AN INVESTIGATION INTO TOBACCO DEPENDENCY MEDICATION ADHERENCE BEHAVIOURS AND THEIR ROLE IN THE TREATMENT OF TOBACCO ADDICTION

by

CAROL JANE SANDERS

A thesis submitted to The University of Birmingham for the degree of DOCTOR OF PHILOSOPHY

Institute of Clinical Sciences
School of Pharmacy
College of Medical and Dental Sciences
University of Birmingham

Final Submission Date 15/08/2025

DECLARATION

I declare that this thesis is based on the original work of the author and has not been previously presented for a degree award. Full reference has been provided to all literature utilised, and the contribution of research made by others has been acknowledged.

The double blind randomised controlled trial was conducted between 2003-2007, in order to test the efficacy of nortriptyline plus nicotine replacement therapy (NRT) versus NRT plus placebo in smoking cessation. The RCT was carried out in the Department of Public Health and Epidemiology at the University of Birmingham. The initial trial protocol was developed by the following Professor Paul Aveyard, University of Birmingham, Mike Murphy, Mark Drury, Robert Walton, Karen Brown, University of Oxford and Mike Bradburn, Cancer Research UK Medical Statistics Unit, Oxford. Some of the material from the RCT within this thesis has been previously published in the following journal:

> Aveyard P., Sanders C., *et al*. (2008). A pragmatic randomised controlled trial of nortriptyline plus nicotine replacement versus placebo plus nicotine replacement for smoking cessation. *British Medical Journal* (Aveyard et al., 2008).

The quantitative chapter that retrospectively analysed the trial date in regard to exploring adherence with smoking cessation medication was my original idea and was carried out by myself whilst supervised by Professor John Marriott at the Institute of Clinical Sciences, College of Medical and Dental Sciences at The University of Birmingham. The qualitative aspects of the thesis are my original ideas and was carried out by myself whilst supervised by Dr Antje Lindenmeyer at the Social Studies in Medicine, Institute of Applied Health Research at The University of Birmingham.

Signed: Carol J Sanders Date: *15/08/2025*

ACKNOWLEDGEMENT

First and foremost, I would like to extend my very sincere thanks to my supervisors John Marriott and Antje Lindenmeyer: to John, for kind, supportive, guidance and for believing in a PhD student he inherited – it has been a privilege to be supervised by him; and to Antje who also inherited me, Antje's kindness and methodological guidance has been invaluable. A special thank you to the late Dr George Doswell for his thoughts and inspiration. I am grateful to Dr Mathew Richardson for statistical advice and his gentle guidance, friendship and humour.

The RCT was funded by Cancer Research UK (CRUK). The RCT and qualitative study were conducted within the NHS Stop Smoking Services in South Birmingham – thank you to their support; without which the PhD would not have happened.

Thank you to the numerous professional colleagues over the lifetime of this study; I am indebted to their help with this PhD journey and for providing the fuel needed to complete the write up.

Warm thanks to my family, especially my dear father who died during 2021, my beautiful, wonderful daughter Phoebe, my dearest friends, for their love and support.

Finally, I would like to acknowledge the patients and clinicians who contributed their time and thoughts to this thesis.

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LIST OF ABBREVIATIONS

Term	Abbreviation
Evidence-based medicine	EBM
Fagerström Test for Nicotine Dependence	FTND
Hospital Anxiety and Depression Scale	HADS
Healthcare professionals	HCPs
Quality of Life	QoL
Smoking cessation	SC
Medicines and Healthcare products Regulatory Agency	MHRA
Mobile health	mHealth
National Health Service	NHS
NHS stop smoking services	NHS SSSs
National Institute for Health and Care Excellence	NICE
Nicotine Replacement Therapy	NRT
Randomised controlled trial	RCT
Smoking Cessation and Nortriptyline and Genetics	*SCANAG*
Tobacco dependence	TD
Tobacco dependency medications	TDMs
Virtual reality therapy	VRT

ABSTRACT

Effective pharmacotherapy is central to tobacco dependence treatment, yet medication adherence remains a persistent challenge, undermining both clinical outcomes and the internal validity of randomised controlled trials (RCTs). This thesis adopts a mixed-methods approach to critically examine the personal, relational, and structural factors influencing adherence to tobacco dependence medications (TDMs) among individuals seeking support through NHS stop smoking services (SSS).

The research integrates three interrelated components: (1) a meta-ethnography synthesising qualitative studies on TDM adherence; (2) a primary qualitative study exploring beliefs and experiences of smokers using pharmacotherapy; and (3) a retrospective critical appraisal of adherence patterns within a pragmatic RCT evaluating nortriptyline plus nicotine replacement therapy. Guided by a critical realist perspective and informed by the *PRIME* theory of motivation, the study embraces methodological pluralism to offer a pragmatic, theory-driven analysis of real-world adherence behaviours.

Findings reveal that adherence to TDMs is shaped less by isolated individual factors and more by dynamic psychosocial processes, health service interactions, and systemic constraints. Participants' beliefs about medication efficacy, side effects, and autonomy often conflicted with biomedical assumptions embedded in standard treatment paradigms. Communication quality, relational continuity, and practitioner empathy emerged as pivotal determinants of engagement. The RCT analysis highlighted inconsistent adherence and exposed design limitations related to participant selection, attrition, and measurement validity, underscoring the need for multilevel strategies in trial design and implementation.

This thesis contributes to the field by advancing a nuanced understanding of medication adherence as a socially situated, context-sensitive phenomenon. It proposes a shift from narrow behaviourist models toward personalised, relational approaches to adherence support. Furthermore, it emphasises

the importance of authentic patient and public involvement (PPI) in research co-design, particularly in shaping future TDM trials that are both scientifically rigorous and patient centred.

Considering evolving post-pandemic health behaviours, widening inequalities, and an expanding digital health landscape, the findings remain timely and relevant. Recommendations include embedding co-produced adherence strategies within routine SSS delivery, integrating psychosocial screening tools, and redesigning RCTs to reflect real-world complexities. Future research should further explore critical ‘decision points’ in medication trajectories, such as initiation, discontinuation, and re-engagement, within the lived contexts of smokers navigating cessation.

CHAPTER 1 BACKGROUND TO THE THESIS

This chapter marks the beginning of the empirical component of my PhD journey, and I begin here because it reflects where my understanding of adherence truly deepened and my own thinking about adherence within smoking cessation RCTs truly shifted. As a clinician with a long-standing interest in public health, I initially approached the issue of tobacco dependence medication (TDM) adherence through a medical model and pharmacological lens. However, it was through my observations and hearing directly from smokers, researchers and SC practitioners, that I came to see adherence as a socially embedded, relational, and often emotionally charged process. These conversations were pivotal: they reshaped how I understood the concept of "non-compliance" and challenged the assumptions I brought into this research. Starting here is not just a structural decision; it reflects the intellectual turning point in my PhD journey. It was through listening to the lived experiences of smokers, trial participants and SC practitioners that I began to see adherence not as an individual failing, but as something shaped by relationships, systems, and values. These conversations were transformative, both personally and intellectually, and shaped the questions I asked, the way I analysed data, and ultimately the direction of this thesis. It felt both logical and necessary to begin with a background to the thesis, where my own learning began.

Reflection is central to rigorous qualitative research. It enables the researcher to account for their positionality, critically examine interpretive assumptions, and enhance transparency in meaning-making processes (Finlay, 2002). In this thesis, reflexive practice supported ethical sensitivity and theoretical depth, particularly in navigating the tensions between researcher-clinician identity and participant experience. The context of this PhD is significant. The study was conducted and completed over a period marked by a global pandemic, health service disruption, and widening health inequalities. These broader societal conditions influenced both the focus of the research and the practical realities of data collection and participant engagement. They also reaffirmed the importance

of understanding adherence as a dynamic, situated, and relational process, shaped as much by external systems as by individual choices. This thesis also takes place within a rapidly evolving landscape. Over the past two decades, stop smoking support in the UK has been shaped by significant political, social, and technological change. The widespread emergence of vaping as both a consumer trend and harm reduction tool has profoundly influenced patterns of smoking and cessation, offered new opportunities but also introducing regulatory, behavioural, and clinical uncertainty. Meanwhile, policy changes, including funding cuts, public health restructuring, and shifting government priorities, have contributed to a fragmentation of NHS Stop Smoking Services (SSS) and a move toward more localised, digital, or pharmacy-based provision. Alongside these developments, a growing range of alternative cessation supports, including mobile health apps, behavioural AI tools, and digitally mediated peer support, have transformed how people attempt to quit. Understanding how these macro-level changes are experienced by individuals, both those trying to quit and those supporting them, is central to this chapter. It is here, through lived accounts, that the wider context meets the personal experience of medication use.

1.1 My journey to the PhD

My prior clinical nursing experience provides a deep familiarity with patient care pathways, communication styles, and the day-to-day operational realities of NHS SSSs. This insider knowledge enabled me to frame my research questions in ways that were immediately relevant to frontline practice. My professional understanding of health inequalities, patient engagement challenges, and the tension between policy directives and individual choice informed the pragmatic design of my mixed methods approach. However, such familiarity may have carried implicit assumptions, for example, regarding what constitutes “successful” adherence or the relative importance of pharmacological versus behavioural support, that required ongoing reflexive awareness.

My nursing background likely provided me with a strong appreciation of medicines optimisation, adherence counselling, and the real-world constraints patients face in taking tobacco TDMs as prescribed. This likely enriched my qualitative interviewing, allowing me to probe practical adherence barriers (e.g., side-effects, dosing schedules, polypharmacy). Yet, there is a potential risk that my professional emphasis on medication safety and adherence may have subtly shaped the interpretation of participants' ambivalence toward pharmacotherapy, potentially framing it more as a challenge to be overcome than as a valid expression of patient agency.

My clinical lens likely heightened my sensitivity to the psychosocial complexities of nicotine dependence, particularly the interplay of habit, identity, and motivation. My direct patient contact would have enhanced my empathy and rapport with participants, supporting rich data generation in the qualitative study. However, clinical proximity can also produce "insider bias" where patients' narratives are interpreted considering prior clinical encounters rather than emergent research data. This underlines the importance of my use of a clear theoretical framework (*PRIME Theory*) to anchor interpretations.

My nursing identity likely influenced the power dynamics in my qualitative interviews. Participants may have perceived me not only as a researcher but also as a health professional, potentially shaping their willingness to disclose non-adherence or scepticism toward TDMs. This could have introduced a degree of social desirability bias, especially in discussions around "willpower" versus "medication reliance." My insider role also means that I was embedded in NHS service cultures, which may have influenced how I conceptualised systemic barriers, emphasising operational fixes rather than deeper structural determinants.

My use of mixed methods, meta-ethnography, qualitative interviews, and retrospective RCT analysis, demonstrated a conscious effort to triangulate perspectives and avoid over-reliance on my clinical worldview. The meta-ethnography provided a counterpoint by foregrounding patients' own words

from diverse contexts, some of which challenged my preconceptions. The qualitative study benefited from my clinical communication skills and capacity to create safe spaces for disclosure. The RCT analysis, while more distanced from personal interaction, allowed me to test hypotheses emerging from the qualitative work against larger datasets, further mitigating potential bias.

Overall, my clinical nursing background has been both a strength and a challenge. It gave me unparalleled insight into patient realities, access to practice settings, and a professional capacity for empathetic engagement. At the same time, it required sustained reflexivity to ensure that my interpretations were grounded in participants' lived experiences rather than filtered through prior professional assumptions. This interplay of insider knowledge and methodological rigour is a defining feature of my thesis and a key contributor to its applied relevance.

As a PhD student, my curiosity about medication adherence with SC treatments emerged by unexpected poor adherence observed during a clinical trial I was involved in. Despite participants receiving evidence-based pharmacotherapy and behavioural support, many failed to initiate or maintain consistent use of their prescribed medications. This raised critical questions for me: what psychological, social, or contextual factors are influencing their decisions? Is there a mismatch between clinical expectations and real-world experiences? I became deeply interested in understanding the nuanced reasons behind non-adherence, particularly how individual beliefs, motivations, and perceptions of medication shape smoking cessation outcomes.

My journey into doctoral research has also been shaped by a deep-rooted commitment to evidence-based clinical practice and an enduring interest in preventative and behavioural health approaches. I began my career as a clinical nurse, working across both acute and community settings. Early on, I recognised the powerful intersection between physical health and lifestyle behaviours, particularly smoking, which remains a persistent cause of ill health and barrier to recovery for many patients (Pirie et al., 2013). Over time, my clinical curiosity evolved into a desire to contribute more directly to the

public health evidence base, prompting my transition into the role of a research nurse in 2003 within the Department of Public Health at the University of Birmingham. Appendix 1 provides a salient timeline of key milestones in smoking, smoking cessation, and medication adherence research and highlights pivotal scientific, public health, and policy developments relevant to tobacco control and the use of pharmacological therapies.

My curiosity about smoking and the UK public health agenda stems from its enduring status as a leading cause of preventable illness and death, despite decades of intervention (ONS, 2024). I'm particularly interested in how national strategies, such as "*Smokefree 2030*", are shaped by evidence, politics, and social inequality. The persistent disparities in smoking rates among low-income and marginalised groups raise important questions about the effectiveness and equity of current approaches (Hiscock et al., 2011). This has driven my desire to explore how public health policies are designed, implemented, and experienced, and how they might be better aligned with the lived realities of smokers.

The history of smoking in public health spans from its rise in the early 20th century, driven by mass marketing and social norms, to its decline following landmark research linking tobacco to cancer and heart disease (Doll and Hill, 1950). Smoking cessation (SC) efforts gained momentum through UK government policy measures, nicotine replacement therapies, and behavioural interventions (Hartmann-Boyce et al., 2021b, Stead and Lancaster, 2016). The UK has led in tobacco control, with significant reductions in prevalence of smoking over recent decades (ONS, 2024). More recently, vaping has emerged as a dominant trend, particularly among smokers seeking harm reduction (McNeill et al., 2020). While evidence supports e-cigarettes as less harmful alternatives, ongoing debates remain regarding their long-term safety and appeal to younger populations. SC refers to activities that aim to support people who smoke to stop smoking (NICE, 2018). Treatments aimed at SC are among the most cost-effective interventions in health care (PHE, 2022b). Most people treated in a single episode, however, eventually return to smoking; those who do return to smoking

relapse while receiving treatment, and therefore more effective interventions are needed (Hajek et al., 2013).

1.2 My PhD journey during the *SCANAG* trial

As part of my role, as a "research nurse", with the Department of Public Health and Epidemiology at the University of Birmingham, I had the privilege of supporting a pragmatic clinical smoking cessation trial, conducted between 2003-2007, alongside a team of experienced researchers. This trial (Smoking Cessation and Nortriptyline and Genetics (*SCANAG*)) was a double blind pragmatic randomised controlled trial (RCT) testing the effectiveness of a combination pharmacotherapy regimen for smoking cessation (Aveyard et al., 2008). This trial aimed to evaluate whether the concurrent use of nortriptyline and nicotine replacement therapy could improve quit rates in real-world clinical NHS Stop Smoking Services (NHS SSS) settings. My responsibilities ranged from training the NHS SSS staff about the trial protocol requirements, participant recruitment and consent, to monitoring adverse events and supporting data collection in accordance with *Good Clinical Practice* (GCP) guidelines. This hands-on experience highlighted both the complexities and rewards of real-world research, and it matched my interest in health behaviours, health psychology, tobacco control and clinical trial methodology. This was the context in which my research curiosity regarding medication adherence began.

A significant learning point was that trial participants did not behave with the trial medication as expected; various non-adherence medication behaviours emerged. Medication adherence is a multifaceted behaviour influenced by a dynamic interplay of biological, psychological, social, and systemic factors (Osterberg and Blaschke, 2005). From a pharmacological perspective, the pharmacokinetics and pharmacodynamics of a drug, including side effects, dosing frequency, and therapeutic outcomes, heavily influence a patient's willingness and ability to adhere to a regimen (Vrijens and Urquhart, 2014). For example, medications with complex dosing schedules or unpleasant

side effects often lead to reduced adherence. Furthermore, the patient's understanding of the pharmacological action of the drug, whether they believe it is effective or necessary, shapes how it is taken (Kvarnström et al., 2021).

My observation with hundreds of smokers desperate to quit smoking who enrolled onto the RCT, was that their adherence with the trial medication was mostly very poor and the reasons stated from discussions with smokers seeking to quit and NHS SC advisers were varied. The non-adherence behaviour was at odds with their desperation to quit smoking. Adherence to the trial medication was a primary determinant of treatment success and this protocol violation (e.g. not starting, taking less than the prescribed dose regimen or stopping the trial medication prematurely) compromised the 'fair' comparison, which was protected by randomisation, and potentially biased the estimate of treatment effect. These findings suggest that investigators should make every effort to conduct intent-to-treat analyses, address adherence measurement and reporting methodology and undertake and report findings from multiple analytic strategies to provide a more complete understanding of the effects of the treatments studied. Moreover, regardless of the strategy used, investigators should clearly describe their handling of data from participants who violate the study protocol re medication adherence (Gossec et al., 2007). Medication adherence is likely an indicator of research quality and treatment acceptance by participants. Improved reporting of medication adherence may enhance the interpretation of study quality and results (Eliasson et al., 2020b). Sub optimal medication adherence has been reported for over two decades; guidelines to on how adherence should be measured, analysed and reported in clinical trials were eventually published in 2018 (De Geest et al., 2018).

Clinical trials of behavioural interventions, such as SC, frequently suffer from low levels of adherence with estimates indicating that between 25% and 50% of research participants are not adherent to medications (Robiner, 2005). The extent to which patient nonadherence has flawed clinical research has in some cases been underestimated. High degrees of non-adherence in randomized controlled trials (RCTs) can lead to failure to detect a true treatment effect (O′Kelly and Ratitch, 2014).

Inadequate adherence in clinical trials contributes to significantly increased study costs, complicates statistical analysis and threatens study validity (Robiner, 2005, Ellis et al., 2000, Martin et al., 2000). Reporting of medication adherence and study-drug discontinuation in RCTs investigating smoking cessation or outcome endpoints in smokers are inconsistent, making it difficult to compare studies and evaluate their impact on outcomes.

In clinical drug trial settings, a high frequency of non-adherence results in failure to detect a true difference, due to the loss of statistical power (Gossec et al., 2007). In addition, a high frequency of study drug discontinuation, which can be due to poor treatment adherence as well as several factors, such as adverse events, drop-out from the study or withdrawal owing to protocol specified events hospitalisation, can also lead to a false negative study outcome because of loss of statistical power (Guobing and Copas, 2004). Consistent reporting of the causes of drug discontinuation is needed to compare studies with respect to the contribution of non-adherence to discontinuation and evaluate their impact on clinical outcomes (Eliasson et al., 2020a).

1.3 Evidence-based medicine

Evidence-Based Medicine (EBM) has traditionally been defined by the pursuit of best evidence to inform clinical practice, with a particular emphasis on methodological rigour and reproducibility. Historically, EBM has prioritised a hierarchy of evidence in which systematic reviews and randomised controlled trials (RCTs) are positioned at the apex, offering high levels of internal validity. While RCTs remain an essential tool for evaluating therapeutic efficacy, their application to complex behavioural interventions, such as tobacco dependence treatment, requires closer scrutiny.

In the context of TDM adherence, this scrutiny is particularly relevant. Although RCTs are often considered the gold standard, they frequently fail to capture the relational, contextual, and behavioural dynamics that influence real-world medication use. Participants in smoking cessation trials are often highly selected and may not reflect the broader population of tobacco users served by NHS Stop

Smoking Services. The structured, time-limited nature of trials, coupled with rigid protocol adherence, diverges significantly from the varied and often unpredictable trajectories of medication use in routine care. As such, trial findings may conflate pharmacological inefficacy with behavioural non-adherence, obscuring the true reasons behind suboptimal outcomes (Deaton and Cartwright, 2018).

Contemporary critiques of EBM have challenged the rigidity of the evidence hierarchy, advocating instead for more nuanced typologies of evidence. These frameworks recognise that different research questions require different methodologies and that qualitative inquiry can play a central role in evaluating intervention acceptability, user experience, contextual relevance, and service delivery (White and Adams, 2018, Greenhalgh et al., 2014). In the case of TDM adherence, qualitative methods are particularly valuable in illuminating the meanings, beliefs, and social processes that underpin engagement with medication.

Moreover, the legitimacy of evidence does not rest solely on statistical robustness, but also on its resonance with clinical, practitioner, and patient knowledge. Greenhalgh *et al*. (2014) argue for a shift toward 'real evidence-based medicine,' which integrates empirical data with patient narratives, clinical judgement, and contextual understanding. This is echoed in my study's critical realist approach, which seeks to understand not just whether adherence occurs, but how and why it is sustained, disrupted, or rejected in everyday practice.

Therefore, this thesis adopts a mixed methods approach that foregrounds both the quantitative patterns and the qualitative meanings of TDM adherence. In doing so, it contributes to a growing body of work that reframes adherence not as a purely individual behaviour to be measured, but as a socially situated practice shaped by power, trust, knowledge, and service design. Understanding and addressing these complexities is central to improving the relevance, effectiveness, and equity of tobacco dependence treatment and public health research more broadly.

I did not expect that, despite the increasing utilisation of SC medications such as NRT, bupropion and varenicline, relatively little was known about adherence to these regimens. At the time of the clinical trial (*SCANAG*) research was focused on clinical efficacy rather than real-world use, overlooking how smokers engaged with treatments over time. Moreover, the dominance of biomedical models obscured the behavioural and psychosocial dimensions of adherence. Without integrating behavioural science and lived experience, our understanding remains fragmented and interventions risk being poorly targeted.

Efforts to improve TD treatment outcomes require a better understanding of the particular barriers to and facilitators of adherence to SC therapy, and of smoker experiences of taking a treatment which is a complex process. Factors associated with non-adherent behaviour can be organised into the following interacting domains: (1) socioeconomic factors; (2) health professional and health services-related factors; (3) characteristics of the treatment regimen; (4) characteristics of the disease and (5) patient-related factors (WHO, 2003). Furthermore, to better understand patients' medicine taking, many researchers have examined cognitive factors such as patients' perception of their disease, and investigated which factors can be changed to enable more effective behavioural intervention (Horne et al., 2013a, Clifford et al., 2008). To improve adherence to TDMs, there is a need for new concepts, for example by exploring differing needs of individuals and the nature of their information needs within the field of SC therapies being recognised as one of the most cost-effective health interventions, long-term adherence is generally poor.

The *SCANAG* trial protocol development did not consider that from a sociological standpoint where adherence is not merely an individual choice but is embedded in a broader social context. Social determinants of health, such as socioeconomic status, cultural beliefs, health literacy, and access to healthcare, all play a pivotal role. Moreover, the patient-provider relationship significantly impacts adherence; trust, communication, and shared decision-making foster greater compliance.

Psychological factors such as depression, cognitive decline, or denial of illness further complicate adherence. The perception of illness severity and perceived susceptibility to complications also modulate behaviour. Importantly, systemic issues, like fragmented healthcare systems, inadequate follow-up, and poor care coordination, can disrupt continuity and monitoring, reducing adherence rates.

Nicotine addiction significantly undermines adherence to medications prescribed to support smoking cessation, such as nicotine replacement therapy (NRT), varenicline, or bupropion (Raupach et al., 2013). The addiction drive to smoke, rooted in neurobiological reinforcement and behavioural conditioning, often overrides rational decision-making, leading individuals to abandon treatment prematurely. Cravings, withdrawal symptoms, and the immediate gratification of smoking contrast sharply with the delayed benefits of cessation medications (Smith and Roberts, 2025). Additionally, ambivalence about quitting, low self-efficacy, and mistrust in pharmacotherapy reduce motivation to persist with medications. To improve adherence, cessation interventions must address both the physiological dependence and the psychological ambivalence that define nicotine addiction; this was not addressed as part of the *SCANAG* trial protocol.

Ultimately, my experience of the *SCANAG* trial meant that I conceptualised medication adherence not as a simple matter of patient education or willpower but as a complex phenomenon requiring an integrated approach that considers the pharmacological properties of the medication, the social context of the patient, and the systemic supports in place. Interventions should be multifactorial, targeting regimen simplification, patient empowerment, social support, and healthcare access, to effectively address the complex behaviour of adherence. Medication adherence did not emerge as a critical issue in tobacco dependency research until the early 2000s, when large-scale clinical trials began to highlight a consistent gap between prescription and actual usage of smoking cessation pharmacotherapies. While nicotine replacement therapy (NRT), bupropion, and later varenicline were shown to significantly improve quit rates in controlled settings, real-world outcomes were often far

less impressive. Researchers observed that many individuals either did not initiate prescribed medications, discontinued them prematurely, or used them inconsistently. This discrepancy prompted a shift in focus toward understanding the behavioural and psychological barriers to adherence in the context of nicotine addiction.

It became increasingly evident, over the course of my PhD studies from my research experiences and the literature, that tobacco dependence, marked by strong craving, habitual use, and ambivalence about quitting, could directly undermine sustained medication use. Withdrawal symptoms, lack of immediate perceived benefit, and ongoing triggers to smoke made it difficult for individuals to engage consistently with cessation medications. Additionally, stigma, low self-efficacy, and misinformation contributed to distrust or misuse of pharmacotherapy. These findings underscored that medication adherence is not simply a matter of patient education, but a core challenge within tobacco treatment. As a result, adherence-enhancing strategies, such as behavioural counselling, motivational interviewing, and simplified regimens, have become central to evidence-based tobacco dependence treatment.

1.4 My PhD training

Recognising a gap in my formal academic training, I completed a Master's degree in Health Sciences at the University of Birmingham prior to my PhD. This was a useful foundation as it provided insight into research methods, project management and research governance., I pursued an opportunity to enrol in a part time PhD programme with a strong applied health research focus. As smoking is a public health issue and recognising that my PhD journey would be enhanced by further formal training I attended various available Master of Public Health modules at the University of Birmingham, where I received structured training in clinical trial design, implementation science, and advanced quantitative and qualitative methods. The University Graduate School provided a postgraduate researcher (PGR) community with a vibrant researcher network, training and social

space. The academic environment not only sharpened my methodological skills but also gave me the space to engage critically with the literature and other researchers on addiction, harm reduction, medication adherence behaviours and behavioural change interventions. My doctoral research builds directly on my prior clinical and research experiences, examining medication adherence behaviours within the context of pharmacotherapy in NHS smoking cessation services and through a pragmatic trial lens.

Medication adherence is a fundamental determinant of both the internal and external validity of clinical trials evaluating stop smoking medications (Vrijens and Urquhart, 2014). My PhD thesis findings emphasise that the design, implementation, and interpretation of these trials hinge on accurate measurement and promotion of adherence. Without consistent use of the intervention as intended, it becomes difficult to assess the true efficacy of pharmacotherapies such as nicotine replacement therapy (NRT), bupropion, or varenicline. Adherence acts as a critical mediator between intervention and outcome; poor adherence dilutes treatment effects and can lead to underestimating the true potential of cessation aids. In the design phase, researchers must incorporate adherence-promoting features such as patient education, behavioural support, and user-friendly dosing schedules. Randomisation and blinding help minimise bias, but without monitoring adherence, through self-report, pill counts, or biomarkers, the interpretation of trial results remains vulnerable.

Adherence should be a predefined outcome in statistical analyses, with subgroup comparisons to understand how outcomes differ between adherent and non-adherent participants. During implementation, adherence monitoring and support are crucial to trial reliability. Addressing barriers such as side effects, motivation fluctuations, and social influences is essential to maintain engagement. Moreover, a clinical trial must distinguish between pharmacological failure and behavioural non-adherence when interpreting lack of efficacy (Davies et al., 2025). Finally, adherence data directly impacts generalisability. If trial participants are more adherent than typical users, efficacy findings may not translate to real-world effectiveness. Conversely, poor adherence in

trials can obscure medication benefits and lead to misleading public health guidance. Therefore, medication adherence is not a peripheral issue but central to the success and relevance of smoking cessation trials (Williams and Green, 2024). Designing studies that reflect real-world adherence challenges enhances both scientific validity and the utility of findings for health policy and clinical practice (Gupta and Lee, 2025).

1.5 My PhD context

As a PhD student, the context of my research was significantly disrupted by a combination of personal life challenges and the wider impact of the COVID-19 pandemic. Personal circumstances, including unexpected family responsibilities and health-related issues, affected my ability to maintain consistent academic progress. In parallel, the pandemic caused major disruptions to data collection, participant recruitment, and access to university resources, leading to delays in key milestones. Remote working and social isolation also impacted my focus and wellbeing. These factors, both personal and structural, have extended my timeline and required me to adapt my research approach and expectations. The trajectory of my research, like that of many others, was significantly affected by personal circumstances and the coronavirus (COVID-19) pandemic which caused periods of non-research activity. My PhD timeline was disrupted related to lockdown and social distancing restrictions; each chapter was affected by the pandemic practically and changed smoking behaviour. While the COVID-19 pandemic triggered quit attempts among many smokers, it led some to smoke more and others to relapse back to smoking (Gravely et al., 2021). Diverse effects of lockdown, COVID-19 as a catalyst for stopping smoking, changes in vaping and change and challenges for NHS SSSs, boredom and stress created by the pandemic impacted individuals' smoking and vaping behaviours (Kayhan et al., 2020). Smoking cessation methods in the UK have evolved from brief advice and nicotine replacement therapies to a more comprehensive approach incorporating behavioural support, pharmacotherapy (including varenicline and combination therapies), digital interventions, and e-cigarettes (Onwuzo et al., 2024). Contemporary strategies prioritise personalised,

accessible, and pragmatic solutions to address diverse needs and reduce tobacco-related health inequalities (Alexander et al., 2025).

I also returned to clinical practice within the NHS during the pandemic which, alongside personal, family and health issues, added to delays of my PhD completion. While all these challenges were undoubtedly difficult, they also prompted me to reflect and re-evaluate how research is designed and delivered pragmatically. My PhD journey has constantly reminded me of the need for flexible, responsive trial protocols and the importance of digital modalities for both intervention delivery and data collection. My PhD topics and selected methodologies have evolved over the lifetime of the PhD. Medication adherence behaviour has shifted from a purely compliance-based model to one recognising the sociocultural, psychological, and structural factors influencing patients' choices (Kvarnström et al., 2021). Greater emphasis is now placed on shared decision-making, health literacy, digital monitoring, and addressing systemic barriers, reflecting a more nuanced, patient-centred understanding of adherence within complex social contexts (Elwynn et al., 2012, Vestbo and Anderson, 2025). These research findings have informed the adaptive design of my PhD and reinforced the importance of embedding resilience and equity into future public health research.

The unprecedented COVID-19 pandemic starting in early 2020 caused an unexpected context of a global crisis for everyone. As a doctoral student I was completing and writing up my doctoral thesis and inevitably the pandemic disrupted my thesis progress as I returned to clinical practice to support the NHS. The COVID-19 pandemic, its associated health risks and its impact on social activity has influenced smoking behaviour, SC, medication adherence behaviour and health behaviour change.

At the final stages of my PhD complete, I remain committed by the potential impact of high-quality, pragmatic research on frontline healthcare. My journey from bedside to researcher has been marked by both challenges and growth, and I remain committed to bridging the gap between research and clinical practice, especially in tackling preventable health issues such as smoking, raising awareness

of medication adherence behaviours and importance of person-centered care. My PhD journey has led me to predict that future research in smoking cessation and medication adherence will prioritise personalised interventions, digital health integration, and equity-focused approaches. Emphasis will be placed on real-world effectiveness, addressing health inequalities, understanding behavioural mechanisms, and leveraging mixed methods research to optimise engagement, adherence, and long-term outcomes across diverse and underserved populations in the UK.

At the end of my PhD journey, I view medical sociology as essential to understanding smoking and medication adherence because it situates health behaviours within broader social, cultural, and structural contexts. Smoking is not just a biological addiction, but a practice shaped by identity, stress, stigma, and social norms. Similarly, adherence to cessation medications involves more than clinical instructions, it reflects beliefs about medicine, personal agency, and trust in healthcare systems. Medical sociology allowed me to critically explore how these factors influence individual choices and health outcomes, and to challenge assumptions that behaviour change is purely rational or individual. This perspective deepens both analysis and intervention design. Smoking, SC, and medication adherence in the UK understood through a sociological lens acknowledges the complex interplay of individual agency, social structures, and cultural context (Webster and al., 2025, ONS, 2024). Smoking, historically embedded in working-class identity and social rituals, has declined significantly due to public health campaigns, legislation, and shifting norms (Williams and Green, 2024). However, smoking remains patterned by deprivation, with higher prevalence among socioeconomically disadvantaged groups (ONS, 2024). SC, once focused on individual willpower and medicalised interventions, now increasingly incorporates behavioural support and harm reduction approaches such as vaping (Rojas et al., 2025). Yet, access and engagement with cessation services often reflect broader social inequalities, including trust in health systems, stigma, and digital exclusion (DHSC, 2023, Khan, 2022). Vaping emerged as a SC option towards the end of this PhD timeline (ASH, 2023). It has significantly altered the smoking landscape, offering a harm reduction

tool that aids cessation for some while raising concerns about youth uptake. Its dual role necessitates nuanced research into long-term health effects, behavioural trajectories, and policy implications to balance public health benefits with potential unintended consequences (Rojas et al., 2025, DHSC, 2023).

I found during the clinical trial that medication adherence behaviour similarly transcends biomedical explanations. While traditionally viewed through a compliance lens (Aronson, 2007), adherence is now understood as a dynamic, negotiated practice shaped by beliefs, side effects, healthcare relationships, and daily life constraints (Vestbo and Anderson, 2025). Qualitative research has been instrumental in revealing how individuals make sense of medications and navigate conflicting priorities (Gittleman et al., 2024). In both SC and adherence, research must prioritise patient-centred, context-sensitive strategies that address not only behavioural change but also the structural and relational conditions that support sustained engagement, especially in communities historically underserved by mainstream public health interventions.

1.6 Why I chose a mixed methods PhD methodology

A mixed methods approach to investigate smoking and medication adherence because it allowed for a comprehensive understanding of both behavioural patterns and the underlying reasons behind them. Quantitative data helps identify trends, adherence rates, and correlations, while qualitative insights reveal the beliefs, motivations, and contextual barriers influencing smoker behaviour. This combination provides a richer, more nuanced picture than either method alone. Given the complexity of tobacco dependence and the variability in how individuals engage with cessation medications, mixed methods offer the flexibility and depth needed to explore both measurable outcomes and lived experiences. Mixed methodology is essential in understanding SC and medication adherence behaviours, as it combines the strengths of quantitative and qualitative research. Quantitative approaches measure prevalence, effectiveness, and patterns, offering generalisability and statistical

insight. Qualitative methods, meanwhile, provide depth, uncovering motivations, lived experiences, and contextual barriers. Together, they enable a comprehensive understanding of complex health behaviours, informing more effective, equitable interventions. In public health, mixed methods support the design of person-centred approaches, enhance implementation strategies, and ensure that evidence is not only robust but also grounded in the realities of diverse populations, particularly those facing structural disadvantages in accessing care.

As few studies have investigated adherence to tobacco dependence treatment; there is a need to better understand the factors that influence adherence behaviours with TDMs. A mixed methods approach was utilised as smoking, SC and medication adherence behaviours are complex and the overall purpose and central premise of mixed methods studies is that the use of quantitative and qualitative approaches in combination provides a better understanding of research complex phenomena than either approach alone. This involved the intentional collection of both quantitative and qualitative data to answer the research questions. It was envisaged that there would be more insight to be gained from the combination of both qualitative and quantitative research methods rather than either form by itself. The qualitative data collection preceded the quantitative data analysis, as intention was to first explore the problem of poor TDM adherence and then to follow up on that exploration with quantitative data analysis, so that the results could be applied to adult smoker populations.

1.7 Structure of the thesis

The structure of the thesis reflects its central aim: to move beyond individualistic or purely pharmacological explanations of non-adherence and to foreground the relational, sociocultural, and systemic dimensions of medication use in tobacco cessation. By combining diverse methods and perspectives, the thesis offers a multi-layered and practice-relevant understanding of TDM adherence, one that is responsive to both lived experience and health system realities. The PhD thesis describes an expanded understanding of the problem of low adherence to SC medications and the negative

impact this has on long-term abstinence. By following the meta-ethnography and qualitative phases with a reflective exploration of medication adherence during the pragmatic RCT designed to test the efficacy of nortriptyline plus NRT with placebo plus NRT for SC, with the intention to also attempt to explain the mechanism behind the quantitative results in the RCT and the implication to SC clinical practice and SC RCT design. Globally, smoking remains a leading cause of preventable death, with smoking prevalence, cessation varying by country and resource availability (WHO, 2025). While high-income countries see declining rates, low- and middle-income nations face rising tobacco use (WHO, 2025). Medication adherence challenges persist worldwide, influenced by health literacy, access, cultural beliefs, and health system capacity (WHO, 2003).

The PhD adopted a three-phase, mixed qualitative design to investigate the complexities surrounding medication adherence for smoking cessation, particularly within the context of pharmacological interventions offered by NHS SSSs. Drawing from public health, pharmacy, and medical sociology perspectives, the thesis aimed to provide a robust, multi-level exploration of SC medication adherence behaviour, beliefs, and treatment efficacy. The thesis plan was designed to gain an evidence basis for stop smoking in a concerted manner through the thesis, which culminated in a critique of the *SCANAG* trial in the hindsight of experience and evidence and knowledge gained during the qualitative phases presented in the chapters of the thesis. The study phases were as follows:

Phase 1: A meta-ethnography.

Phase 2: A qualitative study designed to explore beliefs and attitudes by people who seek help to stop smoking within a NHS SSSs and choose a smoking medication to support their quit attempt.

Phase 3: Reflections of medication adherence during from the pragmatic RCT designed to test the efficacy of nortriptyline plus NRT with placebo plus NRT for SC.

This carefully staged sequence allows the thesis to move from abstraction to application, from literature to lived experience to critical trial appraisal, each step enabling a more holistic and grounded understanding of what adherence means, why it fails, and how it might be better supported in public health practice. The substantive chapters in this thesis represent three investigations all on the same theme of adherence behaviours with medication to help adults to stop smoking. Despite the increasing utilisation of TDM medications, such as NRT, bupropion and varenicline, relatively little is known about adherence to these regimens. This thesis examined medication adherence among adults seeking to quit smoking utilising a mixed methods approach as both smoking and medication adherence behaviours are complex. This involved collection of both quantitative and qualitative data and the combination of the strengths of each to answer the thesis research questions (Creswell, 2018).

This meta-ethnography comes first in the empirical sequence because it lays a conceptual and thematic foundation. By synthesising existing qualitative research on TDM adherence, the meta-ethnography identifies recurring constructs, such as perceptions of medication safety, relational support, autonomy, stigma, and experiential ambivalence. This synthesis not only highlights knowledge gaps in the literature but also refines the interview questions and sensitising concepts for the subsequent primary qualitative study in phase 2. It also serves a secondary purpose: to situate the thesis within an existing evidence base, justifying the need for further exploration of under-theorised and under-represented user experiences in real-world NHS contexts.

The meta-ethnography identified and synthesised the best available qualitative evidence on adult smokers' experiences, meanings and beliefs regarding TDMs and their importance to adherence behaviours. Synthesising existing qualitative research through meta-ethnography provided a strong foundational understanding of the shared and divergent experiences of individuals attempting to quit smoking. Meta-ethnography goes beyond systematic reviews by offering interpretive synthesis, enabling conceptual innovation (Noblit and Hare, 1988). The synthesises develops interpretive themes that identify common patterns across studies, such as trust in medication, relational support,

and identity disruption, while revealing contradictions in how adherence is framed by researchers versus service users. This synthesis informs the development of the interview study and supports theoretical refinement. This phase provided a theory-informed lens through which identified themes, psychosocial context of TDM behaviours, willpower predilection and resisting medications that shaped smokers' medication adherence behaviours. These insights informed the development of phase 2 (a qualitative study).

Building directly on the themes identified in phase 1, the meta-ethnography, phase 2 presents new empirical data derived from in-depth interviews with service users and SC practitioners. It is positioned here to enable an inductive, grounded engagement with real-world experience, adding depth and nuance to the broader patterns described in the meta-ethnography. Importantly, phase 2 expands the lens by incorporating the perspectives of smokers, whose voices are often underrepresented in adherence research. Their insights expose the institutional logics, relational constraints, and value judgements that shape adherence support in practice.

The qualitative study examined adult smokers' TDM adherence from their own perspective by exploring their experiences and beliefs. By understanding the subjective beliefs, meanings, and attitudes of individuals who actively sought NHS stop smoking help and choose pharmacotherapy was helpful to unpacking adherence behaviours. The smokers held complex, ambivalent views about medications, shaped by stigma, identity, and prior experience (Bell et al., 2010; Lawton et al., 2006). This phased used in-depth interviews to explore how individuals' beliefs about medications, e.g. varenicline, NRT, or bupropion, influenced their quit attempt trajectories and adherence, illuminating the cultural and social embeddedness of medication use. Drawing on semi-structured interviews with smokers, this study presents an in-depth thematic analysis (Guest et al., 2012) of real-world adherence experiences. The findings expose the relational, emotional, and moral dimensions of adherence, and surface the tensions between professional guidance and personal agency (Pope and Mays, 2020). The role of practitioner continuity, stigma, and implicit expectations is explored in detail, offering insights

that challenge linear models of 'compliance'. By understanding the subjective beliefs, meanings, and attitudes of individuals who actively sought NHS SC help and choose pharmacotherapy was helpful to unpacking adherence behaviours (Vestbo and Anderson, 2025). The smokers held complex, ambivalent views about medications, shaped by stigma, identity, and prior experience (Bell et al., 2010; Lawton et al., 2006). This phased used in-depth interviews (Silverman, 2017) to explore how individuals' beliefs about medications, e.g. varenicline, NRT, or bupropion, influenced their quit attempt trajectories and adherence, illuminating the cultural and social embeddedness of medication use (Williams and Green, 2024). This phase provides the rich, contextualised knowledge that is essential for interpreting the patterns observed in phase 3.

Phase 3 is placed last in the empirical sequence because it applies the insights gained in phases 1 and 2 to interrogate a concrete, real-world trial. Here, the thesis moves from exploring how adherence is experienced and supported, to how it is operationalised and measured within a high-level evidence framework (CASP, 2024). Rather than treating the trial data at face value, this chapter adopts a critical lens, interrogating the trial's assumptions, design limitations, and adherence metrics. The reader is now equipped, with the experiential insights of phase 1 and the thematic map from phase 2 to understand why and how the trial's portrayal of adherence may diverge from lived realities. The analysis challenges the dominant narrative of non-responsiveness to treatment and instead repositions non-adherence because of structural design, relational fragmentation, and epistemological oversights. Thus, this final empirical phase closes the loop, drawing together behaviour, context, and system, thereby preparing the ground for integration and theoretical synthesis in Chapter 7.

Phase 3 undertook a retrospective exploration of the *SCANAG* trial and examined factors that may have affected medication adherence behaviours with a SC trial medication to provide a deeper understanding of what aspects of adherence behaviours with SC medications need to be considered to help people quit smoking. This final phase bridged clinical trials and clinical practice by embedding a qualitative reflection within the *SCANAG* pragmatic randomised controlled trial (RCT). It allowed

for real-world exploration of adherence trajectories, side effect management, and patient perspectives on taking medications under trial conditions. The thesis qualitative work uncovered why some participants adhered while others don't, providing context to RCT outcomes and strengthening translational relevance (Sanders et al., 2019). The thesis's pragmatic design reflects real-life service delivery and evaluates an underused but potentially cost-effective treatment (nortriptyline), aligning with NHS goals for tobacco harm reduction (PHE, 2022b). Simultaneously, the qualitative lens interrogates the lived experience of trial participation, particularly in how trust, self-efficacy, and medicalisation intersect with adherence. This phase undertakes a critical secondary analysis of adherence data from a pragmatic RCT involving nortriptyline and nicotine replacement therapy. The analysis examines methodological limitations in trial design and implementation, highlighting issues of recruitment bias, retention, adherence measurement, and real-world generalisability. The findings demonstrate how RCTs can both illuminate, and obscure key dynamics of medication use when not attuned to behavioural context.

The discussion chapter, (chapter 7), draws together the findings across methodological strands using critical realist triangulation. It explores the interplay between individual agency, structural constraints, and service design in shaping adherence outcomes. The discussion articulates a reconceptualisation of adherence as a relational, negotiated, and temporally fluid practice, challenging dominant framings in addiction science and health behaviour models. The implications for practice, policy, and future trial design are critically examined. This thesis provides a theoretically informed, contextually grounded, and clinically relevant contribution to understanding SC medication adherence. It addresses the persistent public health challenge of low adherence and underuse of pharmacotherapies in quitting smoking, using a mixed method approach grounded in real-world settings and patient perspectives. The meta-ethnography synthesis, lived experience, and *SCANAG* trial reflections ensured both depth and breadth, making the findings relevant for clinicians, pharmacists, policymakers, and researchers.

The final chapter summarises the thesis's contributions to knowledge and outlines practical recommendations for enhancing patient-centred adherence support. It advocates for the integration of co-produced interventions, practitioner training in relational care, and broader systemic reforms within NHS SSS. Directions for future research are proposed, with a focus on longitudinal adherence trajectories, digital self-management tools, and health equity. This thesis adopts a mixed-methods, theory-driven, and critically reflective structure, designed to investigate the complex and multifactorial nature of adherence to tobacco dependence medications (TDMs) within NHS SSS. The structure reflects the epistemological orientation of the research, rooted in critical realism, which recognises that adherence is shaped by interacting biological, psychological, social, and structural mechanisms that operate across different levels of reality. The thesis unfolds across several interlinked chapters, each fulfilling a distinct analytical and conceptual purpose while collectively building a coherent narrative that bridges evidence, theory, and practice.

The *SCANAG* Trial served a deliberate and foundational role in the thesis, the starting point of my personal and intellectual journey through this PhD. Beginning here reflects the moment my understanding of TDM adherence began to shift. As a clinician with decades of experience, I entered this research with assumptions shaped by evidence-based practice and behaviour change theory. Yet, it was through hearing the stories of smokers, trial participants, researchers and SC practitioners, listening to their struggles, values, decisions, and constraints, that I came to see adherence differently: not as a behaviour to be corrected, but as a process negotiated within personal, relational, and systemic contexts. The voices presented in this thesis were not only central to answering the research questions; they also profoundly influenced the structure of the thesis itself. Their complexity required a framework that could hold multiple truths, resist reductive interpretations, and acknowledge how people's lives are shaped by shifting services, policy changes, and social meanings. It is from these insights that the rest of the thesis unfolds.

By beginning with qualitative inquiry grounded in lived experience, I have intentionally prioritised the real-world context in which adherence decisions are made. This approach echoes and builds upon the theoretical critique presented in the introduction chapter, where the limitations of hierarchies of evidence and behaviourist assumptions were first interrogated. The understandings developed in this chapter laid the groundwork for the next stages of the thesis: a re-examination of adherence within trial settings, and ultimately, a call for more relational, patient-centred, and inclusive models of public health research and service design. This background chapter is not just a presentation of findings, it is the beginning of the story, of this thesis, and of a shift in how I understand the behaviours and meaning of medication adherence within SC.

CHAPTER 2 INTRODUCTION TO THE THESIS

The introduction chapter establishes the research context, identifies knowledge gaps, and outlines the thesis rationale. It structured to first present the historical and contemporary context of smoking in the UK, including prevalence, socioeconomic patterns, and the evolving policy landscape. It then reviews the health impacts of smoking, the development of NHS SSSs, and available pharmacological and non-pharmacological cessation approaches. This is followed by an overview of medication adherence and its relevance to tobacco dependence treatment, underpinned by health behaviour theories such as *PRIME*. Finally, the chapter provides the rationale for the thesis aims, objectives, research questions, methodology and structure of the thesis.

2.1 A brief history of smoking

Historically, smoking was endorsed by the medical profession, with doctors featured in tobacco advertisements and limited awareness of health risks. Today, public health leads global efforts to reduce smoking, driven by robust evidence linking tobacco to disease. This reversal reflects profound shifts in scientific understanding, ethics, and public health priorities. Tobacco has been growing wild in the Americas for nearly 8000 years and used by various cultures, populations and widespread adoption globally. By the 1700s, smoking had become more widespread, and a tobacco industry had developed. During the 1920s the first medical reports linking smoking to lung cancer began to appear (Doll, 1999). However, in the 1930s and 1940s, smoking became the socially prevalent for both men and women and most physicians smoked. At the same time, there was rising public anxiety about the health risks of cigarette smoking. At the beginning of the fifties, research was published showing a statistical link between smoking and lung cancer (Doll and Hill, 1952). Sixty years ago smoking was the norm and the harm caused by smoking went largely unacknowledged until the Royal College of Physicians (RCP) report published in 1962, described the health risks of smoking unequivocally (RCP, 1962): the effect was a social shift in attitudes to smoking (Alamar and Glantz, 2006). This

report, using the research of Sir Richard Doll and Sir Austin Bradford Hill (Doll and Hill, 1952), made a strong epidemiological case for the harm caused by smoking to health. Worldwide, smoking remains the most important preventable cause of premature death and disability (Killen et al., 2000). There is a strong relationship between cigarette smoking and social disadvantage (Hiscock et al., 2011). Smokers from deprived areas have low awareness of services available to help them, and hold misconceptions about their availability and effectiveness (Paul et al., 2010) (Williams and Green, 2024).

Despite decades of research and anti-tobacco messaging, nicotine addiction remains an important public health problem leading to hundreds of thousands of deaths each year. Almost 6 million people still smoke in England; smoking remains the single biggest cause of preventable illness and death and is still one of the largest causes of health disparities (ONS, 2021, ONS, 2024). Every year tens of thousands of people die prematurely from smoking, with thirty times as many suffering from cancer, cardiovascular, respiratory disease and dementia caused by smoking. Stopping smoking is the best thing a smoker can do for their health. Making smoking obsolete in England would lift enable nearly 2.6 million adults and 1 million children out of poverty (Khan, 2022, Williams and Green, 2024).

Tobacco dependency medications (TDMs) effectively aid initial abstinence and decrease lapse risk (Cahill et al., 2013); however, globally, most smoking cessation (SC) attempts are unassisted. NHS stop smoking services (SSSs) provide evidence based and cost-effective support to quit attempts (NICE, 2018, Stead and Lancaster, 2016). Evidence indicates that, although the majority of current smokers are motivated to quit, the number of people using NHS SSSs to help them quit continues to decline (Lacobucci, 2017). This may be because in recent years, e-cigarettes have become prevalent, generating uncertainty within clinical SC practice and amongst smokers. There is a lack of international consensus regarding the role of using e-cigarettes as a tool for SC. Public Health England (PHE) and NHS Health Scotland advocate e-cigarettes in contrast to other public health bodies such as the World Health Organisation.

A recent UK trial found that, smokers who used e-cigarettes when combined with behavioural support to quit smoking were twice as likely to succeed as smokers who used other nicotine replacement products (Hajek et al., 2019). In contrast, a qualitative study found that both smokers seeking to quit and SC advisors had ambivalent attitudes towards e-cigarettes with regards to efficacy, health risks and incompatibility to SC goals (Tamimi, 2017). Overall, long-term quit success through NHS SSSs remains low (Dobbie et al., 2015) partly explained by poor TDM adherence. Previous studies have found several factors that partly explain TDM underuse such as side effects, cost and access, satisfaction, lack of awareness or knowledge, prior experience of using TDMs, perceived poor efficacy or concerns about safety and dependency (Pacek et al., 2018, Vestbo and Anderson, 2025). Adherence to medication may be determined by other factors such as socioeconomic resources and individuals' beliefs trust or expectations. Poor medication adherence is considered a potential contributor to disparities in health outcomes (McQuaid and Landier, 2018).

The history of smoking reflects shifting cultural norms, aggressive tobacco industry influence, and evolving public health responses. Once glamorised and socially embedded, smoking's harms prompted regulatory action and behaviour change. However, historical inequities, targeted marketing, and delayed policy interventions continue to shape present-day disparities and resistance to tobacco control measures.

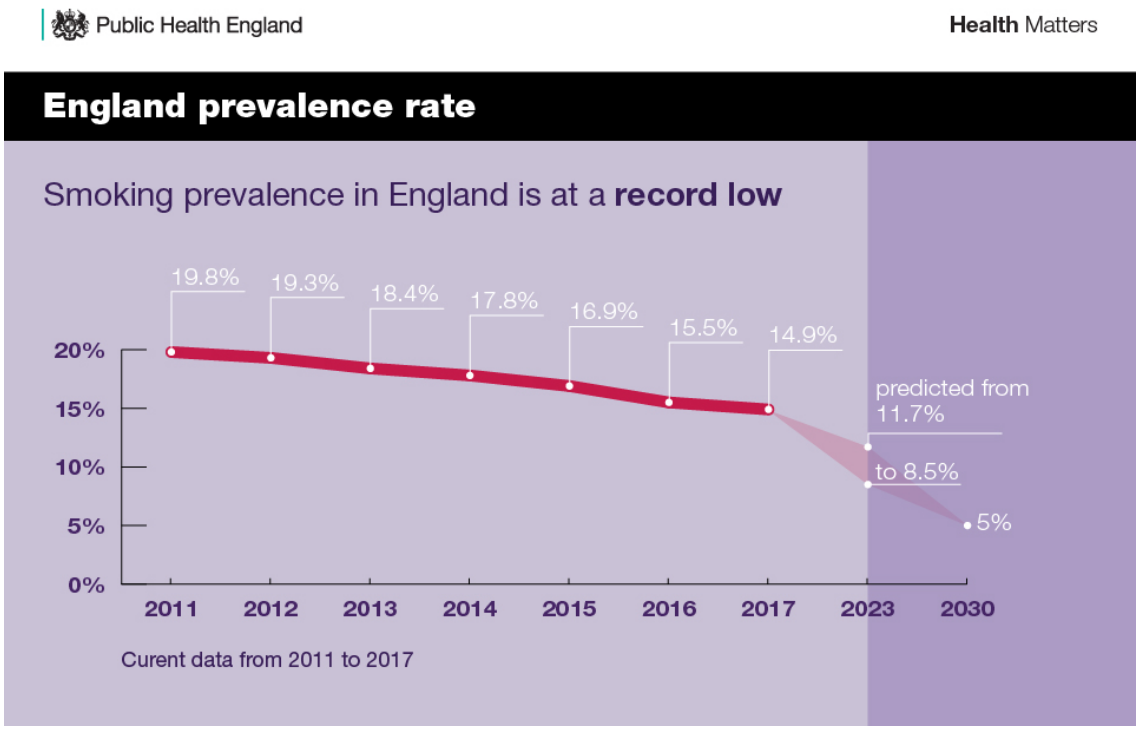
2.2 Smoking prevalence

Smoking remains a controversial issue in society; despite tobacco being the only consumer product that causes mortality half of its regular users and smoking remains an addiction for many people (Peto, 2006). Cigarette smoking prevalence among adults (aged 16+) in Great Britain has fallen by around two-thirds since the late 1940s (ONS, 2020, ONS, 2024). During the last 10 years, the prevalence of cigarette smoking in England has decreased from 21.1% in 2008 to 14.1% in 2019 to 11.9% in 2025 (this equates to around 6.9 million in the population) (as reported by the Office for

National Statistics (ONS, 2024). The proportion of adults who have never smoked cigarettes has increased over the years, from 25% of men and 49% of women in 1974 to 56.4% and 64.1% respectively in 2019; the proportion from more disadvantaged backgrounds has not changed significantly (ONS, 2024). Smoking contributes to health inequalities, causes 16% of all UK deaths (NHS, 2020) and costs the National Health Service (NHS) circa £2bn annually (Callum et al., 2011). The UK smokefree 2030 target will be missed by 7 years.

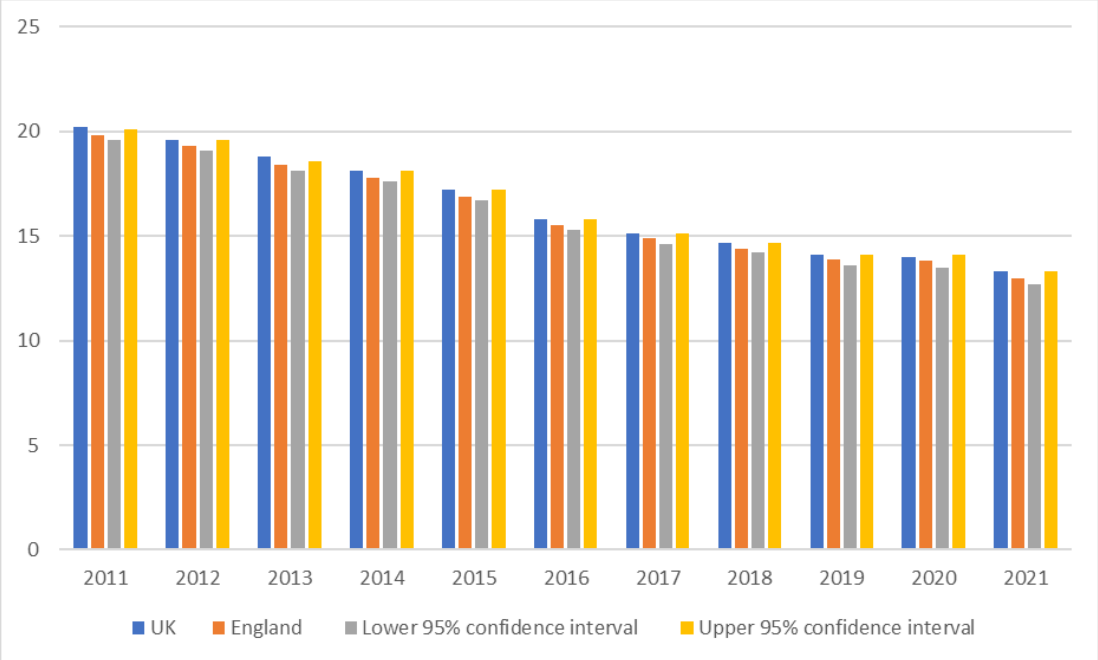
There are concerns that in spite of falls in smoking prevalence, a more dependent, 'hardened' smoking population remains (Warner and Burns, 2003, Emery et al., 2000). However, other studies have found that the mean number of cigarettes smoked per day (another indicator of cigarette dependence) has declined as smoking prevalence falls (ONS, 2020, ONS, 2024). Lower levels of cigarette dependence consistently predict greater quit success (Vangeli et al., 2011), signifying potential to further reduce English population smoking prevalence. Public Health England (PHE) current target is for smoking prevalence to be reduced to 5% or less by 2030 (PHE, 2022b) (figure1).

Figure 1: Smoking prevalence in England (PHE)



In 2019, the government set an objective for England to be smokefree by 2030, meaning only 5% of the population would smoke by then. Without further action, England will miss the target by at least 7 years, and the poorest areas in society will not meet it until 2044. To achieve the target, there is a need to accelerate the rate of decline of people who smoke, by 40% (PHE, 2022a).

Figure 2: Proportion who were current smokers, all persons aged 18 years and over, UK, 2011 to 2021. Source: Office for National Statistics – Annual Population Survey (2020)



Current smokers in the UK are disproportionately from disadvantaged backgrounds, with higher rates among those experiencing mental ill health and socioeconomic hardship. Future trends suggest continued overall decline, but persistent clustering in marginalised groups. Without targeted, equity-focused interventions, smoking may increasingly become concentrated among the most vulnerable, deepening health inequalities.

2.3 The problem of tobacco dependency

Over the past 30 years, more than 200 million deaths have been caused by smoking tobacco use, and annual economic costs due to smoking tobacco use exceed US$1 trillion (Goodchild et al.,

2018). With more than 1 billion current smokers globally in 2019, these numbers are likely to increase over the coming decades (Reitsma and al., 2021). The enormous health and economic consequences of the global tobacco epidemic make tobacco control a clear and urgent public health priority. Smoking remains a leading cause of preventable death, driving cancers, cardiovascular and respiratory diseases, and significant healthcare costs (Khan, 2022). It exacerbates health inequalities, disproportionately affecting lower socioeconomic groups, and imposes social, economic, and environmental burdens, making it a critical target for public health intervention and tobacco control policies (DHSC, 2023). Tobacco use remains one of the leading causes of preventable illness and death worldwide (WHO, 2025). In England, smoking is responsible for approximately 64,000 deaths each year and remains a major contributor to health inequalities (ONS, 2024).

Historically, the UK has made significant progress in reducing smoking prevalence through comprehensive tobacco control measures, including public awareness campaigns, tobacco taxation, smoke-free legislation, smoking cessation services and digital technologies. Although UK smoking prevalence has declined to 11.9% of adults (ONS, 2024) and continues a downward trend, certain groups, particularly those from lower socioeconomic backgrounds, continue to smoke at disproportionately high rates (WHO, 2025, Wilder et al., 2021). In recent years, smoking prevalence in the UK continues a downward trend. However, smoking prevalence can vary across different regions and demographic groups within the UK. The prevalence of current smokers in the routine and manual occupation group (aged 18 to 64) in 2023 was 19.5%. Over the next decade, UK smoking rates will likely continue to decline, driven by stricter regulation, shifting social norms, and vaping uptake (DHSC, 2023). However, disparities will persist, with higher prevalence among disadvantaged groups. Emerging nicotine products and evolving policy debates will reshape cessation strategies and public perceptions of tobacco use.

Smoking prevalence varies widely across the world, reflecting complex interactions between cultural norms, economic development, tobacco control policies, and industry influence(WHO, 2025). In

high-income countries such as the UK, Australia, and Canada, smoking rates have declined substantially over recent decades, often to below 15%, due to comprehensive tobacco control strategies, strong regulation, public health campaigns, and widespread access to cessation support (Reitsma and al., 2021). In contrast, many low and middle-income countries (LMICs) still have high prevalence, particularly among men, with rates exceeding 40% in some regions, such as parts of Eastern Europe and Southeast Asia (WHO, 2025).

UK smoking prevalence has declined to historic lows due to sustained tobacco control (DHSC, 2023), yet rates remain disproportionately high among lower socioeconomic groups, people with mental health conditions, and some ethnic minorities. This persistence highlights structural inequalities, the limits of current interventions, and the need for more targeted, culturally competent cessation strategies.

2.4 Costs of smoking

There is no clear consensus on the factors that should be included in calculating the cost of smoking; estimates of the cost of smoking that span a wide range and are subject to debate. Smoking remains a significant public health challenge as it causes more preventable death and disability in the UK than any other avoidable factor; if current patterns continue the WHO subsequently estimates that more than 8 million people will die prematurely yearly from tobacco use 7 million of those deaths are the result of direct tobacco use while around 1.2 million are the result of non-smokers being exposed to second-hand smoke (WHO, 2020). In 2020, 13% of all deaths in people aged 35 or over in England – 74,600 deaths – were estimated as being attributable to smoking including 54% of cancer deaths and 48% of deaths owing to respiratory diseases (NHS, 2020). In addition, in 2017, an estimated 14% (15,700) of deaths from circulatory diseases and 45% (800) of deaths from diseases of the digestive system were attributable to smoking (NHS, 2020). Cigarette smoking is also related to a higher susceptibility to pulmonary bacterial and viral infections. Previous studies have shown that smokers

are twice more likely to contract influenza and have more severe symptoms than non-smokers (Adams, 2020).

There were 506,100 hospital admissions attributable to smoking, similar to 2018/19 but 10% higher than 2009/10 when there were 461,700 (NHS, 2020). NHS Hospital Episode Statistics for England, as reported in Statistics on Smoking in England (NHS, 2020), show that in 2017/18 there were around 1.8 million hospital admissions for adults aged 35 and over with a primary diagnosis of a disease that could potentially be caused by smoking. For every person who dies because of smoking, at least 30 people live with a serious smoking-related illness. On average, smokers die 10 years earlier than non-smokers (Jha et al., 2013). Smoking has an impact on people's perceptions of health, with smokers in some age groups twice as likely as non-smokers of a similar age to feel that they are not in good health (ASH, 2020). Reducing smoking prevalence is therefore crucial to improving public health. More than a billion people around the world smoke tobacco, and the vast majority live in low-income and middle-income countries or belong to more disadvantaged socio-economic groups (WHO, 2020, Hiscock et al., 2012). Current estimates suggest that the overall cost of smoking to the UK economy may be up to £14 billion per year (DH, 2017, ASH, 2019). The Office for National Statistics estimates that the total UK household expenditure on tobacco in 2015 was to £19.3 billion (HSCIC, 2016). Smoking is one of the main causes of health inequalities in England, since poorer people are more likely to smoke; the harm is concentrated in more disadvantaged communities and groups (PHE, 2022b).

The proportion of current smokers is significantly higher among unemployed persons (26.8%) (ONS, 2020). The Department of Health's 2017 Tobacco Control Plan for England (DH, 2017) estimated the overall cost of smoking as £11 billion per year. Action on Smoking and Health provide a 2017 figure that smoking in England has an overall societal cost of £12.6 billion (ASH, 2022). Provisional HMRC estimates for 2020 tax receipts give a total of £5,947 million, compared to 9.29 billion pounds in the previous financial year (HMRC, 2021). Monthly total tobacco cash receipts are calculated by

summing the receipts from a variety of different cigarette types and other tobacco products. Total tobacco receipts for the current financial year to date (April 2020 to October 2020) are £5,947 million, which is £688 million (13.1%) higher than the same period in the financial year ending 2019. Smokers impose costs on society for health services from smoking related diseases. While cost saving is a benefit, the principal benefit of smoking cessation is the health gain associated with a longer living, healthier population.

Smoking continues to impose substantial global and national economic burdens (Allender et al., 2009). In the UK, smoking-related healthcare costs are estimated at over £2.4 billion annually, with wider societal costs, including lost productivity, social care, and premature mortality, exceeding £17 billion (ASH, 2022). Globally, tobacco use costs economies more than US$1.4 trillion each year in healthcare and productivity losses (Goodchild et al., 2018). These costs disproportionately impact low and middle income countries, where healthcare resources are already limited (WHO, 2025). Beyond economic impacts, smoking drives significant human costs through preventable disease, disability, and reduced quality of life, reinforcing health inequalities and straining public health systems, making tobacco control a critical economic as well as health priority (PHE, 2022b). Current analyses risk oversimplification by focusing on aggregate figures, masking regional and demographic disparities. Comprehensive tobacco economics must integrate these inequities, account for emerging nicotine products, and inform targeted interventions to achieve both fiscal and public health gains.

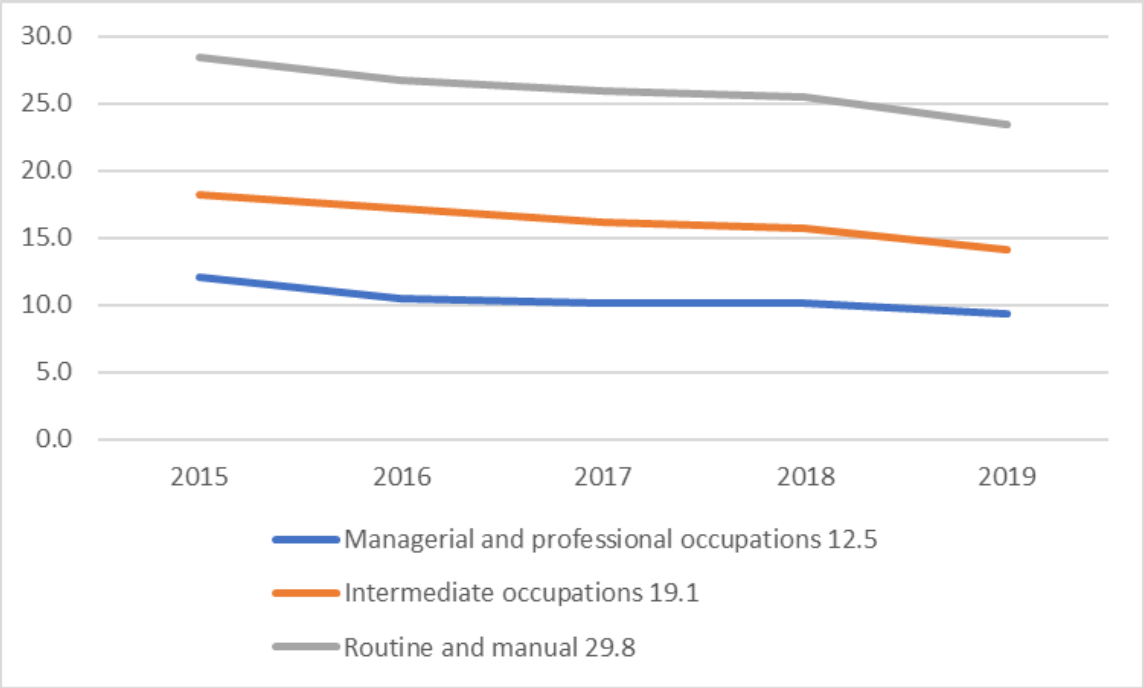
The UK's future smoking-related economic impact will likely decline with falling prevalence yet remain substantial due to persistent high rates in disadvantaged groups (ONS, 2024). Healthcare costs, lost productivity, and social care demands will disproportionately burden deprived communities (PHE, 2022b). Without targeted prevention and cessation strategies, tobacco will continue driving entrenched economic and health inequalities.

2.5 Smoker characteristics in England

There is little analysis of representative data to describe whether important characteristics of smoking and quitting behaviour have changed over time. In the UK in 2022, 14.6% of men smoked compared with 11.2% of women (ONS, 2024). Those aged 25 to 34 years continue to have the highest proportion of current smokers (16.3% circa 1.4 million people). In Great Britain in 2022, 5.2% (an increase from 4.9% in 2021) of respondents said they currently used an e-cigarette, this equates to nearly 3 million adults (ONS, 2024). Cigarette dependence appears to have decreased, as indicated by a reduction in the average number of cigarettes smoked daily and longer time to the first cigarette (Garnett et al., 2020). A recent comparison of English smokers between 2008 and 2017 found that smoking and quitting behaviour, independent of any changes in their socio-demographic characteristics, has changed substantially (Garnett et al., 2020). Smoking habits are associated with a variety of different characteristics and tends to be associated with inequality, defined for example, by a person's occupation (Figure 3) category, unemployment, being unmarried, unqualified and having poor health (ONS, 2020).

Smoker characteristics are useful to the design of appropriately targeted policies and interventions to reduce smoking prevalence further. There have been several changes in tobacco control policy in England since 2007 that may partly explain changes in smokers' characteristics. Over time, smokers' characteristics have evolved in response to shifting social norms, public health campaigns, and regulatory measures (PHE, 2022a). Demographically, smoking prevalence has declined among certain groups, particularly educated individuals and the affluent, while remaining disproportionately high among marginalised, economically deprived populations (ONS, 2024). Moreover, patterns of smoking initiation have shifted, with fewer starting at younger ages. Despite these changes, challenges persist, such as the emergence of new tobacco products and disparities in cessation efforts; the need for continued research and targeted interventions remains (Khan, 2022).

Figure 3: Smoking prevalence continued to be higher in routine and manual occupations than in managerial and professional occupations. Source: Office for National Statistics – Annual Population Survey (2020)



Although there is an overall decline in smoking prevalence in the UK there remains a large gap in smoking prevalence and levels of nicotine dependence between people with and without mental health problems. Around 1 in 3 cigarettes in Britain is smoked by someone with a mental health condition; among adults with a serious mental illness, 40.5% smoke (PHE, 2022b). Compared with non-smokers with mental health problems, smokers with mental health problems spend longer time in hospital and less time out of hospital (Prochaska et al., 2014). Engagement with SC interventions is often undermined by smokers (and health professionals) belief that smoking alleviates feelings of depression, stabilizes mood, and relieves stress (Lightfoot et al., 2020). High smoking rates among people with mental health conditions are the single largest contributor to their 10 to 20-year reduced life expectancy (RCP, 2013). Since the COVID-19 pandemic, smoker characteristics have shifted in complex ways. Some individuals, motivated by heightened health risk awareness, quit or reduced smoking, while others increased use due to stress, isolation, and economic hardship.

Smoking prevalence is disproportionately higher in lower socioeconomic groups due to a complex interplay of structural, social, and psychological factors (Revie et al., 2022). Poverty, job insecurity, and housing instability create chronic stress, for which smoking is often used as a coping mechanism (Kassel et al., 2003). Limited access to healthcare, targeted tobacco marketing in deprived areas, and reduced exposure to cessation support perpetuate smoking patterns (WHO, 2025, Patel and Thompson, 2025). Lower educational attainment can restrict awareness of long-term health risks, while social norms within disadvantaged communities may normalise smoking (Williams and Green, 2024, Hiscock et al., 2011). Intergenerational cycles of tobacco use further entrench the habit, making cessation harder without tailored, culturally sensitive, and accessible interventions. NHS SSSs often underperform in addressing smoking in lower socioeconomic groups because they insufficiently tackle the structural and social determinants driving tobacco use. Services are typically designed for individual behaviour change (Lancaster and Stead, 2017), yet fail to account for poverty, unstable housing, and chronic stress that undermine quit attempts. Appointment-based models may be inaccessible due to inflexible work patterns or transport costs, while messaging often overlooks the lived realities and social norms of disadvantaged communities.

Without integrating financial, social, and cultural support into cessation pathways, SSSs risk reinforcing health inequalities rather than reducing them, leaving the heaviest burden on the poorest. By 2030 and beyond, smoking in the UK will likely be concentrated among socioeconomically disadvantaged groups, people with mental health conditions, and marginalised communities (Buss et al., 2025). These entrenched patterns risk creating a “hard core” of smokers, resistant to conventional interventions, requiring innovative, equity-focused strategies to prevent widening health and social inequalities. Health inequalities are preventable differences in health outcomes between different population groups. Reducing health inequalities remains a key goal of public policy in England. In 2019, the government set an objective for England to be smokefree by 2030, meaning only 5% of the

population would smoke by then. Without further action, England will miss the smokefree 2030 target by at least 7 years, and the poorest areas in society will not meet it until 2044.

2.6 The COVID-19 pandemic

In the recent era of the viral pandemic owing to the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) causing the 2019 coronavirus disease (COVID-19), smoking has been assumed to be possibly associated with an adverse prognosis. The rate of decline in adult smoking prevalence in England stagnated during the COVID-19 pandemic through to 2022 (Jackson et al., 2023b). The coronavirus (COVID-19) pandemic has exacerbated heath inequalities in England. Evidence emerged that smoking was associated with more severe disease, a greater risk of hospital admission and excess mortality in people with COVID-19 admitted to hospital (Liu et al., 2020, George et al., 2020, Patanavanich and Glantz, 2020). The COVID-19 pandemic, its associated health risks and its impact on social activity may have influenced smoking and SC in several ways. COVID-19 is primarily a respiratory illness, and smoking adversely impacts the respiratory and immune systems, which may have incentivised smokers to quit. It may have contributed to the lower UK prevalence of smoking by providing a 'teachable moment' that increased the salience of smoking associated health risks and prompt people to make healthy changes to their behaviour (Lawson and Flocke, 2009).

Many smokers believed that smoking helped to relieve stress and reported smoking as a means of coping with high levels of stress (Kassel et al., 2003). Previous pandemics have resulted in significant consequences for mental health (Kayhan et al., 2020). During COVID-19 people experienced higher than usual levels of stress related to social isolation, employment, finances, caring responsibilities and concerns about catching or becoming ill from the virus (Jia et al., 2020). The COVID-19 pandemic was a population-level stressor of unprecedented global proportions, and consequently led to significant psychological trauma (e.g., stress, anxiety, depression, fear, and feelings of isolation and loneliness). COVID-19 had mixed effects on smoking behaviours: heightened health risk

awareness prompted some to quit, while stress, isolation, and economic hardship increased smoking for others (Gravely et al., 2021). Disparities have widened (Jackson et al., 2020a), with disadvantaged groups less likely to quit. Service disruptions and mistrust in health messaging have further complicated cessation, reinforcing pre-existing health inequalities.

2.7 The COVID-19 pandemic impact on smoking behaviours

The COVID-19 pandemic introduced new dynamics in smoking behaviour. Concerns about respiratory health prompted some smokers to cut down or attempt to quit to reduce their risk of complications from COVID-19 (Gravely et al., 2021). Alternatively, people smoked more in an attempt to cope with higher levels of stress or to relieve boredom (Parrott, 1999). Following the COVID-19 lockdown in March 2020, monthly cross-sectional surveys found that smokers in England were more likely than before lockdown to report trying to quit smoking; rates of SC and use of remote cessation support were higher (Jackson et al., 2020b). Some individuals attempted to quit due to heightened awareness of respiratory health, while others increased consumption due to stress, boredom, or disrupted routines (Jackson et al., 2020b).

The pandemic imposed sudden lifestyle changes and uncertainty about the future (Serafini et al., 2020). Therefore, understanding the interaction between COVID-19 and smoking behaviour is important. A recent cross-sectional survey found that though nearly half of smokers reported thinking about quitting because of COVID-19, the vast majority did not change their smoking behaviour; smokers were more likely to try and quit or reduce their smoking if they had greater concern about susceptibility and severity of COVID-19 related to smoking (Gravely et al., 2021). Several studies have examined the impact of COVID-19 pandemic on smoking behaviours across a range of countries; a systematic review (Almeda and Gómez-Gómez, 2022) reported varied behaviours among smokers during the pandemic (increasing or decreasing smoking, or no change in smoking).

A national study in the UK showed that smokers who experienced significant stress about becoming seriously ill from COVID-19 were more likely to increase smoking, while other studies suggest that smokers who had greater concern of getting COVID-19 and / or those who perceive that smoking increases the risk of COVID-19, were more likely to be motivated to quit, reduce smoking or make a quit attempt (Jackson et al., 2020a). Smokers reported lower adherence to COVID-19 protective behaviours guidelines despite being more worried than non-smokers about catching or becoming seriously ill from COVID-19 (Jackson et al., 2020a). Therefore, for some smokers, the linkage between COVID-19 and smoking appears to have motivated cessation thoughts and behaviours. In contrast, for the many smokers who did not change their behaviour, or increased smoking, they may not have considered that smoking poses a COVID-19-related risk to them and were not overly motivated to quit. A recent large cross-sectional survey findings suggest that the global health and economic shock caused by COVID-19 did not result in net changes in smokers' behaviour (Gravely et al., 2021). The rate of decline in adult smoking prevalence in England stagnated during the COVID-19 pandemic through to 2022 (Jackson et al., 2023b). The COVID-19 pandemic has exacerbated socioeconomic inequalities (Jackson et al., 2020a).

How the pandemic affected smoking behaviour has implications for provision and targeting of cessation support; providing an unprecedented opportune time to encourage and support quitting tobacco use by offering cessation services, pharmacotherapy (e.g., TDMs and nicotine replacement therapies) and behavioural counselling. Post pandemic, it is crucial to assist the world's more than one billion tobacco users, who might also be at increased risk of severe illness from COVID-19, to get the services that can increase the likelihood of successfully quitting tobacco use and accelerate the progress towards a tobacco-free world. It is not known whether smokers are more worried about developing COVID-19 or becoming seriously ill from the disease, which could affect their intention to quit (Jackson et al., 2023b).

2.8 Smoking and SC behaviour

Smoking is a socially patterned behaviour; substantially higher prevalence of smoking in groups with greater socio-economic disadvantage is a key driver of health inequalities (Hiscock et al., 2012). The act of smoking consists of several behaviours and are actions taken by a person that are associated with the burning and inhalation of a substance (Lader and Goddard, 2003). Tobacco smoking is a learned behavior that results in a physical addiction to nicotine for the majority of smokers (RCP, 2000). Most people experiment with smoking during adolescence and do not intend to become regular, addicted, or dependent smokers (Vu et al., 2018). Smoking behaviour is the result of multifactorial influences (i.e., social, economic, environmental, behavioural and physiological) and varies across the life course affecting smoking trajectories (ONS, 2020). Accordingly, stopping smoking can be difficult for many individuals, and it is recommended that interventions include behavioural and pharmacological support. Smoking behaviour theories emphasise the central importance of an individual's motivation and capabilities to quit an addiction with limited reference to context and social factors.

Theories such as *PRIME* (West and Brown, 2013) offer valuable frameworks for analysing motivation, capability, and treatment engagement. Moreover, non-adherence in tobacco dependence trials risks underestimating medication efficacy and impeding translation into practice. *PRIME* (*P*lans, *R*esponses, *I*mpulses, *M*otives, *E*valuations) (West, 2006) has been applied to smokers in attempting to explain how quit attempts are made. *PRIME* states that the decision to quit smoking is based on a smoker's evaluative beliefs (positive or negative) about smoking, which influence motivation to quit or not. This involves internal tensions (impulses and urges to smoke) and external triggers (e.g., cues in the environment) to determine subsequent behaviour. Improving the conceptualisation of SC medication adherence and differentiating each dynamic behavior in the adherence process may allow for more effective identification of targets for NRT adherence promoting interventions. Currently, TD research lacks a prominent theory for thinking about

adherence to TDMs and relevant factors for intervention. Several different health behavior theories and frameworks have been applied to TDM adherence, such as the health belief model, motivational interviewing, social cognitive theory, transtheoretical model, self-regulation/common sense model, and the capability, opportunity, motivation, and behavior (*COM-B*) model. Framing TDM adherence behaviours in theoretical models enables a structured exploration of behavioural mechanisms of these complex activities. Engaging with smokers about their perceptions and knowledge, readiness to quit, and their socioeconomic status when advising them on the use of NRT for SC could improve the real-world effectiveness of these medications through improved adherence (Styklunas et al., 2021). Smoking follows a steep social gradient, with higher prevalence in disadvantaged groups. Yet, cessation support, particularly pharmacotherapy, often targets individual behaviour, overlooking structural determinants. Bridging this mismatch is essential for policy, research, and clinical practice to address health inequalities and ensure interventions reflect the lived realities of those most affected.

Understanding smoking and smoking cessation behaviours and the contexts in which they occur is essential for developing effective evidence-based behaviour change interventions and policies and for reducing avoidable morbidity and mortality. Health behaviour change theories are many and as diverse as the different concepts that they attempt to explain and combine, they also reflect a range of disciplines (including medicine, psychology and sociology) (Michie et al., 2014b). Interventions have been targeted at behavioural risk factors for both smoking (Lancaster and Stead, 2017, Stead and Lancaster, 2016, Stead and Lancaster, 2017) and medication adherence behaviours (e.g. consistent usage, following instructions, seeking support, *etc*.) (Nieuwlaat et al., 2014, Haynes et al., 2008). Efficacy tends to be modest, with substantial heterogeneity of short-term and long-term effects (Michie et al., 2008). Behavioural change techniques for SC are complex and work in multiple ways making it problematic to determine the most effective components (Hartmann-Boyce et al., 2021b).

Over the past decades there has been modest improvement in the effectiveness of behavioural interventions, and it has been argued that a key reason is a lack of a shared language for describing

the content, including the "active ingredients" of SC interventions (Michie et al., 2011a). This has limited the possibility of replicating effective interventions, synthesising evidence and understanding the causal mechanisms underlying behaviour change (Pacek et al., 2018). A recent study (Foo et al., 2025) explored the role of community health workers (CHWs) in supporting SC among adults with serious mental illness. The mixed-methods analysis found that greater CHW-participant engagement was associated with higher tobacco abstinence rates. The concept of the 'person-as-intervention' marks a critical shift in how we understand SC (Zeeman et al., 2023). It acknowledges that while pharmacotherapies like NRT or varenicline are important, their success often hinges not on the medication alone, but on the quality of the therapeutic relationship, the consistency of practitioner support, and the meaning the individual assigns to the quitting process.

A RCT study (Swan et al., 2010) found that treatment outcomes were significantly improved when pharmacotherapy was combined with tailored, practitioner-led behavioural counselling, supporting the concept that the person delivering the intervention matters. In this framing, the practitioner, their empathy, communication, continuity, and capacity to personalise care, becomes the active ingredient alongside the pharmacological agent. This aligns with evidence from relational sociology and behavioural science, which shows that trust, alliance, and shared decision-making significantly influence adherence and quit success (Chen et al., 2025). This prospective cohort study demonstrated that participants who received shared decision-making (SDM), integrated cessation counselling showed higher medication adherence (39.1% vs 28.6%) and were more likely to use cessation pharmacotherapies (83.4% vs 71.9%), though 24-week abstinence rates were not significantly different. A meta-analysis (Cahill et al., 2014) found that tailored psychological counselling produces superior outcomes compared with pharmacotherapy alone. It supports the interpretation that practitioner-delivered, relational elements of care are key active ingredients in cessation success. In clinical SC practice, there is a need for service models that recognise the practitioner not merely as a deliverer of treatment, but as a core component of the intervention itself. The literature robustly links

trust and shared decision-making to adherence, yet over-rely on self-report, underexplore structural inequities, and seldom assess sustained quit outcomes in real world SC contexts.

SC reduces subsequent morbidity and mortality (NICE, 2018). Determinants of successful SC that have been consistently reported include: lifetime tobacco exposure, educational attainment, alcohol drinking, marital status, occupational classification, disease morbidity and second-hand smoke exposure (Freund et al., 1992, NHS, 2020, Richardson et al., 2019). Attempts to quit and cut down have decreased, as has use of behavioural support such as NHS SSSs, highlighting the need to reinstate and improve easy to access effective services. Of those smokers making quit attempts, fewer use no support while more use pharmacological support, owing probably to the rapid rise in the prevalence of e-cigarette use as a tool for quitting smoking (Garnett et al., 2020). Tobacco dependence (TD) is a chronic, relapsing condition driven by addiction to nicotine. However, cessation treatment can help people quit (Hartmann-Boyce et al., 2021b).

Nicotine dependency is generally assumed to be a considerable barrier to cessation (RCP, 2000), and studies have indicated that the large majority of on-going smokers frequently fail to overcome nicotine withdrawal symptoms despite their intention to quit (Hughes et al., 2004). Theories of smoking (West and Brown, 2013) and SC (Prochaska and DiClemente, 1983) differ in their conceptualisations of the relative importance of and inter-relationships between these factors. Smoking, a behavior with detrimental health effects, is often deeply ingrained in individuals due to addiction to nicotine and social or psychological factors (stress, anxiety, depression, and social influences) (West, 2016). SC requires resolving physical addiction, psychological dependence, and managing withdrawal symptoms. Nicotine itself is physiologically and psychologically addictive (West and Brown, 2013), in a similar way to heroin and cocaine and the overwhelming majority of smokers are strongly dependent on nicotine which is a substantial obstacle to smokers who choose to quit (Hajek et al., 2013). Sixty-five percent of smokers want to quit their habit, but are unable to do so (ONS, 2020) (PHE, 2022b). Smoking is a chronic disorder characterised by the development of an

addiction status mainly owing to nicotine thus smokers are generally unable to quit smoking without help (West and Brown, 2013). The severity of addiction can be quantified through simple and validated screening tools, such as the *Fagerström Test for Nicotine Dependence* (FTND) (Heatherton and Fagerström, 1991).

Today's SC behaviours reflect a mix of traditional and evolving approaches, shaped by social norms, technology, and widening inequalities (Mohd Noordin et al., 2023, ONS, 2024). Many smokers still attempt to stop unaided, often relying on willpower, despite evidence that behavioural support and pharmacotherapy significantly improve success rates (Mersha et al., 2021). E-cigarettes have emerged as the most popular cessation aid in the UK (Rojas et al., 2025), reflecting perceptions of reduced harm, affordability, and accessibility, but their role remains contested in policy and public discourse. Socioeconomic disparities remain stark, with disadvantaged groups less likely to access NHS Stop Smoking Services and more likely to relapse, highlighting the limits of current service reach and design.

In the future, cessation behaviours are likely to be increasingly personalised, integrating pharmacogenomics, AI-driven behavioural support, and just-in-time adaptive interventions (NICE, 2025, van Vliet et al., 2024). E-cigarettes and other reduced-risk products may be embedded within structured "step-down" quitting models, particularly for hard-to-reach groups. Social trends, such as declining smoking acceptability, stronger regulation, and increased focus on mental health, may motivate quitting but also risk leaving a concentrated "hard core" of smokers resistant to conventional interventions. Effective strategies will need to combine culturally competent, equity-focused service delivery with innovative, flexible tools that address both the biological and social dimensions of TD. Without this, inequalities in smoking-related harm may deepen.

2.9 Treatment of tobacco dependency

Although many smokers successfully quit smoking unaided, SC interventions are effective and increase chances of successful quitting. The salient feature of TD is the craving to feel the

pharmacological effects of nicotine and the avoidance of unpleasant withdrawal symptoms. "Relapse" means going back to smoking regularly; it is common and occurs during the first days following the attempt of discontinuing smoking, when withdrawal symptoms are generally more severe (Hendricks et al., 2006). Different strategies are available to treat TD that include both non-pharmacological (behavioural counselling); (Stead and Lancaster, 2017), (Lancaster and Stead, 2017) and pharmacological therapies (Cahill et al., 2013). Under usual circumstances in England, a wide range of pharmacological and behavioural support is available for SC. Accessing such support has likely been more difficult under social distancing and lockdown restrictions (Jackson et al., 2020b). While remote support (e.g. telephone support, websites, smartphone applications (apps)) that can be accessed from home is widely available, uptake by smokers has been low (Perski et al., 2019, Bendotti et al., 2023). Relapse is the most likely outcome of any SC attempt (Hajek et al., 2013), even those made with the benefit intensive psychosocial treatment and pharmacotherapy (Piasecki, 2006).

Treatments aimed at SC are among the most cost-effective interventions in health care (Shahab, 2015). However, the effectiveness of NRT in real-world settings has not reached the effectiveness levels found in randomised trials (Kotz et al., 2014). This is thought to be due, in part, to sub- optimal adherence (Gupta and Lee, 2025). Most people treated in a single treatment episode, however, eventually return to smoking. Most of those who do return to smoking relapse while receiving treatment, and therefore more effective interventions are needed. Inadequate medication adherence in clinical trials contributes to significantly increased study costs, complicates statistical analysis and threatens study validity (Robiner, 2005, Ellis et al., 2000, Martin et al., 2000). Clinical trials of behavioural interventions frequently suffer from low levels of medication adherence with estimates suggesting that between 25 and 50% of research participants are not adherent (Robiner, 2005). The extent to which patient nonadherence has flawed clinical research has in some cases been underestimated (Eliasson et al., 2020b).

A comprehensive review of interventions to increase medication adherence and improve related outcomes using a variety of approaches found their effects were inconsistent; only a few clinical trials improved both adherence and clinical outcomes (Nieuwlaat et al., 2014). The most effective medication adherence interventions adopted comprehensive approaches involving a range of strategies, were high-intensity, and tailored to individual patients (Haynes et al., 2008). HCPs (i.e., physicians, nurses, pharmacists) played a key role in supporting, promoting and monitoring medicines adherence in chronic conditions. Patient-centred approaches to improve adherence are considered promising (Kuntz et al., 2014); however their effectiveness remains unclear. In the absence of a single definitive intervention to address non-adherence, current NICE Guidelines combine trial evidence of interventions and explanatory studies of non-adherence (NICE, 2009). The dearth of evidence underpinned by health psychology theory is of concern given its importance for informing intervention design and implementation. Recent literature has also made the case for considering medication adherence as a dynamic rather than static variable (Gupta and Lee, 2025), comprised of multiple behaviours that may vary within an individual over time (Vrijens et al., 2012).

The treatment of TD today is grounded in a combination of behavioural support and pharmacological interventions, including NRT, varenicline, and bupropion (NICE, 2018). In the UK, NHS SSSs provide structured behavioural counselling alongside these medications, significantly improving quit rates compared to unaided attempts (NHS, 2023). However, uptake of SSSs has declined, with many smokers opting for self-directed methods, particularly e-cigarettes, due to perceptions of convenience, cost-effectiveness, and autonomy (Rojas et al., 2025). Persistent barriers include mistrust of medications, limited awareness of service availability, cultural inappropriateness of interventions, and inadequate targeting of disadvantaged populations where prevalence remains highest (Vestbo and Anderson, 2025).

Looking to the future, treatment is likely to become increasingly personalised, integrating pharmacogenomics to match medications to genetic profiles, AI-driven behavioural support, and just-

in-time adaptive interventions that deliver timely prompts based on real-time risk indicators (Onwuzo et al., 2024, Bendotti et al., 2023). Harm reduction approaches, such as structured vape-to-abstinence programmes, may become formalised within clinical pathways, especially for populations resistant to traditional pharmacotherapy(NICE, 2025). Mental health integration will be essential, recognising the bidirectional link between TD and psychological distress (Lightfoot et al., 2020). The challenge will be ensuring equitable access to these innovations, avoiding the risk that technological advancements primarily benefit more affluent smokers while leaving marginalised groups with limited, less effective options (Williams and Green, 2024).

2.10 NHS stop smoking services (SSSs)

In England, NHS SSSs offer behavioural support alongside pharmacological treatments such as NRT, varenicline, and nortriptyline. Electronic cigarettes have also emerged as popular cessation tools (Hajek et al., 2019). However, despite their proven efficacy, adherence to pharmacotherapy remains suboptimal, limiting the real-world effectiveness of these interventions (Beard et al., 2021, Shiffman et al., 2008c). The aim of NHS SSSs is to provide evidence-based, accessible, and personalised support to help smokers quit, reduce tobacco-related harm, and improve health outcomes (Song et al., 2020). This includes behavioural counselling, pharmacological aids, and relapse prevention, with a focus on addressing health inequalities and supporting high-risk, disadvantaged populations (NICE, 2018). The UK has one of the most comprehensive stop smoking approaches globally, combining behavioural support with licensed pharmacotherapies to address both the psychological and physiological components of addiction. SSSs provide evidence based and cost-effective support to quit attempts (NICE, 2018, Stead and Lancaster, 2016). Evidence indicates that, although the majority of current smokers are motivated to quit, the number of people using NHS SSSs to help them quit continues to decline (Lacobucci, 2017, Buss et al., 2025). Overall, long-term quit success through NHS SSSs remains low (Dobbie et al., 2015) partly explained by poor TDM adherence (Vestbo and Anderson, 2025). There is robust scientific evidence showing that comprehensive SC interventions

are essential to reducing tobacco use (Onwuzo et al., 2024, Hartmann-Boyce et al., 2021a). The COVID-19 pandemic presented an unprecedented opportunity to provide evidence-based, comprehensive SC services to tobacco users and strengthen tobacco control policies (Jackson et al., 2023b).

The foundation of UK SSSs lies in behavioural support, which is typically delivered through local NHS SSSs (Hartmann-Boyce et al., 2021b). Support is provided in individual or group settings by trained advisors and may now include digital and telephone-based options. In the UK, NHS Stop Smoking Advisers are typically trained through *National Centre for Smoking Cessation and Training* (NCSCT, 2019) accredited programmes. Training covers evidence-based behavioural support, pharmacotherapy options, motivational interviewing, and tailoring interventions. Advisers are expected to apply guidelines consistently while adapting support to individual needs, particularly among disadvantaged populations. Behavioural interventions help clients understand triggers, manage cravings, and build coping strategies, and are shown to significantly increase quit success when combined with pharmacotherapy (Lancaster and Stead, 2017, Hartmann-Boyce et al., 2021b). Pharmacological treatments available on the NHS include NRT in various forms (patches, gum, lozenges, inhalators, sprays) (Hartmann-Boyce et al., 2018), varenicline (subject to availability post-supply issues), and bupropion (Howes et al., 2020). These medications work by reducing withdrawal symptoms and cravings and are typically offered for 8–12 weeks alongside behavioural support (Onwuzo et al., 2024).

Emerging treatments, such as e-cigarettes, are now increasingly recognised within UK policy and clinical guidance (Hartmann-Boyce et al., 2022). While not currently licensed as medicines, they are endorsed by bodies like the *National Institute for Health and Care Excellence* (NICE) and the *Royal College of Physicians* as effective tools for harm reduction and SC, particularly for smokers who have not succeeded with other methods. The growing role of e-cigarettes in smoking cessation, though their use remains a topic of significant debate. On one hand, a substantial body of evidence,

particularly from the UK, suggests that e-cigarettes can be effective in helping smokers quit (Thomas et al., 2021). Studies, including Cochrane reviews, indicate that e-cigarettes may outperform traditional NRT when combined with behavioural support (Hartmann-Boyce et al., 2022). They offer a similar behavioural and sensory experience to smoking, which may enhance user satisfaction and adherence compared to other cessation methods. However, concerns persist about the long-term health effects, which are not yet fully understood due to the relatively recent emergence of these products. E-cigarettes are not risk-free, and public health messaging must carefully balance promoting them as a cessation aid for adult smokers while preventing uptake among young people and non-smokers (Khouja et al., 2024). Additionally, e-cigarette use without behavioural support may result in dual use, continued smoking alongside vaping, which diminishes cessation benefits (McNeill et al., 2020). Regulatory and ethical challenges also arise, particularly regarding industry involvement and marketing strategies. E-cigarette use without behavioural support may lead to dual use, continued smoking alongside vaping, which limits health gains and undermines cessation goals. This pattern raises regulatory and ethical concerns, particularly around the influence of industry marketing, product appeal, and the need for safeguards to prevent unintended normalisation of nicotine use among vulnerable groups (ASH, 2021). Within NHS SSSs, e-cigarettes are increasingly offered as a cessation aid alongside licensed medications. While evidence supports their effectiveness, delivery is guided by careful harm reduction principles. Services emphasise behavioural support, monitor for dual use, and remain cautious about long-term safety and the evolving regulatory landscape surrounding vaping products (McNeill et al., 2020).

In summary, while e-cigarettes have a legitimate role as a harm reduction tool for smokers unable or unwilling to quit using licensed treatments, they require careful regulation, ongoing research, and targeted support to maximise public health benefit. UK stop smoking treatment emphasises accessibility, with services prioritising high-need groups, such as pregnant women, people with mental health conditions, and those in deprived areas (PHE, 2022b). Despite this, variations in

funding and delivery across regions can impact service quality and reach. In conclusion, the UK's stop smoking treatment model is robust and evidence-led, however continued investment and innovation are needed to address disparities and evolving tobacco use patterns.

2.11 Pharmacological therapies for tobacco dependence

Different pharmacological strategies are available to treat TD. In the United Kingdom, three pharmacotherapies, i.e. varenicline, bupropion and NRT, are licensed by the Medicines and Healthcare products Regulatory Agency (MHRA) and recommended by the National Institute for Health and Care Excellence (NICE) for smoking cessation (NICE, 2018) are effective cessation aides for people who are assessed as nicotine dependent (Cahill et al., 2013). TDMs effectively aid initial attempt to quit and decrease relapse risk (Cahill et al., 2013); however, globally, most SC attempts are unassisted and consequently long term abstinent rates are poor (Chaiton et al., 2016). It is well accepted that TDMs are effective and safe in real-world settings(Howes et al., 2020, Hartmann-Boyce et al., 2018). NRT, varenicline and bupropion are the main pharmacological strategies available for SC; the pharmacological approach to SC is safe and effective, and therefore TDMs should be offered to everyone willing to quit smoking (Cahill et al., 2013). NRT, the utilised TDM most commonly, is available as patches or as shorter acting oral forms (lozenges, chewing gum, nasal sprays), reduces urges and withdrawal symptoms by substituting for nicotine inhaled via tobacco smoke (Cummings and A., 2005). NRT is effective as part of a strategy to promote SC increasing the rate of long-term quitting by approximately 50% to 70% regardless of setting (Stead et al., 2012b). April 2022 to March 2023, approximately 54% of smokers who set a quit date with NHS SSSs successfully quit smoking at four weeks post-quit (NHS, 2023).

NRT has been the mainstay of smoking cessation therapy for >15 years and has been accepted as first-line pharmacotherapy for SC because of its safety and efficacy profile (West, 2017). Oral varenicline is a nicotinic receptor partial agonist that binds less effectively than nicotine to receptors

(Ebbert et al., 2010). The aim is to reduce smoking withdrawal symptoms and the pleasure people usually experience when they smoke (Cahill et al., 2016). Antidepressant medications are primarily used for the treatment of depression and disorders of negative affect and have been effectively used to aid SC (Hall et al., 2002) providing an alternative to frontline SC therapies, such as NRT, and nicotine agonists, such as varenicline. Bupropion and nortriptyline are effective pharmacological aids for SC (Howes et al., 2020). Oral bupropion is a nicotinic receptor antagonist with dopaminergic and adrenergic actions (NICE, 2002). It may work by blocking effects of nicotine, relieving withdrawal, or reducing depressed mood (Richmond and Zwar, 2003). Of the antidepressant medications indicated for SC, the most commonly used is bupropion, the second most commonly tested medication for SC is the tricyclic antidepressant nortriptyline which enhances noradrenergic and serotonergic activity by blocking reuptake of these neurotransmitters (Benowitz and Peng, 2000). There is no evidence of higher quit rates when combining bupropion with either NRT or varenicline relative to each drug taken alone (Howes et al., 2020). For smokers, the choice among the therapies is based largely on their preference, with a few notable exceptions for smokers with comorbidities or contraindications to certain drugs (NICE, 2018). It is important that smokers who receive pharmacotherapy receive a full course, which will vary depending on the individual smoker. A full course for NRT or bupropion is at least 8 weeks, and at least 12 weeks for varenicline (NICE, 2018). Smokers may have difficulties using of TDMs. There is high-certainty evidence to suggest that people using bupropion are more likely to stop taking the medicine because of unpleasant effects than those taking a placebo (Howes et al., 2020).

TDMs are essential tools in the treatment of TD, yet they are not without limitations. Licensed pharmacotherapies, NRT, bupropion, and varenicline, have been consistently shown to increase quit rates compared to placebo (Howes et al., 2020, Hartmann-Boyce et al., 2018). They work primarily by reducing withdrawal symptoms and cravings, helping to stabilise motivation during the critical early phase of cessation. Among these, varenicline has shown the highest efficacy in clinical trials

(Peng et al., 2017). However, real-world effectiveness is often lower than trial outcomes due to poor adherence, premature discontinuation, and underutilisation (Catz et al., 2011). Many smokers either do not access medications, use them incorrectly, or stop treatment too early (Vestbo and Anderson, 2025). Moreover, these medications do not address the behavioural and social dimensions of smoking, which are central to long-term cessation success (Vestbo and Anderson, 2025). Another critical issue is access and equity; while medications are available on the NHS in the UK, disparities persist, with lower uptake among socioeconomically disadvantaged groups and those with mental health conditions, populations most burdened by smoking (Murray et al., 2009, Williams and Green, 2024).

Pharmacological therapies for TD currently primarily include NRT, varenicline, and bupropion. When combined with behavioural support, these treatments can double, or triple quit rates compared to unaided attempts (Onwuzo et al., 2024). In the UK, NHS SSSs routinely offer these medications, but uptake has been declining (Buss et al., 2025), partly due to the increasing popularity of e-cigarettes, mistrust in medications, and perceptions of side effects or ineffectiveness. Access and adherence remain uneven, with disadvantaged populations less likely to use pharmacotherapy effectively, contributing to persistent health inequalities. Furthermore, global supply issues, such as the recent varenicline shortage, have highlighted vulnerabilities in treatment provision. In the future, pharmacological therapies are likely to become more targeted and integrated with technological support (Perski et al., 2019). Advances in pharmacogenomics may enable clinicians to tailor treatments to individual genetic profiles, optimising efficacy and minimising side effects (Lessov-Schlaggar et al., 2008). Digital adherence tools, including AI-driven reminders and feedback, could address one of the biggest barriers identified in current practice, (NICE, 2025, van Vliet et al., 2024) low and inconsistent medication use. Novel agents targeting neurobiological pathways beyond nicotinic receptors are in development, potentially expanding the therapeutic toolkit (Hoogsteder et al., 2012). However, to ensure impact, these innovations must be embedded in equitable, culturally competent service delivery models, preventing a widening gap in tobacco-related health outcomes.

2.12 Electronic cigarettes

Electronic cigarettes (e-cigarettes) are nicotine delivery devices that use a battery to aerosolize nicotine (Britton and Bogdanovica, 2014). Many e-cigarette products are available and vary in the rate and amount of nicotine delivery. Because tobacco is not burned, these devices are likely to be safer than continuing to smoke conventional tobacco cigarettes (ASH, 2021). However, their safety with long-term use is uncertain (Pisinger and Dossing, 2014). There is a lack of international consensus regarding the role of using e-cigarettes as a tool for SC. While evidence supports e-cigarettes as a harm-reduction tool (Hartmann-Boyce et al., 2021c), uncertainties over long-term safety, dual use, youth uptake, regulatory inconsistency, and industry influence complicate their integration into sustainable smoking cessation strategies.

A landmark randomised trial (Hajek et al., 2019) provided robust evidence that nicotine-containing e-cigarettes, when combined with behavioural support, are more effective in helping smokers quit than traditional nicotine replacement therapies. In response, Public Health England (PHE) and NHS Health Scotland advocated e-cigarettes in contrast to other public health bodies such as the World Health Organisation who emphasize that these products are being marketed aggressively to youth, using attractive flavours and designs, with minimal safeguards in nearly 90 countries (WHO, 2025). The role of e-cigarettes in SC treatment remains unclear The results of randomised trials are mixed, although a meta-analysis concluded that there is moderately good evidence that e-cigarettes were more effective for SC than nicotine replacement products or e-cigarettes without nicotine (Hartmann-Boyce et al., 2021c). E-cigarettes have huge promise, although there is limited evidence on how to use them best to assist SC, how safe they are long-term and whether they have unintended consequences (ASH, 2018). The overall impact of e-cigarettes on public health remains a question of debate. Although e-cigarettes showed promise as cessation tools, more research is needed on their long-term effectiveness and safety (Thomas et al., 2021). While e-cigarette use may represent harm reduction for adult smokers, few would suggest a benefit of nicotine vaping in adolescence when the

brain is still developing. E-cigarettes have surpassed conventional cigarettes in popularity, with 32% of 15-year-olds surveyed reporting e-cigarette use at some point and 20% in the past 30 days (Salari et al., 2024).

The literature on e-cigarettes reveals mixed evidence: while some studies suggest potential for SC, concerns persist about dual use, youth uptake, and unknown long-term harms. Regulatory, ethical, and marketing challenges complicate their role, demanding cautious, evidence-based integration into cessation strategies alongside robust surveillance and adaptive public health policy. Future SC strategies involving e-cigarettes remain contested; evidence suggests potential harm reduction, yet youth initiation, dual use, and uncertain long-term risks undermine confidence. Without stringent regulation, equitable access, and robust longitudinal research, their promise may be outweighed by unintended public health consequences, particularly in nicotine dependence trajectories and relapse prevention (Hartmann-Boyce et al., 2022) (Goniewicz et al., 2019).

2.13 SC treatment innovations

Although some research has shown that successful quit attempts made without any form of pharmacological and / or behavioural support (Lancaster et al., 2006), one of the main predictors of effectiveness is medication adherence; a crucial component of the pharmacological treatment of smoking (Mersha et al., 2021). SC rates are further improved when these medications are provided together with multi-session behavioural counselling (e.g. Quitline, NHS cessation clinic) (Stead and Lancaster, 2016). Adherence to TDMs is reported to be inconsistent and low (WHO, 2003, Quinn et al., 2020, Pacek et al., 2018). Improving adherence to TDMs requires a comprehensive intervention approach involving various stakeholders pre-clinical trial design.

Since most smokers who attempt to quit still fail to achieve long-term abstinence, and most smokers relapse in the first 8 days, the need for better SC approaches is of major importance. Prospects for the pharmacotherapy of SC include the use of nicotine receptor subtype-specific agonists and antagonists,

targeted to deal with specific reinforcement and / or specific withdrawal symptoms. Development of nicotine antibodies that might neutralise the effects of nicotine could be effective in the future. A potential new treatment in SC and relapse prevention is nicotine vaccination which is based on active immunisation against the nicotine molecule. Immunisation stimulates the immune system to produce nicotine-specific antibodies that sequester nicotine in the blood stream, after inhaling tobacco products (Hoogsteder et al., 2012). One of the advantages of nicotine vaccination is the increased treatment adherence compared to other SC therapies owing to the mode of administration, and the persistence of antibodies after vaccinations are completed, which may serve a role to maintain abstinence and prevent relapse (Hoogsteder et al., 2012).

Evidence indicates that smokers trying to quit in the future may benefit from a more tailored drug treatment plan to target individual physical cravings – possibly even through a DNA test. Research has shown that addressing the psychological and social aspects of addiction is critical in preventing people from relapsing (Baumeister, 2017, Hajek et al., 2013). In terms of SC, mobile health (mHealth) has become a powerful coadjutant tool (Chu et al., 2021). Technological innovations are increasingly offering novel services and tools to support SC attempts. Digital therapeutics (e.g. NHS Quit smoking app, *QuitGuide*, *Clickotine*) for SC offer several advantages over traditional SC methods; they provide increased access to support and resources, empowering individuals to quit smoking tailored to their preferences. Through interactive features like goal setting, progress tracking, and personalised feedback, digital therapeutics enhance engagement and motivation. Digital therapeutics leverage cutting-edge technology to deliver tailored interventions that address individual needs and preferences. Utilisation of algorithms and artificial intelligence (e.g. Quit Sense) to analyse user data, identify patterns, provide targeted interventions, maximising effectiveness and personalisation (Bendotti et al., 2023).

The future of e-cigarettes in the smoking cessation arena is likely to remain dynamic and contested, shaped by evolving evidence, regulatory decisions, and societal attitudes. E-cigarettes emerged as a

widely used harm reduction tool, especially among smokers who have not succeeded with conventional cessation methods. In the UK, public health bodies such as NICE and the Royal College of Physicians support their use in smoking cessation, citing evidence that they are significantly less harmful than combustible tobacco and can aid quitting. The e-cigarette role will depend heavily on balancing risk and benefit. To maximise public health gains, e-cigarettes must be promoted specifically as quit aids for adult smokers, not lifestyle products for the wider population. Robust regulation of marketing, product standards, and flavours will be essential to prevent youth uptake and unintended normalisation of nicotine use. Research priorities include long-term safety, patterns of dual use, and their effectiveness across diverse populations. There is also scope to integrate e-cigarettes more systematically into cessation services, especially for disadvantaged groups with high smoking rates. In summary, e-cigarettes are likely to remain a controversial but potentially valuable component of a broader tobacco harm reduction and cessation strategy.

Future UK SC interventions will need to integrate personalised pharmacogenomics, digital behavioural support, and real-time biometric feedback (Prom-Wormley et al., 2023, Mattock and al., 2023). NHS services may adopt artificial intelligence (AI) AI-driven tailoring, culturally adapted programmes, and hybrid vape-to-abstinence models. Conversational AI (chatbots and dialogue systems) is an emerging tool for tobacco cessation that has the potential to emulate personalised human support and increase engagement; however there is limited evidence of effectiveness (Bendotti et al., 2023). Greater emphasis should be placed on addressing social determinants, sustaining motivation, and reducing inequalities in access and outcomes across diverse communities.

2.14 Non-pharmacological tobacco dependence therapies

TDMs can be combined with non-pharmacological strategies (behavioural support) (Stead and Lancaster, 2016), which are validated approaches to aid quit attempts and can help more people to stop smoking for six months or longer, without causing unwanted effects (Hartmann-Boyce et al.,

2021b). Behavioural support provides an alternative or addition to TDMs to help people stop smoking. The behavioural support offered by stop smoking services can be a combination of health education, motivational interviewing and, occasionally, more intensive psychotherapy such as cognitive behavioural therapy, which focuses non-pharmacological support, such as behavioural counselling and digital apps, offers additional avenues but varies in accessibility and impact (NICE, 2008, Onwuzo et al., 2024).

Understanding the behavioural, psychological, and social factors that influence treatment adherence is essential (Vestbo and Anderson, 2025). Quitting is not simply a matter of choice for most tobacco users (Mohd Noordin et al., 2023) (Styklunas et al., 2021), but involves a struggle as smoking is woven into everyday life, and can be physiologically, psychologically, and socially reinforcing (Caleyachetty et al., 2012). Many factors, including media depictions and cultural and societal aspects of tobacco use, combine with tobacco's addictive capacity, making quitting difficult. on changing thoughts and actions about smoking via group sessions or one-to-one (Kirchner et al., 2012). Individual behavioural support involves scheduled one-to-one meetings between someone who smokes and a counsellor trained in SC (Lancaster and Stead, 2017). Support typically involves weekly sessions over a period of at least 4 weeks after the quit date and is normally combined with pharmacotherapy (NICE, 2018). Group behavioural support involves scheduled meetings offered weekly for at least the first 4 weeks of a quit attempt (that is, for 4 weeks after the quit date) and is normally combined with pharmacotherapy (Stead and Lancaster, 2017). While this literature recognises the multi-layered nature of TD, it risks underplaying structural and relational determinants of adherence, such as socioeconomic disadvantage, stigma, and healthcare trust (Gupta and Lee, 2025). Behavioural support models are well-evidenced, yet effectiveness may falter without tailoring to individual contexts and integrating ongoing, adaptive, and culturally competent engagement strategies.

Combining behavioural treatments with first-line pharmacotherapies is recommended where possible, however the size of the treatment effect with different TD treatment combinations and in different settings and populations is unclear (Stead and Lancaster, 2016). Surveys suggest that the proportion of people who use both types of treatment when attempting to stop smoking is low (Shiffman et al., 2008a). The need for widely accessible behavioural support programmes in TD is clear. Obstacles to TD support include limited access and adherence to effective interventions. Tailoring behavioural support provides a future direction (RCGPs, 2009). Smartphone applications could play an integral role in reducing the personal and societal costs of smoking owing to their high population reach and immediate accessibility. Recent research has showed promise with virtual reality therapy (VRT) which is a method of psychotherapy that uses virtual reality technology to treat patients; the VRT smartphone-based *MindCotine* digital intervention to support SC showed great potential with regard to participant adherence and initial efficacy (Goldenhersch et al., 2020). *MindCotine* is a digital platform designed to assist individuals in quitting smoking through mindfulness-based techniques. It offers personalised programs that combine mindfulness meditation, cognitive behavioural therapy (CBT), and behavioural change strategies to address the psychological aspects of addiction. However, participant adherence remains a challenge, and SC apps struggle to maintain high levels of adherence, thus limiting their potential effectiveness (Abroms et al., 2013). Behavioural change interventions have been found to often be delivered inconsistently resulting in variations in outcomes (Lorencatto et al., 2013).

This section emphasises the synergy between TDMs and behavioural support, aligning with strong evidence that combined approaches yield higher quit rates (Stead and Lancaster, 2016). However, it also found persistent gaps in reach, uptake, and adherence. Despite robust trial evidence, population-level use of combined pharmacological and behavioural interventions remains suboptimal (Shiffman et al., 2008c), partly due to access barriers, perceived stigma, and limited tailoring to diverse social contexts. The literature tends to focus on individual motivation and counselling quality, while

underrepresenting structural determinants such as socioeconomic disadvantage, cultural norms, and healthcare trust, all of which shape engagement and adherence (Gupta and Lee, 2025). Digital innovations, such as smartphone apps and virtual reality therapy (Goldenhersch et al., 2020), offer promise through scalability and personalisation. Yet, consistent with broader digital health literature (Abroms et al., 2013) adherence to these platforms is typically low, with novelty often outpacing sustained engagement. Furthermore, behavioural change interventions are frequently delivered inconsistently (Lorencatto et al., 2013), limiting fidelity and reproducibility. Future directions require integrating behavioural support within broader, adaptive systems of care that address both individual and structural barriers. This includes culturally competent delivery, real-time monitoring of adherence, and embedding behavioural interventions into everyday environments to normalise quitting and sustain engagement over time.

2.15 Medication adherence

Hippocrates (400 BC) was the first to note that some patients do not take their prescribed medicines and often complained the treatment did not help. Despite four decades of adherence research, there is still no uniformity in the terminology used to describe deviation from prescribed regimens. Within the literature the concept of adherence as been used synonymously with the terms of compliance, concordance and therapeutic alliance. Medication adherence, defined as "*the extent to which patients take medication as prescribed by their healthcare professionals*" (HCPs) is an important aspect of treatment efficacy, healthcare costs and patient safety (Osterberg and Blaschke, 2005). In response to problematic terminology in the literature on medication adherence medication adherence has evolved from the WHO's (2001) operational framing "*the extent to which a patient follows medical instructions*" to the more behaviourally nuanced tripartite model of initiation, implementation, and discontinuation with persistence measured as time from initiation to discontinuation (Vrijens et al., 2012). The lack of agreed definition of the concept of adherence agreement has undermined the development of a guiding theoretical framework. The seminal work of Horne and colleagues (Horne

et al., 2013b), the *Necessity-Concerns Framework* (NCF), suggests that adherence is influenced by implicit judgements of personal need for the treatment (necessity beliefs) and concerns about the potential adverse consequences of taking it. (Vrijens et al., 2012). This latter definition is widely adopted in adherence science, particularly within the EMERGE reporting framework (De Geest et al., 2018), because it offers temporal granularity, supports objective measurement, and aligns with pharmacoepidemiological study designs.

However, while the tripartite model is a methodological advance, it has limitations. First, it remains predominantly biomedical and prescriptive, focusing on concordance with a healthcare professional's orders rather than acknowledging that patient decisions are embedded in social, cultural, and contextual realities. Second, it assumes a clear "prescribed regimen" and overlooks cases where regimens are intentionally modified by patients or jointly negotiated with clinicians (so-called *intelligent non-adherence*). Third, its linear conceptualisation underplays non-linear adherence patterns such as intermittent dosing, drug holidays, or regimen switching, which are increasingly common in chronic disease management. Fourth, it underrepresents the influence of patient–provider communication quality, health literacy, and shared decision-making, factors shown to significantly affect both initiation and persistence. A future-oriented definition could integrate biomedical precision with patient-centredness: *medication adherence is the dynamic, context-dependent process by which individuals initiate, implement, modify, and / or discontinue prescribed pharmacotherapy, in alignment with jointly agreed treatment goals, influenced by personal beliefs, social circumstances, and healthcare interactions.* Such a definition retains the tripartite structure for measurement but recognises that adherence is negotiated, situated, and shaped by bidirectional engagement between patient and provider. It also accommodates contemporary shifts toward personalised medicine, self-management, and digital adherence support tools.

Internationally, medication non-adherence is recognised as a major public health issue with serious consequences (WHO, 2003). It is estimated that £300m of NHS prescribed medicines are wasted each

year (Hazell and Robson, 2015). Adhering to prescribed medication regimens is a complex behaviour requiring the ability to access prescribed medication and the cognitive capacity and motivation to take it. Non-adherence may occur at initiation (the medication is not started), implementation (delay, omitting or taking extra doses during treatment) or persistence (premature discontinuation) phases of medication use (Vrijens et al., 2012). Non-adherence negatively affects the efficacy, safety and costs of therapies (Gast and Mathes, 2019). Internationally, medication non-adherence is recognised as a major public health issue with serious consequences (WHO, 2003). Average adherence to medication ranges from 50 to 79% among patients suffering from chronic diseases. It is estimated that £300m of NHS prescribed medicines are wasted each year (Hazell and Robson, 2015).

Currently, there is no "*gold standard*" measurement of medication adherence and most research measures are objective. Common methods include, medication possession ratio (MPR), self-reported adherence, electronic monitoring devices, pharmacy refill records and biological markers (Vrijens and Urquhart, 2014). Self-reported adherence is subject to bias, while objective measures such as electronic monitoring or biochemical validation are less frequently employed due to cost and logistical challenges. Self-reports have the following advantages: they are brief, inexpensive and applicable in various settings. In addition, they can provide immediate feedback at the point of care and reveal underlying issues that contribute to non-adherence (Voils et al., 2011). Although self-reports carry a potential risk of misstatements or response biases, they provide a reasonably accurate estimate of adherence (Osterberg and Blaschke, 2005). Non-adherence can be measured directly or indirectly. Direct methods of assessing medication non-adherence detect the presence of the drug in a patient's body using assays for the drug, drug metabolites, or other markers in urine, blood, or other bodily fluids. Such methods are rarely used because of their high cost and inability to provide feedback at the point of care (Voils et al., 2011). Indirect methods measure medication non-adherence by analysing behaviour and include electronic drug monitoring, pill counts, pharmacy refills, medical record review, directly observed therapy, clinician assessment and self-reports. Different

measurement methods yield different predictors of adherence and further complicated by the definition of adherence varying from pharmacotherapy to pharmacotherapy and often varies within studies of a single treatment modality. Inconsistency of measurement of adherence hinders comparability across studies and weakens evidence synthesis. Future research should prioritise standardised, multimodal adherence assessment to improve reliability and inform best practices (Vestbo and Anderson, 2025).

In terms of intervention research, emerging technologies such as mobile health (*mHealth*) tools, AI conversational agents, and financial incentives show promise in supporting medication adherence (Alexander and al., 2025) (van Vliet et al., 2024, Giovanazzi et al., 2022). Adopting healthy behavior is vital for preventing chronic diseases. Mobile health (*mHealth*) interventions utilising virtual coaches (i.e., artificial intelligence conversational agents) can offer scalable and cost-effective solutions (van Vliet et al., 2024). Yet, these novel approaches require rigorous evaluation for efficacy, scalability, and acceptability across diverse populations. The excitement around technology should not overshadow the persistent need for fundamental adherence supports, including education, counselling, and healthcare access.

Finally, the temporal dimension of adherence of how medication-taking behaviour changes over time is often underexplored. Longitudinal designs that monitor adherence beyond the initial weeks of cessation efforts can better inform sustained behaviour change strategies (Smith and Roberts, 2025). Relapse prevention and ongoing support are vital for long-term abstinence but remain underrepresented in adherence research. Medication adherence in the context of smoking cessation is a critical yet under-addressed aspect of both research and clinical practice. Although evidence-based pharmacotherapies, such as nicotine replacement therapy (NRT), varenicline, and bupropion, significantly increase quit rates, their real-world effectiveness is often compromised by poor adherence.

Medication adherence remains a multifaceted and evolving construct, central to the efficacy, safety, and cost-effectiveness of pharmacotherapy. The progression from early notions of compliance to the WHO's operational framing, and subsequently to the tripartite model proposed by Vrijens et al. (2012), represents an important methodological advance, enabling more precise temporal measurement and aligning with modern pharmacoepidemiological research. However, despite these conceptual refinements, significant limitations persist. Current dominant definitions are still largely biomedical, often positioning adherence as a unidirectional fulfilment of prescriber instructions, with insufficient recognition of the dynamic, negotiated nature of medication-taking in real-world contexts. Social, cultural, economic, and relational determinants, such as health literacy, trust, and shared decision-making, are frequently underrepresented, even though evidence shows they play a critical role in initiation, implementation, and persistence. Furthermore, the tripartite framework does not adequately capture non-linear adherence behaviours, such as intermittent use, dose modification, or the strategic balancing of side effects and perceived benefits, which are common in chronic disease management.

Given this complexity, a patient-centric approach is not merely preferable but essential (Halladay et al., 2015). Such an approach moves beyond compliance-oriented models of adherence to embrace a relational paradigm grounded in collaborative decision-making, empathy, and continuity of practitioner support (Kuntz et al., 2014). The therapeutic relationship itself, built on respect, shared understanding, and adaptability, can act as a key driver of engagement and persistence with medications. In this sense, adherence is not a one-off decision but a dynamic, evolving process shaped by ongoing interaction and relational reinforcement (Smith and Roberts, 2025).

Moreover, qualitative evidence suggests that when individuals feel seen, heard, and supported in their quitting journey, they are more likely to internalise the behavioural goals associated with cessation and to view medication use as part of a broader narrative of self-efficacy and transformation (Williams and Green, 2024, Kvarnström et al., 2021). This aligns with theories of behavioural

medicine that prioritise autonomy-supportive environments, identity change, and motivational reinforcement over externally imposed control. To improve adherence meaningfully, interventions must therefore centre on longitudinal, personalised engagement, rather than one-size-fits-all advice. In short, the relationship is the intervention, and understanding the patient in their social context is as critical as prescribing the right pharmacotherapy. Research on adherence frequently adopts an individualistic lens, focusing on patient behaviour without sufficiently addressing the social and structural context. Factors such as socioeconomic disadvantage, stigma, mistrust in healthcare, and competing life demands are often overlooked (Gupta and Lee, 2025). For example, a smoker from a low-income background may struggle to prioritise medication adherence over other pressing concerns (Vestbo and Anderson, 2025). Moreover, cultural beliefs and social norms about medications or smoking itself may influence engagement in ways not captured by standard adherence metrics (Wilder et al., 2021, Shiratani et al., 2024).

One strength of recent research is the increasing use of mixed methods designs, which combine quantitative adherence data (e.g., pill counts, biochemical verification) with qualitative insights from patient interviews or focus groups (Gupta and Lee, 2025). This holistic approach allows researchers to capture not only the "what" of adherence rates but also the "why" behind patient behaviours. For instance, qualitative data often reveal barriers such as side effects, lack of perceived efficacy, social influences, and structural issues like access and cost. These nuanced findings underscore the importance of addressing adherence beyond mere prescription and point toward the need for personalised, patient-centered interventions.

However, despite methodological advances, many studies still face limitations related to sample diversity and generalisability (Webster and al., 2025). A significant proportion of adherence research focuses on specific populations, such as middle-aged adults in clinical trials or urban smokers, limiting applicability to marginalised groups disproportionately affected by tobacco use, including low-income populations, racial and ethnic minorities, and those with comorbid mental health

conditions. This gap is critical, as social determinants of health heavily influence adherence behaviours (Williams and Green, 2024, McCarthy et al., 2016). Research that incorporates social context and structural barriers will enhance intervention relevance and equity.

From a public health perspective, the absence of a universally accepted, patient-centred definition continues to hinder the development of targeted interventions, robust theory, and comparable measurement across studies (Voils et al., 2011, De Geest et al., 2018). The estimated £300 million in wasted NHS medicines annually (Hazell and Robson, 2015, Gast and Mathes, 2019) underscores the urgent need for frameworks that bridge biomedical precision with behavioural and contextual realities. A more future-proof definition should integrate the tripartite structure for measurement with an explicit acknowledgment that adherence is a context-dependent, co-produced process (Horne et al., 2013a). It should encompass the interplay of personal beliefs, social circumstances, digital health supports, and clinical interactions. Such an approach would not only enhance research validity but also strengthen intervention design shifting the focus from simply measuring deviation to actively understanding and supporting the lived realities of patients managing long-term pharmacotherapy.

2.16 Adherence to TDM medications

Medication adherence is a cornerstone of effective smoking cessation interventions, yet it remains a complex and multifaceted challenge. Research in this domain has grown substantially, integrating behavioural, psychological, and socio-environmental perspectives to better understand why patients either comply or fail to comply with prescribed cessation pharmacotherapies, such as nicotine replacement therapy (NRT), bupropion, and varenicline. Medication adherence directly impacts the effectiveness of TD treatment. Failure to adhere to TDM regimens can lead to treatment failure, disease progression, complications, and mortality.

Efficacious pharmacological interventions for TD are available but poor adherence to these treatments limit their efficacy and the absolute proportion of smokers able to quit using these methods

remains low (Pacek et al., 2018, Cahill et al., 2014). The barriers to TDM adherence, largely driven by social determinants of health such as socioeconomic background and health literacy, are magnified by the novel coronavirus pandemic. The reasons for TDM non-adherence are as multifaceted as they are complex, meaning a patient-centric approach is the only way to improve adherence via ongoing relationships that helps people to commit to, and engage with, behaviour change. The reasons for non-adherence to TDMs are profoundly multifaceted, encompassing biological, psychological, social, and structural influences. These include concerns about side effects, misperceptions about the necessity or efficacy of treatment, fluctuating motivation, stigma associated with medication use, lack of social support, and limited continuity of care. Crucially, these factors do not operate in isolation, they are embedded in the wider context of an individual's lived experience, including socioeconomic status, previous quit attempts, beliefs about addiction, and trust in health systems (Mohd Noordin et al., 2023).

Factors that influence adherence to TDMs remain unclear; for example, we know little about the ways in which smokers' perceptions and experiences of TDMs influence adherence. A recent meta-ethnography (chapter 4) (Sanders et al., 2019) found that smokers are active decision makers regarding using TDMs. For HCPs to work in partnership with smokers, knowledge of smokers' poor TDM adherence during quit attempts is required. Research on lay perspectives regarding adherence to TDMs is sparse and there remains a paucity of literature to inform the design of effective TDM adherence promoting interventions. There are many reported barriers and facilitators of SC medication adherence (Pacek et al., 2018); in particular, patients' treatment-related beliefs are important for their adherence behaviours as medication-related concerns and necessity-beliefs predict adherence (Horne et al., 2013b). The perspective of patients, carers and HCPs often differs in terms of the determinants of medication adherence owing to priorities and knowledge of the situation. Estimates of the rate of adherence to TDMs ranges widely between studies and countries (WHO, 2003). Additionally, TD is a unique treatment context with specific adherence issues. TDM adherence

is shaped by several complex factors: dependence on tobacco, preference not to use medications, fear of side effects, depression, gender, weight gain, cravings, withdrawal symptoms, low motivation to quit smoking, poor social support and fear of dependency on TDMs (Pacek et al., 2018). In contrast, motivation, access to free TDMs and SC support have been found to increase adherence to TDMs (Hollands et al., 2019).

Adherence to SC pharmacotherapies, such as NRT, varenicline, and bupropion, is a pivotal determinant of quit success. However, real-world adherence remains suboptimal, despite strong efficacy observed in clinical trials. This discrepancy has significant implications for clinical practice, research interpretation, and policy development. Studies consistently report that a substantial proportion of individuals prescribed cessation medications either never initiate treatment or discontinue prematurely. Up to 50% of users do not follow prescribed dosing regimens, and many discontinue before the optimal 10–12 week course, well below levels required for therapeutic benefit (WHO, 2003). Poor adherence is strongly associated with lower quit rates: for instance, in Ontario stop-smoking workshops, participants who used less than "most" of a 10-week NRT course had significantly reduced odds of abstinence at six months (AOR ~0.43 or lower) compared to "full" users (Burns and Levinson, 2008). Adherence is influenced by both individual-level factors (e.g. motivation, beliefs, dependence severity) and wider socio-behavioural factors such as social support and socioeconomic status (Kvarnström et al., 2021). Negative attitudes about medication safety, low confidence, and low perceived need predict poor adherence (Vestbo and Anderson, 2025). Conversely, higher nicotine dependence and prior positive experience with cessation medications can improve adherence.

The issue of medication adherence with stop smoking treatments must be examined within the broader cultural and social meanings that individuals attach to smoking, quitting, and the use of pharmaceutical interventions. Research consistently shows that while pharmacotherapies such as NRT, varenicline, and bupropion are clinically effective, their real-world uptake and sustained use

remain suboptimal. A key sociological factor underpinning this is the smoker's predilection for willpower as the preferred mechanism for quitting. Many smokers perceive stopping smoking as a test of personal strength, self-discipline, or moral resolve. This "willpower narrative" is deeply embedded in social and cultural discourse, often reinforced by public health messaging that valorises self-control and individual responsibility (Kotz et al., 2014, Smith et al., 2015b). Consequently, accepting medication can be interpreted by smokers as an admission of weakness or failure, undermining their sense of agency. This creates a psychological and symbolic barrier to adherence, even when individuals are struggling to quit smoking unaided.

Additionally, there is a broader cultural scepticism about medication use, particularly for behavioural or lifestyle issues. Some smokers express concern about becoming dependent on cessation aids, or view medication as unnatural, unnecessary, or intrusive. These beliefs intersect with issues of trust in medical institutions and pharmaceutical industries, especially among marginalised populations. Moreover, the framing of smoking as a personal choice rather than a complex dependency can obscure the legitimacy of medical treatment. This stigma contributes to the underutilisation of pharmacotherapies and premature discontinuation of use. In conclusion, improving medication adherence requires more than addressing practical barriers; it demands a sociologically informed approach that challenges cultural assumptions about willpower, reframes medication as a legitimate and empowering tool, and builds trust in cessation services, particularly among populations where medicalisation is viewed with ambivalence or resistance. The literature identifies that medication adherence to stop smoking medication is shaped not only by access and clinical efficacy, but by a complex web of beliefs, attitudes, social influences, and structural factors (Vestbo and Anderson, 2025). Qualitative studies have found that adherence is shaped by individuals' baseline beliefs and experiential learning during cessation, limited engagement and program uptake in community pharmacy settings (Webster and al., 2025, Horne et al., 2013a). Concerns over safety, necessity, technique, stigma, and beliefs around self-quitting frequently undermine adherence, particularly in

vulnerable groups like pregnant women (Black et al., 2012). Health professionals' approaches and healthcare messaging also play crucial roles (Free et al., 2011).

The literature highlights the need for tailored, theory-informed interventions that address beliefs, provide practical skill-building, and support individuals through stages of uptake, consistent use, and persistence (Horne et al., 2013a). These studies collectively highlight that: (i) positive attitudes and mental health status (e.g., absence of depression) predict better adherence (Malone et al., 2018), (ii) pragmatic features, such as delivery setting (pharmacy, mobile app) (Chu et al., 2021) and communication, impact uptake and sustained use, (iii) real-world adherence is lower than in controlled settings (Patel and Thompson, 2025), leading to lower quit rates and that (iv) specific groups (e.g., pregnant women, low-SEP, homeless) face unique adherence challenges (Williams and Green, 2024). This evidence underscores the importance of rigorous measurement methods, comparative designs, and population-specific insights in understanding and improving medication adherence among smokers (Giovanazzi et al., 2022, Voils et al., 2011).

Adherence to TDMs today remains a significant challenge (Smith and Roberts, 2025), undermining treatment efficacy despite strong evidence that sustained, correct use of pharmacotherapies, such as NRT, varenicline, and bupropion, can markedly improve quit rates (Onwuzo et al., 2024). Non-adherence is driven by multiple factors: side effect concerns, perceived ineffectiveness, preference for "natural" quitting, and misconceptions about medication safety, often reinforced by past negative experiences (Smith and Roberts, 2025). Psychosocial influences, such as reliance on willpower, mistrust in pharmaceutical products, and stigma associated with seeking help, further reduce consistent use (Webster and al., 2025). Adherence disparities are pronounced among disadvantaged populations, where competing life pressures and limited-service engagement hinder optimal medication use (Williams and Green, 2024).

In the future, improving adherence will require a shift toward personalised, responsive support. Digital health tools, including AI-driven reminders, just-in-time adaptive interventions, and real-time adherence monitoring, could provide targeted encouragement at moments of high relapse risk (Goldenhersch et al., 2020, Chu et al., 2021). Pharmacogenomic tailoring of treatments may increase perceived relevance and confidence in medications (Mattock and al., 2023), while integration of adherence support into broader social and mental health care could address underlying barriers (Kvarnström et al., 2018). However, the risk remains that such innovations may primarily benefit more affluent or digitally connected smokers unless equity-focused design and outreach are embedded from the outset (Hiscock et al., 2011). Without addressing structural and cultural barriers, adherence gaps will persist.

2.17 Adherence to pharmacological therapies and behavioural support for tobacco dependence

Efficacious pharmacological interventions for TD are available but poor adherence to these treatments limit their efficacy and the absolute proportion of smokers able to quit using these methods remains low (Pacek et al., 2018, Cahill et al., 2014). TDM nonadherence is a challenge to both clinical practice and research that contributes to lower SC rates (Raupach et al., 2013). Adherence to TDMs range widely between studies and countries (WHO, 2003). Studies have shown that many smokers who use medications for TD do so at a lower dose and for less time than the evidence suggests is optimal (Swan et al., 2010, Pacek et al., 2018, Hays et al., 2010). Burns and Levinson (Burns and Levinson, 2008) reported that users of NRT, on average, continue medication for less than half the time for which it was prescribed. Other studies have found that adherence with the recommended length of treatment occurs among 50% or fewer NRT users (Alterman et al., 1999, Lam et al., 2005, Cooper et al., 2004). Estimates indicate that 20% of smokers who receive prescriptions for smoking cessation medication never fill that prescription (Solberg et al., 2010, Zeng et al., 2011). Nicotine patch adherence has been defined as the use of all patches distributed (Cooper et al., 2004), the

proportion of patches used and to evaluate a cut-off (i.e., 80% of patches used) (Berg et al., 2013, Okuyemi et al., 2010) or the total number of patches used, evaluated as a continuous variable (Fish et al., 2009). Adherence to bupropion and varenicline is often reported with an 80% adherence cut-off imposed (Browning et al., 2016, Shelley et al., 2015, van Boven and Vemer, 2016). Adherence to varenicline has also been quantified based on "purposeful nonadherence" (i.e., not adhering to the medication regimen because the smoker feels better or experiences adverse effects) (Catz et al., 2011) and adherence to bupropion has also been measured based on full, partial, and nonadherence during the past 7 days (Grandi et al., 2016).

Poor adherence with the recommended treatment length is significant because substantial evidence both observational and within the context of clinical trials indicates that greater medication adherence is associated with greater abstinence from smoking (Catz et al., 2011, Hollands et al., 2013, Liberman et al., 2013, Shiffman, 2007) even after controlling for potential bias owing to reverse causation (Raupach et al., 2013). TD is a unique treatment context with specific adherence issues (Sanders et al., 2019, Hollands et al., 2019). TDM adherence is shaped by several complex factors: dependence on tobacco, preference not to use medications, fear of side effects, depression, gender, weight gain, cravings, withdrawal symptoms, low motivation to quit smoking, poor social support and fear of dependency on TDMs (Pacek et al., 2018). In contrast, motivation, access to free TDMs and SC support have been found to increase adherence to TDMs (Hollands et al., 2019). Previous studies have found several factors that partly explain TDM underuse such as side effects, cost and access, satisfaction, lack of awareness or knowledge, prior experience of using TDMs, perceived poor efficacy or concerns about safety and dependency (Pacek et al., 2018). Adherence to medication may be determined by other factors such as socioeconomic resources and individuals' beliefs, trust or expectations. Poor medication adherence is considered a potential contributor to disparities in health outcomes (McQuaid and Landier, 2018).

Evidence shows NHS stop smoking interventions recommended for adults are effective (Song et al., 2020, Bauld et al., 2010). Clinical UK practice guidelines recommend that healthcare providers offer smokers who are prepared to make a quit attempt both pharmacotherapy and behavioural support. Staff delivering behavioural interventions must be trained to the NCSCT training standard (NCSCT, 2019, NICE, 2018). As outlined above, In the UK specialist stop-smoking service combines extended face-to-face support with TDMs. Systematic reviews (Lancaster and Stead, 2017, Stead and Lancaster, 2017, Taylor et al., 2017, Whittaker et al., 2012) have consistently shown that behavioural interventions can effectively increase rates of SC, but with substantial heterogeneity in the strengths of effects. Recent systematic reviews (Hartmann-Boyce et al., 2021b, Black et al., 2020) also concluded that providing behavioural support for smokers using established TDMs will increase the proportion of successful SC attempts. Additional relevant research has focused on identifying the components that contribute most to the success of behaviour support interventions which could be specifically helpful for those with poor success rates for quitting, such as people with histories of depressive disorder or substance abuse (Ussher et al., 2012, Prochaska et al., 2004).

Research on lay perspectives regarding adherence to TDMs is sparse and there remains a paucity of literature to inform the design of effective TDM adherence promoting interventions. Medication adherence is crucial in managing long-term health conditions, ensuring optimal treatment outcomes and quality of life. Qualitative studies highlight complex factors influencing adherence, including beliefs about illness, medication, and healthcare providers' influence; these are developing patient-centered interventions to enhance adherence and improve health outcomes in various medical contexts (Inder et al., 2019, Marshall and Wolfe, 2012). Factors that influence adherence to TDMs remain unclear; for example, little is known about the ways in which smokers' perceptions and experiences of TDMs influence adherence. A meta-ethnography (Sanders et al., 2019) found that smokers are active decision makers regarding TDM use. For HCPs to work in partnership with smokers, acknowledgement and management of smokers' poor TDM adherence during quit attempts

is required for smokers to achieve long term quit success. Current guidance in England on medicines adherence emphasises both patient and health professional perceptions and practicalities for improving medication adherence (NICE, 2009). Between 2008 and 2017 in England, smokers appear to have become less dependent on cigarettes but less likely to try to quit or cut down (NHS, 2020). Of those who tried to quit, fewer used behavioural support and more used pharmacological support (Perski et al., 2019).

The science of behaviour change has advanced rapidly in the past decade and understanding of the types of interventions likely to be effective for specific behaviours, target populations and contexts has improved (PHE, 2020). Interventions to increase TDM adherence are delivered alongside general behavioural support for SC. These interventions include components to change perceptions about TDMs by addressing individuals' beliefs about the value of taking TDMs or providing additional support to overcome barriers to adherence. In addition, they and consider reasons to take it or concerns about doing so; currently there is insufficient evidence to confirm which approach is more effective (Hollands et al., 2019). Raupach *et al.,* (2013) found that one factor that determines the success of a SC program (SCP) is patient compliance, which affects the treatment success, treatment cost, and health economics.

Future innovations in TDM adherence are likely to combine biomedical , technological, and behavioural strategies, including:

1. *Pharmacogenomics & precision prescribing* (Salloum et al., 2018, Wichman et al., 2025): tailoring NRT, varenicline, or future drugs to an individual's genetic profile to optimise efficacy and reduce side effects.
2. *Just-in-Time Adaptive Interventions* (JITAIs) (Yang et al., 2023): mobile or wearable devices delivering timely prompts, coping strategies, or dosage reminders at high-risk moments for relapse.
3. Digital adherence monitoring (van Onzenoort et al., 2009): smart pill bottles, sensor-enabled inhalers, or blister packs that track use and integrate with apps or NHS systems.

4. *AI-driven behavioural coaching* (van Vliet et al., 2024): chatbots or virtual health assistants providing motivational interviewing and personalised adherence support 24/7.
5. *Gamification & incentive systems* (Alexander et al., 2025): reward-based adherence programmes linked to quit milestones, especially for younger or tech-savvy users.
6. *Integrated mental health and cessation care* (Inder et al., 2019*)*: addressing psychological barriers and co-occurring conditions to improve adherence sustainability.
7. *Culturally tailored adherence tools* (McQuaid and Landier, 2018, Foo et al., 2025): interventions designed for specific communities, addressing language, beliefs, and health literacy.
8. *Combination harm-reduction models* (Onwuzo et al., 2024): integrating e-cigarettes or nicotine pouches with pharmacotherapy in structured tapering plans to maintain engagement

These innovations could significantly improve quit outcomes while reducing health inequalities, provided implementation avoids exacerbating existing digital and socioeconomic disparities.

2.18 Health behaviour theories and adherence

Adhering to prescribed medication regimens is a complex behaviour requiring the ability to access prescribed medication and the cognitive capacity and motivation to take it. There are many reported barriers and facilitators of medication adherence (Pacek et al., 2018). In particular, patients' treatment-related beliefs are important for their adherence behaviours as medication-related concerns and necessity-beliefs predict adherence (Horne et al., 2013b). The perspective of patients, carers and HCPs often differs in terms of the determinants of medication adherence owing to priorities and knowledge of the situation. Intentional medication adherence involves patients consciously deciding whether to adhere to prescribed regimens, considering factors like beliefs, concerns, and understanding (Gast and Mathes, 2019, Horne et al., 2013a). Non-intentional adherence, on the other hand, stems from forgetfulness, lack of understanding, or physical limitations (Kardas et al., 2013). Both impact treatment outcomes and require tailored interventions for improved adherence.

A comprehensive review of interventions to increase medication adherence and improve related outcomes using a variety of approaches found their effects were inconsistent; only a few clinical trials

improved both adherence and clinical outcomes (Nieuwlaat et al., 2014). The most effective medication adherence interventions adopted comprehensive approaches involving a range of strategies, were high-intensity and tailored to individual patients (Haynes et al., 2008). HCPs (i.e., physicians, nurses, pharmacists) played a key role in supporting, promoting and monitoring medicines adherence in chronic conditions. Patient-centred approaches to improve adherence are considered promising (Kuntz et al., 2014), however, their effectiveness remains unclear. The potential role of pharmacists in SC services is underutilised despite literature and the accessibility of community pharmacies supporting a role for pharmacists in addressing tobacco use and dependence (Ellis Hilts et al., 2024). In the absence of a single definitive intervention to address non-adherence, current NICE Guidelines combine trial evidence of interventions and explanatory studies of non-adherence (NICE, 2009). Part of the difficulty with addressing non-adherence is its complexity, as adherence can be influenced by multiple factors (Nieuwlaat et al., 2014).

Contemporary behaviour change frameworks such as the *Theoretical Domains Framework* (TDF) (Michie et al., 2005) and *Behaviour Change Technique* (BCT) taxonomy (Michie et al., 2011b) have been used across a range of health behaviours, and they are increasing applied within medication adherence research. However, from a critical sociological and public health perspective, both frameworks have been subject to important critiques regarding reductionism, contextual neglect, and practical utility. The TDF seeks to integrate multiple psychological theories into a single, synthesised framework of behavioural determinants, encompassing domains such as beliefs, skills, social influences, and environmental context (Cane et al., 2012). While its breadth is a strength, critics argue that its underlying assumptions remain psychologically individualistic, often underplaying the structural and relational determinants of health behaviour. From a sociological lens, the TDF's emphasis on cognitive drivers risks marginalising social inequalities, power dynamics, and the lived experience of individuals in complex systems (Kelly and Barker, 2016).

The BCT taxonomy, (Michie et al., 2014a), provides a standardised language for specifying and coding intervention components. Although its development marked a major methodological advance, it has also been critiqued for decontextualising techniques from their delivery and meaning. For example, "social support (unspecified)" or "feedback on behaviour" may be coded identically across studies, despite significant differences in tone, cultural context, or interpersonal dynamics, factors that may influence effectiveness. Moreover, some argue that the taxonomy's reliance on highly specified, modular techniques may inhibit creative, practitioner-led adaptation in real-world settings (Atkins and Michie, 2015). From a critical standpoint, both frameworks contribute to the standardisation and replicability of behavioural science in health but may also obscure complexity and overstate intervention "mechanics" at the expense of meaning, narrative, and context. Researchers have therefore called for integration with critical realist, participatory, or systems-based approaches that embrace complexity and local adaptation.

Theories of behaviour change stress the central importance of an individual's motivation to quit an addiction. Contemporary behaviour change frameworks such as the Theoretical Domains Framework (Michie et al., 2005) and Behaviour Change Technique (BCT) taxonomy (Michie et al., 2011b) have been used across a range of health behaviours, and they are increasing applied within medication adherence research. The seminal work of Horne and colleagues (Horne et al., 2013b), the Necessity-Concerns Framework, suggests that adherence is influenced by implicit judgements of personal need for the treatment (necessity beliefs) and concerns about the potential adverse consequences of taking it. The application of behavioural change theories to smoking cessation research has been foundational in shaping interventions yet remains complex and contested across disciplines.

From a public health perspective, theories such as the *Health Belief Model* (HBM), *Theory of Planned Behaviour* (TPB), and *Transtheoretical Model* (TTM) have helped segment populations by readiness to change, perceived risk, and self-efficacy. These models support scalable interventions and policy development. However, they often assume rational decision-making, overlooking the habitual and

emotionally charged nature of smoking. TD research has shown that smoking is not solely a behavioural choice but a neurobiological addiction. Models focusing on intention or risk perception underplay the physiological addiction to nicotine, craving cycles, and withdrawal symptoms, which can override even the strongest motivation to quit. Thus, integrating pharmacotherapy with behavioural support remains critical. Health behaviour theories frequently lack attention to structural and social determinants, such as poverty, stress, cultural norms, and stigma, that influence both smoking initiation and cessation. Individual-level models risk placing undue responsibility on smokers, ignoring broader systemic barriers.

Newer frameworks like *PRIME* (West, 2006)and *COM-B* (Capability, Opportunity, Motivation – Behaviour) offer more dynamic, real-time perspectives on behaviour. These models better account for the interplay between psychological states, environmental triggers, and biological urges. *PRIME* underpins digital tools such as the *SmokeFree* app, which deliver just-in-time motivational support by intervening at the moment of craving or lapse (West, 2006, Brown and West, 2014). This integration of real-time adaptive features reflects *PRIME's* emphasis on moment-to-moment impulses and responses However, they can be difficult to operationalise and may require more complex, personalised intervention designs (Sanders et al., 2019). In conclusion, while behavioural change theories have enriched SC research, no single model is sufficient. Multidisciplinary approaches that combine cognitive, biological, social, and structural insights are essential to develop effective, equitable, and sustainable cessation interventions (Gupta and Lee, 2025). There is a growing consensus that no single disciplinary lens is sufficient to address the complexity of smoking behaviour. However, while the aspiration is sound, its implementation presents both conceptual and practical challenges. Cognitive and behavioural psychology explains individual motivations, self-regulation, and decision-making, foundational for interventions like cognitive behavioural therapy (CBT) and motivational interviewing (Miller and Rollnick, 2023). Biological mechanisms, such as nicotine dependence and neuroadaptation, justify pharmacological interventions (e.g., NRT,

bupropion, varenicline) and highlight the physiological barriers to cessation (Benowitz, 2010). Social and structural factors, including stress, socioeconomic status, stigma, and availability of services, strongly influence smoking uptake, relapse, and quit success. These are especially relevant in explaining the social gradient in smoking (Graham, 2012). A systems-level integration of these dimensions supports more equitable intervention design, addressing both the *why* (motivation/addiction) and the *how* (access and delivery). Multidisciplinary frameworks may either over-simplify by favouring one domain (e.g., biology in addiction medicine) or become unwieldy by attempting to integrate too many components without clear pathways for implementation. Translation into practice is uneven: many SC services remain heavily reliant on individual-level behavioural models, often neglecting structural interventions such as poverty reduction, housing support, or anti-tobacco regulation enforcement.

PRIME is a comprehensive, dynamic model of motivation that proposes that behaviour at any moment is governed by plans, responses, impulses, motives, and evaluations, hence the acronym *PRIME*. Unlike traditional static models (e.g., stages of change), it focuses on moment-to-moment motivation and offers a detailed account of how desires, habits, and environmental cues interact to produce behaviour. It is especially influential in tobacco addiction science, where it helps explain why people may relapse despite strong intentions to quit, and why short-term urges can override long-term goals. *PRIME* has been applied to:

- SC services: Understanding why some individuals relapse despite strong quit intentions.
- Digital interventions: Designing apps like *Smoke Free* and *Quit Genius*, which deliver moment-based motivational prompts.
- Health behaviour research: Informing intervention mapping by linking cognitive, emotional, and environmental influences on behaviour.

It complements the *COM-B* model and *Behaviour Change Wheel*, also developed by West and Michie (Michie et al., 2014a), by offering a motivational substrate that explains how internal drivers of

behaviour change fluctuate and respond to interventions. *PRIME* explains the interplay of physiological dependence, identity, emotion, and social environment in smoking and cessation (West and Brown, 2013).

2.19 Effect of non-adherence on tobacco dependence medication trials

Few studies provide detailed data on adherence to TDMs such as number of prescribed doses taken during a monitored period, monitored days during which the correct number of doses were taken or whether or not the prescribed intervals between doses taken were respected (WHO, 2003). TDM trials typically record daily smoking behaviour but base data analyses on summary outcome measures of abstinence at selected time points. The limited evidence indicates that participants in TDM trials may drop out for several reasons such as patient-related factors, age, gender, education, nicotine dependence, concern about the medication and adverse effects of the medication (Belita and Sidani, 2015, Heffner et al., 2010). High dropout and low response rates are problematic for SC interventions - regardless of the reason for dropping out of TDM trials participants who do so are usually found to be smoking at follow-up. Studies indicate that patient dropout from SCPs is not random; dropout was found to be more common in patients with low socioeconomic status, those without sufficient knowledge about their health, and those of black race (Siddiqui et al., 1996).

However, non-attendee patients of SCC follow-up visits and those who failed to regularly use TDMs as prescribed were excluded from most studies. Consequently, the features of this non-adherence group of patients are not well known. Adherence and awareness of the target population adherence behaviours are essential for the structuring of SCP design to meet the specific needs of these patients and thus achieve long term quit success. Attrition or withdrawal of participants from smoking cessation intervention studies has negative methodological and clinical consequences. It poses a major threat to statistical conclusion and internal and external validity of the findings. A conventional analysis of SC data uses end-of-treatment (EOT) smoking status as the outcome in a logistic

regression model, estimating the odds ratio (OR) for treatment with adjustment for predictors of quit probability (Hughes et al., 2013).

Non adherence distorts TDM trials (NRT, bupropion, varenicline), adherent participants are 2–3 times more likely to quit successfully compared to non-adherent participants (Raupach et al., 2013). Non adherence is common, early drop-off, and unequally distributed across arms (e.g., more adverse-effect–driven discontinuation on varenicline) (Mersha et al., 2021) . In classic intention-to-treat (ITT) analyses this yields effect-size dilution, trial efficacy looks lower than the drug's biologic effect, while per-protocol / as-treated analyses risk selection bias (adherent participants differ systematically: motivation, dependence, comorbidity) (Pacek et al., 2018). Missed doses and early discontinuation are often informative (linked to craving, side effects, or relapse), so standard missing-at-random imputation misclassifies exposure and outcome, directing estimates toward the null (Hollands et al., 2015). Non-adherence undermines the population-level impact of smoking cessation strategies. While clinical trials report efficacy under controlled conditions, these findings rarely translate directly into community settings, where adherence is typically lower. Research often fails to reflect real-world usage patterns, and public health policies have historically prioritised access over sustained engagement. More robust monitoring and evaluation of adherence within implementation studies are needed to bridge the gap between clinical efficacy and public health impact.

Measurement is another fault-line: pill counts, self-report, or refill proxies overestimate adherence; electronic monitoring (e.g., MEMS) captures opening events, not ingestion; biochemical checks (cotinine, plasma drug) are precise but costly and infrequent (Vrijens and Urquhart, 2014). Few trials model time-varying adherence despite quit risk being highly dynamic in the first 2–4 weeks (Davies et al., 2025). Contamination (off-protocol NRT / e-cig use) further blurs contrasts in pragmatic trials (Pacek et al., 2018).

Design choices can improve internal but harm external validity (Fiorentino et al., 2022). Adherence run-ins, intensive reminder systems, or frequent visits "engineer" higher adherence than routine care, inflating efficacy but limiting generalisability (Giovanazzi et al., 2022). Conversely, highly pragmatic designs mirror real-world adherence yet risk underestimating pharmacologic potential. A middle path is to pre-specify adherence estimates and analyse using causal methods (e.g., complier average causal effect, instrumental variables, marginal structural models) with robust sensitivity analyses for non-random missingness (Fiorentino et al., 2022). Reporting is often insufficient, many trials do not define adherence (initiation, implementation, persistence), do not present exposure–response curves, and rarely publish early discontinuation reasons stratified by arm (Giovanazzi et al., 2022). This obscures mechanisms (e.g., nausea → discontinuation → relapse) that are actionable in practice (Pacek et al., 2018).

There is a paucity of literature that demonstrates the statistical impact of adherence on the effectiveness of SC pharmacotherapies. However, a systematic review showing that smokers who adhered to prescribed regimens of nicotine replacement therapy (NRT), varenicline, or bupropion were two to three times more likely to achieve abstinence compared to non-adherent participants Raupach *et al*. (2014). Hollands *et al*. (2015) confirmed these findings in a meta-analysis, noting that non-adherence significantly attenuates measured treatment efficacy and can bias both intention-to-treat and per-protocol analyses. Pacek *et al*. (2018) similarly reported that consistent use of cessation medications substantially increased quit rates, with effect sizes varying by drug type and population. Mersha *et al*. (2021) further quantified this relationship, showing that high adherence more than doubled cessation success rates across diverse study settings. The available literature underscore that poor adherence is a major determinant of trial outcomes and real-world effectiveness, making adherence support a critical target for both research and clinical practice in TD treatment (Mersha et al., 2021).

In TD research, adherence is intimately tied to the physiological and psychological grip of nicotine addiction (Benowitz, 2010). Medications are intended not only to reduce withdrawal symptoms but also to weaken the reinforcing cycle of addiction (Howes et al., 2020, Hartmann-Boyce et al., 2018). However, individuals often discontinue treatment prematurely due to delayed gratification, side effects, or persistent cravings (Shiffman et al., 2008c). Despite this, many trials treat non-adherence as a methodological nuisance rather than a core phenomenon of interest. Emerging evidence suggests that higher adherence correlates strongly with successful quitting (Shiffman, 2007), yet research into adherence-enhancing interventions, such as medication counselling, reminder systems, or digital support, remains limited and fragmented (Pacek et al., 2018).

2.20 Conclusions

The literature on smoking and SC consistently identifies TD as a chronic, relapsing condition, sustained by a combination of nicotine's neuropharmacological effects and entrenched social, cultural, and psychological factors (West, 2017). While pharmacotherapies such as NRT, varenicline, and bupropion have proven efficacy (Cahill et al., 2014), their real-world impact is constrained by suboptimal medication adherence (Shiffman et al., 2008c). In the context of TDMs, adherence is often undermined by side effects, misperceptions about safety, social stigma, and competing life priorities, with behavioural and structural determinants frequently underexplored in trials (Mersha et al., 2021, Raupach et al., 2013).

SC remains one of the most impactful public health interventions for reducing morbidity and mortality, yet it continues to be shaped by complex interactions between biological addiction, psychological processes, and social context (WHO, 2025). While pharmacotherapies and behavioural support are proven to increase quit success, their effectiveness in real-world settings is often limited by variable engagement and sustained use (WHO, 2003). This highlights a persistent gap between the controlled conditions of clinical trials and the diverse realities of smokers attempting to quit within

community and NHS SSS settings. SC is not solely a matter of individual willpower or pharmacological efficacy, but a socially negotiated process shaped by identity, trust, health beliefs, and broader structural determinants. Addressing these complexities requires moving beyond narrow biomedical framings to incorporate relational, cultural, and contextual dimensions into intervention design.

Medication adherence remains a multifaceted and evolving construct, central to the efficacy, safety, and cost-effectiveness of pharmacotherapy. The progression from early notions of compliance to the WHO's operational framing, and subsequently to the tripartite model proposed by Vrijens et al. (2012), represents an important methodological advance, enabling more precise temporal measurement and aligning with modern pharmacoepidemiological research. However, despite these conceptual refinements, significant limitations persist. Current dominant definitions are still largely biomedical, often positioning adherence as a unidirectional fulfilment of prescriber instructions, with insufficient recognition of the dynamic, negotiated nature of medication-taking in real-world contexts. Social, cultural, economic, and relational determinants, such as health literacy, trust, and shared decision-making, are frequently underrepresented, even though evidence shows they play a critical role in initiation, implementation, and persistence (Dilles et al., 2023). Furthermore, the tripartite framework does not adequately capture non-linear adherence behaviours, such as intermittent use, dose modification, or the strategic balancing of side effects and perceived benefits, which are common in chronic disease management, including tobacco dependence.

From a public health perspective, the absence of a universally accepted, patient-centred definition continues to hinder the development of targeted interventions, robust theory, and comparable measurement across studies. The estimated £300 million in wasted NHS medicines annually (Hazell and Robson, 2015) underscores a need for frameworks that bridge biomedical precision with behavioural and contextual realities. Innovative digital adherence technologies offer promise in this

regard, particularly when they are integrated with personalised behavioural support, social acceptability, and patient priorities (Kardas, 2024).

A more future proof definition should integrate the tripartite structure for measurement with an explicit acknowledgment that adherence is a context-dependent, co-produced process (Eliasson et al., 2020a). It should encompass the interplay of personal beliefs, social circumstances, digital health supports, and clinical interactions (Vestbo and Anderson, 2025, Alexander et al., 2025). Such an approach would not only enhance research validity but also strengthen intervention design, shifting the focus from simply measuring deviation to actively understanding and supporting the lived realities of patients managing long-term pharmacotherapy.

CHAPTER 3 METHODOLOGICAL APPROACHES

3.1 Purpose of the thesis

The overarching aim of this thesis was to explore and critically examine the beliefs, behaviours, and contextual factors influencing adherence to tobacco dependence medications (TDMs) among adults attempting to quit smoking within NHS SSSs. Specifically, it sought to generate knowledge to improve clinical practice and trial design by identifying modifiable influences on TDM adherence. Through a sequential mixed methods design, this thesis contributes a nuanced understanding of the behavioural and systemic factors affecting medication adherence, situating individual decisions within broader social, structural, and relational contexts.

3.2 Research aims

1. Investigate medication adherence behaviour in adult SC.
2. Discover key factors involved.

3.3 Research objectives

1. To explore and improve understanding of how adult smoker's experiences and beliefs regarding SC medications and their importance to adherence behaviours by synthesizing knowledge from published qualitative studies from smokers' perspectives.
2. To explore adult smokers attempting to quit perceptions of SC medication by exploring in-depth, smokers' beliefs, experiences and attitudes towards TDMs to help explain poor TDM adherence.
3. To retrospectively critically analyse the design and methods within the pragmatic randomised clinical trial RCT Smoking Cessation and Nortriptyline and Genetics (*SCANAG*).

3.4 Research questions

1. How do adult smokers' experiences and beliefs regarding SC medications affect their adherence behaviours?
2. What are the views & meanings of SC medications of adults seeking to stop smoking in a NHS SSS?
3. Is the *PRIME Theory of Motivation* sufficient to describe and explain SC medication adherence behaviours within a NHS SSS context?
4. How did adherence to SC medication in adult smokers seeking support in a pragmatic trial Smoking Cessation and Nortriptyline and Genetics (*SCANAG*) undertaken in NHS SSSs affect the trial quality?

3.5 Research Design and Philosophical Assumptions

This thesis employed a pragmatist mixed methods approach, integrating qualitative and quantitative methodologies across three interrelated phases: (1) a meta-ethnography of qualitative studies on smokers' perceptions of TDMs, (2) a primary qualitative study with NHS SSS clients, and (3) a retrospective critique of a pragmatic randomised controlled trial (RCT) assessing nortriptyline + nicotine replacement therapy (NRT) versus placebo + NRT. The pragmatist paradigm was selected not simply for methodological plurality but because it aligns with the complex and situated nature of smoking cessation and medication adherence. As both behaviours are dynamic, context-sensitive, and driven by psychological, social, and structural determinants, no single method was deemed sufficient to capture their intricacies (Creswell & Plano Clark, 2018). Pragmatism prioritises problem-solving, real-world application, and flexibility, making it particularly appropriate for health behaviour research where patient experience, lived reality, and intervention feasibility intersect. Mixed methods research (MMR), often described as a third paradigm, offers a systematic way to integrate the strengths of both qualitative and quantitative approaches (Tashakkori et al., 2020). In this thesis,

integration occurred through design (sequential phases), methods (meta-ethnography, interviews, retrospective analysis), and interpretation (triangulation and synthesis). The phases were deliberately designed to inform and build upon one another—qualitative insights shaped the interpretation of RCT findings, and the retrospective analysis helped contextualise adherence patterns observed in prior literature and fieldwork.

Generally, it is accepted that the philosophy behind qualitative and quantitative studies is significantly different even though in practice researchers frequently apply both methodologies, making the reality less dichotomized. The philosophy of qualitative research is "interpretive, humanistic, and naturalistic" (Creswell, 2018). It places significant importance on subjectivity. The ontological assumption is that there is no single reality but it encompasses multiple realities for any phenomenon (Speziale and Carpenter, 2012). The quantitative approach emerged from a positivist paradigm. A positivist paradigm places considerable value on "rationality, objectivity, prediction and control" (Gray and Grove, 2020). "The ontological assumption is that there is one reality, which exists and can be validated through the senses" (Brink and Wood, 1998). Mixed methods research (MMR) has been described as a third research paradigm that combines qualitative and quantitative research methods. Pragmatism is a paradigm that includes ideas, methods, approaches, principals, or a mix of these to explain a solution to a research problem and is the approach used for this thesis. Pragmatism focuses on what can be achieved or what works rather than on the positivists' principle of absolute truth or reality. Pragmatism accepts a flexible approach to solving research problems. According to pragmatism there cannot be one way to solve a problem, but a mix of approaches can better help solve a problem and find the truth. Pragmatists believe that there cannot be a single reality but multiple realities. The pragmatism paradigm follows both positivism and interpretivism to seek the answers to the problems.

The choice of mixed-methods research was not due to the merits and demerits of different approaches, but the nature of the research problem as both smoking and medication adherence behaviours are

complex (Creswell, 2018). This thesis involved a synthesis of qualitative studies of adult smokers' perspectives of SC medications, a retrospective analysis of trial data, collection of qualitative data and the combination of the strengths of these approaches to answer the research questions (Creswell, 2018). It was envisaged that more insight was to be gained from the combination of both qualitative and quantitative research methods rather than either form by itself. The mixed methods approach (Table 1) provided an expanded understanding of the problem of low adherence to SC medications and the negative impact this has on long-term abstinence.

Table 1: The mixed method approach (Tashakkori et al., 2020).

Timing	**Weighting**	**Merging the data**	**Theorizing**
Sequential: Meta-ethnography qual and studies first to allow for detailed exploration of key concepts and informed the retrospective analysis of the clinical trial.	Equal	The thesis merged data from the meta-ethnography, qual and pragmatic clinical trial to provide a comprehensive analysis of the research problem.	The guiding theory for the entire thesis: *PRIME Theory* http://www.*primetheory*.com/index.php This theory provided a theoretical lens and was used as an overarching perspective and framework of the PhD topic and methodology.

Connecting quantitative and qualitative data sought to develop a more complete understanding of adult SC medication behaviours. By following the meta-ethnography and qualitative phases of the present study with the quantitative research, the intention was to also attempt to explain the mechanism behind the quantitative results. The study phases were as follows:

I. Phase 1: A meta-ethnography of adult smokers' perspectives of TDMs. A meta-ethnographic synthesis of qualitative studies (2005–2020) was conducted to understand

adult smokers' lived experiences with TDMs. The line-of-argument synthesis identified recurring themes of resistance, ambivalence, and reliance on willpower, highlighting the disconnect between clinical expectations and smokers' perceptions of pharmacotherapy.

II. Phase 2: A qualitative study designed to explore beliefs and attitudes of people who seek help to stop smoking within a NHS SSS and choose a smoking medication to support their quit attempt. Semi-structured interviews were conducted with 10 purposively sampled adults accessing a West Midlands NHS SSS who opted for TDMs. This phase explored beliefs, relational influences, and emotional drivers of medication use, offering insight into both facilitators and barriers to adherence. Data were thematically analysed and interpreted through the lens of *PRIME Theory*.

III. Phase 3: Retrospective critical analysis of adherence behaviour issues within a pragmatic RCT designed to test the efficacy of nortriptyline plus NRT compared to placebo plus NRT for SC. Using the CASP framework, a critical analysis of the *SCANAG* trial evaluated adherence patterns, protocol assumptions, and outcome interpretation. The retrospective analysis identified design limitations, particularly around the lack of behavioural adherence measurement, and raised questions about how RCTs assess pharmacological efficacy without accounting for real-world use patterns.

Integration occurred through a sequential explanatory design. The meta-ethnography and qualitative study shaped the questions asked of the RCT data and guided interpretation of inconsistencies or patterns. Triangulation allowed comparison across methods, illuminating points of convergence (e.g. low motivation as a key barrier) and divergence (e.g. structural vs personal explanations for non-adherence). The "point of interface" (Creswell, 2018, Tashakkori et al., 2020) occurred during interpretation, where cross-phase insights were synthesised to answer the research questions

holistically. The phases were intentionally integrated rather than keeping them separate; the approach taken was to utilise the meta-ethnography and qualitative study findings from interview questions to inform the dataset for data analysis from the original RCT. Integration therefore occurred by connecting the analysis from each phase of the study (Creswell, 2018). The substantive chapters 4-6 in this thesis represent three independent investigations, all on the theme of medication adherence to TD medications. Each chapter provides more detail of its methodical approach, justification of the research method, detail of the chosen method, tools used for data collection, approach to how the data was analysed and design limitations.

3.6 Theoretical Framework: PRIME Theory

PRIME (West, 2006) was adopted as the overarching theoretical framework guiding this thesis. It conceptualises motivation as arising in real-time from interacting *P*lans, *R*esponses, *I*mpulses, *M*otives, and *E*valuations. *PRIME* foregrounds the dynamic and emotionally situated aspects of behaviour, challenging linear models of decision-making. It was particularly well-suited to explore smoking and TDM adherence, which are often influenced by moment-to-moment impulses and shifting motives that override longer-term intentions. The theory informed not only the design of qualitative interview questions but also the interpretation of findings across all phases. For instance, it helped explain why rational evaluations (e.g. “smoking is harmful”) often fail to translate into consistent medication adherence. However, while conceptually robust, *PRIME* remains difficult to operationalise quantitatively, and its focus on intrapersonal dynamics risks overlooking social and systemic influences, an important critique addressed in this thesis by integrating perspectives from medical sociology and public health.

PRIME, developed by Professor Robert West (West, 2006), offers a comprehensive, dynamic framework for understanding human behaviour, particularly in health contexts like SC and provides an integrated cognitive, emotional, and behavioural components into a unified model. At the heart of

PRIME is the idea that motivation is not a static trait but a constantly shifting state that arises from competing internal influences. *Plans* represent long-term intentions or goals, such as a desire to quit smoking. *Evaluations* are beliefs and judgments about behaviours, such as viewing smoking as harmful. *Motives* reflect moment-to-moment desires or needs, which can fluctuate and conflict e.g., wanting to quit smoking while also wanting the relief it provides. *Impulses* are urges or automatic tendencies to act, and *Responses* are the actual behaviours performed. Critically, *PRIME* asserts that behaviour is driven directly by impulses and motives, not by rational plans or evaluations alone. For example, a smoker may genuinely believe that quitting is important (*evaluation*) and have a structured quit plan yet still smoke when faced with a strong craving (*impulse*). This explains why insight or intention alone often fails to change behaviour. The theory emphasises the importance of supporting motivation at the point of action, by strengthening positive motives and reducing competing impulses. It also encourages designing interventions that account for fluctuating motivation, such as just-in-time support, cue management, and behavioural reinforcement.

In summary, *PRIME* provides a nuanced, real-time understanding of motivation that is particularly well-suited to addressing complex, habitual behaviours like smoking. The theory is a comprehensive, real-time model of motivation highly relevant to smoking cessation research. Its strength lies in acknowledging that behaviour is driven by immediate motives and impulses, rather than abstract plans or evaluations. This aligns well with the lived experience of smokers, who often relapse despite strong intentions to quit and knowledge of smoking's harms. The theory highlights the fluid, situational nature of motivation, making it a valuable framework for designing interventions that address real-time triggers, cravings, and environmental cues. In SC, it highlights how motivation, immediate impulses, and personal evaluations influence adherence to medication (Beard et al., 2013a). However, its application in empirical research presents challenges. *PRIME* is conceptually rich but difficult to operationalise. Terms like "motives" and "impulses" are dynamic and subjective, making them hard to measure reliably in standardised studies. This limits its predictive power and

complicates the development of robust, testable hypotheses. Additionally, while it accounts for intrapersonal dynamics well, it underemphasises structural and social determinants of smoking, such as socioeconomic context or access to cessation support. Despite these limitations, *PRIME* has influenced the development of real-time, adaptive interventions, such as mobile health tools that provide support at the point of need (Ubhi et al., 2015). *PRIME* is theoretically compelling and behaviourally realistic but requires further empirical refinement to maximise its utility in smoking cessation research.

Sustained SC medication adherence depends on aligning motives with planned goals and managing impulses that may lead to relapse or noncompliance. Qualitative literature provides in-depth insights into the factors influencing adherence behaviours, offering valuable perspectives for healthcare professionals and researchers. Smokers often report low intrinsic motivation due to unreadiness, low self-efficacy and ambivalent thoughts on quitting cigarette (Mohd Noordin et al., 2023, Styklunas et al., 2021). Furthermore, there is often an overemphasis on individual-level factors in explaining adherence, with insufficient attention paid to broader systemic influences (Gast and Mathes, 2019). For example, healthcare system factors such as provider training, communication quality, and follow-up support are rarely central to adherence studies but have significant implications for medication use. The healthcare environment and policy frameworks, such as insurance coverage for cessation medications, shape adherence opportunities and should be more systematically integrated into research models (Patel and Thompson, 2025).

This mixed-methods thesis advances understanding by combining patient-centred perspectives with real-world clinical data. It also contributes to methodological literature by demonstrating how behavioural theory, critical appraisal tools, and sociological framing can be productively integrated in health research. The use of *PRIME*, while innovative, is critically examined for its applicability and limitations. The inclusion of a meta-ethnographic synthesis further grounds the research in the

wider qualitative literature, while the RCT critique contributes practical insights into how adherence should be more meaningfully addressed in future trials.

CHAPTER 4 META-ETHNOGRAPHY

This chapter reports on a meta-ethnography of adult smokers' perspectives of TDMs. The aim of this chapter is to explore and improve understanding of adult smokers' experiences and beliefs regarding TDMs and their importance to adherence behaviours by synthesizing knowledge from published qualitative studies from smokers' perspectives. The meta-ethnography offered a rigorous method for synthesising multiple qualitative studies to advance understanding of adult smokers' experiences, views and beliefs about TDMs. Section 2.1 details the meta-ethnography design and literature search methods; section 2.2 details the critical appraisal; 2.3 details data abstraction; 2.4 the synthesis; and 2.5 the results. The chapter concludes by discussing the inter-relationship between the identified three themes which are illustrated as a model of smokers' TDM adherence and non-adherence behaviours (Figure 2).

4.1 Study design

A synthesis of qualitative studies of adult smokers' perspectives of TDMs published between 1990 – March 2016 was undertaken using meta-ethnography (Noblit and Hare, 1988). Meta-ethnography is the most commonly used meta-synthesis technique for qualitative analysis; it is a robust and analytical process of synthesising qualitative studies (France et al., 2016). According to Bondas and Hall (2007) "the goal of a meta-ethnography is to generate findings that are 'more than the sum of the parts' through a process of clarification of patterns in data" (Bondas and Hall, 2007). A rigorous meta-ethnography can construct new conceptual understandings of complex healthcare issues and contribute to the understanding of patient experiences (Campbell et al., 2011, Atkins et al., 2008). Meta-ethnography continues to develop and guidance to inform the decision-making process at key stages of the qualitative synthesis exists; although consensus on best practice is yet to be published (Kastner et al., 2012, France et al., 2016, France et al., 2015, Wong et al., 2013). Noblit and Hare's

seven-step iterative process remains the primary organising framework for conducting meta-ethnography (Noblit and Hare, 1988).

4.2 Search methods

Published qualitative studies exploring adults' experiences, views and beliefs of TDMs were included. No language restrictions were applied, and the search included all studies from 1990 to March 2016. A search strategy was created following the background reading of published literature, titles, reference lists and abstracts and other relevant reviews to find terms, spellings, topic language in the field of medication adherence with TDMs, spellings; the search strategy was refined in response to the literature found. The search criteria were guided by the Sample, Phenomenon of Interest, Design, Evaluation, Research type (SPIDER) framework (Cooke et al., 2012). Using key word sets and medical subject headings, seven databases were searched (MEDLINE, EMBASE, PsycINFO, ASSIA, PubMed, Web of Science, CINAHL) during April 2016. Example search syntax is provided in appendix 2. Hand searches of reference lists of retrieved articles and journals were also included. Hand searching aimed to ensure complete coverage of articles which may not have been indexed by databases.

4.3 Ethical considerations

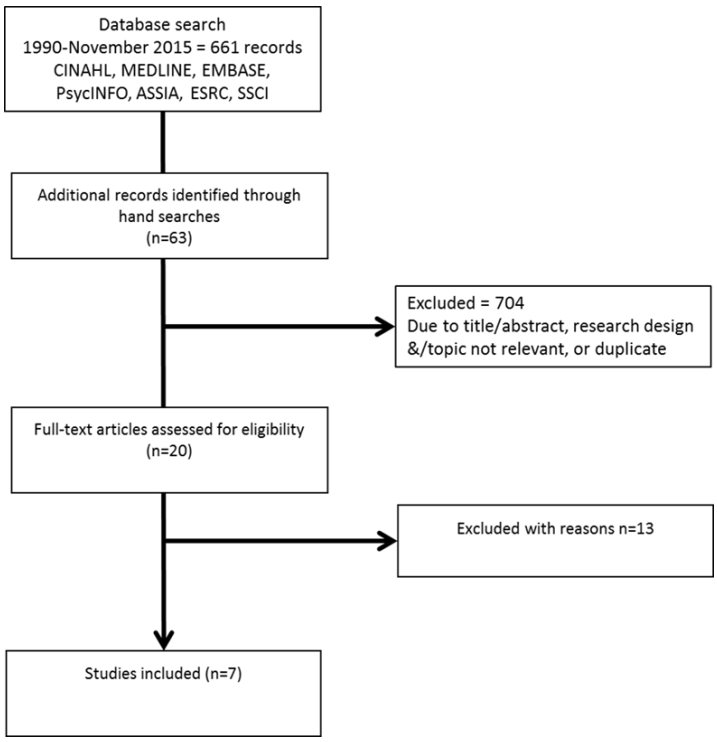
Meta-ethnography, as an interpretive synthesis of qualitative studies, presents unique ethical challenges that extend beyond traditional primary research. Researchers must navigate the ethical terrain of representation, consent, and transparency when reinterpreting participants' lived experiences from existing studies. Although meta-ethnographers do not engage directly with participants, they bear a responsibility to honour the original context, voice, and intent of those narratives. While consent should have been covered by the original studies, the researchers critically assessed whether each study data aligned with ethical norms. Clear documentation of interpretive decisions, translation processes, and conceptual frameworks was undertaken to maintain academic

integrity and allow for scrutiny. Researchers ensured misrepresenting or decontextualising participant quotes and themes, ensuring fidelity to the original meaning. Clear documentation of interpretive decisions, translation processes, and conceptual frameworks was essential to maintain academic integrity and allow for scrutiny. Clear documentation of interpretive decisions, translation processes, and conceptual frameworks was essential to maintain academic integrity and allowed scrutiny.

4.4 Search outcome

The search yielded 724 potentially relevant papers (Figure 4). Titles and abstracts of all studies found from the literature searches were reviewed for eligibility. 704 were excluded because they were duplicates, irrelevant, did not state ethical considerations, or not qualitative in design. This resulted in 20 papers for inclusion that were then read in full to ensure their relevance to the meta-ethnography. Papers were eliminated at this stage primarily because they did not report primary research, adults' experiences, views and beliefs of TDMs, or were quantitative studies that did not have a significant qualitative component. This further reduced the number of papers to 7.

Figure 4 Flow chart of study inclusion and exclusion (PRISMA 2009)



The 7 papers considered relevant, according to the search strategy using the Standardized appraisal tools from the Joanna Briggs Institute (JBI) System for the Unified Management Assessment and Review of Information (SUMARI) package, were then assessed for methodological quality (appendices 2-3) (JBI, 2014a). Evidence from these studies included the views, perceptions, attitudes, expectations, beliefs and experiences of 370+ diverse cultural/ethnic background former or current smokers of both genders and aged ≥18 years. Included studies aimed to understand the low use of TDMs including within ethnic minority groups but lacked in-depth analysis of perceptions of TDMs. Interpretations were mostly limited to a description of TDMs use or non-use within a biomedical model, interpreting TDM underuse as a deviant behaviour. The rationality of TDM taking and barriers to TDM use was predominantly conceptualised as relating to cultural factors, individual misconceptions or inadequate understanding of the medication.

4.5 Quality appraisal

Noblit and Hare's pivotal 1988 book provides no precise guidance on how to appraise studies for inclusion in a meta-ethnography (Noblit and Hare, 1988). Subsequent methodological developments provide researchers with qualitative quality appraisal (QA) tools (Hawker et al., 2002). I agree with the concept that that research can and should be assessed for quality; thus, all included studies were assessed for eligibility, quality and risk of bias. Study clarity and methodological quality was assessed utilising a standardised appraisal tool from the Joanna Briggs Institute (JBI, 2014b) (appendix 3). Secondly, studies were scored as having a low, high, or unclear risk of bias (appendix 4). Thirteen articles were excluded owing to a lack of relevance to the review and / or ineligible study design e.g. they did not provide an explicit account of a theoretical framework or a clear description of methods (Table 2). The seven papers were included as they were of sufficient quality, clearly reported on study proceedings and aimed to explain the phenomena they investigated. A description of the seven included studies is given in Table 2. The papers are listed pragmatically in alphabetical order based on the first authors' surname.

Table 2: Table of included studies

Paper number	Source paper (n=7)	Country and setting	Participants	Medication type	Methodology	Indicative finding
1	Burgess, *et al.* (2007)	USA, Minneapolis/St Paul Community	26 American Indian	NRT only	Qualitative descriptive approach Focus Groups x6	Participants held negative attitudes toward pharmacotherapy for smoking cessation, including worries about side effects, scepticism about effectiveness, and dislike of medications in general. Negative attitudes were grounded partly in a lack of trust in conventional medicine.
2	Carpenter, *et al.* (2011)	USA, South Carolina Community	70 African American, European American, Hispanic	NRT only	Qualitative descriptive approach Focus Groups x9	There was a general lack of knowledge of NRT effects and its efficacy, with only moderate knowledge of the mechanism by which NRT works. Concerns about NRT safety were expressed in all groups, with particular apprehension about addictive potential and possible interactions with other medications. Results highlight enduring misperceptions about NRT that likely undermine usage.
3	Fu, *et al.* (2007)	USA, Minneapolis/Minnesota Community	95 African American,	NRT and Bupropion	Qualitative descriptive approach	The cultural value of mental control and self-determination was seen as most important to quit smoking. Pharmacotherapy was rarely

			American Indians, Southeast Asians (Hmong, Vietnamese)		Focus Groups x16	utilized and participants had low knowledge and poor understanding of the benefits of pharmacotherapy.
4	Levinson, *et al.* (2006)	USA, Colorado Community	49 Latino	NRT and Bupropion	Qualitative descriptive approach Focus Groups x6	The use of medications to treat nicotine dependence and facilitate withdrawal is not an accepted construct. Five major themes related to perceptions that smoking is a weakness rather than an illness, pharmaceuticals are to be generally avoided, NRT is mistrusted, and rejection of bupropion and misconceptions are regarding smoking and cessation.
5	Tsang, *et al.* (2014)	USA Community	39 Chinese and Vietnamese	NRT only	Qualitative descriptive approach In-depth Interviews x39	Both smokers and their family members believed strongly in willpower and a sense of personal responsibility as the primary drivers for stopping smoking. Those who do use NRT often use it incorrectly, following their own preferences rather than product instructions.

6	Vogt, *et al.* (2008)	UK South London GP practice	27 British	NRT and Bupropion	Qualitative descriptive approach Semi-structured interviews x27	Smokers' motivations to use nicotine dependence medications vary with their expectations that these medications will be effective. Expectations appear to be influenced by perceptions related to the ability of these medications to control cravings to smoke. An aversion to conventional pharmacology and an expectation that consumption of nicotine dependence treatment is unpleasant also were associated with smokers' motivations to use TDMs. Interventions aimed at increasing the likelihood with which smokers use TDMs may be more successful if they address these outcome expectations.
7	White, *et al.* (2006)	UK Newcastle on Tyne Community	73 UK Bangladeshi and Pakistani	NRT and Bupropion	Qualitative descriptive approach In-depth interviews x6	Willpower was the most common approach to quitting. There is a need to adapt and test effective smoking cessation interventions to make them culturally acceptable to ethnic minority communities.

4.6 Data abstraction

The data was combined by following Noblit and Hare's (1988) rigorous process of meta-ethnography, including reciprocally translating the findings from each included study into those from all the other studies in the synthesis (Noblit and Hare, 1988). Following the techniques described by Noblit and Hare (1988): (i) reciprocal translation (looking for similarities across studies) and (ii) refutational analysis (identifying differences or challenges to the emerging concepts and looking for alternate accounts) and (iii) the development of a 'line of argument' that considers both the similarities and differences found in the studies. Differences were pursued as rigorously as similarities and comparisons across concepts and settings were continuously explored, for example, the extent to which an emerging interpretation was relevant across different TDMs. To ensure alternative perspectives were made transparent they were discussed with a view to enriching the analysis. This was undertaken via robust discussion between authors and comparison with existing literature on tobacco dependency, medication adherence and health behaviour change. Findings were systematically reviewed and integrated. Participant quotes extracted from included studies are tabulated within Table 3.

Table 3: Participant quotes extracted from included studies

Theme	Quote	Author
Psychosocial context of TDM behaviours	*''I decided that I was not going to smoke. I managed without cigarettes the whole day. But then at the end of the day I would start arguing with the family for one reason or another reason, and then would start smoking again''*	(White et al., 2006)
	"When you smoke, you'll set a bad example. You think you can tell your children not to smoke later?	(Tsang et al., 2014)

	No way. The second thing is about your parents. . . . If you smoke, you [are] not listening to their advice, that means you [do] not fulfil your filial duties."	
	''I think that made a big impression on me. I was like, 'Hey when I grow up I'm going to smoke.'' ''one of the obstacles against quitting I think is friends and family that smoke.''	
	"I used [the nicotine gum and patch] separately. I was scared of the level of nicotine in my body."	(Tsang et al., 2014)
	"I thought it was just the nicotine in there that they're giving you. What good is that? I'm not putting anything on me with nicotine, you know. It's not quitting, it's like changing one for another."	(Levinson et al., 2006)
Predilection for willpower and "natural" methods to achieve quit success	*"No medicines can help to cure [nicotine] addiction. Chewing gums, eating plums, or snacks perhaps might help a little, but medicines are just impossible."*	(Tsang et al., 2014)
	"Most people would probably think it's okay, although I've got…I don't know if the same subconscious feeling with other people, it's just sort of if you take pills to me it's sort of somehow a sign of giving up and being weak. I'd rather do it myself and find the strength myself."	(Vogt et al., 2008)
	"*Well it's tablets [bupropion] to take and I don't really take any…. I try to avoid all of that…I try to*	(Vogt et al., 2008)

	use more natural things than tablets. Because it's [natural things] better for your body…"	
	"In my case, after I came up with my decision and determination, I could quit easily." Another smoker stated, "When I decide to quit smoking, my determination will surpass all. There is nothing more than [your] determination. . . . If you are not determined, you will deviate easily."	(Tsang et al., 2014)
	"at least with cold turkey, it is free and you know you are not hurting yourself"	(Burgess et al., 2007).
	"I think at the end of the day it's a matter of willpower, yeah"	(Vogt et al., 2008)
	"It's probably just psychological, but I feel like if I just stop smoking but start like being addicted to a patch, then what's the point, I'd rather just brave it out."	(Vogt et al., 2008)
Resisting medications	*"Like in every commercial you can see they have like those gross side effects. You know, I'm so surprised they only put them on TV. I wouldn't want any of that type of and I'm so afraid of damaging the liver and all the organs inside from taking medicines …"*	(Burgess et al., 2007).
	"Why would you take something to stop smoking and then get three or four different side effects? When you only got one with smoking."	(Fu et al., 2007).

	"The fear of unknown, and hearing all those side effects, which I have heard of, would keep me away from even trying the product."	(Levinson et al., 2006)
	"Well it's mainly the craving for the nicotine isn't it, and I mean they're [NRT] actually giving you a certain amount of nicotine which helps stop the craving…."	(Vogt et al., 2008)
	"…cause they work and that means that you are going to stop taking them eventually, right, not going to transfer, your money spent on cigarettes to money spent on medicine for the rest of your life."	(Carpenter et al., 2011)
	"It made me feel real funny, real different. I could just feel the stuff going into you. ... I just didn't like it."	(Levinson et al., 2006)
	"I think that'd [bupropion] be the one, it has to be strong, something boom, that would just take that craving away, ... I think I need a chemical, for me I need a chemical, something strong, to take the craving away…"	(Vogt et al., 2008)
	''I am quite sceptical about tablets and stuff so I wouldn't want to get into that habit. I wouldn't be happy about using Zyban [Bupropion]''	(White et al., 2006)
	"*That word [antidepressant]. Sounds like you're messed up in the head. ... I don't think I'm a depressed person. ... It's labelling you as a—as a*	(Levinson et al., 2006)

	what?—as a depressant. That scares a person. That's scary."	

4.7 Synthesis

Data synthesis consisted of studies that explored the perceptions, experiences and expectations of NRT amongst ethnically diverse adult smokers: four studies also included bupropion; none of the studies investigated varenicline or e-cigarettes. Study characteristics were extracted from the papers using the standardised JBI data extraction tool for Interpretative & Critical Research (appendix 5). First-order findings (quotations) were used to support second-order interpretations (authors' analyses) to gain new insight into the relationships between SC and TDM adherence. Once themes became apparent, a process of refutational inquiry (refutational translation) was undertaken, looking for differences across studies to ensure findings were rigorously presented and to ensure that the process did not miss anything that may add or disprove the findings. Common themes were then summarised in a statement or 'line of argument synthesis' (Noblit & Hare 1988). Direct quotations from participants were used to illustrate their experiences.

Reading the studies was central to the meta-ethnographic process undertaken and had different purposes throughout the process, for example critical appraisal, organisation, comparison, to contrast, data extraction and verification. Primary themes, as reported in the included studies, were interpreted as reflecting participants' understandings, attitudes, meanings and expectations of TDMs within the context of smoking cessation. Secondary themes, located in the discussion and conclusion section of each study, were understood as authors' interpretations of participants' understandings. The included papers were processed in chronological order. The first three papers (see table 4) provided the structure into which the remaining four papers were translated. Reciprocal Translation Analysis (RTA) (Noblit and Hare, 1988) provided the process approach for integrating the data into a coherent argument. This allowed for codes to be compared, contrasted and provisionally grouped into broad areas of similarity. This generated a reduced set of translations about how TDMs were perceived and

experienced within the context of smoking cessation in different cultures. Seven "translations" were created and expressed as "lines of argument" (Noblit and Hare, 1988) in order to depict facilitators or barriers of TDM adherence. The themes reflected the medication setting that encompassed nuances of everyday lives affected by long smoking histories, chronic deprivation and cultural dynamics. The synthesis represents a new understanding, based on translation and interpretation of the meaning of findings in primary studies. Extracted data were organised by gathering and then organising concepts that contributed to the development of three themes (Table 4).

Table 4 Translations and lines of argument

Translations	**Line of argument 1**	**Line of argument 2**
TD medication behaviours in the context of sociocultural circumstances	Smokers feel they are behaving correctly when they resist TDMs as they seek to act in the same way as the majority in their social group and align with a resistance to medications.	Importance of Psychosocial context of TDM behaviours.
Smokers oscillate between accepting the medical model of treating nicotine addiction and natural methods		
Rejection of the "medical model" approach of treating nicotine addiction with medications	It is the social norm to believe that willpower is an essential ingredient to stopping smoking.	Predilection for willpower and "natural" methods to achieve quit success.
Smokers' appraisal and experiences of TDMs side effects	The interpretation of TDMs becomes compatible with existing fears about medicines.	Resisting medications.

4.8 Results

4.8.1 Concepts in the synthesis

The process of lines-of-argument revealed the perceptions and experiences of TDM adherence (facilitators) or hindered (barriers) smokers to attempt to quit using an available TDM. The themes related to smokers' mediation of complex elements that form unstable TDMs adherence behaviour. Resistance to medication emerged from the synthesis as an important theme. Smokers' discourse about TDMs challenged medical evidence rather than depicting a passive acceptance of it. The synthesis indicated that decision making about TDMs was associated with dynamic processes of dealing with Nicotine Withdrawal Symptoms (NWSs) within the context of psychosocial factors that mostly supported smoking behaviour and rejected TDM use. Findings are presented in these three main themes:

1. Psychosocial context of TDM behaviours
2. Willpower predilection
3. Resisting medications

4.8.2 Psychosocial context of TDM behaviours

Smokers face difficult and emotional challenges when they attempt to quit. Habitually smoking was seen to be helpful to alleviation high levels of stress and compatible with social environments. Participants' narratives suggest TDMs use is embedded in a psychosocial context, which is not influenced by existing guidelines for SC. The meaning of smoking and cessation were strongly fashioned via dynamic social interactions, conflicts and shared cultural traditions and roles. Narratives conveyed a complex, uncomfortable and dynamic lived experience of SC. Smokers described conflicts within themselves and with their significant others about their smoking choices and subsequent behaviours.

''I think that made a big impression on me…'Hey when I grow up I'm going to smoke.'' ''one of the obstacles against quitting I think is friends and family that smoke.'' (Burgess et al., 2007)

This psychosocial context caused abrupt termination of SC decisions resulting in a relapse to smoking. In contrast some positive ideas about smoking, others expressed strong dislike of it, explaining the negative impact that smoking has on them personally and also their family relationships. Smokers' narratives revealed conflicting thoughts about SC. Some were influenced by their personal relationships to stop smoking but had low motivation to do so. Most participants were unaware of available TDMs and behavioural support. Smokers' narratives suggested cognitive dissonance (Festinger, 1957) about smoking (e.g. believing smoking is harmful and simultaneously holding its importance to their social interactions). Such conflicting beliefs destabilised adherence to TDMs as smokers tended to alter their beliefs intentionally to stop the cognitive dissonance. Smoking was a well-established, common behaviour amongst participants; the ease of availability of cigarettes and normalisation of smoking behaviour was evident. The presence of smoking among family members and peer groups contributed to the early formation of smoking behaviours and was a strong barrier to cessation. Within the included studies most beliefs about TDMs had been formed within social contexts where medications were feared. Most participants had little understanding of TDMs and worried about taking them; paradoxically, the use of TDMs was in conflict with their desire to stop smoking. Perceptions of TDMs properties detracted from TDM initiation and adherence. Participants, who expressed a desire to stop smoking, feared unpleasant nicotine withdrawal symptoms (NWSs) and although aware of TDMs their negative perceptions of them stopped them from using them. Decisions to use TDMs are not made solely by isolated persons, but rather they reflect choices made by groups of people associated to each other both directly and indirectly. Smokers are psychosocially connected; this influenced their adherence to TDMs.

4.8.3 Willpower predilection

Unaided SC was cited as the most popular method of quitting. Participants had low motivation to use TDMs. Reasons for avoidance of TDMs included fear of side effects, a general aversion to medication, connotations of mental illness, or belief that willpower alone controls successful cessation. Many participants feared becoming dependent on medicinal treatments. They described smoking as more of a personal weakness and a failure of their willpower than an illness. These negative attitudes toward pharmacotherapy were linked to feelings of mistrust in conventional health care, with natural interventions considered to be more desirable. Participants preferred to "tough it out" or use non-medicinal substances to help them stop smoking, for example, chewing gum, chamomile tea, fruit, exercise and sweets (candy). They used these strategies to alleviate cravings during quitting; these "natural" methods were supported by their family members who validated the idea that willpower determined SC success rather than using TDMs. The perception that "willpower" is superior to TDMs was reinforced by concerns about safety; quitting using willpower alone provided a sense of accomplishment and demonstrated strength of character. Participants believed that without sufficient willpower a smoker would not be able to stop smoking:

> *''Well I think it is mainly the willpower. If somebody wants to give the cigarettes up it depends how strong he is…nowadays there are lots of expensive cigarette patches and everything on the market. I don't believe they can help somebody to stop smoking if they don't want to'' (White et al., 2006)*

Use of TDMs was perceived as a weakness and an uncomfortable reflection of having a lack of willpower. A perceived lack of willpower was used by some participants to justify their inability to stop smoking. Male narratives associated willpower with bravery and strength of character. Taking TDMs conflicted with a strongly held belief amongst participants that willpower is the remedy to smoking. As participants' capacity for active willpower was limited and not a constantly available

resource, fluctuating adherence to TDMs regimens and SC behaviours was seen as influenced by the person's willpower.

4.8.4 Resisting medications

'Resistance to TDMs' emerged as an important theme for smokers who seek to reconcile their smoking, quitting choices and behaviours within complex contexts of long smoking histories, failed quit attempts, chronic deprivation and cultural factors. Beliefs and interpretations of TDMs were not fixed but oscillated within different SC circumstances. These interpretations arguably align with an existing general tendency for people to resist taking medicines (Britten, 1996). This predilection to resist medicines resulted in dynamic behaviour with TDMs; deliberately choosing to avoid or reduce TDMs was a theme recurring in the studies. Participants had knowledge of TDMs (e.g. over the counter NRT) but perceived the taking of medicines as undesirable and many of the participants' feared dependence and strongly resisted TDMs.

> ''*I'm not very much of a pill person…. I think someone taking pills for quit[ting] smoking, I'd think they're crazy….*''(Burgess et al., 2007).

Non-adherence to TDMs was common because of fears of taking medicines, risk of dependency and smokers' suspicions about the plausibility of their ability to help them stop smoking. Worry about side effects is augmented by (i) inaccurate knowledge about the potential risks and (ii) the perception of incidence of likely occurrence of harm. Paradoxically, smoking was often considered safer than using TDMs. Participants actively assessed TDMs, especially their safety and addictive potential. NRT and bupropion were regarded differently as TDMs. NRTs were partially understood regarding how they stopped cravings or replaced the purpose of cigarettes (or not). Some participants understood that the nicotine in NRT reduced or stopped cravings for cigarettes. However, not all participants shared this view of NRT and were unconvinced nicotine replacement was plausible. Some participants recognised that NRT was safer than continued smoking but this belief was incongruent with stronger negative opinions and scepticism of NRT.

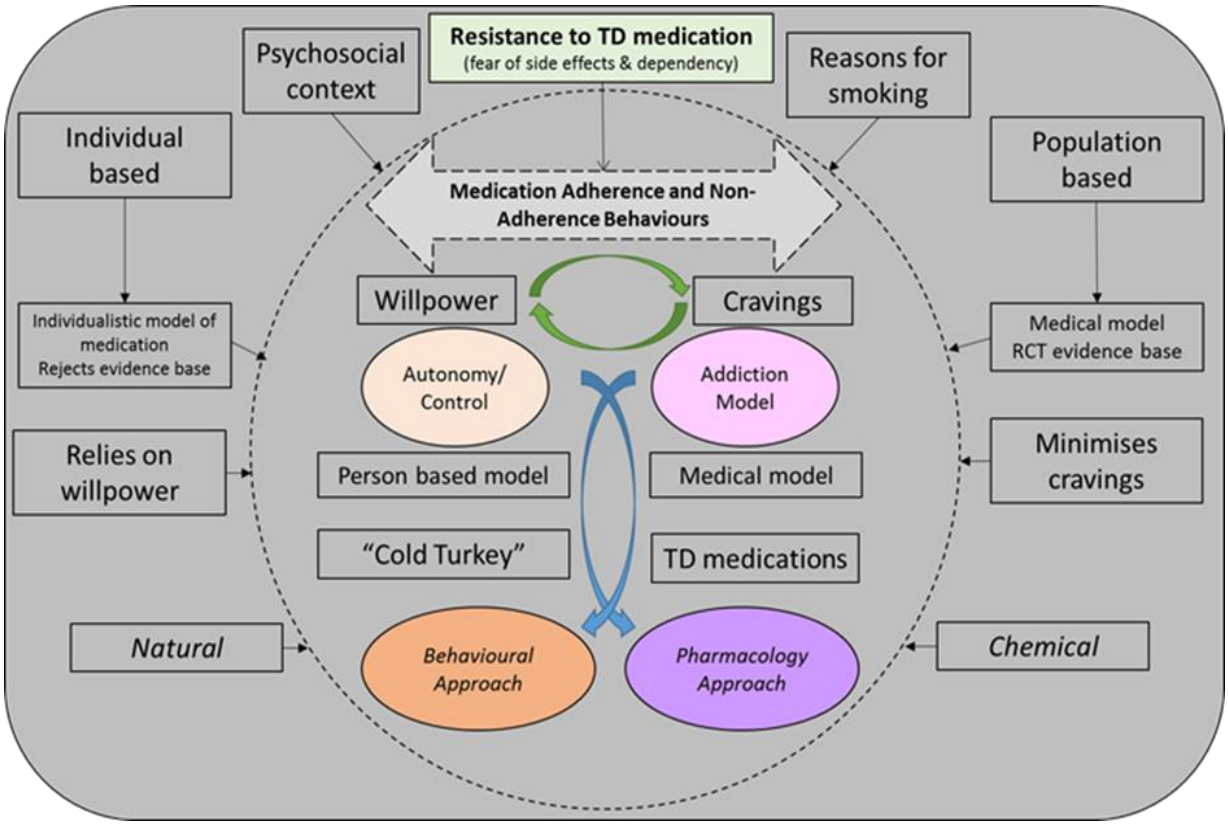
The idea of taking bupropion met with more apprehension amongst participants than NRT use. Bupropion was perceived more as a medicine owing to its oral dose form; this connected strongly with attitudes against medication and intensified worries about side effects. Bupropion was considered a potent drug; this led to perceptions of it being dangerous, a powerful chemical substance and unnatural. For some participants the interpretation of bupropion being powerful was the attraction for its use. However, participants quickly rejected it once they knew it as an anti-depressant. This knowledge provoked negative views associated with mental health problems, fear of side effects, and general dislike of medicines. Bupropion was generally perceived as having dangerous adverse effects and interfering with the body's natural state. Perceptions about TDMs appear to also be formed within an economic discourse, e.g. comparing the financial costs of TDMs with that of cigarettes. Resistance to TDMs appeared to be a complex combination of individual and social group beliefs. The extent to which TDMs were resisted depended on how it was perceived within their social network and strength of preference for resisting medication.

4.9 Conceptual model

Following this, the synthesis was then expressed as a 'line of argument' and presented as a conceptual model (Figure 5). I became aware of the eMERGe project (France et al., 2015) after undertaking this study and have retrospectively carefully considered the eMERGe web resources (France et al., 2019) to assure the best practice of conducting the meta-ethnography has been followed. The inter-relationship between the identified three themes is illustrated as a model of smokers' TDM adherence and non-adherence behaviours (Figure 2). It depicts oscillation between psychosocially driven beliefs about TDMs that mostly do not resonate with the current medical model of TD treatment. TDMs were mostly judged ineffective, resisted and rejected because of potential side effects, limited efficacy, incompatibility with willpower and inability to address reasons for smoking other than nicotine addiction. The complexity of the effect of facilitators and barriers is significant. The person is placed at the centre of the model within their dynamic TDM adherence behaviours. Unpleasant NWSs fit with the medical model of TD addiction and need for a pharmacological approach. This

conflicts with a preference for willpower and natural methods to quit smoking. Factors identified from the line-of-argument translation operate as facets of smokers' experiences of smoking, SC and medication beliefs within the real world. This creates an insecure milieu for TDM adherence behaviour, which oscillates in response. Therefore, the model does not classify smokers into fixed categories or locate them on a specific trajectory of adherence behaviour at a given time point.

Figure 5 A model of smokers' TDMs adherence and non-adherence behaviours



4.10 Beliefs about tobacco dependency medications

Attitudes to TDM adherence had multifactorial influences with different 'moderators' being shaped by individuals' contexts. Beliefs and perceptions surrounding the importance of willpower in the SC process emerged as important. High resistance towards TDMs was evident, despite participants struggling to stop smoking. This indicates that smokers may have specific reasons for poor medication adherence compared to other medication conditions. There was a strong preference for "natural" methods to aid cessation. There are several key factors involved here. Facilitators and barriers were neither constant nor binary influences on smokers' TDM adherence behaviour. There

was confused knowledge about safety, efficacy and functional benefits of TDMs. Smokers' perceptions of TDMs appeared to be shaped by their judgement of the ability of TDMs to control cravings to smoke. Most participants preferred to avoid the use of TDMs. A dislike of medications in general contributed to a negative view of TDMs specifically. This dynamic cognition undermines the dominant medical discourse regarding SC that strongly asserts the efficacy of behavioural support and TDMs for SC (Stead et al., 2012a).

4.11 Resistance to medications

'Resistance' in regard to medication taking has emerged as a concept from a previous qualitative synthesis (Pound et al., 2005). Pound *et al.,* (2005) defined medication resistance as "the ways in which people take medicines and attempt to minimise their intake". This work has been further developed (Britten et al., 2010) and the concept of resistance has been updated as referring to the various ways in which people behave with medicines. Although most participants in the included studies resisted TDMs, some positive attributes of TDMs were expressed, mainly by those who had experienced the benefits of TDMs in previous quit attempts. Most participants preferred willpower alone; this has been found in other studies (Smith et al., 2015a, Etter and Schneider, 2013). Willpower preference and resistance to TDMs needs to be acknowledged by health professionals and used to inform tailor TDM adherence advice. Arguably willpower is an underestimated concept, though commonly associated with SC by smokers, clinicians and researchers. Different stakeholders within SC are likely to have a different understanding of what willpower means (Smith et al., 2015b). It would be beneficial to explore willpower within health behaviour change and establish its relationship to medication adherence.

4.12 Beliefs about smoking cessation and use of medications

Smokers' narratives revealed the presence of psychological discomfort from conflicting attitudes or beliefs about SC and use of TDMs, which resonated with cognitive dissonance theory (Festinger, 1957). TDMs emerged as ambiguous aids to quitting whose meanings were still being negotiated by

those seeking to quit smoking. Arguably, smokers' oscillating SC thoughts and TDM use is a representation of inconsistent beliefs owing to numerous and conflicting social interactions. Smokers' experience and discourse about TDMs challenged medical evidence rather than encouraging passive acceptance of it. This synthesis indicates that decision making about TDMs was influenced by dynamic processes of dealing with NWSs within the context of psychosocial factors that mostly supported smoking behaviour and rejected medication use. Nurses should ascertain smokers' concerns about TDMs; it may be helpful to achieve this by encouraging them to share their TDM experiences and concerns.

A propensity to reject TDMs and substantial preference for willpower emerged from the synthesis. Smokers opted for TDMs in particular situations, such as for quick alleviation of their NWSs or when they had a previous history of several failed quit attempts. In the present review, smokers made decisions to avoid, modify or stop a prescribed TDM regimen for multi-faceted reasons manifested from their cultural context and everyday lives. Resistance to TDMs, the role of willpower, the psychosocial context of TDM adherence behaviours, fear of dependency and the preference for "natural" methods need further investigation. A better understanding may help people achieve long-term SC. Nurses should facilitate SC by ascertaining TD treatment perceptions, encouraging openness about TDM concerns and tailoring support to the individual. Adherence support needs to be part of patient-centered care and shared decision-making (NICE, 2009); respecting a person's beliefs about TDMs is fundamental to nursing practice and supporting adherence (NMC, 2015).

Using the meta-ethnographic approach enabled development of a model of smokers' TDMs adherence and non-adherence behaviours by comparing and re-interpreting across seven individual qualitative studies. Plausible themes were developed that can be used by policy makers and clinicians to inform discussions with smokers to improve TDM decision-making and adherence.

4.13 Limitations

However, despite attempts to undertake a comprehensive search some studies may have been missed. It is recognised that searching the qualitative literature can be problematic (Hannes and Macaitis, 2012). Studies included were descriptive and used thematic analysis; it was unclear if the studies analysed the data based on pre-specified theoretical assumptions on the ontological or epistemological status of qualitative data or on medication adherence. Instead, included studies presented findings as inherently characteristic of smokers' concerns and difficulties of SC. This generalised the needs and experiences of individual smokers and did not address the complexities of TDMs behaviours. None of the studies worked from a definition of adherence or within available typologies of medication adherence, despite the extensive theorisation in the literature. Further, most of the data was descriptively reported providing little interpretation of the causes or consequences of differences between prescribed and actual use of TDMs. Included studies were from either the UK or USA, where SC programmes align with similar guidelines and best practices. However, it is acknowledged that the studies were undertaken in differently funded systems of health care limiting the transferability of the present findings.

Noblit and Hare's meta-ethnography remains a powerful qualitative synthesis methodology. However, it is not without limitations, particularly when applied to complex behavioural health issues like smoking cessation and medication adherence. A major limitation is the subjectivity and lack of reproducibility inherent in the interpretive synthesis process. While the method encourages deep engagement with primary data, it lacks a standardised procedure for selecting, appraising, and translating studies. This can undermine transparency, a concern when informing evidence-based interventions and policy. Within tobacco dependency treatment, the method may oversimplify divergent findings through its emphasis on conceptual translation. Important nuances, such as context-specific factors influencing adherence to tobacco dependence medications (TDMs), can be lost in the pursuit of theoretical coherence. Additionally, older studies with outmoded treatment paradigms may dilute the relevance of synthesis in a rapidly evolving field.

The method's reliance on published data means that rich pharmacological and adherence-specific information is often underrepresented. Adherence is typically treated narratively or behaviourally in qualitative studies, which may limit its analytical depth in meta-ethnographic synthesis. While the method aligns well with constructivist paradigms, its limited engagement with structural determinants of health, such as inequality, race, or neoliberal policy shifts, may underplay broader socio-political forces shaping smoking behaviours and treatment perceptions. Finally, practical limitations include the time- and labour-intensive nature of synthesis, and potential difficulties in managing large bodies of qualitative literature. Without clear inclusion parameters or theoretical focus, findings risk becoming thematically descriptive rather than theoretically generative. Despite these limitations, when conducted reflexively and rigorously, meta-ethnography remains a valuable tool for understanding lived experience in health research (France et al., 2016, Campbell et al., 2011).

4.14 Strengths

This review provides a synthesis of published qualitative literature on smokers' views, perceptions, attitudes, expectations, beliefs and experiences of TDMs and their importance to adherence behaviours. It is the first metasynthesis to explore TDM adherence. The small number of studies indicates that little research attention has focused on smokers' views of TDMs, their beliefs regarding utilising TDMs and the reasons for preferring unassisted cessation. It is anticipated that this metasynthesis may improve awareness of the complexity of TDM adherence behaviours by providing an understanding of what facilitates or thwarts adult smokers in choosing and adhering to TDMs.

Noblit and Hare's (1988) meta-ethnography is a seminal and methodologically rigorous approach to synthesising qualitative research. Distinct from quantitative meta-analysis, this method enables the interpretive integration of qualitative studies, facilitating the generation of new conceptual understandings rather than aggregating findings. This is especially valuable in complex areas such as tobacco dependency and medication adherence, where lived experience, identity, and context critically shape health behaviours. Meta-ethnography offers a way to explore how smokers experience cessation interventions in diverse settings, making it highly relevant to service design and

policy implementation. It supports health promotion strategies that are grounded in the realities of users' beliefs, fears, and motivations. The methodology allows a nuanced synthesis of psychological, social, and behavioural dimensions of tobacco dependency treatment. It acknowledges the non-linear and ambivalent nature of quitting, moving beyond clinical outcomes to the meaning smokers assign to treatments, including pharmacotherapy and non-pharmacological aids. Further the meta-ethnography insights surface the cultural and emotional undercurrents that influence whether and how people use prescribed treatments, essential knowledge for tailoring interventions and improving compliance with TDMs.

This method exemplifies the interpretivist paradigm, enabling theoretical innovation through reciprocal translation, refutational synthesis, and line-of-argument construction. It allows for the deconstruction of power relations embedded in healthcare and captures the symbolic meanings attached to smoking, quitting, and the role of medicine. Overall, Noblit and Hare's methodology is particularly suited to addressing socially embedded health behaviours like smoking. When applied rigorously, it allows researchers to create theoretical generalisations that inform both academic and applied fields (France et al., 2019).

4.15 Conclusions

Smokers' narratives revealed diverse concerns and perceptions of TDMs that led to nonadherence behaviour. Many of the issues identified were potentially modifiable by existing medication adherence or health behaviour change interventions. The psychosocial context of TDM behaviours, TDM resistance and preference for willpower emerged from the synthesis as important – this translated into deliberate non-adherence. Low confidence in TDMs and experienced failure of TDMs to address multi-faceted and often conflicting reasons for smoking resulting in the predilection for willpower and legitimised non-adherence behaviours. TDMs were often incompatible with individual views and beliefs about taking medications, especially in the long term. Complete TDM adherence and persistence was unachievable within powerful anti-medication social contexts and individuals'

desire to be in control of their lives. Healthcare professionals should work in partnership with smokers, so their preferences and concerns are utilised to either help improve TDMs adherence or avoid the prescription of medication which is not taken. Future research should be aimed at understanding healthcare professionals' perceptions and practices of assessing medication adherence in smokers that may guide interventions to resolve this important issue of medication nonadherence. Research to further understand how a smokers' predilection for willpower augments the resistance to TDMs is required. This may help in achieving improved long-term quit outcomes. Personalised TDM adherence interventions are likely to be most effective to help improve long-term SC outcomes.

4.16 Reflections on the meta-ethnography July 2025

This meta-ethnography synthesised qualitative studies on adult smokers' perspectives of tobacco dependence medications (TDMs). Key themes emerged: fears of side effects, beliefs that quitting unaided preserves moral pride, distrust of pharmaceutical interventions, and the centrality of willpower narratives. Since this synthesis was completed, England has witnessed pivotal shifts. The availability of e-cigarettes has grown rapidly: over 5.6 million adults now vape, and dual use has surged from 17 % in 2021 to 32 % in 2024 (ONS, 2024, Jackson et al., 2023a). Public Health England and NHS campaigns continue to encourage vaping as a harm-reduction tool (DHSC, 2023). Meanwhile, smoking rates have declined further, reinforcing the meta-ethnography findings about smokers' preference for alternative quitting tools and natural quitting. The COVID-19 pandemic added complexity (Jackson et al., 2023b); smoking was consistently identified as a risk factor for serious illness and hospitalisation and heightened risk raised the stakes for cessation, yet also amplified distrust in medication-based approaches, some framed medication offers as coercive. Importantly, the UK government's "Quit for COVID" campaign relied heavily on willpower messaging, which resonated with smokers' moralistic self-framing (Rojas et al., 2025, Notley et al., 2025). Sociopolitical currents have reinforced this self-reliance: during Boris Johnson's tenure, several policies were criticised as "nanny state" overreach framing regulation of tobacco and vape

sales as infringements on freedom; COVID had augmented these perceptions (Jackson et al., 2023b). These discourses link to earlier qualitative findings outlined above where participants viewed medication prompts as patronising interventions and preferred unaided cessation. A pharmaceutical distrust persists (Vestbo and Anderson, 2025), but the growing legitimisation of vaping as a consumer choice aligns with smokers' desire for autonomy (Gravely et al., 2021), suggesting a pathway to integrate flexibility in cessation offerings that respects self-governance while promoting harm reduction.

The meta-ethnography highlighted that smokers frequently attribute success to willpower, believing medication diminishes personal agency. Since then, this belief has ebbed and flowed. During the pandemic and amid debates over vape regulation, willpower regained prominence as a social virtue. Consequently, medication adherence remains challenging: smokers often discontinue treatments when their resolve weakens, perceiving pills or patches as conflicting with self-discipline. To counter this, interventions must reconceptualise medication, not as a substitute but as a reinforcement of willpower. Supporting autonomy while normalising pharmacotherapy could enhance adherence in future stop-smoking pathways.

In order to integrate these changes within the meta-ethnography, a further literature search was undertaken during June 2025 which identified a further five qualitative studies (Table 5) providing important insights that both support and expand upon findings from the initial meta-ethnography. These studies reveal both continuity and evolution in smokers' attitudes, shaped by newer cessation tools, changing health contexts, and broader public health discourses. Together, these studies suggest that while fundamental themes remain consistent, such as agency, trust, and perceived necessity, emerging narratives around e-cigarettes, co-morbidity, and participatory design are reshaping the landscape of TDM acceptability and adherence.

Table 5 Qualitative studies published after the initial meta-ethnography

Author	Country	Key relevance to the meta-ethnography
Shiratani *et al*. (2024)	Japan	Reinforces the original meta-ethnographic themes of habitual smoking as culturally ingrained and quitting as a personal responsibility. Participants' scepticism about medication, shaped by beliefs in natural recovery and willpower, resonated prior findings. However, this study adds a sociocultural layer specific to Japanese norms of endurance and stoicism, broadening the applicability of meta-ethnographic conclusions across cultures.
Rojas *et al.* (2025)	United States	Provides novel insight into perceptions of e-cigarettes in formal cessation services. Unlike earlier studies where TDMs were framed as external aids conflicting with identity, e-cigarettes were often seen as bridging personal agency and medical support. This suggests a shift in how nicotine delivery technologies are conceptualised, aligning better with smokers' autonomy-focused narratives identified in prior meta-ethnographic themes.
Trigg *et al.* (2024)	Australia	Underscores structural barriers to TDM use among individuals in addiction recovery. Although similar to earlier findings of mistrust in pharmacotherapy, their study situates adherence within systemic constraints (e.g., lack of tailored support post-discharge), offering a more institutional critique absent in earlier syntheses.

Gittleman *et al.* (2024)	Germany	Highlights how comorbidities, such as cancer, further complicate attitudes toward TDMs. Safety concerns, low perceived relevance, and medication fatigue contribute to ambivalence, mirroring earlier concerns about side effects but emphasising the role of medical complexity.
Dyson *et al.* (2023)	UK	Emphasises co-design and service-user engagement, showing how relational and participatory approaches can reshape attitudes toward pharmacological support. Their findings directly challenge the "top-down" perception of TDMs found in earlier meta-ethnographies, pointing to the need for culturally sensitive and collaborative cessation strategies.

Integrating these five recently published qualitative studies, with the earlier meta-ethnography revealed important developments in understanding smokers' treatment preferences, barriers to medication adherence, and evolving cessation behaviours. The original meta-ethnography identified several core themes: distrust of pharmacological aids, the valorisation of willpower, concerns about side effects, and a preference for unaided cessation rooted in autonomy and identity. Each of the new studies builds upon these themes while also expanding them in light of changing contexts.

Beliefs in self-discipline and quitting "naturally" persist globally, highlighting how cultural values shape medication aversion (Shiratani et al., 2024). This study resonated with the original meta-ethnography's finding that many smokers view quitting with medication as undermining personal strength or authenticity. As e-cigarettes are generally accepted as less harmful than tobacco, this may be considered a desirable harm reduction strategy. However, the health effects of long-term e-cigarette use remain unclear. They are often framed not as a "treatment" but as a lifestyle adaptation, making them more congruent with smokers' identities, a contrast to how prescription medications

were problematised in earlier studies. A shift toward e-cigarettes and user-involved service design represent new, more acceptable forms of support (Dyson et al., 2023) and (Rojas et al., 2025). E-cigarettes appear to blur the line between pharmacological aid and behavioural choice. Studies deepen the discussion by situating medication adherence within complex social and health contexts (Trigg et al., 2024). Smokers managing co-occurring substance use or cancer express concerns about TDM safety, priorities, and relevance (Gittleman et al., 2024). These studies suggest that adherence is not solely about belief systems but is influenced by competing health concerns and institutional settings, gaps in the original meta-ethnography's more individual-centred focus.

Together, these newer studies indicate that while themes like willpower and mistrust of TDMs endure, the landscape is shifting. Acceptance of alternative nicotine delivery systems, involvement in service design, and recognition of structural and health-specific barriers suggest a more nuanced, context-sensitive understanding of adherence. Future cessation interventions must balance support with autonomy and tailor medication messaging to diverse life circumstances. Since 2014, several significant social, political, and technological shifts have influenced smoking behaviours, public attitudes toward tobacco dependence medications (TDMs), and healthcare engagement. These developments are important to consider when interpreting or updating the findings of a meta-ethnography focused on adult smokers' experiences and beliefs. During the Johnson premiership (2019–2022), political rhetoric often challenged perceived state interference in personal choices. This reinforced resistance to public health campaigns and medical interventions, especially among those who value individual autonomy. The rise of social media and mistrust in government health messaging, particularly among ethnic minority groups and lower-income populations, has altered how people interpret medication information (Zarocostas, 2021). Misconceptions about safety and side effects of TDMs may now be more deeply rooted or reinforced by online peer networks rather than healthcare professionals (Badje et al., 2021). Zarocostas (2021) describes the "*infodemic*" phenomenon during the COVID-19 pandemic, where misinformation proliferated via social media, and notes its damaging effects on public trust in government health messaging. Mistrust rooted in

perceived contradictions and politicisation of health information undermines public engagement with health guidance, including preventive services. Badje et al. (2021) provide empirical evidence that smokers in the UK are more likely to hold negative beliefs about biomedical interventions, driven by mistrust in authorities and concerns about commercial motives. This mistrust is associated with hesitancy toward vaccination and may parallel scepticism toward smoking cessation medications or health provider advice. For policy and clinical practice, these findings highlight how social media-fuelled mistrust can directly impair medication adherence and reduce the effectiveness of cessation programs—suggesting a need for tailored, transparent communication strategies that rebuild trust and engage smokers meaningfully with evidence-based cessation aids.

The growing popularity of vaping, particularly among younger and mid-life adults, has reshaped public and individual perceptions of smoking cessation tools. Many smokers now perceive vapes as more acceptable, accessible, and less medicalised than TDMs like varenicline or NRT, often describing them as lifestyle products rather than health interventions. This shift challenges earlier narratives of reliance on "formal" medications and repositions the role of willpower, self-regulation, and autonomy in cessation efforts.

As outlined above, the COVID-19 pandemic (2020–2022) heightened public awareness of respiratory vulnerability, particularly among smokers. For some, this triggered quit attempts, but for others, it reinforced stress-induced smoking or mistrust in government and pharmaceutical messaging, factors that can negatively influence adherence to cessation medications (Gravely et al., 2021). It also amplified digital inequalities, influencing how different social groups accessed cessation services (ONS, 2024). While, the UK has seen growing income inequality and austerity policies since 2014, most recently a cost-of-living crisis has exacerbated the pressures felt by those in most deprived circumstances, who are also most likely to be smokers (Onwuzo et al., 2024, Williams and Green, 2024). These pressures impact access to medications, prioritisation of health behaviours, and levels of trust in institutions. Smokers in deprived communities may increasingly reject medicalised

cessation support or feel underserved by NHS Stop Smoking Services. In turn, this influences attitudes toward taking prescribed medications for smoking cessation, with some smokers favouring unaided quitting to maintain personal agency.

These developments suggest that a meta-ethnography based solely on pre-2014 studies may underrepresent emerging cessation behaviours, the social legitimacy of vaping, and growing institutional mistrust. An updated synthesis should account for these shifts, perhaps incorporating studies from the COVID-19 era and post-2015 qualitative research to enhance contemporary relevance and transferability. Incorporating these post-2015 studies into the meta-ethnography would enrich the analysis, capturing transformative social narratives around vaping, pandemic response, and evolving user identities.

CHAPTER 5 QUALITATIVE STUDY OF SMOKER'S PERSPECTIVES ON TOBACCO DEPENDENCE MEDICATIONS

This chapter presents the findings of a qualitative study exploring adult smokers' perspectives on tobacco dependence medications (TDMs) and their adherence during a quit attempt supported by an urban NHS Stop Smoking Service. Understanding how individuals engage with or disengage from pharmacological support requires a close examination of the beliefs, meanings, and lived experiences that shape their smoking cessation journey. While medication adherence is a well-documented challenge in public health, its specific dynamics within smoking cessation remain underexplored and are often oversimplified through biomedical or individualist lenses. This chapter adopts a medical sociological and behavioural lens, investigating why adherence to TDMs remains suboptimal despite their clinical efficacy. It foregrounds smokers' voices to illuminate how cultural expectations, prior quit experiences, perceived medication utility, and relationships with healthcare systems interact to shape decisions around medication use.

The study employed a flexible, inductive qualitative design situated within an interpretivist paradigm and underpinned by *PRIME,* a motivational framework that accounts for the real-time, shifting interplay of motives, impulses, plans, and evaluations. Data were collected through semi-structured interviews and analysed using thematic analysis (Braun and Clarke, 2013), allowing for rich, in-depth exploration of meaning-making around medication adherence. To enhance the translational potential of the findings, persona methodology was used in the latter stages of analysis. Personas—composite characters grounded in the coded data, were developed to represent archetypal smoker behaviours and belief profiles. These personas synthesised themes across cases, making the findings more accessible to practice and policy stakeholders, and illuminating the variability in smokers' motivations, trust, and support needs during quit attempts.

The chapter is structured into sections that provide the theoretical and methodological framework, including justification for thematic analysis and persona development. Describes the study design,

methods, sampling, and analytic process. Presents key findings as a set of interrelated themes, illustrated with participant quotations and introduces personas that reflect typical adherence pathways. offers a critical discussion of the findings and introduces a conceptual model (Figure 5) illustrating the layered influences on TDM adherence. In prioritising smokers' perspectives and constructing representative personas, this chapter provides valuable insight for designing more person-centred, contextually appropriate smoking cessation interventions.

5.1 The conceptual framework of PRIME theory

Smoking is not simply a rational behaviour but is shaped by moment-to-moment impulses and fluctuating motivation. Combined behavioural and pharmacological support is more effective than pharmacotherapy alone (Stead and Lancaster, 2016). Traditional "plans" to quit are often overridden unless real-time behavioural support is provided. Depressive symptoms can lower motivation to quit, and increase impulses to smoke, even among those with strong intentions (Beard et al., 2013b). While traditional behavioural models often assume a rational, linear decision-making process, *PRIME Theory of Motivation* (West, 2006) (*P*lans, *R*esponses, *I*mpulses, Motives, *E*valuations) recognises the fluctuating, moment-to-moment nature of motivation and behaviour, features especially salient in the context of SC and medication adherence. Effective cessation interventions must address not only knowledge and intentions, but also impulses, emotional needs, and environmental triggers (Hartmann-Boyce et al., 2021b). *PRIME* introduces a real-time model of motivation that better explains addictive behaviours like smoking than static models and that SC interventions need to respond dynamically to motivational states (Ubhi et al., 2015). It highlights that impulses and motives, not just intentions or evaluations, drive moment-to-moment decisions to smoke or quit and emphasises the need for interventions to target motivation at the point of action (e.g. cravings) (West, 2006). *PRIME* provides a realistic and dynamic model for understanding non-adherence and relapse. Effective cessation interventions must address not only knowledge and intentions, but also impulses, emotional needs, and environmental triggers. *PRIME* helps explain why motivation wanes, and how

ongoing behavioural support (e.g., via SMS, counselling) sustains quit attempts (Hartmann-Boyce et al., 2021b).

The utilisation of *PRIME* was essential to this qualitative study to provide a dynamic, real-time understanding of how smokers navigate medication use during quit attempts. *PRIME* offered a conceptual framework capable of accommodating the complexities smoker's decisions about using TDMs by illustrating how a person may plan to quit, evaluate smoking as harmful, yet still relapse under the pressure of immediate urges (Moan and Rise, 2005, West, 2006). Using *PRIME* helped guide data interpretation beyond static attitudes or beliefs, highlighting the importance of affect, internal conflict, and the interplay of conscious and unconscious processes in shaping adherence. It also provided a valuable lens to inform persona development and to link lived experience with theoretically grounded categories, allowing for more nuanced intervention design grounded in smokers' actual motivational landscapes. *PRIME* as a conceptual framework provided a comprehensive, dynamic model of human motivation and behaviour, making it particularly well-suited to understanding the complex and fluctuating processes involved in tobacco dependence, quit attempts and medication adherence.

PRIME situates smoking behaviour within the context of everyday decision-making, allowing the researcher to explore how social, emotional, and environmental influences impact motivation to quit and to adhere to treatment. This aligned with the PhD's emphasis on real-world applicability and the design of more responsive cessation services. The theory is uniquely valuable because it recognises that motivation is not static, but constantly influenced by changing desires, impulses, and opportunities. This dynamic framing helps explain relapse, inconsistent medication use, and the gap between intention and sustained behaviour. Medication adherence is a longstanding challenge, often oversimplified as a rational, compliance-based issue. *PRIME* allows for a nuanced understanding of non-adherence, highlighting how even well-intentioned smokers may not follow treatment plans due to shifting motives and internal conflicts, thus informing more personalised pharmaceutical care.

PRIME captures the interplay between individual agency and structural factors, enabling deep exploration of how cultural meanings, beliefs about medication, and identity shape both quitting and adherence behaviours. In summary, *PRIME* Theory provided a psychologically robust and sociologically sensitive lens through which to explore medication use and cessation, enhancing the analytical depth and translational value of this qualitative study.

5.2 Study design

This qualitative study is based on in-depth interviews with smokers attending an urban NHS SSS situated in a deprived area in Birmingham, UK between November 2014 and April 2015. The SSS was located in a densely populated, socioeconomically disadvantaged, and ethnically diverse community. The area had a high proportion of residents from South Asian backgrounds, particularly Pakistani, Bangladeshi, and Indian communities, alongside Somali and other African populations. White British residents were a minority. The area faced persistent health inequalities, including elevated smoking rates, high rates of cardiovascular disease, and poor mental health. Overcrowded housing, unemployment, and limited access to healthcare compounded these issues. Birmingham's NHS stop smoking services (SSS) have operated for over two decades, originating in 1999–2000, offering fully funded, locally accessible behavioural and pharmacological support as part of a longstanding national public health commitment. Birmingham's SSSs are delivered through GP surgeries, pharmacies, and community hubs, at the time of the study, were typically offering free behavioural support and 12 weeks of treatment, including nicotine replacement therapy, varenicline, or bupropion, with specialist advisers guiding smokers through quit planning, CO monitoring, and relapse prevention (NICE, 2008). The study aim was to uncover and understand adult smokers' TDM adherence from their own perspective; this methodological approach was selected as it allowed a flexible exploration of participants' experiences and beliefs (Silverman, 2011, Smith, 2008).

5.3 Recruitment and eligibility of study participants

A purposive approach was initially planned to recruit a sample of smokers aged over 18 currently engaged in quit attempts using TDMs. Purposive sampling is a non-probability method where participants are deliberately selected based on characteristics relevant to the research question, allowing for in-depth exploration of specific phenomena (Palinkas et al., 2015, Silverman, 2011). It's commonly used in qualitative studies to ensure information-rich cases contribute to theoretical understanding. Originally, a purposive sampling strategy was developed based on characteristics relevant to the research question (Ritchie et al., 2013) to ensure depth and richness in understanding participants lived experiences and the contextual factors influencing them. The inclusion criteria were defined as participants must:

- Be aged 18 or older.
- Be currently enrolled in the Birmingham-based NHS Stop Smoking Service hosting the study.
- Be making a new quit attempt (defined as a self-defined serious effort to stop smoking).
- Be using or have used a pharmacological stop smoking aid (e.g., NRT, varenicline, bupropion, or combination therapies) during the current or prior attempts.
- Have had at least one previous quit attempt involving pharmacological treatment.
- Willing to volunteer participation in the study.

However, eventually a convenience sampling approach was chosen, asking everyone accessing the SSS (detailed above) to participate if they fully met the above inclusion criteria. This decision was made due to practical constraints, for example, low numbers of people willing to participate, limited participant time spent at the SSS, study recruitment procedure via the SSS clinical team and the study recruitment advert being limited to the SSS building and not distributed in the local community (see Table 6 for participant demographics). Convenience sampling is a non-probability technique where participants are selected based on ease of access and availability (Etikan et al., 2016); in this study, this was their attendance at a specific NHS SSS clinic. Though cost-effective and time-efficient, it risks bias and limited generalisability as participants are too similar which reduces the range of

perspectives they can offer (Creswell, 2018, Ritchie et al., 2013) Participants received no reimbursement for taking part. Advertising posters (appendix 6) inviting smokers to discuss their opinions about TDMs were placed in the SSS 2 months ahead of recruitment. The SSS SC Advisers asked for interested people to volunteer to take part; eleven smokers from a White British ethnic background volunteered; a convenient appointment with myself, the researcher, for each study volunteer was arranged by the SC adviser and they were given a *Participant Information Sheet*. It is well recognised that white people tend to be more likely to take part in research due to a mix of structural, cultural, and historical factors. Studies show that mistrust of research, rooted in histories of exploitation and unethical treatment, reduces participation among ethnic minorities (Farooqi et al., 2022). Additionally, research recruitment often relies on networks, institutions, and communication styles that align more closely with white, middle-class populations. Language barriers, lack of representation among researchers, and culturally insensitive study designs further alienate diverse groups. Evidence highlights that without deliberate strategies, such as community engagement, inclusive methods, and reflexivity, research remains skewed toward white participants, limiting its relevance and equity (Lloyd et al., 2008).

Participants were formally enrolled into the study after an initial appointment with the SSS advisor where they had selected their TDMs. In line with clinical SC support, this was ahead of their quit date in Week One of their behavioural support group (NCSCT, 2019), with the aim to obtain interviews four weeks after their quit date. Recruitment aimed to obtain enough data to sufficiently describe the phenomenon of interest and address the research question (Silverman, 2011) (Pope and Mays, 2020). As a PhD student conducting an unfunded and time-limited qualitative study, I had a time window of 3 months for recruitment and enrolled all eleven participants that volunteered during this time with no further attempts at recruitment, deciding that they were sufficient to provide a broad range of experiences with stop smoking medications and insights regarding medication adherence. The study aimed to explore in-depth experiences rather than achieve data saturation, which was not feasible within the timeframe. While saturation is often a standard goal in qualitative research (Saunders et

al., 2018), my focus was on capturing a range of perspectives within realistic study boundaries. This decision allowed for meaningful analysis while acknowledging the methodological limitations imposed by the study's scope and available resources.

Table 6: Characteristics of study participants

Characteristic	**n=11 participants**
Mean age, years (SD) (range)	47 (11.27) (31-65)
Gender, percent (number of participants)	
Female	55% (n=6)
Male	45% (n=5)
Ethnicity, percent (number of participants)	
White, British	100% (n=11)
Age of smoking initiation, years (range)	15 (13-17)
Fagerström score, percent (number of participants)	
7 to 10 points = highly dependent	82% (9)
4 to 6 points = moderately dependent	18% (2)
less than 4 points = minimally dependent	0% (0)
Number of cigarettes smoked per day, percent (number of participants)	
10 or fewer	0% (0)
11-20	18% (2)
21-30	18% (2)
31 or more	64% (7)
Number of cigarettes smoked per day (cpd), Mean (range)	32cpd (20-60)
Time to first cigarette of the day, percent (number of participants)	
<5 min	36% (4)
5-30 min	45% (5)
31-60 min	18% (2)
>60 min	0% (0)
Ever used nicotine replacement therapy in attempt to quit percent (number of participants)	
Yes	8 (73%)
No	3 (27%)

Ever used pharmacotherapy (varenicline *(Champix*) or bupropion (*Zyban*) in attempt to quit percent (number of participants) Yes No	 10 (91%) 1 (9%)
Number of previous quit attempts, total for cohort, Mean	40 (4)
Adherence behaviour group, percent (number of participants) Group A: fully adherent Group B: partially adherent Group C: nonadherent	 55% (6) 27% (3) 18% (2)
SC medication used to aid their current quit attempt, percent (number of participants) NRT (any form of NRT such as gum, patch, inhaler, tablet/lozenge, nasal spray) Champix Zyban No SC medication	 18% (2) 73% (8) 0% (0) 9% (1)

5.4 Interviews

Data was collected between November 2014 and April 2015. An initial meeting was set up with each participant, prior to arranging a date and time for the face-to-face interviews in which participants consented, in writing, to the study after full explanation of what was involved. All the interviews were conducted by CJS. A short survey was completed by participants before the start of the interviews to gain insight into their demographic characteristics, TDM use, smoking history and TD (assessed using the Fagerström Test for Cigarette Dependence (FTCD) (Heatherton and Fagerström, 1991)). An interview guide (appendix 7) was developed to explore how the views, beliefs and experiences of adult smokers shaped their adherence behaviours. The interview guide was designed to provide structure and direction to the interview to ensure that relevant data was collected. The interview was semi-structured and allowed a range of questions to be asked but also enabled flexibility for a wide range of responses. It enabled probing into topics raised and did not restrict the interview to only pre-determined questions, providing opportunity for participants to reply in their

own words about their experiences (Bowling, 2009). The interview schedule was mostly open-ended questions, allowing the interview to adopt a neutral position; the questions were derived from integrating knowledge and concepts from the existing literature regarding TDMs and adherence behaviours with medications. Utilising an interview schedule enabled a focus on the study's purpose and allowed the participant to speak freely about his/her attitudes, experiences, perceptions and beliefs. I endeavoured to remain as neutral as possible and avoided leading questions so that any influence on the interviewee's response was minimised. At interview the researcher explored experiences, perceptions and understandings of TDMs and how these affected adherence behaviours. Topics included thoughts about TDMs, past and current experiences with TDMs, and the most appropriate way for SC health professionals to help the respondent and other smokers adhere to TDMs. Participants were encouraged to say what they really felt and not to worry about whether or not this would be acceptable to the researcher. Interviews lasted up to 90 min in a private room within an NHS SSS and were audio recorded. The main topics were experiences, views, meanings and beliefs held about TDMs and e-cigarettes, barriers to adherence and suggestions for reducing these barriers. Questions were guided by concepts from *PRIME* Theory, for example asking for details of plans to quit or return to smoking and evaluative beliefs about smoking and TDMs.

5.5 Ethical considerations

Ethics committee approval was obtained from the following three bodies (i) NHS Health Research Authority (REC 13/SW/0173), (ii) the University of Birmingham and (iii) the NHS Sandwell and Birmingham research and development department. The study was approved by all three ethics committees. The approval process ensured that conducting the qualitative study within an NHS SSS was undertaken within ethical principles that safeguarded participants and upheld research integrity. Given the sensitive nature of SC and medication adherence, often involving personal health struggles, addiction, and behavioural change, I ensured informed consent before each interview appointment, confidentiality, and voluntary participation were rigorously maintained. Smokers were provided with a *Participant Information Sheet* during their SSS clinic visit outlining details of the study and the

opportunity to contact the researcher if they had any enquiries before confirming their involvement. All participants were assured of confidentiality, the anonymous processing of the data and that SSS staff did not have access to the data. The researcher (CJS) had no access to SC patient records. The researcher remained attuned to power dynamics, avoided coercion and ensured participants felt safe to share their experiences without judgment. Reflexivity was key: the researcher critically examined her own biases and positionality, especially when interpreting narratives around non-adherence or relapse. Data protection under GDPR was upheld via anonymisation and secure storage of transcripts and recordings. The researcher balanced the dual goals of generating meaningful insights and minimising harm, ensuring that participation did not exacerbate distress or undermine the participants quit attempt and that findings were used to improve service delivery and patient outcomes.

5.6 Analysis

Braun and Clarke's (2006) thematic analysis is a widely used qualitative method for identifying, analysing, and reporting patterns (themes) within data. This approach provided a flexible method for exploring the complex qualitative data with transparency and rigour. It consists of the following six recursive stages:

1. Familiarisation with the data: immersing oneself by reading and re-reading transcripts or texts, noting initial ideas.
2. Generating initial codes: systematically coding interesting features across the dataset, organizing data into meaningful groups.
3. Searching for themes: collating codes into potential themes, gathering all relevant data for each theme.
4. Reviewing themes: checking themes against coded extracts and the entire dataset to ensure coherence and distinctness.
5. Defining and naming themes: refining specifics of each theme, identifying the essence and generating clear, concise names.

6. Producing the report: weaving analytic narrative with data extracts to tell a compelling, coherent story addressing the research question.

Transcripts were imported into NVivo software for coding, using Braun and Clarke's thematic analysis method (Braun and Clarke, 2006). Step 2 of the process included (i) generation of initial descriptive content codes and (ii) consolidation of codes in 'higher order' analytic themes to produce an interpretation (Saldana, 2013). Steps 3-5 involved grouping codes into themes, systematically interpreting patterns and relationships within the data to develop a conceptual framework that explains the phenomenon under study. Through iterative analysis, these themes were examined for connections, hierarchies, and causal links. Once themes were developed, participants' accounts were further interpretated using the elements of *PRIME* theory. This means that the analysis was both inductive, from the accounts (experiences and views) of participants, and deductive, through being informed by the conceptual framework of *PRIME* theory (also reflected in the study objectives and the topics chosen for the interviews) as well as the existing literature. Several drafts of the analysis were generated and reviewed / reworked until interpretation was agreed by the researcher and supervisors. I then abstracted these findings into a visual or narrative model (Figure 6) that represents the key constructs and their interactions. The model aims to offer a coherent, evidence-based explanation grounded directly in the study participants' experiences it was created following the data analysis process which involved systematically interpreting patterns and relationships within the data to develop a conceptual framework that explains the phenomenon under study. This process began with coding raw data, followed by grouping codes into themes or categories. Through iterative analysis, using thematic, these themes were examined for connections, hierarchies, and causal links.

To assure methodological rigour, the researcher undertook an "audit trail" outlining decisions made throughout the process of data collection and analysis (Lincoln and Guba, 1985) and documented their discussions on coding and analysis of data as a method of checking plausibility of emerging themes, the paths taken to arrive at those themes and data interpretations (Braun and Clarke, 2013,

Silverman, 2011). In addition, the transcribed data allowed all authors to revisit the text to check emerging themes and ensure that they remained true to participants' accounts. Details of demographics, smoking characteristics, TDM and adherence history are described in Table 2 allowing readers to contextualise participants' responses. COREQ guidelines were followed in reporting the methods (Tong et al., 2007). I abstracted these findings into a visual or narrative model that represents the key constructs and their interactions. This model offers a coherent, evidence-based explanation grounded directly in the study participants' experiences.

The use of personas was employed as a methodological tool to synthesise qualitative interview data and represent the diversity of SC medication adherence behaviours (Dominello et al., 2025). Personas are composite fictional characters grounded in real data, developed to reflect recurring beliefs, experiences, motivations, and barriers expressed by participants. This approach aligns with interpretivist qualitative research principles, where meaning is co-constructed through thematic analysis and then translated into narrative-driven representations of lived experience (Haldane et al., 2019). The personas were developed after thematic coding of interview transcripts using a framework guided by *PRIME* and sensitised to sociological constructs such as stigma, agency, and healthcare relationships. Each persona was not a reproduction of a single participant, but rather an analytical distillation of common behavioural patterns and belief systems observed across multiple interviews.

Key dimensions used to build the personas included: stage of change, motivation to quit, trust in pharmacotherapy, experience with NHS services, and perception of tobacco dependence. This method allowed the complex, nuanced narratives of individual participants to be presented in an accessible, theory-informed form that could inform practice and policy. For instance, one persona, "*the sceptical relapser*", captured individuals with low trust in medications and high reliance on willpower, highlighting the need for trust-building and reframing support approaches. Another persona reflected service-engaged individuals who required ongoing motivational support to sustain adherence. The use of personas provided a translational bridge between raw data and the design of

tailored interventions. It facilitated stakeholder understanding, especially among practitioners and policy audiences, by humanising abstract themes and illustrating the heterogeneity of smoker experiences and adherence behaviours within real-world service settings.

5.7 Results

As outline above, eleven adult smokers registered with an urban NHS SSS participated in the study. The participants were all long-term, highly nicotine dependent smokers who had failed several previous SC attempts and had a varied adherence history with TDMs. All participants stated that they were motivated to quit and had chosen to use TDMs to support their quit attempt. The process of defining and labelling the themes was guided by the study objectives, PRIME Theory and new concepts developed inductively from the data. Key themes identified in our data were mapped against motivational reasons that may have influenced non-adherence. There was consistency between the study themes and the concepts of *PRIME* Theory i.e. plans, responses, impulses and inhibitory forces (urges), motives (feelings of want or need) evaluations (evaluative beliefs) and the findings of previous research. The central analytical focus, however, were the original, previously unreported themes in our analysis. When grouped, these indicated four new processes that could help explain TDMs adherence behaviours:

1. Evaluating TDMs;
2. Planning to use TDMs;
3. Available support;
4. Experiential learning.

5.8 Evaluating TDMs

PRIME theory states that "we arrive at evaluations through a process of generalisation and deduction". Participants reminisced about their smoking in positive and negative terms which

influenced their acceptance of TDMs. Cognitions about SC were deeply embedded in participants' experiences which evoked their emotions, shaping their ideas about TDMs.

> *"I've got the NRT, why do I need it? I ask myself, why?" (P4)*
>
> *"…I need to have something to help me stop…" (P8)*

TDM experiences led participants to believe that they were not a complete solution; mostly owing to TDMs' inability to stop NWS. Participants' beliefs had both positive and negative dimensions which affected motivation to use TDMs. Participants' evaluations of TDMs were expressed as conflicting emotions and beliefs while reflections on past quit attempts motivated participants to use TDMs. Reflections on past relapses also motivated participants to use TDMs. Beliefs about TDM evolved over time increasing confidence in TDM efficacy.

> *"I think with things like Champix in the past, I didn't do what I was meant to do because I found it too hard...' (P14)*

Most participants articulated strong fears of TDM use (e.g. side effects, dependency). They assessed the risks and benefits of TDMs within their psychosocial context: these TDM evaluations were an important facet of TDM adherence:

> *"…it was so hard, with the mood swings and stuff like that, and I felt really down when I was on the Champix (P2)*
>
> *"…perhaps if I had more motivation, I may have had more tolerance to the side-effects, but when I look back on it I just think it was a horrible experience". (P6)*

This indicates that HCPs should tailor their TDM advice in line with an individual's beliefs to increase TDM adherence.

5.9 Planning to use TDMs

Plans, according to *PRIME* "allow for behaviours to be deferred according to priorities or anticipated opportunity or threat (Michie and West, 2013). The process of planning seemed more important to some participants than the plans that emerged; it provided smokers with "thinking time" about past failed quit attempts. They were frequently challenged by the pressures of addiction to cigarettes which undermined adherence.

> *'This is really hard. I'm struggling. I think on Saturday I'm going to go out and have a few drinks. I won't wear a patch, and I'll smoke.' (P7)*
>
> *"I can't do it without them. So, I guess to me they're essential. I feel that I couldn't cope without the patches, or the lozenges now, but having said that, I'm quite dependent on them. (P1)*

TDM use reflected participants' (i) realisation they needed TDMs in order to implement their desired behaviour change in the face of conflicting wants, needs and urges; (ii) understanding that TDMs provided a way forward that minimised NWSs and (iii) required a shift in deep identity - from smoker to non-smoker.

> *"... the mistakes that I've made, I've rectified them this time around, whereas in the past I used to leave it too long in the morning before having any NRT..." (P5)*

In contrast, participants' who were not fully committed to SC made choices in the way they used TDMs that enabled them to smoke.

> *"I'd smoke through the Champix and make myself feel really ill, and then I'd think, the next day, 'Oh, well, I gave in yesterday. I'm not going to take them [sic Champix] today,' and I'd deliberately not take them (P2)*

Partial adherence, described by some participants, occurred in response to impulses or urges to smoke. Participants then made independent decisions about increasing or decreasing their TDM

doses. Planning activities emerged as useful to achieving TDM adherence. *PRIME* identifies that acting in pursuit of what we most want and need is a central feature of addictive behaviour (West and Brown, 2013). Participants deviated from their plans to use TDMs in response to various stimuli, commonly the urge to smoke, habit, psychosocial factors e.g. significant others, negative emotions:

"I'd deliberately not take Champix for a couple of days because I wanted to smoke…"(P11)

Participant narratives revealed the importance of coping, reassurance and predictability that came with having a cigarette. These needs were not fully replaced by TDMs. They suggested that the prerequisites of an effective TDM was that it replaced the cigarette niche in their life. Conversely, as none of the participants wanted to be viewed as an addict, they believed TDMs should not have characteristics of a cigarette or contain "the enemy" nicotine. All participants were aware of e-cigarettes, and a predominant narrative was that they wanted certainty about their safety and role within SC. Two participants felt that e-cigarettes mimicked smoking a real cigarette and believed that that the use of them was either ineffective or an indication that a person was not ready to quit smoking.

"…these e-cigarettes, and I've been told that because there's been no research into them no one really knows how effective they are or what they do to you…what damage they can do in the long run…I personally don't see them as a replacement, although others obviously do because they are stopping with them..." (P2)

"Before I started out on the patches, I wanted to do the e-cigs, because I'd heard so many good things about them. But it was the fact that they weren't licensed that put me off..." (P3)

"It makes no difference whether it's an e-cigarette or a Benson and Hedges, you're still doing the same habit…" (P6)

Participants did not recognise that their adherence was "poor" in clinical terms, and it was not given as the reason for the difficulties of SC. Participants conveyed how they had actively selected different

TDMs over the course of their journey to stop smoking. They expressed a limited confidence in TDMs with anger and/or denial about their smoking addiction. Some said they quickly stopped TDMs in response to side effects and worried about replacing their addiction to cigarettes with an addiction to medication. These converging cognitions destabilised TDM adherence. Participants displayed differing opinions regarding TDMs; some believed that they were essential to their SC plans, whereas others did not. Most participants held negative views towards TDMs stating that they were concerned about the side effects and were not confident about TDM efficacy. Some participants also held expectations that TDMs were a "quick fix" for their smoking addiction, believing it was their last hope for becoming a non-smoker. Others liked the relief and confidence TDMs provided. Participants' past experiences of TDMs helped to build a schema that was drawn upon to form plans for their subsequent quit attempts. This meant that plans to use TDMs were affected by what happened around them which determined their TDM adherence behaviours.

5.10 Available support

All participants' TDM adherence behaviours were influenced by various social interactions. TDM adherence involved positive (supportive) behaviours by their social circle, such as shared decisions about which TDM to use, and reinforcement such as agreement on how to use TDMs.

> *"We both said that if we were going to do it, it would be with Champix. I think we both see it (Champix) the same way. It's just a tablet. Pop it, finish for the day, sort of thing. Get on with it". (P4)*

In contrast critical (negative) behaviours, such as challenging the participant's smoking, shared complaints/concerns about TDMs or agreed decisions to smoke, led to poor adherence. Family context and cohabitants' smoking status (social support) were influential to participants' SC attempts and decisions regarding TDMs access and adherence behaviour.

"smoking has been my thing and a lot of people round me that have said, oh you know, especially my partner, 'Oh, it is easy to give up, you just make a choice'… to them that might be possible but I find it incredibly difficult to give up without some support. (P7)

Some participants portrayed chaotic lives, carelessness with TDM use and intentional non-adherence. Participants reported stress, conflict and anxiety because of trying to rationalise smoking with family members' concerns regarding the dangers and harms associated with smoking. Participants' addiction to smoking had many significant and enduring impacts on family dynamics and functioning. A greater role for family support might be considered regarding supporting use and adherence with TDM regimens. PRIME theory states that environmental cues can influence the decision to smoke by triggering impulses. SC support accessed by participants influenced TDM adherence behaviours. Most participants were inspired to make a quit attempt by the Stoptober campaign (PHE, 2018) which provided a supportive social context to attempt to quit. Participants found accessing the SSS helpful in providing support to their TDM use. The SSS role was a place to access TDMs but also met participants' social and emotional support.

"When she'd explained what patches did… what Champix did, because she was telling me that you just take a tablet and then it makes you stop smoking, I thought, 'Great.' So that choice was made by the information that she'd given me at the clinic." (P2)

Narratives contained several interactions with HCPs that were very positive and a main source of advice regarding the selection and management of TDM, side effects and regimen modification. However, not all interactions with HCPs were positive. One participant was frustrated that although he did not want to use NRT, the SC adviser issued it regardless:

"I did say to the SC Adviser that I didn't want any medication and she said, 'But when the nicotine receptors in your brain start crawling round for nicotine, you're going to find it very,

very hard'. That's the only thing I disagree with her about. I think she could probably find out more about the person, before shoving the medication at them" (P6)

Another participant recalled a negative experience regarding access to his Champix prescription, the HCP was perceived as unhelpful and unfortunately the participant returned to smoking. Most participants preferred having an active role in TDM decision making which had important effects on adherence:

"I tried again, about three years ago, on Champix... Every time I'd go the prescription wasn't ready or he couldn't see me or he was really busy, so I'd go two, three days without having anything at all. So, I just automatically started smoking again…I think if he was more reliable, I don't think I would be smoking now..." (P4)

5.11 Experiential learning

Participants described in detail their smoking addiction and struggles to stop; this formed a highly negative context for achieving adherence to TDMs. They all had unique histories and relationships with TDMs which shaped their adherence behaviours. Learning from experiences with TDMs led to an increased perception of their role with reducing NWSs; this strongly influenced participants' TDM adherence. When a TDM stopped urges to smoke and NWSs, participants were more likely to persist with TDMs.

"…what I've learnt from the two failures before, is that you must complete the course…" (P7)

"what I did learn about the Champix, I found that there was a learning curve…don't ever think that it is a magic pill; it's not a magic pill, but what it does is, it's a blocker." (P7)

"I'm starting to learn more how they (NRT patches) affect me and how I need to do it, to change it, do you know what I mean..." (P4)

While participants acknowledged TDM benefits, they held strong concerns about dependency and side effects. They described how TDMs added to their problems, particularly noting the experience of intense emotions or unpleasant bodily effects caused by TDMs. The most common reasons given for not taking TDMs were side effects, forgetfulness, deciding to omit a dose, other priorities and emotional reasons which caused changes in physical or mental status. Previous experiences with TDMs that generated unpleasant side effects delayed future initiation of TDMs; significantly some participants associated TDMs with a failed quit attempt that made them feel horrible.

> *"I felt really down when I was on the Champix (P2)*
>
> *"I think for me it didn't help to know that it was blocking the nicotine, because that just made me think, 'Oh, I'm going cold turkey." (P9)*

> *"I think with the Champix it's blocking me getting nicotine, but with these patches, they're giving me nicotine" (P11)*

Asking participants to talk about how they found out about TDMs provided new insights into why TDM adherence is often poor. There exists a disjoint between smokers and HCPs about TDM efficacy; participants' adherence was strongly influenced by their experiential learning rather than advice they received from HCPs. The experiential learning of TDMs formed participants' judgements of TDM efficacy; adherence behaviours were susceptible to participants' experiences.

> *"When you use Champix, you get up in the morning and you haven't got the urge for a cigarette…I can't describe it, it's just weird. They are the best thing ever." (P6)*

Participants had limited faith (confidence) in TDMs, exhibited anger or denial about their addiction and quickly rejected TDMs in response to side effects experienced.

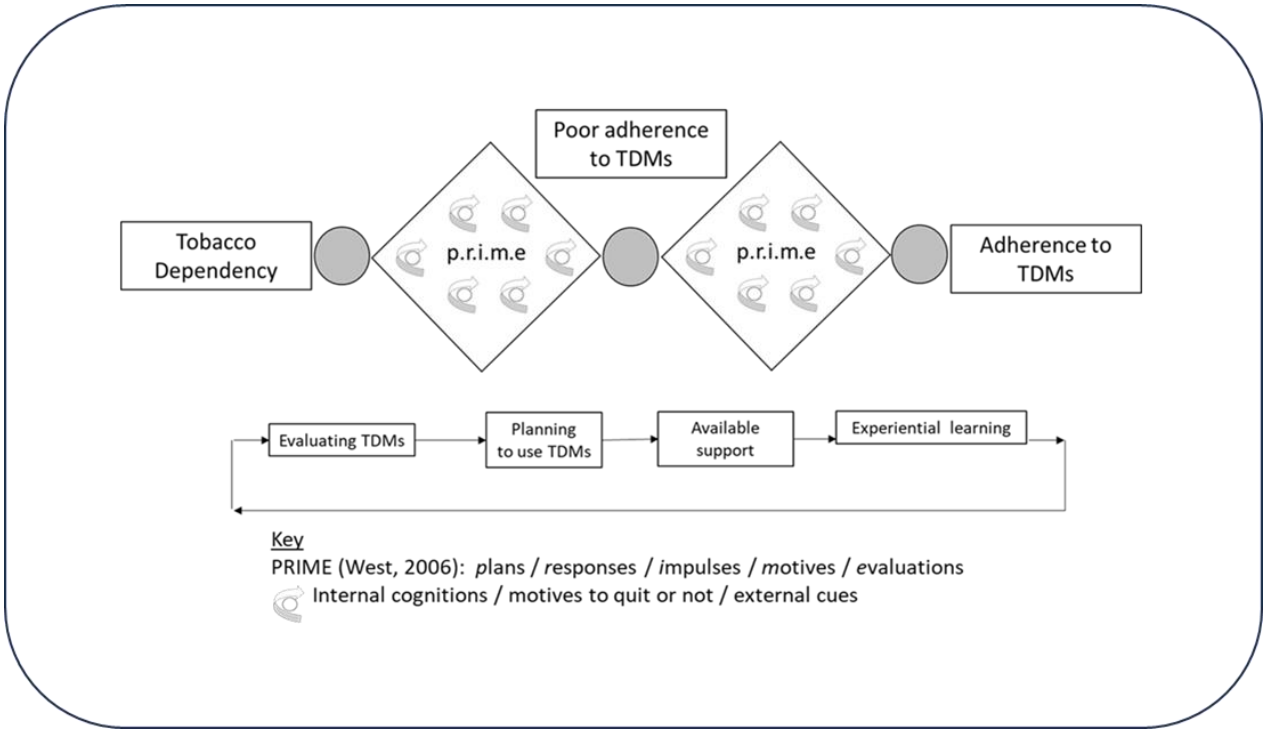
> *"Champix, I found them potent, and I didn't like putting them into my body because of what they did to me, in terms of not feeling well, and the mood and the stomach problems. (P5)*

All participants expressed a strong view of not wanting to replace their addiction to cigarettes with an addiction to TDMs. These converging cognitions were key deterrents to TDM adherence. Participants were unable to express their behaviours in the same terms as HCPs; adherence was not a concept/term they knew. In stressing the negative aspects and addictive potential of TDMs, participants expressed views about TDMs that opposed medical knowledge of TDM benefits.

5.12 Conceptual model

Incorporating the conceptual framework of PRIME theory with the four themes found in the present study, we conceived a model of smokers' TDM adherence (Figure 6). The model depicts the dynamic cognitions and complex processes that, within the context of TD, affect adherence; this model may be helpful to SC policy and clinical practice guideline formulation. This model seeks to help optimise adherence with TDMs and contribute to improving the desired outcomes of SC and avoidance of pharmaceutical waste. Improving the ability to properly assess the risk of TDM non-adherence and deliver interventions aimed at reducing this, may lead to improved SC outcomes.

Figure 6: A model of smokers' TDMs adherence



5.13 Smokers' beliefs about how to stop smoking

As with most smokers (Sanders et al., 2019, Edwards et al., 2014), unassisted quitting was perceived as the optimal way to stop smoking. A history of failed quit attempts caused participants to feel inadequate and frustrated that their willpower alone had not enabled them to quit. Motivation, willpower and commitment have been found to be important to smokers who quit without TDMs (Smith, Chapman, & Dunlop, 2015); all participants understood that those factors affected their SC success. Utilising beliefs about the importance of willpower in SC clinical interactions may be important to improving TDM adherence. Participants were distressed about their smoking addiction and this transferred into fear of becoming dependant on TDMs. Participants' rejection of TDMs, influenced by strong beliefs in unassisted quitting, has been found in other studies (Morphett et al., 2015, Smith et al., 2015b). This belief augments concerns about TDMs and is a factor in poor TDM adherence.

5.14 Evaluations of TDMs

PRIME Theory emphasises plans to develop strategies that assist smokers with quitting smoking. Planning emerged as an intrinsic part of achieving TDM adherence. This study found many complex influences leading to poor TDM adherence. According to *PRIME* Theory, an individual's evaluations inform their motives and intentions to plan a certain course of behaviour. Participants' evaluations, critically of their smoking addiction and past failed quit attempts, eventually led to learning about the role of TDMs and to acceptance that medication was important to their SC solution. Participants cited the inability of TDMs to stop cravings (impulses and urges) for a cigarette as the reason for stopping TDM use. Over time, participants transitioned from unfamiliarity and rejection of TDMs towards critically accepting the role of TDMs in undoing their addiction. The main driver of this transition was experiential learning from past failed quit attempts. This led to acceptance of the need to prevent/respond to impulses to smoke with TDMs.

5.15 Poor TDM adherence

This study found that participants commonly did not use TDMs in accordance with clinical recommendations is consistent with evidence from other studies (WHO, 2003, Balmford et al., 2011, Shiffman, 2003). Poor TDM adherence increased participants' experience of NWS which further weakened perceptions of TDM efficacy. Deliberate non-adherence mostly occurred owing to relapse to smoking; the lived world of nicotine addiction undermines TDMs adherence. Poor TDM adherence has been explained in other studies as being due to: a high level of dependency (Fagerstrom and Hughes, 2002), low mood (Ginsberg et al., 1997), concerns about side effects and future adverse effects (Pacek et al., 2018) and nicotine withdrawal symptoms (Alterman et al., 1999, Gourlay et al., 1994). Participants' attitudes towards TDM options were formed by several diverse, converging, dynamic issues. Participants expressed several concerns about electronic cigarettes (ECs) i.e. that they mimicked smoking, undefined safety, potential for nicotine dependence, and sought evidence of safety from HCPs. There is evidence that ECs help smokers to stop smoking in the long term compared with placebo ECs (Hartmann-Boyce et al., 2021c). The perceived role of ECs as a quit aid was uncertain amongst participants who had concerns about safety and nicotine dependence. This finding is contrary to current academic thought that ECs may have an important role in harm reduction (McNeill et al., 2018). Some participants, as with smokers in general (King et al., 2014), viewed ECs tentatively as being less harmful than smoking but were unsure of their efficacy as aids for SC.

Arguably, the current treatment approach has an overemphasis on the medical model, which underestimates the impact of complex TDM taking cognitions and behaviours that occur. Most participants depicted their smoking behaviour as a "response" (a concept of *PRIME* Theory), to external triggers (social influences) and internal cues (self-image). Participants' narratives revealed that their TDM adherence behaviours were underpinned by responses to complex psychosocial factors and addiction which caused impulsive and conflicted decision making. The study found considerable reluctance to take TDMs and a preference to take as little as possible for a short duration.

This may partly explain why adherence to TDMs has been found to be very low in the long term (< 40%) (WHO, 2003).

5.16 Experiences of TDMs

Participant's experiences of TDMs were deeply personal and their judgements were influenced by their individual context and personality. Improved TDM adherence may be facilitated by a greater emphasis on collaborative approaches that recognises the expertise of both the person attempting to quit smoking and HCPs. Participants did not passively accept what HCPs told them about the need for or how to use TDMs.

5.17 Personas of study participants

Personas, narrative-based, composite representations of user types—are increasingly used in applied health research and behaviour change design to translate qualitative findings into accessible, human-centred insights that support intervention development and service improvement (LeRouge et al., 2013, Pruitt and Grudin, 2003). Unlike traditional case studies or individual participant vignettes, personas are not literal depictions of single participants. Instead, they synthesise recurring patterns across a dataset into fictional yet plausible characters, crafted to reflect typical motivational, behavioural, and contextual profiles. In doing so, personas offer a practical and theory-informed way of maintaining the voice and complexity of the participant while facilitating engagement with policy makers, practitioners, and designers of cessation support.

In this study, the development of personas was informed by the thematic analysis of qualitative interviews with adult smokers engaged in an NHS SSS. Drawing on *PRIME* as the conceptual lens, the analysis focused on participants' shifting motivations, impulses, beliefs about medication, and relational experiences of cessation. Thematic patterns were carefully integrated with demographic and psychosocial characteristics to develop three contrasting personas, each representing a different trajectory of medication adherence and engagement with tobacco dependence treatments.

The personas were crafted as concise, narrative-driven pen portraits that embodied core attributes such as smoking history, character traits, emotional responses, treatment perceptions, and socio-cultural context. Particular attention was paid to how identity, previous quit attempts, structural barriers, and attitudes towards pharmacotherapy informed adherence behaviours. These personas highlighted the lived tensions between planning to quit and the pull of real-time impulses, and the role of trust, stigma, and service relationships in shaping the uptake and persistence with smoking cessation medications.

The use of personas in this qualitative study served both analytical and translational purposes. Analytically, they supported theory-informed synthesis across participants. Practically, they offered a compelling tool for communicating nuanced behavioural patterns in a way that is relatable, actionable, and aligned with person-centred intervention design. In doing so, they contribute to a more holistic understanding of the factors influencing TDM adherence in real-world contexts.

Personas were developed to expand and encapsulate key patterns and experiences emerging from participant narratives. They aimed to synthesise diverse perspectives into coherent, relatable profiles that illuminate variations in medication adherence and SC behaviours. Labelled as "*The Stoic Sceptic*," "*The Overwhelmed Caregiver*," and "*The Independent Realist*", they reflect differing motivations, challenges, and social contexts identified through thematic analysis:

1. **The Stoic Sceptic** represents individuals who view SC medications with suspicion and prefer to rely on personal willpower. They tend to downplay addiction severity, expressing doubts about the effectiveness or necessity of pharmacological support. Their stoicism often masks internal struggles, and they may avoid seeking help due to mistrust of medical interventions or a desire to maintain control.
2. **The Overwhelmed Caregiver** embodies those juggling multiple life stressors, such as caregiving responsibilities, work pressures, and financial constraints. This persona

experiences high levels of stress and limited personal time, which undermine medication adherence despite genuine motivation to quit. The complexity of their circumstances often leads to inconsistent use of cessation aids and feelings of frustration or guilt.

3. **The Independent Realist** is characterised by pragmatic acceptance of tobacco dependence and a balanced approach to quitting. They recognize the value of medication but emphasize self-management and personal responsibility. This persona engages with cessation treatments thoughtfully, weighing benefits and drawbacks, and adapts their strategies based on lived experience and practical considerations.

5.18 Persona James "The Stoic Sceptic"

James is a 58-year-old mechanic from a working-class background who has smoked for over 40 years. He began smoking at 16, and it quickly became part of his daily routine and identity. James had tried to quit multiple times, cold turkey, nicotine patches, and once with varenicline, but experienced unpleasant side effects, including vivid nightmares and nausea. Since then, he had developed a deep mistrust of SC medications, which he viewed as unnecessary "chemicals." James was highly nicotine-dependent, smoking around 25 cigarettes a day. Despite this, he insisted that quitting should be a personal test of willpower. He believed that "real men don’t need pills to quit." He’s proud of having once stayed smoke-free for six weeks without help and still talked about it as proof that he can quit, he just hasn’t found the “right time.” His approach is shaped by a mix of stoicism, scepticism about pharmaceuticals, and a generational belief in self-reliance.

5.19 Persona Angela "The Overwhelmed Caregiver"

Angela is a 45-year-old single mother caring for her elderly father and two teenagers. She started smoking during a stressful period in her late teens and now smokes about 20 cigarettes daily. Over

the years, she has tried various cessation methods, gum, patches, and even a mobile app-based program. However, she found the medications "didn't work for her," claiming they made her anxious and emotionally detached. Angela believes medications "mess with the mind" and fears becoming dependent on them. She is also wary of being judged by healthcare providers, having had past experiences where she felt pressured into trying medications she didn't trust. Though she desperately wants to quit for her children, she believes she needs a "clean break" and insists on quitting naturally. However, between caregiving responsibilities, work, and emotional strain, she never lasted more than a week without relapsing. She carried a sense of guilt and shame, compounded by her belief that failure means weakness.

5.20 Persona Derek "The Independent Realist"

Derek is a 62-year-old retired lorry driver who started smoking at age 13. He smoked about 30 cigarettes a day and openly described himself as "hooked for life," though he had made several serious attempts to quit. He tried nicotine replacement therapy (NRT) and prescribed medication but felt "manipulated" by the side effects, mainly mood changes and stomach upset. For Derek, the benefits of quitting didn't outweigh the perceived costs of taking medications that interfered with his sense of control. He distrusted the pharmaceutical industry, believing that companies "just want to keep you hooked on something else." Derek was pragmatic, he knew the risks of smoking, especially since he has early-stage COPD, but believed quitting is something he needed to "sort out on his own terms." He didn't want lectures or pills, he wanted practical support, someone to talk to who understood his addiction without trying to fix it with medication. He said, "I didn't need drugs to start smoking, I shouldn't need them to stop."

Together, these personas capture diverse attitudes and contextual factors affecting SC behaviours, highlighting the need for tailored support strategies. Further the persona's provide nuanced insights into the heterogeneous experiences and attitudes of smokers attempting cessation, highlighting important implications for tailoring stop smoking treatments and enhancing medication adherence.

The Stoic Sceptic reveals how deep-seated mistrust of pharmacological aids and a strong belief in willpower can undermine engagement with evidence-based cessation support. This persona illustrates the challenge of addressing psychological barriers rooted in self-reliance and scepticism toward medical models of addiction. Understanding this perspective suggests that interventions for such individuals must prioritise building trust, addressing misconceptions, and validating their autonomy, perhaps through motivational interviewing and peer-led support that respects their need for control.

The Overwhelmed Caregiver underscores how external life pressures, such as caregiving, financial stress, and time scarcity, can disrupt medication adherence despite high motivation to quit. This portrait exemplifies the importance of contextual factors beyond individual will, highlighting structural and social determinants of health. Treatment approaches for this group might involve flexible, low-burden support options, such as tailored reminder systems, practical aid for medication management, and integrated social services that address broader stressors, thereby reducing adherence barriers.

The Independent Realist represents a pragmatic and reflective smoker who balances medication use with personal responsibility. This persona suggests that effective cessation strategies should foster informed decision-making, provide clear information about medication benefits and side effects, and support adaptive coping strategies. This group may benefit most from collaborative care models that empower them to personalise their quitting plan while maintaining engagement with professional support.

Collectively, these pen portraits enrich understanding of smoker heterogeneity, moving beyond one-size-fits-all models. They reveal that medication adherence is not solely a biomedical issue but

intersects with beliefs, social roles, and lived realities. Integrating such psychosocial insights into treatment design can improve relevance, acceptability, and ultimately cessation outcomes. Tailored interventions that acknowledge these diverse smokers' typologies promise more effective support and higher adherence rates, advancing public health goals in tobacco control.

5.21 Limitations

The qualitative nature of this study limits the generalisability of the findings to a broader population of individuals with TD. Furthermore, the study was conducted in a single NHS SSS situated in a deprived area. Participants recruited had several prior attempts at SC and experience with TDMs and may not reflect the experiences of smokers seeking to quit for the first time. The participants were a convenience sample with no diversity in ethnicity. Therefore, results may be not generalisable to smokers in other settings. ECs emerged as a controversial SC method during the time period of this study, but were not explored directly regarding its role in increasing adherence to TDMs. Personas inherently simplify and generalize participant experiences, which risks obscuring individual variability and nuances. Without careful grounding in robust data and reflexivity, they may reinforce stereotypes or overlook intersectional factors such as ethnicity, socioeconomic status, or mental health. Moreover, the fictional nature of personas can lead to challenges in maintaining analytic rigor and transparency, particularly if the development process is insufficiently documented. This study, while offering valuable insights into smoking cessation and medication adherence, is subject to several important acknowledged limitations. First, the use of a convenience sample limits the representativeness of the findings. Participants were recruited based on accessibility and willingness to take part, rather than purposive sampling aimed at achieving maximum variation. This may have introduced bias, as individuals who are more motivated or engaged with health services may be overrepresented.

Second, the study exhibited limited ethnic diversity, with all participants identifying as White British. This lack of representation constrains the transferability of the findings across the wider population,

particularly in diverse urban areas where smoking prevalence, cultural beliefs, and access to cessation services may differ substantially among ethnic groups. Perspectives shaped by racial, cultural, and linguistic factors may have been underexplored, which is especially relevant in understanding social influences on medication adherence. There are limitations. *PRIME* Theory, while psychologically rich, may underrepresent structural and social determinants of health such as socioeconomic status, cultural stigma, or healthcare access, factors critical in understanding medication adherence. It was challenging to operationalise without risking overly individualistic interpretations.

Finally, the broad conceptual scope of *PRIME*, while offering a rich lens for understanding motivation, posed challenges for data coding and thematic delineation. Its dynamic and overlapping constructs, such as impulses, motives, and evaluations, necessitated careful operationalisation and a clearly articulated analytic framework established prior to coding to ensure rigour and interpretive clarity. The study's conclusions should be interpreted with caution, particularly in relation to policy or service development intended for multi-ethnic populations. Future research should aim to use purposive or stratified sampling strategies to capture a broader range of experiences and better reflect the complexity of TD across diverse communities.

5.22 Strengths

The qualitative design of this study adds to the existing literature on TDM adherence and provided a more in-depth discussion of the complex reasons for why adherence to TDMs is poor. An important strength of this study was the sample’s in-depth experiences of SC and TDMs. The identification of factors that affect adherence with SC medications and provision of a deeper understanding of adherence behaviours with SC medications are important to NHS SSSs. Insights into people’s perceptions of TDMs in relation to their quit attempt and how he or she is likely to react to differing styles of intervention to increase adherence to SC medications may be useful to health professionals when talking to smokers about stopping smoking and supporting their quit attempt. The use of personas provides a compelling way to humanize and synthesize complex data, making findings more

accessible and actionable. *PRIME* offers significant strengths as a conceptual framework for a qualitative study of smoking cessation and medication adherence. Its core advantage lies in its dynamic and integrative model of motivation, recognising that behaviour results from constantly shifting *P*lans, *R*esponses, *I*mpulses, *M*otives, and *E*valuations. This allowed the researcher to explore how internal conflicts, fluctuating desires, and emotional states shape the decisions to use or avoid stop smoking medications. *PRIME* is especially relevant in capturing non-linear quit attempts, explaining lapses and inconsistent adherence that traditional rational-choice models overlook. Moreover, its emphasis on moment-to-moment influences aligns well with qualitative methods that focus on subjective experience and social context. It encourages nuanced exploration of how identity, habit, and meaning making intersect with pharmacological support. The personas, *The Stoic Sceptic, The Overwhelmed Caregiver*, and *The Independent Realist,* exemplify this strength by vividly capturing diverse smoker experiences, beliefs, and contextual challenges related to medication adherence. This method translates rich qualitative insights into relatable, narrative forms that can guide intervention design and policy.

One of the key strengths of this qualitative study lies in its ability to generate rich, in-depth insights into the lived experiences of individuals attempting to quit smoking using pharmacological aids. Through semi-structured interviews and thematic analysis, the study captured the complexity of medication adherence, including emotional, cognitive, and contextual influences often missed in quantitative research. This depth allows for a more nuanced understanding of behaviours and attitudes towards stop smoking treatments. Another strength is the use of personas to synthesise and communicate findings. By translating thematic data into relatable character profiles, the study enhances accessibility and usability of results for practitioners, policymakers, and service designers.

This approach bridges the gap between abstract analysis and practical application, supporting the development of more tailored, empathetic interventions. Furthermore, the study demonstrated strong methodological transparency, detailing data collection, coding, and theme development processes.

Reflexivity was also evident, with the researcher acknowledging their positionality and potential biases during interpretation. This strengthens the credibility and trustworthiness of the findings. Finally, the focus on real-world, service-level issues, such as time pressures, social roles, and perceptions of treatment, adds applied value, highlighting how qualitative research can directly inform more responsive and effective SC strategies.

5.23 Conclusions

This qualitative study aimed to understand adult smokers' poor TDM adherence during quit attempts via a qualitative approach using the conceptual framework of *PRIME* theory. *PRIME* proved a powerful, flexible tool for understanding the complex health behaviour, smoking cessation and medication adherence, in-depth. Adherence to TDM regimens is a challenging goal, potentially sabotaged by many complex factors. Smokers' TDM literacy and contextual influences are important to TDM adherence. Poor adherence may be difficult to comprehend, though this study does provide some explanation using the conceptual framework of *PRIME* Theory. ECs were viewed negatively by participants who voiced the need for further authoritative safety information. Adherence to TDMs was influenced by smokers' evaluations, plans, access to support and experiential learning highlighting the need for individualised TDM adherence support. The findings of this study are important for future TD clinical practice guideline development if HCPs are to contribute to the further reduction of smoking prevalence.

Understanding of smokers' perceptions of TDMs is an important element of establishing an effective therapeutic relationship. HCPs need to identify where people with TD are in relation to rejection and initiation in TDM decision-making in order to work with them to achieve TDM adherence. It is also important TDM adherence is viewed within a broader context of a holistic framework rather than from a narrower medical discourse. Future efforts to improve adherence to TDMs may need to take the processes outlined in this study into consideration. As this was qualitative research, no inferences about the prevalence of these beliefs, experience and attitudes towards TDMs in the larger population of smokers can be drawn. However, these findings provide valuable insights into complex processes

that influence TDM adherence. Interventions to improve adherence to TDMs need to acknowledge and incorporate smokers' concerns and perspectives. The study findings are of value to clinicians, nurses, policymakers and researchers as it seeks to inform future design of SC interventions that enhance TD treatment engagement, adherence, and long term quit outcomes.

This qualitative study offers important insights into the complex and multifaceted nature of medication adherence within smoking cessation. By investigating participants lived experiences, beliefs, and social contexts, it moves beyond traditional biomedical explanations and highlights the psychosocial and structural factors that shape quit attempts. The use of in-depth interviews, thematic analysis, and the development of personas allowed for the synthesis of individual narratives into accessible, evidence-based characterisations that can inform more person-centred approaches to treatment.

The findings emphasise that adherence to stop smoking medications is not solely a matter of motivation or knowledge but is deeply influenced by factors such as mistrust in pharmacological interventions, competing life demands, and individual identity. These insights challenge one-size-fits-all cessation models and reinforce the need for more tailored support that respects diversity in experience, belief, and context. While the study's limitations, such as convenience sampling and limited ethnic diversity, must be acknowledged, the research nonetheless provides valuable implications for both clinical practice and public health strategy. Future work should aim to build on these findings through more inclusive sampling and longitudinal designs. Ultimately, this study highlights the value of qualitative research in enhancing the understanding of tobacco dependence, medication adherence behaviours and improving the design and delivery of SC interventions and SC clinical trials.

CHAPTER 6 RETROSPECTIVE CRITIQUE OF THE SCANAG RCT

This chapter presents a retrospective critical analysis of the design and methodology of the pragmatic randomised clinical trial (RCT) *Smoking Cessation and Nortriptyline and Genetics* (*SCANAG*), which forms a core foundation of this PhD thesis. The overarching aim was to examine how medication adherence behaviours influence the quality and interpretability of RCTs within the tobacco dependence field. The *SCANAG* trial, published in *BMJ* (Aveyard et al., 2008), highlighted significant challenges in interpreting pharmacological efficacy due to widespread non-adherence among participants who did not take the trial medication as prescribed (Appendix 8). Adherence was inconsistent and frequently low, influenced by a range of behavioural, perceptual, and contextual factors. The chapter builds directly upon the previous two empirical chapters, Chapter 4 (meta-ethnography) and Chapter 5 (qualitative study), both of which identified the multi-layered, socially situated nature of tobacco dependence medication (TDM) adherence. The beliefs, motivations, and structural constraints explored in those chapters informed a more nuanced analysis of the SCANAG trial data, enabling a deeper interrogation of how trial design failed to account for real-world adherence behaviours. In this sense, the analysis is not simply a retrospective appraisal, but a synthesis of sociological insight and clinical trial critique.

Although pragmatic RCTs aim to enhance external validity by simulating real-world conditions, this approach can introduce methodological challenges such as selection bias, attrition bias, and measurement error. These biases, exacerbated by poor adherence, ultimately compromise the reliability and generalisability of findings. Medication adherence is increasingly recognised as a critical determinant of pharmacological treatment outcomes in smoking cessation (Mersha et al., 2021), yet it remains under-acknowledged in trial design and analysis. This chapter is structured around the Critical Appraisal Skills Programme (CASP, 2021), which provides a systematic, question-led framework for evaluating RCT validity, results, and applicability. In addition, I use this framework to explore trial adherence behaviours and the implications for improving future trial

design (Appendix 9). Section 4.1 outlines the SCANAG trial structure and rationale; Section 4.2 analyses the key factors that undermined trial quality; and Section 4.3 explores the implications of poor TDM adherence for trial interpretation and the wider evidence base in tobacco dependency treatment.

6.1 CASP critical appraisal process

Critical Appraisal is the process of carefully and systematically examining research to judge its trustworthiness, and its value and relevance in a particular context (CASP, 2024). Critically appraising the SCANAG RCT involved examining its quality, validity, and relevance to identify its strengths and weaknesses. This allowed judgement of its trustworthiness and applicability to adherence to TDM medications by adult smokers seeking to quit. A careful analysis of the RCT study's methodology, results, and conclusions was undertaken to assess the quality and validity of the study. This helped to determine if the RCT's findings were robust, reliable and applicable to the research context. The CASP RCT checklist provided a series of structured question and ensured all key points were considered. The checklist ensured that the RCT was appraised in a systematic way, it provided structure and ensured all key points were considered; this increased consistency in decision-making by providing a framework. Within each of the checklist's section there are options to record 'Yes', 'No' or 'Can't tell' in response to those questions. There are prompts below the questions that highlight the issues important to consider. The checklist was used systemically, each question answered, and the answers were recorded and the reasons for the answers in the space provided. The checklist also provides a record of decision-making which is transparent for the purpose of quality assurance (appendix 9).

6.2 The scientific context of the *SCANAG* Trial

The *SCANAG* trial was a pragmatic RCT which took place in UK National Health Service SSSs. During the 1980s treatments aimed at SC were established as the most cost effective interventions in health care (West, 2007, Jarvis et al., 1982). Local SSSs were established in England in 1999 as part

of the Government's commitment to help smokers to quit; the first such services in the world. Approximately 15% of the percentage point reduction in smoking prevalence during 2001–2016 in England was attributed to the NHS SSS; uncertainty remains regarding the actual impact of the NHS SSSs (Song et al., 2020). NHS stop smoking services were set up to advise people, who wanted to stop smoking, to make quit attempts using the evidence-based aids that increased their chances of success (behavioural and pharmacotherapy support) (Stead et al., 2008, Stead and Lancaster, 2009, da Costa et al., 2002). At the time of the *SCANAG* trial (Appendix 8) smokers with a previous history of depression or mild current depression had not been shown to successfully quit smoking with antidepressants rather than NRT; it was unclear whether the efficacy of nortriptyline was specific to the unique pharmacology of the medication. The rationale for the use of antidepressant drugs for SC include: (i) depression may be a symptom of nicotine withdrawal, and SC sometimes precipitates depression (Berlin et al., 2010) and (ii) nicotine may have an antidepressant effect that maintains smoking for some smokers; antidepressants may substitute for this effect (Hughes et al., 2014).

Research of the association between smoking, SC and depression led to the evaluation of antidepressants as aids for SC (Hughes et al., 2009). Nortriptyline was considered a promising adjunct for smoking cessation and had been used in several long-term SC trials previously (Hall et al., 1998, Prochazka et al., 1998, da Costa et al., 2002). Nortriptyline was well-tolerated and reduced withdrawal symptoms and was found to be effective in smoking cessation (SC), being suitable for most patients attending SC clinics. These trials found that smokers who take nortriptyline had reduced tobacco withdrawal symptoms and increased long term cessation rates when combined with NRT and a smoking cessation programme. The *SCANAG* trial aimed to provide evidence that nortriptyline adds to the efficacy of NRT for all smokers seeking to quit.

6.3 *SCANAG* trial key results

Overall, 901 people (445 nortriptyline arm, 456 placebo arm) were enrolled between November 2003 and June 2005. They were recruited from 10 NHS stop smoking services and were seen by 45

different advisers. Forty-one were seen in primary care and 860 by specialists. 337 (79%) people in the nortriptyline arm and 325 (75%) in the placebo arm were taking combination treatment on quit day, median 75 mg per day in both groups. Key *SCANAG* trial outcomes are summarised in table 7.

Table 7: SCANAG Trial outcomes

Outcome	**Placebo arm**	**Intervention arm**
6 months lost to follow up	380	404
12 months lost to follow up	380	393
Abstinent from smoking at 6 months	55 of 456 (12%)	72 of 445 (16%)
Total n=127 (14%)	Relative Risk 1.34, 95% Confidence Interval 0.97 to 1.86	
Abstinent from smoking at 12 months	40 (9%)	49 (11%)
Total n=89 (9.8%)	Relative Risk 1.26, 95% Confidence Interval 0.84 to 1.87	

The nortriptyline arm had noticeably higher severity ratings for dry mouth and constipation than the placebo arm, with slightly higher ratings for sweating and feeling shaky. Both groups had similar urges to smoke, but nortriptyline reduced depression and anxiety. Overall, withdrawal symptom scores did not differ. For the intention to treat analysis, people using nortriptyline plus nicotine replacement therapy were slightly more likely to stop smoking on every measure at every follow-up than those using placebo plus nicotine replacement therapy, but the differences were small and not statistically significant.

6.4 Ethical considerations

As a pragmatic trial testing nortriptyline combined with NRT within NHS SSSs it was required to uphold rigorous ethical standards while reflecting real-world clinical practice. Key considerations included informed consent, ensuring participants understood the trial's purpose, risks (e.g. nortriptyline's side effects like dry mouth, constipation, and mood changes), and the voluntary nature of participation. Given the trial's integration into routine SSS care, researchers were required to avoid therapeutic misconception, where participants could conflate research with standard treatment. Data protection under GDPR was strictly observed, with anonymisation and secure handling of health data.

Ethical approval from NHS Research Ethics Committees was mandatory. The trial research team obtained approval from the multicentre research ethics committee and all local research ethics committees for the areas in which the trial took place. Clinical trials authorisation was obtained from the Medicines and Healthcare products Regulatory Agency. Approval was obtained from all NHS research and development offices of the primary care organisations for the areas in which the trial took place.

6.5 *SCANAG* trial design

Trial participants were randomised to either placebo plus NRT or nortriptyline plus NRT. The trial was conducted within NHS smoking cessation services who supplied the nicotine replacement therapy (NRT) for the study, allowing participants to choose from all available NRT products (such as patches, sprays, gum and lozenges). Switching NRT products was allowed and in some services participants were given two or more types of NRT to use simultaneously. Nortriptyline and placebo were provided in 25 mg capsules, maximum daily dose 75 mg. The active drug was coated in a capsule, and the capsule of the placebo was identical. Participants were posted the whole course of drugs from a central pharmacy. They were advised to start their medication one week prior to their quit date and to take 25 mg of either drug for three days, 50 mg for four days, and 75 mg thereafter, a dose found effective in previous trials (Hughes et al., 2009). The participants were advised to take the maximum dose for six weeks and then reduce the dose over a week.

6.6 Medication adherence within the SCANAG RCT

Low patient adherence emerged during the trial as a barrier to realising the benefits of the trial medications that had previously been shown to do more good than harm in clinical trials (Stead et al., 2008, Hughes et al., 2009). All participants were followed closely by the research team in an attempt to assure high medication adherence. At the initial consultation, the research nurse (CJS) discussed issues of medication use with the patient and encouraged them to raise fears and concerns about the medication and how it is used. The trial medication pack included a leaflet that asked participants to

phone the trial secretary to let us know the medication had arrived and reminded participants not to stop the medication without discussing with the trial nurse. The participants were provided written adherence information and issued contact details so that they could raise any concerns about using the medication. The research team observed during the trial that adherence to the medications was problematic (poor adherence) and in response attempted to increase adherence to the trial medications by providing participants with further information of the importance of adherence and raising the issues with the SC advisers to encourage them to promote participant medication adherence. SC advisers were trained in managing the trial drugs, although they remained unfamiliar with the impact of poor medication adherence on the trial quality and were hesitant to mention it with participants. The trial research team encouraged participants with concerns to ring the trial nurse, and they sometimes reduced the dose because of side effects. The trial nurse also made telephone contact with all of the participants between weeks 3-5 to initiate discussion on how the participant was getting on with their medication, to problem solve any side effects and to answer any questions.

The researchers attended as many stop smoking programs as possible later into the cessation attempt to encourage completion of the trial questionnaires and to promote medication adherence. Researchers sought to educate participants about the medication, its expected benefits, and potential side effects and provided clear and accurate information to address any misconceptions or concerns. The SC advisers did seek to create a positive and supportive patient-provider relationship, encouraged open communication and along with the researchers did address participants' medications questions or concerns. There were processes in place to monitor and address participants' concerns or side effects promptly, researchers attempted to provide appropriate support and reassurance. Explicit use of behavioural interventions, such as motivational interviewing or cognitive-behavioural techniques, to promote positive attitudes and beliefs towards medication and adherence could have been adopted. Involving participants in the research process, seeking their input and feedback to enhance their engagement and sense of ownership in the trial would have supported medication adherence.

6.7 *SCANAG* trial medication adherence outcomes

Most people chose NRT patch (70%) in addition to the trial medication. 15% used a NRT oral product. Participants in both arms took a median of two capsules of nortriptyline or placebo daily by quit day, the median dose consumed thereafter was three capsules daily; of note was that there was more variation in the number taken in the nortriptyline arm than placebo arm. Maximum number of capsules to be taken over 8 weeks (56 days) = 148 capsules. Owing to missing data, adherence was only be measured by self-reported pill count on weeks 1, 2, 3, 4, and 7 reducing adherence data to a maximum of 95 capsules. Number of people adherent to ≥80% of 76 capsules = 161 (17.8%). Number of people adherent to <80% of 76 capsules = 740 (82.2%). More people in the nortriptyline arm than in the placebo arm took lower doses. By week 4 of the medication regime 22% (nortriptyline arm) had stopped taken the medication, 18% had reduced the dosage and 61% self-reported taking 3 capsules per day (the prescribed dose) and 44 (22%) of those in the nortriptyline arm were not using nortriptyline. 15 (8%) were taking one capsule daily, 20 (10%) were taking two capsules daily, and 121 (61%) were taking three capsules daily. Of the 445 participants randomised to nortriptyline, by week 4 of the medication regimen, 22% (n=96) had stopped taken the medication, 18% (n=79) had reduced the dosage and 61% (n=270) self-reported taking 3 capsules per day (the prescribed dose). Studies have shown that between 43% and 78% of participants receiving treatment during a clinical trial for chronic conditions can be classified as being compliant (Osterberg and Blaschke, 2005). *SCANAG* trial medication nonadherence was a challenge to the SC clinical practice and undermined the research that aimed to contribute to lower SC rates. As the *SCANAG* research nurse this was my awakening to the problem of poor medication adherence. I was concerned of its impact to the trial outcomes and its data. Medication adherence has held my curiosity ever since.

The impact of *SCANAG* participants not being compliant with their treatment during the trial was significant. Missing data from participants who did not attend all the scheduled visits to the SC clinic meant that an accurate safety and efficacy assessment of the trail medication could not be made. This

ultimately resulted in a poor trial data set and undermined results, data analyses and trial conclusions. There was a financial cost to the sponsors of the trial as participants were not adherent with the trial protocol. Recruitment of participants was slower than anticipated, participants did not stay in the trial and / or were not able to complete all the required sections of the trial, the sponsor was required to support recruitment of additional participants from additional SC services and participants adherence with the trial medication was poor.

Key factors that affected the trial quality

6.8 Quality assurance of the trial

The *SCANAG* trial was conducted between 2003-2007, in order to test the efficacy of nortriptyline plus NRT versus NRT plus placebo in SC. Trial quality assurance was determined by several processes and measures implemented to ensure that the trial was conducted in accordance with good clinical practice (GCP) guidelines and other applicable regulations. Ethics committee approval was secured, and the ethics board reviewed and approved the trial protocol, informed consent forms, and other trial-related documents to ensure the protection of participant rights, welfare, and safety. Compliance with NHS R&D regulatory requirements was essential to maintain trial quality. This included adherence to local regulations, obtaining necessary approvals and agreements, and timely submission of required documentation to those regulatory authorities. The trial protocol defined participant recruitment, data collection and management, adverse event reporting, and trial monitoring. Each participant SC service received comprehensive training from the research team to assist with maintaining trial quality. This included training on the trial protocol, data collection methods, and ethical considerations. The training helped to ensure that all trial personnel were aware of their roles, responsibilities, and the procedures they needed to follow. However, participants, investigators, or study sites deviated from the trial protocol, for example, not dispensing the weekly trial questionnaires, reduced intensity and duration of SC support, variations in quality of medication management and adherence advice, leading to compromised data integrity and potential bias. Non-

adherence to the trial protocol included deviations in participant selection, intervention administration, data collection methods, and follow-up procedures. These deviations undermined the validity and reliability of the study results.

Inadequate participant recruitment and retention was seen early in the trial. Insufficient recruitment would have led to an underpowered study and making it difficult to draw meaningful conclusions. The trial enrolment failed to attract the number of eligible participants within a single NHS SSS and therefore had to increase the number of SSSs and geographical sites involved. Researchers were aware that ensuring consistent and high-quality data and outcomes across those sites was essential to maintaining the integrity and validity of the trial results. Forty-one were seen in primary care and 860 by specialists. Medication adherence was affected by the involvement of multiple health professionals in the trial in several ways. The trial protocol was not delivered in a systematic way across the NHS SSSs participating in the trial. It introduced complexities that impacted participant's ability to adhere to their medication regimen. Trial quality assurance was a comprehensive and ongoing process, involving collaboration among the research team, trial sponsors, ethics committees, regulators, and other stakeholders.

Ensuring that participants have a clear understanding of their medication regimen and the importance of adherence was essential for the success of the trial. The lack of strict control over the trial protocol conditions made it challenging to isolate the effects of the intervention accurately, to measure medication adherence and to support participants to adhere to the trial medication regimen. The poor control of the trial protocol across multiple sites introduced variability and reduced the ability to draw definitive causal conclusions. The need for coordination and standardisation across the different NHS SSSs and locations increased the complexity and cost of the trial. The specific strategies and procedures employed responded to the trial as it was conducted, its complexity, and applicable regulations. While trial quality assurance measures aimed to ensure that the trial was conducted to the highest standards, several challenges and problems still arose. The trial also found retaining

participants throughout the study duration problematic. High participant attrition rates likely introduced bias and affected the representativeness of the study sample. The need for coordination and standardisation across the different SSSs increased the complexity and cost of the trial.

Researchers did provide clear, accurate, and tailored information about the medication, its purpose, expected benefits, and potential side effects which did address misconceptions or concerns participants may have had. SC advisers and researchers sought to create a trusting and supportive patient-provider relationship, encouraged open communication and addressed individuals' questions or doubts. NHS SSS programs involve smokers in shared decision-making processes, allowing them to actively participate in treatment decisions and empowering them to take ownership of their medication regimen (e.g. choice of NRT type). Researchers provided ongoing support and education throughout the trial treatment period, reinforcing positive beliefs about medication and addressing any barriers to adherence. Tailored interventions to participants'' beliefs and concerns, utilising techniques such as motivational interviewing to address ambivalence may have enhanced motivation for adherence.

6.9 Effects of a real-world setting

The term ‘pragmatic controlled trial’ (PCT) was first coined in 1967 by Schwartz and Lellouch and is broadly defined as a RCT whose purpose is to inform decisions about clinical practice. Pragmatic RCTs are conducted in real-world settings. This was a protocol design decision by the SCANAG research team and aimed to enhance the external validity of the findings so that the results could be directly applied to clinical practice, making them more relevant to healthcare decision-making. Our study was set within ten NHS stop smoking services that followed the Maudsley model (Hajek, 1989) of group-based support for SC, and the trial protocol was largely based on this model. A group size was of typically 10-20 participants were provided with a 6 or 7-week NHS smoking cessation programme. By including a diverse range of participants, the RCT aimed at a broader understanding of the intervention's effects across different populations, settings, and contexts. To improve the

generalisability of the findings. A lack of strict control over the study conditions can make it challenging to isolate the effects of the intervention accurately. The real-world setting of the SCANAG trial did introduce confounding factors that may have affected the study outcomes, for example,

- Quality of the ten NHS SSSs varied regarding the SC support provided.
- Participants received conflicting advice regarding medication instructions and recommendations from the different professionals, which led to inconsistencies and confusion.
- The delivery of SC support via intensive group interventions was unattractive for some participants as they did not want to attend SC groups.
- Trust in HCPs and the quality of the patient-provider relationship are essential for medication adherence. In the *SCANAG* trial there was multiple healthcare providers. Thus, participants may not have developed the same level of trust and rapport with each provider, which could have impacted their willingness to adhere to the prescribed trial medications.
- Each health professional was responsible for different aspects of a participant's care, including medication management. This led to issues such as changes in the medication regimen. There was inconsistent information about the importance of medication adherence and potential side effects. This led to confusion and doubts about the trial medications.
- Both inconsistent data collection and participants lost to follow-up undermined medication use which caused missing data and caused poor medication adherence.
- Participants in the trial experienced side effects or had concerns about the medication they were taking. Those concerns were not effectively addressed by the HCPs and might have led to non-adherence.

6.10 Participants' experience of taking part in a clinical trial

Clinical trials are essential for advancing medical knowledge and developing new treatments; they also represent a unique, complex and multifaceted health context for participants. Research participation is determined by multiple factors (Sheridan et al., 2020). This conceptually requires each participant to make sense of their trial participation, to have agency and support to overcome challenges of the RCT treatment context, to be able to manage their disappointment of not being randomised into the active treatment RCT arm, and to manage the emotions and practical demands provoked by the trial context (Wootten et al., 2011, Locock and Smith, 2011). *SCANAG* trial participants were intrigued to be introduced to a new treatment available to help them quit smoking; trial participation required them to complete questionnaires at regular intervals and to have a blood test, agree to closer follow up and to take the trial medication which had the potential to help them to stop smoking but also to cause side effects, such as dry mouth, constipation, feeling dizzy, feeling tired, headaches. Those trial requirements were experienced as either a positive or a burden according to reports from participants or SSS clinicians.

People who volunteered to participate in the *SCANAG* trial did not always have a clear understanding of the trial process or design, despite the best efforts of the SC advisers and researchers. Withdrawal or non-adherence within a clinical trial may be related to participants dissatisfaction with aspects of their trial participation (Verheggen et al., 1998). In the *SCANAG* trial, unintended consequences may have arisen from researcher efforts to give full information required to secure "informed consent" and also to improve medication adherence. The definition of 'enough', and the relative importance of written information versus discussion / advice from researchers varied by *SCANAG* participants. Participants' experiences with participating in the trial, decision-making and practices around medication management were mostly hidden from the view of the researchers and SC advisers as they needed to fit the medications into their unique lives and their attempt to overcome their addition to smoking. Medicines optimisation within a patient-centered approach is arguable best located within shared decision process within the clinical consultation (Kuntz et al., 2014, Lowes, 2007).

Further research is required to explore the experience of smokers' experiences participation in clinical trials to enhance the study design by addressing participants' support and information needs throughout the trial. This crucial as adherence behaviour may partly be an indicator of research quality and trial participation experiences.

6.11 Characteristics of trial participants

Participants who volunteer for a clinical trial differ in important ways from those who do not volunteer or are unable to participate. It can introduce bias in treatment group assignment, leading to differences in outcomes between treatment groups that are not solely attributable to the intervention itself, impacting the internal validity of the trial. For example, they may be more proactive in seeking medical care and more likely to take medication. The trial findings may not accurately reflect the real-world effectiveness or impact of the intervention on the entire smoking target population (Kotz et al., 2014). Studies have found that when smokers quit, between half and two-thirds quit unassisted: they do not consult health professionals, use pharmacotherapy (nicotine-replacement therapy, bupropion or varenicline) (Edwards et al., 2014, Bansal et al., 2004). The *SCANAG* trial aimed to ensure that the trial outcomes were aligned with smokers' preferences and needs; for example, offering a range of NRT. As with most trials, the participants were volunteers. The RCT involved randomising participants to different interventions in routine SC care settings. This raised ethical considerations, such as equipoise and informed consent. The trial did focus on patient-centred outcomes that matter to smokers wanting to quit and aimed to be relevant to clinical SC practice. Patient-centred outcomes are valuable for understanding the true impact of a medical intervention beyond clinical or objective measurements.

The *SCANAG* trial measured via a baseline questionnaire participants' *Quality of Life* (QoL), a broad measure of a participant's overall well-being and satisfaction with their life. A *Fagerstrom Test of Nicotine Dependence* (FTND) was used to assess physical nicotine dependence, and the *Hospital Anxiety and Depression Scale* (HADS) was used to measure participant's anxiety and depression.

182 people did not return baseline questionnaires. 60% (n=719) of the trial population did return a baseline questionnaire. The participants' mean FTND score was 5.4; a score of 5 or more indicates a significant dependence (Fagerstrom and Schneider, 1989). HADS scale: normal population mean (SD) for anxiety is 6.1 (3.8) and for depression is 3.7 (3.1). Score 0-7 is normal, 8-10 borderline, ≥11 caseness (Crawford et al., 2000). HADS scores within the trial showed that 64% (n=230) in the nortriptyline group and 57% (204) in the placebo group had a history of depression; their mean (SD) anxiety score (range 0-21): was 8.0 (3.8) and their mean (SD) depression score was (range 0-21): 4.9 (3.5). Most smokers want to quit but continue because smoking helps relieve stress and provides other mental health benefits (Kassel et al., 2003, Thompson et al., 2003, Clancy et al., 2013). The SCANAG trial participants' HADS scores identified that depression and anxiety symptoms were present and smoking arguably eased their psychological distress over their adult lifetime. SC likely triggered feelings of low mood and irritability as nicotine levels dropped. Smoking helps people to manage stress (Taylor et al., 2021) which partly explains participant relapse to smoking, dropping out of the trial and low medication adherence. Smoking prevalence amongst people with mental illness has declined only slightly and is currently around 32% in the UK (Richardson et al., 2019, Szatkowski and McNeill, 2015).

Depression can have a significant impact on medication adherence, however, the relationship between depression and adherence is complex (Ginsberg et al., 1997, Gast and Mathes, 2019). Depression often leads to a lack of motivation or interest in activities, including taking medications (DiMatteo et al., 2000). Participants may have struggled to find the motivation to adhere to their trial medication regimen, as they may have felt indifferent about their health or their treatment. Depression can lead to cognitive impairments, such as difficulties with memory, concentration, and decision-making (DiMatteo et al., 2000). These cognitive challenges may have made it harder for participants to remember to take their medications consistently. Depressed participants may have experienced negative emotions, such as hopelessness, sadness, and anxiety, which can create emotional barriers to medication adherence. They may have not seen the value in adhering to treatment or believed that

the medication would not help them. In some cases, participants with depression may have been self-medicating with substances like nicotine (smoking), alcohol or other drugs and medications (Bosworth et al., 2012), which may have interfered with their medication adherence and / or exacerbated the need to return to smoking. Depressed participants may have struggled to engage with their SC advisers, the researchers and the medication regimen, causing poor adherence behaviours (Zolnierek and Dimatteo, 2009).

Anxiety, similarly to depression, can have a significant impact on medication adherence, as it can create various challenges and barriers that make it more difficult for individuals to consistently take their prescribed medications (Berlin et al., 2010). Anxiety can lead to a heightened state of alertness and distractibility, making it easier for participants to forget to take their medications (Osterberg and Blaschke, 2005, Kardas et al., 2013). This can be especially problematic for those with busy or stressful lives (Costa and McCrae, 1981). Participants with anxiety may have been preoccupied with worries and intrusive thoughts, which may have interfered with their ability to remember and prioritise taking their trial medications. Anxiety can make individuals more sensitive to physical sensations and side effects. Fear of potential side effects of medications, even though the risk was low, may explain why some participants avoided taking the trial medication (Peng et al., 2020, Sanders et al., 2019). Anxiety often leads to avoidance behaviours. In the context of medication adherence, this can manifest as avoiding taking medication due to fear or discomfort associated with it. Some participants with anxiety disorders may have had compulsive behaviours, such as checking or rechecking their trial medications, which could have created delays or barriers to taking them as per trial medication regimen. Anxiety can cause procrastination and avoidance of tasks that create anxiety (Kvarnström et al., 2018, Rahi et al., 2023). Taking the trial medication may have been perceived as an anxiety-inducing task, leading to delay or avoidance.

6.12 Trial medication side effects

Medication side effects are known to cause nonadherence (Kvarnström et al., 2021, Osterberg and Blaschke, 2005). Proper reporting and management of adverse events is crucial for participant safety and trial integrity. The trial protocol established clear procedures for identifying, documenting, and reporting adverse events and ensured that they were appropriately addressed and communicated to relevant stakeholders (Appendix 8). Experiencing adverse effects or anxiety about potential adverse effects is a major deterrent to patient adherence (Horne et al., 2013a, Clifford et al., 2008). Reported side effects by the trial participants were more common and more severe in those taking active drug (nortriptyline) rather than placebo. A minority of participants reported other side effects, such as headaches, trouble sleeping, vivid dreams and feeling spaced out. Participants randomised to the intervention arm experienced less depression and anxiety early in the quit attempt when the risk of return to smoking is at its highest than those randomised to placebo. The presence of side effects can influence medication adherence in several ways. They can cause physical discomfort or disrupt daily routines. For example, dry mouth, dizziness, or gastrointestinal issues can be uncomfortable and may lead to avoidance of medications. Over 80% of those taking nortriptyline had a dry mouth, more than half experienced constipation and sweating. Many participant's stopped taking nortriptyline or placebo and, to a lesser extent, nicotine replacement therapy, despite continuing to attempt to quit, but rates of discontinuation were similar in each arm and seem not to have been affected by severity of side effects, which differed noticeably only for dry mouth and constipation (Aveyard et al., 2008). When dry mouth persists, it can make chewing, swallowing, and even talking difficult. Constipation can cause abdominal pain and fatigue.

6.13 Measures of adherence with the trial

Adherence in clinical trials remains suboptimal, poorly measured, under-analysed and not fully reported (Eliasson et al., 2020a). Ideally all *SCANAG* participants would have fully received their allocated intervention and adhered to the prescribed medication regimen. Deviations from the

intended intervention undermines RCT quality and impacts the interpretation of the trial results and application to clinical practice (Giovanazzi et al., 2022). Measuring medication adherence in clinical trials is crucial for assessing the validity and reliability of the trial outcomes (Vander Stichele, 1991). Several methods and tools can be used to measure medication adherence in trial settings (Giovanazzi et al., 2022). The trial protocol selected self-reported measures using paper questionnaires distributed via the SC service advisers each week of the SC program. This self-reported measure was relatively easy to implement, cost-effective, and provided insight into participants' medication adherence (appendix 8). Self-reporting is convenient and inexpensive but is subject to recall bias and social desirability bias, as participants may overestimate their adherence (Giovanazzi et al., 2022). Participants were asked a single question about their type and use of NRT use and a separate question that asked if they had taken their trial medication and if so, how many tablets had they taken (a simple pill count).

While pill counts can provide objective data, they do not account for doses missed or explore reasons why. Poor pill counts in clinical trials can have implications for a study's outcomes and validity (Eliasson et al., 2020a). Furthermore, it is crucial to consider the potential impact of measurement methods on participants' adherence behaviours and potential bias. Researchers conducted training sessions for participants to ensure they understood the proper procedure for conducting pill counts and did seek to explain the purpose of the pill count as a measure of adherence, emphasising the importance of their contribution to the study. The trial researchers could have selected available comprehensive, robust and validated measurement tools and methods to obtain a comprehensive assessment of medication adherence within the trial (Vrijens and Urquhart, 2014). Clear and consistent measurement strategies could have been established in the trial protocol to ensure a more accurate and in-depth assessment of medication adherence prior, during and post the trial delivery. However, NHS SC programs sought to engage participants in their own care and educated them about the importance of medication adherence. Researchers and SC advisers provided information about the benefits of adherence, the potential impact on treatment outcomes, and strategies for overcoming

adherence barriers. The *SCANAG* Trial could have used validated assessment tools to measure medication adherence, such as the *Morisky Medication Adherence Scale* (MMAS) or *Medication Adherence Rating Scale* (MARS). Both tools have been designed and validated for assessing medication adherence and would have provided a structured framework for participants to report their adherence. SC clinical trials would benefit from a systematic approach to guide the measurement of adherence within a clinical trial helping to avoid poor understanding of medication adherence in clinical practice and real-world settings (Eliasson et al., 2020a, Peng et al., 2017).

6.14 Medication aesthetics

Medicines can be conceptualised as socially embedded phenomena, representations that have meanings and influence social relationships (Conrad, 1985); medication taking decision taking occurs beyond the clinical setting mostly in participants' social settings and medication adherence is located within "lay pharmacology" (Swinglehurst and Fudge, 2021). Consumers of medications openly discuss the comparative side effects of different drugs via various communication channels; anti-depressants are affected by existing social knowledge, beliefs and experiences (Martin, 2006, Britten et al., 2010). *SCANAG* trial participants' mostly saw them as a poison rather than as a remedy (Sanders et al., in press). Medication aesthetics refers to the sensory attributes or characteristics of medications, including their appearance, taste, smell, texture, and packaging. Aesthetics can have a significant impact on medication adherence, influencing how individuals perceive and experience their medications. The active trial medication Nortriptyline belongs to the group of medicines called tricyclic antidepressants that can also be used to treat depression. Trial participants expressed fears and concern in response to knowing that this type of medication was an antidepressant and they worried they would become addicted to it. Stigma plays an important role in treatment acceptability and adherence for various conditions (Sirey et al., 2001). Perceived stigma associated with mental illness and individuals' views about the illness may have played an important role in adherence with the trial medication. There was stigma associated with taking antidepressant medication. Nortriptyline was associated by participants' with mental illness; views about the illness play an

important role in adherence to treatment for both depression and smoking (Chapple et al., 2004, Black et al., 2012). Beliefs about antidepressant medication are known to vary widely based on individual experiences, knowledge, and cultural factors and affect adherence (DiMatteo et al., 2000). Misconceptions about antidepressants, such as the belief that they are addictive also negatively influence views (Kardas et al., 2013).

From my direct involvement as a researcher in the *SCANAG* trial and through informal discussions with NHS SSS advisers supporting participants, it became apparent that concerns about the trial medication, nortriptyline, were frequently voiced by those considering or taking part in the study. Many participants expressed anxieties about potential dependency and adverse side effects. These apprehensions were not simply clinical in nature but reflected deeper concerns about how pharmacological treatments might interfere with their sense of agency or affect their mental and emotional wellbeing.

Participants often articulated unease about taking an antidepressant for SC, worrying it might alter brain function or have unknown long-term consequences. This scepticism was heightened by the framing of nortriptyline as a psychiatric medication, which carried additional stigma and discomfort for some individuals. While many recognised that willpower alone might be insufficient to manage TD, they were notably more accepting of NRT, which was perceived as more familiar, less intrusive, and more aligned with their understanding of smoking as a behavioural habit rather than a clinical disorder.

In contrast, nortriptyline was viewed by some as excessive or inappropriate, especially among those who did not see themselves as depressed or in need of psychiatric treatment. These observations suggest that participant reluctance may not have stemmed from medication avoidance per se, but from a mismatch between biomedical framing and personal beliefs about what constitutes appropriate support for smoking cessation. Such insights informed later phases of this PhD and emphasise the

importance of aligning pharmacological interventions with user beliefs, explanatory models, and perceived acceptability.

Again, based on my observations during the *SCANAG* trial and informal discussions with NHS SSS Advisers supporting participants, it became clear that some individuals viewed the use of the trial medication, nortriptyline, as a potential sign of weakness. This perception often generated discomfort, particularly when participants contemplated disclosing their participation to others within their social networks. For several individuals, the idea of taking an antidepressant to stop smoking clashed with prevailing norms around self-control and personal responsibility, which framed quitting as an act of willpower rather than one requiring pharmacological support. This social context introduced a layer of tension between participants and their significant others, many of whom also held sceptical or stigmatised views toward antidepressant medications. As a result, some participants appeared reluctant to fully engage with the trial medication or to discuss it openly with family or peers. This inhibited the formation of what could be described as a wider therapeutic alliance within their immediate social environment, an alliance that has been shown to play a vital role in successful behaviour change (Britten, 1996). Such stigma, both internalised and socially reinforced, may have shaped participants' adherence behaviours and contributed to the challenges of integrating trial participation into the broader context of their everyday lives (Sanders et al., in press). These findings reinforce the need to understand smoking cessation not only as a clinical or behavioural process but as one embedded in social relationships and moral judgements about health, dependency, and personal strength.

My role as a researcher embedded in the *SCANAG* trial, combined with insights shared by NHS SSS advisers, indicated that the aesthetic and physical design of the trial medication had a notable influence on participants' adherence behaviours. Several participants commented that the encapsulated medication was uncomfortably large and difficult to swallow, while the royal blue colour was perceived as unappealing. Furthermore, uncertainty regarding whether the capsule

contained active medication or placebo generated anxiety and suspicion, which in some cases contributed to reduced motivation to take the medication as prescribed (Sanders et al., in press). These responses reflect the broader socio behavioural reality that pharmacological adherence is shaped not only by clinical rationale, but also by sensory and symbolic perceptions of the medication. Although nortriptyline is pharmacologically effective, these design-related issues influenced how participants experienced the medication, and ultimately, their willingness to persist with treatment.

As a member of the *SCANAG* trial team, I contributed to decisions about the medication's formulation and presentation. In retrospect, the absence of patient involvement in the pre-trial design stage, particularly regarding capsule appearance, size, and delivery format, represented a missed opportunity to incorporate user preferences that may have improved adherence. Encouraging open dialogue between participants and stop smoking advisers about these concerns could have supported problem-solving or psychological reframing. Additionally, providing alternative dosage forms or flexibility in delivery may have accommodated a wider range of participant needs. This experience highlights the importance of adopting a patient-centred approach in clinical trial design, particularly in trials involving behavioural components and long-term medication use. Adherence is not merely a pharmacological issue but is deeply embedded in user experience, embodiment, and trust—factors that deserve greater attention in tobacco cessation research and practice.

Building on the previous chapter's findings, a truly patient-centred approach to evaluating the efficacy of SC medications demands a broader conceptualisation of what “medication effectiveness” means in practice. This includes not only pharmacological performance but also user experience—encompassing perceived safety, aesthetic acceptability, and alignment with participants’ values and preferences. In the *SCANAG* trial, medication adherence was shaped as much by symbolic and sensory dimensions as by therapeutic outcomes. Participants were encouraged to report any side effects or concerns relating to the trial medication. However, in practice, such communication was limited. Despite repeated prompts from clinical staff, many participants did not disclose their

difficulties with the medication. My reflections during the trial and discussions with NHS SSS advisers suggest several plausible explanations for this limited engagement. These include perceived barriers such as lack of time during consultations, fear of judgment, or uncertainty about what constitutes a "valid" concern. Some participants may have internalised norms of self-reliance or feared being labelled as non-compliant, while others placed greater trust in peer advice or non-clinical information sources (Inder et al., 2019). These findings reinforce the need for healthcare professionals and researchers to create safe, non-hierarchical spaces for participants to voice concerns without fear of moral judgment or clinical reprisal. More relational and dialogic models of care, grounded in trust and mutual respect, may be necessary to elicit meaningful discussions about medication adherence. This also calls for trial designs and health services that move beyond technical efficacy to consider the relational, emotional, and social contexts in which treatment is received, evaluated, and sustained.

6.15 Tobacco dependency

To situate this Chapter within the current landscape of TD treatment and policy, it is important to contextualise recent trends using contemporary literature. As of 2023, it was estimated that approximately 13% of the UK adult population, equivalent to around 8 million individuals aged 18 and over, continued to smoke (ONS, 2021). In response, TD treatment has been prioritised within the NHS Long Term Plan and is positioned as a critical mechanism for supporting the UK government's ambition of a smoke-free generation by 2030 (OHID, 2022). The literature consistently identifies that the most effective treatment pathway for TD involves a combined pharmacological and behavioural approach. Evidence supports the efficacy of NRT, such as patches, alongside prescribed medications like bupropion (Zyban) and varenicline, when used in conjunction with structured behavioural support (Stead and Lancaster, 2016). Despite this, approximately half of all smokers in England still attempt to quit without formal support, relying instead on willpower alone, widely recognised as the least effective method (OHID, 2022). E-cigarettes have now emerged as the most commonly used

quit aid among smokers in England, particularly for those who avoid or mistrust traditional cessation medications (Hartmann-Boyce et al., 2022).

However, TD presents significant barriers to medication adherence. Nicotine's pharmacological effects on cognition, mood regulation, motivation, and executive function may undermine a smoker's ability to initiate and sustain consistent medication-taking behaviours. Withdrawal symptoms, including irritability, anxiety, and disrupted routines, can further interfere with adherence. Smoking rituals, environmental cues, and cravings often take precedence over treatment regimens. Furthermore, tobacco use is frequently comorbid with other unhealthy behaviours or mental health conditions, which may complicate care pathways and exacerbate non-adherence (Hartmann-Boyce et al., 2021c). Although the behavioural sciences offer robust evidence for the efficacy of smoking cessation treatments, there remains a paucity of research explicitly examining interventions aimed at improving adherence to tobacco dependence medications (TDMs) (Haynes et al., 2008). This gap in the literature underscores the rationale for this thesis, which seeks to understand not just the pharmacological aspects of cessation, but also the lived, relational, and behavioural contexts that shape how smokers engage, or fail to engage, with medication-based support.

6.16 Poor TD medication adherence

Medication nonadherence is a challenge in clinical practice and research that contributes to lower SC rates (Raupach et al., 2013). Vrijens et al. (Vrijens and Urquhart, 2014) define medication adherence as "the process by which patients take their medication as prescribed" suggesting that medication adherence is composed of three quantifiable phases: initiation: when patients take their first dose of a prescribed medication, discontinuation: when patients stop taking their prescribed medication, and implementation: the extent to which patients' actual dosing corresponds to the prescribed regimen, from initiation until the last dose (Vrijens et al., 2012). The prevalence of adherence to TD therapy varies widely between studies (5–96%) (WHO, 2003). It is estimated that 20% of smokers who receive prescriptions for TDM never fill that prescription (Solberg et al., 2010). Smokers who

access pharmacotherapies for TD often use them at a lower dose and for less time than evidence suggests is optimal (Hays et al., 2010, Shiffman et al., 2008b, Swan et al., 2010). Adherence with the recommended length of treatment occurs among 50% or fewer NRT users (Burns and Levinson, 2008, Alterman et al., 1999, Cooper et al., 2004). Adherence to NRTs and to other treatments for TD is very low in the long term (< 40%), but it shows a strong positive correlation with better cessation outcomes. Unfortunately, these long-term cessation outcomes are still unsatisfactorily low (< 20%).

6.17 Implications for clinical trials

Limited evidence exists that compare adherence to TDM quit rate efficacy in community-based settings versus clinical trials. Poor adherence with the recommended TD treatment length is significant because substantial evidence, both observational and within the context of clinical trials, indicates that greater medication adherence is associated with greater abstinence from smoking (Raupach et al., 2013, Catz et al., 2011, Hollands et al., 2013, Shiffman, 2007) even after controlling for potential bias due to reverse causation (Raupach et al., 2013). Further, to other key confounders, (Kotz et al., 2014) medication nonadherence likely explains at least part of the discrepancy between efficacy observed in strictly managed clinical trials and real world clinical practice, where nonadherence occurs at higher rates (Pierce and Gilpin, 2002, Hajek et al., 1999).

In summary, improving TDM adherence in clinical trials is essential for ensuring the validity and reliability of study outcomes and for maximising treatment efficacy and achieving successful SC outcomes. Several strategies can be employed to enhance TDM among participants:

1. Tailor interventions to individual needs: recognise that SC is a highly personalised process influenced by various factors such as TD level, motivation to quit, and psychosocial determinants. Offer person-centred treatment plans and support strategies based on participants' unique characteristics and preferences.

2. Offer TDM adherence behavioural support: incorporate behavioural counselling or therapy into SC interventions to address psychological aspects of addiction and enhance coping skills. Behavioural support should target complementing pharmacotherapy and increasing participants' confidence in their ability to quit smoking, thereby promoting adherence to treatment regimens, to promote positive attitudes and beliefs towards medication and adherence.
3. Provide comprehensive education: offer detailed information about the benefits of SC, available treatment options (e.g., pharmacotherapy), potential side effects, and coping strategies for managing cravings and withdrawal symptoms. Educated participants are more likely to understand the importance of adherence and actively engage in treatment.
4. Implement adherence monitoring tools: utilise adherence monitoring tools, such as self-reported diaries, electronic medication monitors, or biochemical validation measures, to track participants' medication use accurately. Regular monitoring allows for early detection of adherence challenges and timely intervention to address them.
5. Create a supportive study environment: form a supportive and nonjudgmental study environment that encourages open communication, fosters peer support, and respects participants' autonomy in their quitting attempt. A positive study experience enhances participant engagement and adherence to treatment recommendations.
6. Involve participants in the research process, seek their input and feedback to enhance their engagement and sense of ownership in the trial to support medication adherence.
7. Further research to explore the experience of smokers' experiences participation in clinical trials to enhance the study design by addressing participants' support and information needs throughout the trial.
8. Utilise available comprehensive, robust and validated measurement tools and methods to obtain a comprehensive assessment of medication adherence within TDM trials.

9. Adopt a broader perspective of medication that incorporates medication safety, aesthetics' and alignment to participants priorities and addresses what matters to them.

6.18 Conclusions

This chapter describes a critical analysis of the design and methods within the pragmatic RCT *SCANAG* retrospectively, using the formal critical appraisal process (CASP, 2021) to assess the validity, results, and applicability of the RCT with a detailed examination of the medication adherence issues that emerged (Table 8). Critical appraisal of *SCANAG*, using the CASP RCT checklist, involved examining its quality, validity, and relevance to identify its strengths and weaknesses. Low patient adherence emerged during the trial as a barrier to realising the benefits of the trial medications. *SCANAG* trial medication nonadherence was a challenge to the SC clinical practice and undermined the research that aimed to contribute to lower SC rates. Clinical trial participation is determined by multiple factors. Participation in a clinical trial is a specific context of taking medication; participants may differ from those who do not volunteer, further, additional support via the research is provided compared to usual clinical care.

As a PhD researcher actively involved in the *SCANAG* trial, through reflective engagement with NHS SSS advisers, I observed that a high proportion of *SCANAG* trial participants had a significant nicotine dependency, anxiety and depression scores; supported by trial data analyses. These factors all can have an impact on medication adherence. Medication side effects are known to cause nonadherence. The *SCANAG* participants experienced various nicotine withdrawal symptoms and simultaneously medication side effects which contributed to poor adherence with the trial medications. The *SCANAG* medication aesthetics, for example, regarding medication type (an antidepressant) and associated stigma, size and colour affected perceptions of safety and interactions with the medication leading to poor adherence in some participants. Poor medication adherence in *SCANAG* presented significant challenges, impacting the validity and reliability of the study outcomes. Various factors contributed to suboptimal adherence, TD, prior failed quit attempts, prior

beliefs and experiences of TDMs, nicotine withdrawal symptoms, existing mental health problems, adverse effects, and participant characteristics such as socioeconomic status, and health literacy. High trial dropout rates, inadequate adherence data collection and measurement undermined analysis of trial outcomes and significance of adherence issues, weakening the quality of reporting and dissemination of the *SCANAG* clinical trial.

Through close involvement in *SCANAG* and routine discussions with front-line stop smoking practitioners, it became apparent that participants beliefs, perceptions, and attitudes towards the trial medication did strongly influence their motivation, decisions, and adherence behaviours. For example, perceived efficacy, concerns about side-effects, beliefs about necessity, perceived control and self-efficacy, cultural and social beliefs, trust and communication were factors that caused poor adherence. Attitudes and beliefs about taking medication are known to vary widely among individuals and can be influenced by personal experiences, cultural factors, societal norms, and beliefs about healthcare. The beliefs and attitudes that participants held about medications had a significant impact on the trial quality and outcomes. Addressing TD alongside medication adherence is crucial for optimising health outcomes in individuals with tobacco-related conditions.

Table 8 Summary of TD medication adherence within the *SCANAG* trial

Clinical Trial Context	**Pragmatic "real" world**
Clinical, medical model, academic context. Clinical trial development based on researchers' understanding. Study design. Study duration.	Home environment lived real world context. Motivated by volunteering, close monitoring and care, impact on daily life; requires additional time and effort, potentially affecting daily routines and responsibilities. Inclusion/exclusion criteria, randomisation process, blinding, data collection methods, trial

	measurements and follow-up procedures. Length of the trial and duration of treatment.
Clinical trial offers a new hope of SC success.	Access to cutting-edge TD interventions. Being a trial participant conflicts with participants real world.
Being a trial participant. Psychological factors. Health beliefs. Socioeconomic factors.	Addiction to nicotine. TD, mental health issues (anxiety, depression, stress), motivation, and coping mechanisms, prior failed quit attempts. Psychological capability impaired. Age, gender, socioeconomic status, health literacy, and comorbidities. Attitudes, perceptions, and beliefs about medication type, efficacy and necessity. Access to healthcare, location of SSS
Burden of attending SC clinics: trial activity demands e.g. completing questionnaires and other invasive data collection methods; costs, time to participate.	Participants level of understanding of (i) the causes and effects of TD and (ii) importance of medication adherence to quit success. Length of the trial and duration of treatment.
Other trial participant experiences (+ve & / -ve) of medication(s). Adverse effects. TDM aesthetics. Complexity of regimen.	Participant and other lay perceptions and opinions of medication, academics and health professionals. Unpleasant or harmful reactions to TDMs. Sensory attributes or characteristics of TDMs, including their appearance, size, taste, smell, texture, and packaging. The number of

	TDMs, dosing frequency, and administration route.
Emotions, psychological burdens of trial participation experiences e.g. allocation to placebo or active medication, failure to stop smoking, loss of participation.	SC beliefs align with willpower not medication. Not perceiving medication as essential to SC success.
Health literacy demands, overwhelming & / too little trial information.	General physical health and mental health and wellbeing status. Coping with stress.
Beneficial effects such as the satisfaction of feeling "useful," gaining "a sense of control," and receiving special attention.	Participants don't take any medication as per regimen.
Quality of experiences with SC health professionals and trial researchers.	Resistance to taking medication. Actively deciding not to take medication. Medication aesthetics.
	Working out placebo v active medication allocation.
	External factors that prevent adherence unable to find time to take the medication, side effects not compatible with life demands / daily routines (work *etc.*), limited social support to taking medication.
	Justifying taking a medication type (e.g. an antidepressant) to lay people.

	How the trial medication fits in the participants life.

The trial protocol did not assess and monitor participants' beliefs and attitudes via validated instruments or qualitative interviews. By incorporating this information into trial design and participant engagement strategies, researchers could have promoted transparency, addressed concerns, and optimised participant experiences, ultimately enhancing the validity and applicability of trial findings. The trial protocol stage would have benefitted from a pre-trial design state undertaking a qualitative study to explore and understand the meaning of medications to participants and to ascertain potential attitudes and beliefs about taking medication to help them stop smoking. The enrolment stage of the trial would have benefited from utilising available tools such as the Decisional Conflict Scale (O'Connor, 1995) which assesses perceptions of uncertainty, feeling informed, and clarity of values regarding medication decisions. As this scale measures confidence and satisfaction with the decision-making process it would have helped the researchers to understand smokers' attitudes and beliefs about their medication choices. The knowledge gained from pre-trial exploration of medication adherence within the context of SC would have helped to design *SCANAG* from a more patient-centred perspective.

Clinical trials are essential for advancing SC knowledge and developing new treatments to enable smokers to quit, but they also represent a unique and sometimes challenging context for participants that can contribute to poor medication adherence. Participating in SC clinical trials is a complex and multifaceted experience; it can be both positive and negative affecting adherence with trial interventions. Researchers and HCPs should design patient-centered trials to support optimal medication adherence which would contribute to RCT quality in several critical ways. Important to reducing medication nonadherence is understanding the characteristics that cause nonadherence both nonmodifiable (sociodemographic,) and modifiable (e.g., smoking, medication factors, resistance to taking medication, forgetfulness, mental health, communication, trust in patient-provider

relationships, support) via intervention. There remains a lack of understanding about the complexity of medication adherence from the patient's perspective within TD RCTs. The viewpoints of healthcare professionals continue to dominate the design of TD RCTs and lack the input of participants. Patient-centred care requires a greater understanding of the daily decisions participants need to make to manage a medication regimen within a clinical trial designed to help them stop smoking and how to effectively navigate the complexity of TDM adherence.

Medication adherence is a critical mediator of treatment outcomes for TD and low rates of adherence undermine clinical trials and SC success. Adherence monitoring and optimisation should be a standard component of TD treatment research. Health programs and policies are recommended to integrate the issue of adherence to TDMs as a core component of TD interventions. This chapter highlights a low level of adherence to TDMs within a pragmatic clinical trial. Moreover, the analyses illustrate the diverse adherence behaviours and a strong association between adherence and successful SC; they also contextualise the trial intervention in the NHS specific clinical communities and population groups. The trial medication was evaluated by participants on acceptability, pragmatics in their lives, and effectiveness. RCT participation is a small part of each participant's real world (Dew et al., 2015). Participant's home settings are more important that the clinical trial context and shape participants' evaluations of TD medication in terms of anticipated and / or experienced side effects and how congruence with medication adherence is navigated within their home environments.

This study indicates the need for a comprehensive multilevel approach to improving adherence and enhancing the effectiveness of TDMs to improve the quality of TDM clinical trials and quit smoking success rates. Improving adherence to TDMs is a complex issue that requires a comprehensive approach, ongoing dialogue with participants regarding home environment impacts and an agile set of interventions rather than focusing on a traditional single intervention strategy. It is recommended to implement a theory-based approach applied, such as the Behaviour Change Wheel (Michie et al.,

2014a), to improve TD clinical trial design and intervention strategy involving various stakeholders to improve adherence to TDMs.

CHAPTER 7 GENERAL DISCUSSION

This PhD set out to investigate the beliefs, experiences, and behaviours associated with smoking cessation and medication adherence among adult smokers in England, using a mixed-methods design that incorporated a meta-ethnography, a qualitative interview study within NHS SSSs, and a retrospective analysis of a pragmatic RCT (*SCANAG*). Together, these phases offer a multidimensional understanding of why individuals do or do not adhere to TDMs and how service structures, personal beliefs, and broader sociopolitical dynamics shape this behaviour. In the pursuit of enhancing public health to end tobacco use, the quality and efficacy of clinical trials for SC were the focal point of the PhD thesis. One critical aspect of successful SC is the adherence to prescribed medications designed to aid individuals in overcoming nicotine dependence.

The discussion chapter serves as the culmination of the research journey, providing a comprehensive analysis and interpretation of the study's findings in the context of existing literature, theoretical frameworks, and research objectives. This chapter provides a synthesis of the results, draws meaningful conclusions, and discusses their implications for the smoking cessation, clinical trials of TDMs within a public health context. In this section, key findings of the research are critically evaluated regarding their significance, and I explore avenues for future research. By critically reflecting on the research process, addressing limitations, and offering insights into broader implications, this discussion aims to contribute to the advancement of knowledge in the discipline and inform future research endeavours.

7.1 Summary of findings

This PhD thesis sought to unravel the complexities surrounding medication adherence, recognising its pivotal role in the overall success of smoking cessation efforts. The synthesis of evidence and use of *PRIME* have provided a comprehensive understanding of the factors shaping adherence behaviours, illuminating the intricate interplay between individual, social, and contextual determinants. The nuances of SC delivery systems in healthcare, including the influence of NHS

SSSs provision and the impact of psychosocial factors on medication adherence have been considered throughout the thesis. The NHS SSSs, introduced in 2000, remain a cornerstone of tobacco control in England. They offer behavioural support and pharmacotherapy, including nicotine replacement therapy (NRT), varenicline (when available), and bupropion, to help people quit smoking. However, despite early success and a strong evidence base (Bauld et al., 2010, McEwen et al., 2006), the SSS model is increasingly challenged by structural, cultural, and economic changes that threaten its future effectiveness and equity. First, the decline in service uptake is a critical concern. Recent Public Health England reports (PHE, 2022b) and NHS Digital data (NHS, 2023) indicate a steady reduction in the number of smokers accessing SSSs, even though the smoking prevalence in disadvantaged communities remains high. Explanations include reduced visibility, local authority budget cuts (following the 2013 transfer of public health to local government), and increased use of unregulated digital resources and vaping products (Beard et al., 2021). This raises questions about the reach and relevance of traditional face-to-face cessation services, particularly for younger and more digitally literate populations.

Second, health inequalities persist. Smoking rates remain disproportionately high among those with mental health problems, low income, and in routine/manual occupations (OHID, 2022). Despite the existence of targeted pathways (e.g., the NHS Long Term Plan's tobacco dependency treatment in mental health trusts), gaps remain in implementation and access. Qualitative studies suggest that many smokers, especially from ethnic minority groups or those with negative experiences of healthcare, distrust pharmacological interventions and prefer to quit unaided or with e-cigarettes (Notley et al., 2025, Brown et al., 2021). These perspectives are underrepresented in SSS design and evaluation.

Third, the emergence of vaping as a preferred cessation aid has transformed the landscape. The increasing preference for e-cigarettes (now the most common quit method in England) raises critical questions for NHS SSSs: should services integrate vape support more systematically, and how should

they address long-term nicotine use? While the UK remains relatively progressive in its harm reduction stance (McNeill et al., 2020), SSSs have yet to develop consistent, evidence-based approaches for incorporating vaping into structured quit plans.

Looking ahead, the future of NHS SSSs may lie in their capacity to evolve into flexible, person-centred hubs. Digital cessation tools (apps, SMS coaching, AI-powered chatbots) can complement rather than replace face-to-face support. However, services must also work harder to co-produce interventions with marginalised smokers, acknowledging cultural norms, mistrust of medicines, and the symbolic meanings of "willpower" and self-reliance (Pound et al., 2005, Onwuzo et al., 2024). Furthermore, national efforts must tackle upstream determinants, poverty, stress, housing instability, that sustain smoking and complicate adherence to cessation medications. In conclusion, while the NHS SSSs have been world-leading, they must adapt to shifting social trends, new technologies, and patient preferences. Their survival and future success depend on political will, cross-sector collaboration, and a move towards more inclusive, participatory service models grounded in contemporary public health realities. The future of NHS SSSs will be shaped by shifting public health priorities, digital innovation, and evolving patterns of tobacco and nicotine use (DHSC, 2023, NICE, 2025). Digital tools, apps, online support communities, and virtual counselling, are likely to expand reach and improve engagement, particularly among tech-savvy users. However, equity will remain a key concern, ensuring that underserved populations maintain access to in-person support. NHS services will continue to adapt under budgetary pressures and strive to be more data-driven, personalised, and inclusive, aiming not only to help individuals quit but to create environments that make smoking less socially and culturally viable.

The data generated have not only elucidated the challenges faced by individuals striving to adhere to TDMs but have also illuminated potential avenues for tailored interventions and policy recommendations. Medication adherence is a labyrinth, and the thesis argues that a one-size-fits-all approach is insufficient. The thesis findings underscore the need for personalised and person-centred

interventions that consider the diverse array of factors influencing adherence. Furthermore, the general discussion explores the implications of these findings for smoking cessation clinical trial design, with potential applications extending beyond smoking cessation to other areas of chronic disease and addiction management.

The preceding chapters of this PhD thesis have explored the multifaceted landscape of adherence to smoking cessation medications, exploring the factors influencing adherence, the impact of poor adherence on smoking cessation clinical trials, and the implications for long-term cessation outcomes. I have written this thesis with each chapter standing as a separate investigation; hence each chapter has its own conclusions. I have presented these here for convenience (Table 9) and offer several overarching conclusions.

Table 9 Conclusions from Chapters 2-4

Thesis Chapter	**Chapter Conclusion**
Chapter 5 Meta-ethnography	• Smokers' narratives revealed diverse concerns and perceptions of TDMs that led to nonadherence behaviour. • Many of the issues identified were potentially modifiable by existing medication adherence or health behaviour change interventions; the psychosocial context of TDM behaviours, resistance to TDMs and preference for willpower emerged from the synthesis as important – this translated into deliberate non-adherence. • Low confidence in TDMs and experienced failure of TDMs to address multi-faceted and often conflicting reasons for smoking resulting in the predilection for willpower and legitimised non-adherence behaviours.

	• TDMs were often incompatible with individuals' views and beliefs about taking medications, especially in the long term. • Complete TDM adherence and persistence was unachievable within powerful anti-medication social contexts and individuals' desire to be in control of their lives. • Nurses should work in partnership with smokers, so their preferences and concerns are utilised to either help improve TDM adherence or avoid the prescription of medication which is not taken. • Personalised TDM adherence interventions are likely to be most effective to help improve long-term SC outcomes.
Chapter 6 Qualitative study	• Adherence to TDM regimens is a challenging goal, potentially sabotaged by many complex factors. • Smokers' TDM literacy and contextual influences are both important to TDM adherence. • Poor adherence may be difficult to comprehend, though this study does provide some explanation using the conceptual framework of *PRIME* Theory. • ECs were viewed negatively by participants who voiced the need for further authoritative safety information. Adherence to TDMs was influenced by smokers' evaluations, plans, access to support and experiential learning highlighting the need for individualised TDM adherence support. • Interventions to improve adherence to TDMs need to acknowledge and incorporate smokers' concerns and perspectives.

Chapter 7 Retrospective critique of the RCT design and outcomes	• There was a low level of adherence to TDMs within this pragmatic clinical trial. • Moreover, my analyses illustrate the diversity of adherence behaviours and a strong association between adherence and successful SC and contextualise the trial intervention in the NHS specific clinical communities and population groups. • Participants' beliefs, perceptions, and attitudes towards the trial medication did strongly influence their motivation, decisions, and adherence behaviours. The beliefs and attitudes that participants held about medications had a significant impact on the trial quality and outcomes. • The trial protocol did not assess and monitor participants' beliefs and attitudes via validated instruments or qualitative interviews. • Participating in SC clinical trials is a complex and multifaceted experience; it can be both positive and negative affecting adherence with trial interventions. Important to reducing medication nonadherence is understanding the characteristics that cause nonadherence both nonmodifiable (sociodemographic,) and modifiable (e.g., smoking, medication factors, resistance to taking medication, forgetfulness, mental health, communication, trust in patient-provider relationships, support) via intervention. • The trial medication was evaluated by participants in regard to acceptability, pragmatics in their lives, and effectiveness; RCT participation is a small part of each participant's real world.

	• Participants home settings are more important that the clinical trial context and shape participants' evaluations of TD medication in terms of anticipated and / or experienced side effects and how congruence with medication adherence is navigated within their home environments. • Medication adherence is a critical mediator of treatment outcomes for TD; low rates of adherence undermine clinical trials and smoking cessation success.

7.2 Interpretation of Results

The following sections provide a detailed analysis and interpretation of each of three thesis chapter findings, including their significance and implications.

7.3 Meta-ethnography

The meta-ethnography synthesised evidence on adult smokers' experiences, meanings and beliefs regarding TDMs and their importance to adherence behaviours. A line-of-argument synthesis captured recurring perceptions and experiences that supported (facilitators) or hindered (barriers) tobacco dependence medication adherence. Three themes relating to smokers' medication use of tobacco dependence medications emerged from the lines of argument process (i) psychosocial context of TDM behaviours, (ii) predilection for willpower and "natural" methods to achieve quit success and (iii) resisting medications. The inter-relationship between the identified themes was illustrated as a model of smokers' TDM adherence and non-adherence behaviours. The model depicted oscillation between psychosocially driven beliefs about TDMs, which mostly did not resonate with the current medical model of tobacco dependence treatment.

Smokers' narratives revealed diverse concerns and perceptions of TDMs that led to nonadherence behaviour. Many of the issues identified were potentially modifiable by existing medication

adherence or health behaviour change interventions. The psychosocial context of TDM behaviours, TDMs resistance and preference for willpower emerged from the synthesis as important – this translated into deliberate non-adherence. Low confidence in TDMs and experienced failure of TDMs to address multi-faceted and often conflicting reasons for smoking resulting in the predilection for willpower and legitimised non-adherence behaviours. TDMs were often incompatible with individual views and beliefs about taking medications, especially in the long term. Complete TDM adherence and persistence was unachievable within powerful anti-medication social contexts and individuals' desire to be in control of their lives. HCPs should work in partnership with smokers, so their preferences and concerns are utilised to either help improve TDMs adherence or avoid the prescription of medication which is not taken. Future research should be aimed at understanding HCPs' perceptions and practices of assessing medication adherence in smokers that may guide interventions to resolve this important issue of medication nonadherence. Research to further understand how a smoker's predilection for willpower augments the resistance to TDMs is required. This may help in achieving improved long-term quit outcomes. Personalised TDM adherence interventions are likely to be most effective to help improve long-term SC outcomes.

Since the endpoint of the original meta-ethnography on adult smokers' perspectives of tobacco dependence medications (TDMs), research (2023–2025) has revealed substantial social and behavioural shifts that deepen the rationale for this PhD and accentuate its contemporary relevance. The dramatic rise in vaping among ex-smokers in England, with over 41% of quit attempts now supported by e-cigarettes, and a tenfold increase in long-term vaping among ex-smokers, particularly younger adults (ONS, 2024). This rapid uptake illustrates that vapes are no longer niche but foundational to cessation frameworks. UK qualitative work (Sherratt et al., 2023) shows that many smokers now see e-cigarettes as a medicalised extension of healthcare, signalling a notable shift in identity and autonomy narratives. By neglecting vaping, earlier meta-ethnographies risk misrepresenting current contexts in which devices function as stand-ins for TDMs. This strengthens the argument for including more recent studies in the meta-ethnography update and reframing the

thesis around mediation, autonomy, and product choice. COVID-era qualitative and longitudinal studies reveal that despite heightened awareness of health risks and institutional messaging, willpower remains deeply valued (Gupta and Lee, 2025). The COVID pandemic prompted some smokers to consider cessation but also heightened stress, leading to inconsistent adherence to pharmacotherapies (Jackson et al., 2023b). This paradox reinforces meta-ethnography themes, witnessing smokers caught between impulse and reason, conflicting with biomedical cessation models. The meta-ethnography would be strengthened by deeper exploration of structural inequalities. Recent qualitative work, such as that on vape access in deprived English communities (Jackson et al., 2023a) and prison release populations (Brown et al., 2021) reveal how economic constraints and service gaps shape cessation behaviours. A limitation of the meta-ethnography is some newer studies post-2023 could not be incorporated into the meta-ethnography, and the COVID-19 pandemic altered smoking behaviours in ways not fully captured by the data.

The meta-ethnography illuminated how smokers often view pharmacological cessation aids with suspicion or ambivalence. Concerns about side effects, loss of autonomy, previous negative experiences, and perceived ineffectiveness were central to participants' narratives. These findings were echoed in the qualitative study, which revealed that even among help-seeking individuals, adherence was undermined by a lack of trust in medications, reliance on willpower, and a preference for non-pharmacological strategies. *PRIME Theory* was employed as a conceptual framework to understand these behaviours, revealing that momentary motivational conflicts and identity-based resistance to medications played a crucial role in shaping adherence.

7.4 Qualitative study

Smokers' narratives revealed diverse concerns and perceptions of TDMs that led to nonadherence behaviour. Many of the issues identified were potentially modifiable by existing medication adherence or health behaviour change interventions. The psychosocial context of TDM behaviours, TDMs resistance and preference for willpower emerged from the synthesis as important – this

translated into deliberate non-adherence. Low confidence in TDMs and experienced failure of TDMs to address multi-faceted and often conflicting reasons for smoking resulted in the predilection for willpower and legitimised non-adherence behaviours. TDMs were often incompatible with individual's views and beliefs about taking medications, especially in the long term. Complete TDM adherence and persistence was unachievable within powerful anti-medication social contexts and individuals' desire to be in control of their lives.

Adherence to TDM regimens is a challenging goal, potentially sabotaged by many complex factors. Smokers' TDM literacy and contextual influences are important to TDM adherence. Poor adherence may be difficult to comprehend, though this study does provide some explanation using the conceptual framework of *PRIME*. ECs were viewed negatively by participants who voiced the need for further authoritative safety information. Adherence to TDMs was influenced by smokers' evaluations, plans, access to support and experiential learning highlighting the need for individualised TDM adherence support.

HCPs should work in partnership with smokers, so their preferences and concerns are utilised to either help improve TDMs adherence or avoid the prescription of medication which is not taken. Future research should be aimed at understanding healthcare professionals' perceptions and practices of assessing medication adherence in smokers that may guide interventions to resolve this important issue of medication nonadherence. Research to further understand how a smoker's predilection for willpower augments the resistance to TDMs is required. This may help in achieving improved long-term quit outcomes. Personalised TDM adherence interventions are likely to be most effective to help improve long-term SC outcomes.

The findings of the qualitative study are important for future TD clinical practice guideline development if HCPs are to contribute to the further reduction of smoking prevalence. As this was qualitative research, no inferences about the prevalence of these beliefs, experience and attitudes towards TDMs in the larger population of smokers can be drawn. The sample for the qualitative study

lacked ethnic diversity, mirroring a broader challenge in cessation research. Future studies should adopt purposive, inclusive sampling strategies and engage with underrepresented communities to address these gaps. However, these findings provided valuable insights into complex processes that influence TDM adherence. Interventions to improve adherence to TDMs need to acknowledge and incorporate smokers' concerns and perspectives.

7.5 Retrospective critique of the RCT design and outcomes

SCANAG formed the foundation of my PhD thesis. The retrospective critical analysis of the design and methods within the trial used the formal critical appraisal process (CASP, 2021) and assessed the validity, results, and applicability of the RCT. Of the 445 participants randomised to nortriptyline by week 4 of the medication regime 22% (n=96) had stopped taken the medication, 18% (n=79) had reduced the dosage and 61% (n=270) self-reported taking 3 capsules per day (the prescribed dose). The impact of *SCANAG* participants not being adherent with their treatment during the trial was significant. Missing data from participants who did not attend all the scheduled visits to the SC clinic meant that an accurate safety and efficacy assessment of the trial medication could not be made. This ultimately resulted in a poor trial data set and undermined results, data analyses and trial conclusions. There was a financial cost to the sponsors of the trial as participants were not adherent with the trial protocol. Recruitment of participants was slower than anticipated, participants did not stay in the trial and / or were not able to complete all the required sections of the trial, the sponsor was required to support recruitment of additional participants from additional NHS SSSs and participants adherence with the trial medication was poor.

Observations drawn from my participatory involvement *SCANAG*, enriched by adviser reflections from the NHS SSSs, indicated that participants' beliefs, perceptions, and attitudes towards the trial medication were found to strongly influence their motivation, decisions, and adherence behaviours. For example, perceived efficacy, concerns about side-effects, beliefs about necessity, perceived control and self-efficacy, cultural and social beliefs, trust and communication were factors that caused

poor adherence. Attitudes and beliefs about taking medication varied widely among participants and were be influenced by personal experiences, cultural factors, societal norms, and beliefs about medication. The beliefs and attitudes that participants held about medications had a significant negative impact on the trial quality and outcomes. This indicates the need for a comprehensive multilevel approach to improving adherence and enhancing the effectiveness of TDMs to improve the quality of TDM clinical trials and quit smoking success rates. Improving adherence to TDMs is a complex issue that requires a comprehensive approach, ongoing dialogue with participants regarding home environment impacts and an agile set of interventions rather than focusing on a traditional single intervention strategy.

The existing RCT data set had significant missing data which limited the exploration of factors that might influence adherence with SC medication and the relationship between adherence with SC medications and abstinence from smoking. This chapter highlighted a low level of adherence to TDMs within *SCANAG*. Moreover, the analyses illustrate the diverse adherence behaviours and a strong association between adherence and successful SC and contextualised the trial intervention in the NHS specific clinical communities and population groups. The trial medication was evaluated by participants regarding acceptability, pragmatics in their lives and effectiveness. RCT participation is a small part of each participant's real world. Participants' home settings are more important than the clinical trial context and shape participants' evaluations of TDM in terms of anticipated and / or experienced side effects and how congruence with medication adherence is navigated within their home environments.

This study indicated the need for a comprehensive multilevel approach to improving adherence and enhancing the effectiveness of TDMs to improve the quality of TDM clinical trials and quit smoking success rates. Improving adherence to TDMs is a complex issue that requires a comprehensive approach, ongoing dialogue with participants regarding home environment impacts and an agile set of interventions rather than focusing on a traditional single intervention strategy. The retrospective

RCT analysis further contextualised these findings by showing that adherence levels were variable and that self-reported beliefs and expectations about medications significantly influenced outcomes. Adherence cannot be fully explained through biomedical or behavioural models alone but must also consider patients' subjective experiences and social contexts.

7.6 Methodological reflections

Mixed methods research methodologies utilised provided a comprehensive understanding of TDM adherence and the implications to SC clinical trials and smokers quit attempts by combining qualitative insights into underlying motivations and barriers and a retrospective critical appraisal of a RCT. The different research methods utilised generated rich, multifaceted data that captured in-depth insights, allowing for a deeper exploration of each chapter's research question. Overall, the research methods strengths allowed for a comprehensive exploration of the thesis research aims and questions by integrating quantitative and qualitative data, providing a more holistic understanding of complex phenomena. Limitations of the research methods employed, include time constraints in terms of data collection, analysis and synthesis. Mixed methods research can add value to TDM clinical trials by providing a comprehensive understanding of interventions' effectiveness, mechanisms of action, and participant experiences. Integrating quantitative data on outcomes with qualitative insights enriches the SC evidence base, informing both clinical practice and policy decisions with a nuanced understanding.

The use of Noblit and Hare's (1988) meta-ethnography approach is a significant strength for synthesising qualitative research on smokers' perspectives of tobacco dependence medications (TDMs). This interpretive methodology enables conceptual translation across diverse studies, generating new insights beyond aggregative review formats (France et al., 2019). The decision to use meta-ethnography aligns well with the aims of this PhD; to understand how smokers make meaning of TDMs, their motivations, and the social contexts influencing adherence.

However, the method is limited by its reliance on existing data, which may omit important population groups (e.g. recent vapers, ethnic minorities, or socioeconomically marginalised individuals underrepresented in published studies). Moreover, without updating the synthesis to include post-2020 studies, the meta-ethnography risks being outdated, particularly given the vaping boom, COVID-19, and shifting public perceptions of pharmacological supports (Notley et al., 2025). The qualitiative study adds essential contemporaneous empirical depth. The use of semi-structured interviews is appropriate for exploring complex, sensitive topics such as personal beliefs, mistrust of medications, and ambivalence about quitting. The application of *PRIME* as a guiding framework helped to structure data analysis around motivation, impulses, and evaluative beliefs (West and Brown, 2013). Despite its richness, the qualitative study was limited by a lack of diversity in its sample, as all participants were drawn from a single urban SSS in Birmingham and were of one ethnic group (white). Broader representativeness could have been enhanced by including rural services or services with specific minority outreach. Additionally, while theoretical guidance is a strength, it may risk imposing a framework too rigidly, potentially overlooking alternative explanatory models (e.g., *COM-B*, social practice theory).

Since the completion of the meta-ethnography, several social and policy changes have influenced the smoking cessation landscape. The proliferation of e-cigarettes, particularly among those seeking unaided cessation, has offered an alternative to traditional TDMs, changing the perception of what constitutes "legitimate" cessation support. Additionally, the COVID-19 pandemic brought new health anxieties and intensified risk awareness, prompting some smokers to quit while reinforcing fatalism in others. *The Johnson government's* resistance to perceived "nanny state" interventions complicated public health messaging and influenced trust in government-endorsed cessation tools. Recent studies (Beard et al., 2021, Notley et al., 2025, Vestbo and Anderson, 2025, Rojas et al., 2025) have shown an increase in vape-related quitting attempts and a continued decline in traditional pharmacotherapy use. These trends point to a need for services to remain responsive and to acknowledge that the SC

journey is highly individualised. The thesis findings highlight the importance of flexible, user-centred approaches that can adapt to evolving norms, technologies, and user expectations.

The retrospective analysis of *SCANAG* phase demonstrated innovative methodological triangulation by reanalysing RCT data qualitatively. The approach enriched traditional effectiveness findings by examining why and how participants adhere (or not) to medications like nortriptyline and NRT. This retrospective design provided real-world explanatory insight, countering the artificiality often associated with RCT conditions. The main weakness here lies in secondary data constraints: participants' perspectives on adherence were not explicitly gathered during the RCT, meaning interpretation is dependent on proxy data (e.g. medication use via self-reported questionnaires). This limits the depth of insight into experiential and motivational factors compared to prospective qualitative inquiry. Furthermore, retrospective analysis lacks control over data quality and may inadvertently introduce bias in interpreting participants' intentions.

The sequential, mixed-methods design is conceptually sound. The meta-ethnography provided a foundation of existing knowledge, the qualitative study contributed new empirical data grounded in lived experience, and the retrospective RCT analysis bridged subjective perspectives with real-world behaviour in a clinical trial. This triangulation enables a richer understanding of adherence than any single method would provide alone. However, integration across phases could be strengthened by a formal mixed-methods synthesis strategy, for example, using joint display matrices (Fetters et al., 2013) or framework synthesis to align findings across paradigms. The reflexive commentary on the researcher's positionality, especially in interpreting RCT data through a qualitative lens, enhanced rigour and transparency.

This PhD's methodological architecture demonstrates a thoughtful and innovative design appropriate to the research aims. It balances the conceptual (meta-ethnography), empirical (qualitative interviews), and translational (retrospective RCT analysis) in a way that few studies achieve in SC

and medication adherence research. However, future versions could strengthen integration, expand sample diversity, and adopt more formal tools for synthesising mixed-methods findings.

7.7 Theoretical implications

The aim of this study was to investigate beliefs about medication held by people wanting to stop smoking in order to provide a deeper understanding of aspects of adherence with tobacco dependency medications that need to be considered to help people quit smoking. *PRIME* (West, 2006) was selected as it related to my observations during the clinical trial where motivation to participate and access the medication was high but subsequent medication adherence behaviours were poor and did not align with intention. The theory posits that the decision to quit smoking is based on a smoker's evaluative beliefs about smoking (either positive or negative), which influence motives to either continue or quit (Uppal et al., 2013). *PRIME* provided valuable insights for understanding the intricacies of motivational processes and an organising framework to account for what is known; it helped to explain adherence to smoking cessation medications. Improving TDM adherence in SC interventions has significant theoretical implications for health behavior change theories. It reinforces the importance of self-efficacy, as consistent adherence to TDMs enhances individuals' belief in their ability to quit smoking successfully. Additionally, it aligns with the principles of social cognitive theory by emphasising the role of environmental factors, such as social support and counselling, in promoting adherence. Moreover, it underscores the relevance of the transtheoretical model, as adherence represents a crucial stage in the behavior change process, leading to sustained SC and improved health outcomes.

The theoretical implications of this PhD are multifaceted. They advance understanding in the domains of health behaviour theory, medication adherence, and tobacco dependency from a qualitative and mixed-methods perspective. This thesis applies *PRIME* as a conceptual framework to explore why smokers may or may not adhere to TDMs. Findings suggest that medication adherence is not a linear decision but a dynamic and emotionally mediated process, involving fluctuating motivation,

ambivalence, and moment-to-moment impulses. The thesis supports and extends *PRIME* by illustrating how real-world medication use is embedded in socio-emotional and biographical contexts. It also critiques the theory's individualistic assumptions, pointing to a need for greater integration with sociological models of structure, stigma, and trust (Goffman, 1963). Traditional models of medication adherence (e.g. the *Necessity-Concerns Framework*, (Horne et al., 1999) often assume rational decision-making. However, the qualitative data in this thesis illustrate that non-adherence may reflect resistance, mistrust, experiential knowledge, or preference for 'natural quitting' rather than forgetfulness or irrationality. The findings advocate for a broader, more contextualised understanding of adherence, one that incorporates embodied knowledge, identity, and past experiences with medications.

The findings challenge assumptions in public health behavioural models that rely on nudging individuals toward medication use through default options or incentives (Thaler and Sunstein, 2008). Many smokers actively reject pharmacological approaches as part of a moral or cultural identity, preferring to stop smoking "unaided" or with e-cigarettes. This underscores the need to move beyond individualist models of behaviour change and integrate cultural and relational theories of health behaviour. By identifying key beliefs, mistrust, and attitudes toward medications among smokers in NHS SSSs, the thesis offers theoretically grounded insights for tailoring service delivery, e.g., using motivational interviewing, narrative-based support, or shared decision-making, all framed within *PRIME*.

This thesis extends the utility of *PRIME* by applying it in real-world, NHS-based cessation contexts. It demonstrates how motivation, identity, and decision-making occur in flux, influenced by real-time social and psychological processes. Furthermore, the findings resonate with sociological theories of medical compliance and health behaviour theories, such as the *Health Belief Model* (HBM) and theories of lay expertise, suggesting that SC interventions must account for both internal cognitive processes and external social structures. *HBM* offers a useful framework to interpret key findings

from this thesis. It suggests that individuals' engagement with health behaviours, such as using tobacco dependence medications (TDMs), is shaped by their perceived susceptibility to harm, perceived severity of the condition, perceived benefits and barriers of treatment, cues to action, and self-efficacy. These constructs align with participants' beliefs uncovered in this study. Some smokers underestimated their personal risk (low perceived susceptibility) or did not view smoking-related illness as sufficiently immediate or severe to warrant pharmacological intervention. Others acknowledged the potential benefits of TDMs but expressed concerns about dependency, side effects, and the stigma of antidepressant use (high perceived barriers), which deterred adherence. Self-efficacy also influenced behaviour; those with lower confidence in quitting were more likely to disengage from both medication and behavioural support. While *HBM* helps explain many of the behavioural patterns observed, this thesis also reveals the limitations of purely cognitive models. It shows that decisions about TDM adherence are shaped not only by beliefs but also by emotions, social norms, identity, and moment-to-moment motivational shifts. These findings support integrating *HBM* with dynamic behavioural theories, such as *PRIME*, to better inform patient-centred cessation interventions.

The mixed-methods design was a key strength of this thesis, allowing for the triangulation of findings and providing both depth and breadth in understanding medication adherence in smoking cessation. Each component contributed complementary insights: the meta-ethnography established a foundational understanding of smokers' beliefs about TDMs; the qualitative study offered rich, first-hand accounts from individuals engaged in NHS SSS; and the retrospective analysis of *SCANAG* provided a pragmatic lens on how adherence issues manifest in trial settings.

However, the sequential structure also presented certain limitations. The meta-ethnography, conducted early in the research process, may have missed relevant studies published later, particularly those reflecting the evolving context of e-cigarette use and post-pandemic behavioural changes. The qualitative study, while providing in-depth and theoretically informed data, was context-specific and

limited in generalisability beyond the urban NHS SSS setting. The retrospective analysis of the RCT, although valuable in exposing real-world adherence challenges, was constrained by the absence of fine-grained behavioural and psychosocial data, which limited the ability to directly link non-adherence to the motivational or relational factors identified in earlier phases. Together, these reflections underscore the value, and complexity, of integrating multiple methods to examine a behaviour as dynamic and context sensitive as SC.

The NHS SSSs remain a crucial part of England's tobacco control strategy. However, this thesis suggests that service redesign is needed to build trust, offer more personalised pathways, and incorporate behavioural and motivational support alongside pharmacological treatment. Practitioners should receive training in motivational interviewing, cultural competence, and real-time behavioural assessment. Public health messaging should address misconceptions about medications while respecting the autonomy and lived experiences of smokers. The thesis also underscores the need for funding stability and investment in research-practice partnerships to continuously adapt services to emerging evidence and shifting public attitudes.

This PhD contributes methodologically to theory by demonstrating how interpretive synthesis (meta-ethnography), primary qualitative research, and secondary RCT data can be integrated using a conceptual framework (*PRIME*). This contributes to the growing field of mixed-methods theory-building in implementation science and behaviour change. The PhD offers a theoretically nuanced account of medication adherence in smoking cessation, challenging and extending existing models, especially in relation to *PRIME*. It underscores the need for theory that better captures agency, mistrust, and the lived realities of marginalised groups, and offers a framework for more responsive and personalised cessation support in public health practice.

This PhD contributes to a growing interdisciplinary literature that recognises smoking cessation as a socially and psychologically embedded process, shaped not only by individual motivation but also by identity, interpersonal trust, cultural narratives, and structural conditions. It repositions medication

adherence in SC not merely as a clinical compliance issue but as a sociocultural practice, influenced by the meanings people attach to medications, their relationships with healthcare systems, and the moral discourses surrounding willpower, addiction, and self-management. By foregrounding the lived experiences of smokers and illuminating how these intersect with pharmacological interventions, this research challenges the dominance of purely biomedical or behavioural models. It demonstrates the critical value of qualitative inquiry in uncovering the relational, emotional, and symbolic dimensions of adherence behaviour, factors that are often overlooked in trial design and policy discourse. Future research and public health practice should continue to integrate these qualitative and person-centred perspectives to inform the development of SC interventions that are more acceptable, equitable, and contextually grounded. Only by aligning treatment strategies with the realities and values of those they intend to support can we begin to address the persistent gaps in SC outcomes and optimise the use of TDMs.

CHAPTER 8 CONCLUSIONS

This PhD concludes at a pivotal moment in UK tobacco control history. As the timeline (appendix 1) illustrates, SC has evolved through clinical, social, and policy lenses, with recent years highlighting persistent inequalities, declining smoking rates, and the complex role of pharmacotherapy and vaping. Since COVID-19, socio-behavioural shifts and renewed policy ambition (e.g., Khan Review) have reshaped service delivery and public discourse. This thesis responds to longstanding research gaps around beliefs, medication adherence, and structural barriers. Moving forward, the UK's tobacco endgame vision demands more nuanced, inclusive approaches, centred on trust, equity, and evidence, to support all smokers toward sustained cessation.

Public health has followed predominantly a positivist approach based on epidemiology; a quantitative discipline. Over the last two decades there has been a well-documented move away from seeing any one research method as the 'gold standard'. The public health impact of interventions is often not realised because the stakeholders have not been involved in the development of the preventive strategies or interventions intended for them. To answer the four research questions, the thesis included qualitative and quantitative components. Generally, it is accepted that the philosophy behind qualitative and quantitative studies are significantly different (Creswell, 2018). My general position pertaining to this thesis was a pragmatist perspective because multiple factors impacting SC and medication adherence had been already identified. The mixed methods research encouraged the use of multiple paradigms (i.e. beliefs and values), rather than the typical association of certain paradigms with quantitative research and others with qualitative research. Each part of the thesis was meaningful and appropriate to the specific context of the thesis in seeking to understand poor medication in *SCANAG*.

SC holds paramount importance in public health, with profound implications for both individual well-being and societal health. Medication adherence is a critical aspect of healthcare with far-reaching implications for individual health outcomes, healthcare systems and public health. Medication

adherence in the context of SC is of paramount importance for achieving successful outcomes in the journey toward being smoke free. Adherence to TDMs, such as NRT or prescription medications, significantly increases the likelihood of successful quitting. Medication adherence is also essential in the effectiveness of SC clinical trials and their efficacy interventions in a smoker's complex real world. Patient engagement in clinical trial design is a pivotal and transformative aspect that significantly enhances the research process and its outcomes. The traditional approach to clinical trials often centered around the perspectives of researchers and healthcare professionals. *SCANAG* trial took a traditional biomedical approach, and the outcome was poor medication adherence.

Researchers should recognise the unique insights and experiences that patients bring to the design process; this would ensure that clinical trials address questions and outcomes that matter most to those directly affected by smoking and interventions to help them quit. A patient-centred approach increases the relevance of the research, making it more meaningful and applicable to the those it aims to benefit. Patient engagement contributes valuable insights into the practical aspects of study design, such as the feasibility of trial protocols, the acceptability of interventions (e.g. medication characteristics) and the burden of participation. This collaboration helps researchers develop more realistic and patient-friendly study designs, potentially increasing recruitment, retention rates and improve medication adherence. The meta-ethnography and qualitative studies found that patients are experts in their own experiences, and the retrospective analyses of *SCANAG* demonstrated the significance of their involvement in identifying acceptable medication interventions to aid smoking cessation. Incorporating patient-reported outcomes would ensure that smoking clinical trials capture not only the clinical efficacy of interventions but also the impact on patients' quality of life, symptoms, and overall well-being.

Cross-national comparisons (e.g., New Zealand's Smokefree 2025, Australia's vape restrictions) highlight that the UK's relatively harm-reduction-friendly regulatory environment enables vaping

more than in other Anglophone countries. Weaker justification for UK specificity in the thesis could be remedied by contrasting how attitudes and adherence vary under divergent policy frameworks. Since 2014, the magnitude of change in the smoking cessation landscape, particularly through vaping's mainstreaming, global inequalities, and persistent motivational narratives, underscores the need for an updated and context-sensitive meta-ethnography. Explicitly incorporating newer UK qualitative studies alongside vaping's quantitative prominence, integrating structural health determinants, and situating the project in an international context will significantly enhance the thesis's theoretical depth, practical relevance, and policy impact.

8.1 Proposed model of medication adherence with TDMs in clinical trials

My model of improving medication adherence with smoking cessation medication(s) within a clinical trial proposes that medication adherence is addressed at each critical stage of the trial. The proposed model (Figure 6) is described below and the corresponding terms and definitions are summarised in Table 10.

Table 10 Summary of the thesis model and definitions

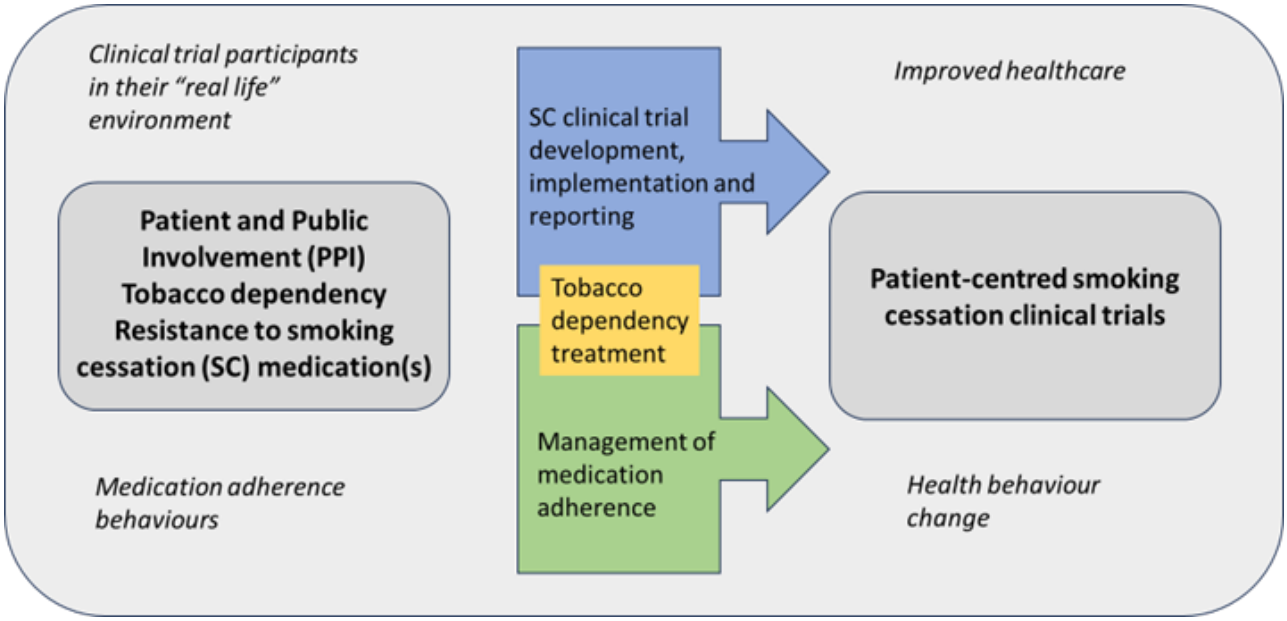
Clinical trial stage	Taxonomy	Definition	Outcome
Feasibility pre-trial stage. Qualitative study(s).	Patient and Public Involvement (PPI). TD. Resistance to TDMS.	Exposing of contexts and psychosocial behavioural. processes that may derail or amplify outcomes. Various stakeholder involvement; patient, family and carers, providers and prescribers.	Informed & modified trial protocol.
Pilot Trial	Refine trial protocol in response to outcomes from feasibility study(s).	To assess the feasibility/acceptability of an approach and intervention(s) to be used in the main study. Identify behavioural strategies, such as goal setting, self-monitoring, and reinforcement. Design medication and packaging aesthetics. Develop patient education about medication adherence. To determine reasonable tolerances and inform trial procedures to enhance adherence.	Optimised protocol.

Main Trial	Trial implemented with optimal adherence.	Medication adherence, measurement & analysis. Management of adherence. Close monitoring of adherence e.g. use of digital technologies, telehealth / virtual care. Tailored interventions components to support medication adherence. Implement medication management systems. Implement communication to optimise medication adherence. To ensure internal validity, reliable outcome interpretation, and ethical treatment of participants. To rigorously evaluate the safety and efficacy of TDMs, and optimal adherence to ensure the integrity of the trial evaluations. Personalised TDM adherence trial interventions enhances the credibility of trial results, supports the translation of research findings into clinical practice, and upholds the ethical principles of participant well-being and justice.	Enhances credibility of trial results. Enabled translation of research findings into clinical practice. Trial upholds the ethical principles of participant involvement in SC clinical trials.
Post Trial	Follow established reporting guidelines	SC clinical trial outcomes are reported with precision, integrity, and ethical consideration, fostering trust in the research community and promoting evidence-based healthcare practices.	Gold standard reporting of SC trials and medication adherence

	(e.g., CONSORT, EMERGE)		Accurate conclusions regarding SC medication treatment effect. Essential insights needed for informed decision making in SC medication development.
Context of SC clinical trials	Principal domains of contextual influences on TDM effectiveness	Clinical trial participants in their “real life” environment Medication adherence behaviours	To address the importance of contextual variation for the interpretation of clinical trial findings. Improved healthcare system. Health behaviour change.

The proposed model (Figure 7) identifies key elements required to achieve patient-centred SC clinical trials proposing necessity of (i) patient and public involvement, (ii) management of medication adherence, (iii) SC clinical development, implementation reporting within the context of participants "real life" environment and medication adherence behaviours to the improvement of healthcare and health behaviours change.

Figure 7 Illustration of TDM trial development and the process of medication adherence management



In response to each thesis chapter findings, this model has resulted in a new conceptual foundation for a transparent taxonomy of SC clinical trials. The terms and definitions are focused on promoting importance and transparency of key concepts and methods to aid in the consideration, measurement, management, analysis and interpretation of TDM adherence within clinical trials.

8.2 Innovation and Strengths

The key outcome of this study was the identification of key factors that inform future clinical practices and RCT design regarding tobacco dependency medications. As the PhD student, I had established strong links with local NHS SSSs; this was important regarding conducting the qualitative study and also to ensure the contemporary relevance of its focus to clinical practice. *SCANAG* (published in a

reputable journal) provided initial curiosity towards factors that might influence adherence with TDMs and the relationship between adherence with TDMs and abstinence from smoking. The clarity and coherence of *PRIME* provided a strong guide for the thesis. Utilising a well-defined theoretical perspective helped guide the research questions and hypotheses, contributing to a cohesive thesis narrative. The meta-ethnography of smoking cessation medication adherence qualitative literature is innovative and was undertaken in collaboration with a qualitative researcher; it was published in a reputable journal.

Collectively, the three chapters (meta-ethnography, qualitative explorations and the retrospective critique of the RCT design and outcomes) provide a good level of depth and balance. The benefits of mixed methods research lie in its ability to offer a more complete, valid, and practically relevant understanding of research questions. This approach was particularly advantageous to investigating complex phenomena, medical adherence to smoking cessation medications, that require both breadth and depth of inquiry. The strengths of the three approaches complemented each other, providing a richer and more nuanced picture of the phenomenon smoking cessation medication adherence.

8.3 Limitations

The meta-ethnography was originally located within an interpretivist world view and aimed at reviewing small numbers of qualitative studies, often involving small sample sizes. Despite attempts to undertake a comprehensive search, some studies may have been missed. Studies included were descriptive and used thematic analysis; it was unclear if the studies analysed the data based on pre-specified theoretical assumptions on the ontological or epistemological status of qualitative data or on medication adherence. These problems may mean the resultant meta-ethnography reflected a thematic synthesis of evidence rather than a conceptual development of evidence, resulting in meta-ethnographies that do not reach the intended level of analytical depth. The meta-ethnography findings were presented as inherently characteristic of smokers' concerns and difficulties of SC. This generalised the needs and experiences of individual smokers and did not fully address the

complexities of TDMs behaviours. None of the studies worked from a definition of adherence or within available typologies of medication adherence, despite the extensive theorisation in the literature. Further, most of the data was descriptively reported providing little interpretation of the causes or consequences of differences between prescribed and actual use of TDMs. Included studies were from either the UK or USA, where SC programmes align with similar guidelines and best practices. It was acknowledged that the studies were undertaken in differently funded systems of health care (UK and USA) limiting the transferability of the present findings. It was possible that during the process of analysis the findings became interpreted so much that they lost their grounding or association with the included studies.

The qualitative nature of limits the generalisability of the qualitative study findings to a broader population of individuals with TD. Furthermore, the study was conducted in a single NHS SSS situated in a deprived area. Participants recruited had several prior attempts at SC and experience with TDMs and may not reflect the experiences of smokers seeking to quit for the first time. Therefore, results may be not generalisable to smokers in other settings. Electronic cigarettes have emerged as a controversial SC method, but these were not explored directly regarding their role in increasing adherence to TDMs.

A weakness of the retrospective chapter is that it generated a great deal of missing data. Missing data reduced the representativeness of the sample and had the potential to distort inferences about the population. I did explore dealing with the missing data by imputing (i.e., filling in) the missing values. There are no established guidelines about an acceptable percentage of missing data which imputation will have benefits. Adherence to the *SCANAG* trial medication was inconsistent and low due to diverse factors. Although pragmatic RCTs aim to minimise bias, the real-world nature of the study design introduced various biases, such as selection bias, attrition bias, and measurement bias. These biases impacted the validity and reliability of the trial findings. This chapter was therefore structured in accordance with a formal critical appraisal process (CASP, 2021) which through a series

of eleven questions assessed the validity, results, and applicability of the RCT and enabled exploration of the trial medication adherence.

8.4 Anticipated benefits of this research

The aim of this thesis was to investigate beliefs about medication held by people who wanted to stop smoking to provide a deeper understanding of what aspects of adherence with TDMs need to be considered to help people quit smoking. I believe that the value of understanding medication adherence behaviour with SC clinical trials is that it will lead to a new generation of interventions to enable people to stop smoking. An achievement of this thesis is the provision of a deeper pragmatic understanding of the process by which adults attempting to quit smoking adhere or not to TDMs and how this behaviour is influenced. The knowledge generated aims to contribute to the development of targeted interventions to increase adherence with TDMs and support NHS SSSs tobacco addiction treatment programs. Further, adherence to SC clinical trial medication is important to trial outcomes. The meta-ethnographic review focused on interpretations made the researchers and characteristically could generate hypotheses, achieve higher-level theorising, reconcile consensus and contradictions within individual qualitative studies and uniquely derived more formalised new knowledge about smokers' medication use. The line-of-argument synthesis captured recurring perceptions and experiences that supported (facilitators) or hindered (barriers) TDM adherence.

The process of utilising *PRIME* as the theoretical framework for the qualitative study enabled the development of knowledge of underlying principles of adherence behaviours with SC medications within the context of NHS SSSs; these could be useful to policy and service developments. SC pharmacotherapy adherence has been understudied in the literature; hence this study provides a valuable addition to SC clinical practice and research studying tobacco addiction interventions and adherence with medications used to support health behaviour change. Further, examination of sociodemographic differences in smoking, and quitting barriers and motivations, may help create interventions tailored for particular groups. The retrospective critique of *SCANAG* found that

participants not being adherent with their treatment during the trial was significant, it caused missing data which resulted in a poor trial data set that undermined results, data analyses and trial conclusions. Further participant's beliefs, perceptions, and attitudes towards the trial medication were found to strongly influence their motivation, decisions, and adherence behaviours. Patient engagement in smoking clinical trial design is not just a moral imperative but also a pragmatic strategy that enriches the entire research process. It would lead to more relevant, feasible, and patient-centred trials, ultimately improving the quality and impact of smoking cessation clinical research on public health outcomes.

In summary, patient engagement in clinical trial design is not just a moral imperative but also a pragmatic strategy that enriches the entire research process. It would lead to more relevant, feasible, and patient-centred trials, ultimately improving the quality and impact of SC research on public health outcomes. Smokers' attitudes, beliefs, underuse and resistance towards TDMs suggests that research and policy need to focus on increasing smokers' implicit motivation to quit improving TDM medication adherence, even for those who classify themselves as having high motivation to quit mostly have poor levels of TDM medication adherence. During SC attempts, targeted medication adherence information and further education about NHS SSSs is required to increase medication adherence, this should be delivered using a theoretical health behaviour change framework. Overall, this study has important implications for developing effective SC interventions and policies that address the complex factors influencing smoking medication adherence behaviour among adults seeking to quit.

RECOMMENDATIONS

Based on the findings of this PhD and considering contemporary research and policy developments, several recommendations are proposed for future research, clinical practice, and policy in smoking cessation and medication adherence. I have several personal conclusions on the role of this thesis in the future.

First, qualitative research in this area should continue to adopt purposive and theoretically informed sampling strategies that ensure inclusion of underrepresented populations, particularly ethnic minority smokers and those living in socioeconomically deprived areas. These groups often experience disproportionate tobacco-related harm yet remain underserved and underrepresented in research. Studies must acknowledge historical mistrust in institutions and ensure culturally competent, co-designed research approaches that build trust and empower participation. I think researchers and clinicians know more about the theoretical, conceptual and methodical issues of SC, than they do about smokers' understanding of their TD treatment options and their decisions to adhere to them. Addressing the problem of non-adherence with TDMs needs close collaboration between clinicians, researchers and smokers to develop effectives methods to minimise the problem of non-adherence. Patients today expect to take a more active role in their own care, and SC, they are active in their decision making and evaluate of TDMs for themselves whether the medication is safe, fits into their life, is compatible with their significant others' beliefs about medications. I believe that clinicians and researcher communications with smokers is a key determinant to predicting both adherence and non-adherence; patient and public involvement in research is essential to future SC medication trial development and the process of medication adherence management.

The meta-ethnography study found three themes relating to smokers' medication use of tobacco dependence medications which emerged from the lines of argument process: (i) psychosocial context of tobacco dependence medication behaviours, (ii) predilection for willpower and "natural" methods to achieve quit success and (iii) resisting medications. *PRIME* and many other health psychology-

based theoretical frameworks used in SC or medication adherence research contribute to understanding of the psychology and behaviour of adherence. I believe that the capacity of these theoretical approaches to generate effective TD interventions has yet to be fully evaluated and this remains a key challenge for future TD adherence research and the development of TDMs. I think it is important for research to provide a more complete explanation of TDM adherence behaviours than research that provides "single point" decisions about TDMs (e.g. initiation, lapses back to smoking, within psychosocial contexts of taking them) is important to improving TDM adherence. Further, theoretical and practical application of *PRIME* is recommended. This model, focused on moment-to-moment motivation and internal conflict, offers a valuable lens for understanding adherence to tobacco dependence medications. Future interventions could utilise real-time ecological momentary assessment (EMA) methods to measure fluctuations in adherence, cravings, and motivation, allowing interventions to respond dynamically to relapse risks.

Second, NHS SSSs must shift towards more individualised, relational models of care that consider personal experiences with pharmacotherapy, beliefs about medication, and non-clinical drivers of behaviour, such as identity, autonomy, stigma, and social context. Rather than defaulting to pharmacological treatment pathways, services should integrate meaningful behavioural and peer-led support, digital options that do not exacerbate inequalities, and patient-led treatment plans.

Third, researchers should consider mixed methods designs with longitudinal follow-up to explore how broader societal and political shifts, such as changes in legislation, the growth of e-cigarettes, and public health narratives, impact medication use, service uptake, and cessation outcomes. The post-COVID landscape has seen new dynamics in digital health, health anxieties, and health autonomy, all of which intersect with smoking cessation efforts.

Fourth, training for stop smoking practitioners should be expanded to incorporate findings from sociological research on medication beliefs, stigma, and lay knowledge. Helping professionals

understand why individuals may resist or discontinue medications despite their efficacy can foster more supportive, non-judgemental care environments.

Fifth, at the policy level, greater funding and structural support is needed for local SSSs, especially in areas of high deprivation. As the *Khan Review* (2022) recommended, efforts to deliver a smoke-free generation must be matched by robust, community-sensitive services that accommodate a variety of cessation routes, including vaping and psychological support.

Finally, comparative research between the UK and other countries (e.g., New Zealand, Australia) pursuing endgame policies could offer insights into the interplay between individual behaviour and national policy. This PhD contributes to that evidence base by examining how medication adherence is not simply a clinical issue but one shaped by trust, policy, power, and lived experience. I think that an important avenue for future research would focus on the identification and removal of barriers to adherence to TDMs. The model developed from the meta-ethnography study depicted oscillation between psychosocially driven beliefs about TDMs, which mostly did not resonate with the current medical model of TD treatment. I think it is important that research that acknowledges what the smoker thinks about the TDM, how that influences what they do, would identify certain cognitions which underpin smoker's adherence decisions. The qualitative study concluded that personalised TDM adherence interventions are likely to be most effective to help improve long-term SC outcomes. The retrospective critique of the RCT indicated the need for a comprehensive multilevel approach to improving adherence and enhancing the effectiveness of TDMs to improve the quality of TDM clinical trials and quit smoking success rates. Improving adherence to TDMs is a complex issue that requires a comprehensive approach, ongoing dialogue with participants regarding home environment impacts and an agile set of interventions rather than focusing on a traditional single intervention strategy.

My PhD journey has led me to believe theoretical frameworks should emphasise that smokers make active decision about whether to follow the treatment advice on the basis of whether it makes sense

in their lives, their experiences and beliefs about medications and how they should stop smoking, and ideas about the nature of tobacco addiction, and how adherence / non-adherence is perceived to affect it. Taken together, the recommendations seek to inform more responsive, equitable, and theoretically grounded approaches to smoking cessation and tobacco dependency treatment in the UK and beyond. Future research should be aimed at understanding HCPs' perceptions and practices of assessing medication adherence in smokers; this may guide interventions to resolve this important issue of medication nonadherence. Research to further understand how a smoker's predilection for willpower augments resistance to TDMs is required. I believe that this would help in achieving improved long-term quit outcomes. Stopping smoking prolongs life and reduces morbidity. Overall, I think smoker-informed, novel SC treatments and tailored medication adherence management interventions, which are congruent with a smoker's psychosocial context and align with their medication beliefs, are likely to be most effective to help improve long-term SC outcomes.

Since 2023, significant social and behavioural shifts have influenced the SC landscape in the UK. Public attitudes towards nicotine use have been increasingly shaped by the normalisation of vaping, alongside growing ambivalence towards pharmaceutical smoking cessation treatments. Contemporary literature has noted a marked increase in the use of e-cigarettes as first-line quit attempts, even in NHS-supported contexts (ASH, 2023, Rojas et al., 2025). This trend reflects changing preferences among smokers, many of whom perceive vaping as a more controllable, less medicalised, and socially acceptable alternative to pharmacological therapies (Notley et al., 2025).

Simultaneously, wider social changes, including post-pandemic public health fatigue, declining trust in state health institutions, and a cost-of-living crisis, have further complicated engagement with formal cessation services (Jackson et al., 2024, Khouja et al., 2024). Smokers increasingly value autonomy and personal agency in cessation, reinforcing earlier thesis findings on the importance of identity, willpower, and lay expertise in shaping medication adherence. This evolving context reinforces the necessity of culturally and contextually adaptive services. It also strengthens the case

for integrating patient-centred approaches that value non-pharmacological and hybrid cessation methods. More recent studies (Vestbo and Anderson, 2025, Gupta and Lee, 2025) have called for the development of "blended cessation models" combining digital tools, peer-led support, and brief pharmacological interventions, tailored to motivational readiness and social background. Therefore, this thesis's recommendations for personalised, trust-based NHS SSS models remain highly relevant. The findings also suggest future directions: integrating real-time behavioural analytics, co-designed services, and a more nuanced public health narrative around pharmacotherapy. The field is shifting from a universal pharmacological approach to a multimodal, individualised paradigm. Embedding such models in NHS SSSs will ensure greater adherence and sustained cessation outcomes in an increasingly diverse and digital health environment.

This thesis set out to explore why adherence to tobacco dependence medications (TDMs) remains suboptimal, despite their proven clinical efficacy, and to examine this issue through a socio behavioural and person-centred lens. Using a mixed-methods design, comprising a meta-ethnography, a qualitative study, and a retrospective analysis of a pragmatic randomised controlled trial (RCT), this research illuminated the complex interplay of beliefs, identities, motivations, and contextual influences that shape smokers' engagement with pharmacological support. Across all three phases, it became clear that medication adherence is not simply a function of understanding, access, or clinical recommendation. Rather, it is a socially embedded process, influenced by personal histories, perceived norms, emotional states, trust in healthcare systems, and the symbolic meanings attached to both smoking and medication. These findings challenge prevailing models that frame non-adherence as an individual deficit and instead argue for a more holistic, sociological approach to understanding and supporting SC.

Importantly, the thesis also highlights how the design and delivery of SC trials and services must evolve. Incorporating patient perspectives into medication development, trial design, and treatment

delivery is critical. Behavioural science alone is insufficient if not informed by qualitative insights that reflect real-world complexity.

This research contributes original knowledge by identifying the barriers to TDM adherence not only as behavioural or motivational, but as relational and sociocultural. It calls for a shift in how TD is treated and understood: from compliance to collaboration, from efficacy to experience. Future interventions must move beyond "what works" in controlled conditions to consider "what matters" to smokers navigating the challenges of quitting. By grounding cessation strategies in lived experience, we can create more responsive, equitable, and ultimately more effective public health approaches to ending tobacco use.

CHAPTER 9 APPENDICES

9.1 Appendix 1 Timeline: *Smoking, Smoking Cessation, and Medication Adherence Research Milestones*

1950s–1970s: Foundations

- **1950** – *Doll & Hill* publish first case-control study linking smoking and lung cancer.
- **1964** – U.S. Surgeon General's report conclusively links smoking to serious health risks.
- **1965–1970s** – Early behavioural cessation programs developed; nicotine considered primarily a behavioural habit, not pharmacological dependency.
- **1970s** – Introduction of *Health Belief Model (HBM)*
    - Emphasised perceived severity, susceptibility, benefits, and barriers as predictors of health behaviour. *HBM* (Rosenstock) laid groundwork for understanding perceptions of illness risk and treatment benefit.
    - Provided a foundational psychological model to explain medication adherence.
- **1971** – First national anti-smoking campaigns begin in the UK.

1980s: Understanding Nicotine Dependence

- **1980s** – Early research focuses on behavioural models (e.g., *Theory of Planned Behaviour (TPB*).
- **1982** – Role of 'Concordance' and Patient Autonomy
    - Sociologists began to challenge the compliance model, arguing for a shift toward shared decision-making.
    - Introduced the idea that adherence must reflect patient values, culture, and autonomy.
    - Medical sociologists begin rejecting paternalistic "compliance" narratives in favour of patient-centred views.
- **1988** – U.S. Surgeon General declares nicotine to be addictive, on par with heroin and cocaine.
- **1984–1988** – Emergence of the *HBM* and *TPB* in smoking behaviour research.
- **1986** – First nicotine replacement therapies (NRT) introduced (e.g., nicotine gum).

1990s: Pharmacotherapy and Behavioural Models

- **1992** – First transdermal nicotine patches approved for over-the-counter use in the U.S.
- **1995** – Varenicline and bupropion (non-nicotine pharmacotherapies) enter clinical trials.
- **1999** – *West and Shiffman* propose the *PRIME Theory* of motivation in addiction.
- **1990s** – Adherence research begins to explore the psychosocial barriers to medication use in smoking cessation.

- **1995** – Kleinman's Explanatory Models of Illness
    - Arthur Kleinman highlighted cultural and social influences on patients' interpretations of illness and treatment.
- **1997** – UK's From Compliance to Concordance report formally shifts discourse to negotiated treatment relationships.

1998 – White Paper "*Smoking Kills*" (Department of Health)

- The first comprehensive UK government strategy on tobacco control.
- Proposed the establishment of *NHS Stop Smoking Services* (SSSs).
    - SSSs introduced via the White Paper *Smoking Kills*, a landmark public health intervention.
- Recognised smoking as the leading cause of preventable illness and death.

2000 – Launch of SSSs

- Nationwide rollout offering behavioural support and pharmacotherapy (NRT, later varenicline and bupropion).
- SSSs were free and accessible via primary care, pharmacies, and community settings.
- 2000 – Concordance Framework (UK)
    - Move away from "compliance" to "concordance" in medication adherence literature.
    - Recognised the importance of respecting patient beliefs and negotiating treatment decisions.
- 2001 – Bupropion licensed for smoking cessation.
- 2006 – Varenicline (Champix) approved by NICE.
- Focus on behavioural support + pharmacotherapy as best practice.
- Emergence of sociological studies exploring stigma, identity, and motivation in smokers' experiences.

2000s: Adherence and Combined Approaches

- **2000s** – Increasing focus on medication adherence and real-world effectiveness vs. efficacy.
- **2003** – WHO Framework Convention on Tobacco Control (FCTC) signed, influencing global cessation efforts.
- **2004** – NICE (UK) publishes first smoking cessation guidelines incorporating pharmacological therapies.

- **2004** – NICE Guidelines Begin Emphasising Patient Experience
    - NICE CG76 and later guidance began incorporating patient preferences and social contexts into adherence recommendations. NICE includes patient views and experience in early adherence guidelines.
- **2005–2010** – Growth in Qualitative Adherence Research

  Studies used interviews, ethnographies, and grounded theory to explore how trust, identity, and stigma affect adherence, particularly for chronic conditions and mental health.
- **2005** – Pound *et al*.'s synthesis of qualitative studies documents complex moral, emotional, and identity work in medicine-taking.
- **2006** – Varenicline (Champix) approved in UK and US; widely studied in clinical trials.
- **2008** – *Hajek et al.* and *West et al.* publish influential studies on pharmacotherapy efficacy and real-world effectiveness.

2008: NICE Public Health Guidance PH10

- Provided evidence-based recommendations on smoking cessation services in primary care, workplaces, and other settings.
- Emphasised combined behavioural support and pharmacological aids.

2010s: Population-Level Interventions and E-cigarettes

- **2011** – Necessity-Concerns Framework (NCF) Gaining Influence
    - Horne *et al*. advanced a model focusing on beliefs about necessity of medication vs. concerns about harms.
    - Research focuses on chronic illness, intentional vs. unintentional nonadherence, and role of doctor-patient trust.
- **2013** – NICE issues updated guidance (PH48) incorporating behavioural support and multi-therapy approaches.
- **2014–2018** – Rise of e-cigarette use prompts comparative studies on effectiveness vs. NRT and medications.
- **2015** – PHE endorses e-cigarettes as 95% less harmful than smoking.
- **2016** – Cochrane review on e-cigarettes and traditional cessation methods updated.
- **2016–2018** – Research into Health Literacy, Digital Support, and Social Inequities

    - Increasing focus on how structural factors (language, culture, healthcare communication) influence patient understanding and expectations around medications.
    - Research focuses on chronic illness, intentional vs. unintentional nonadherence, and role of doctor-patient trust.
- Widespread cuts to local authority public health budgets begin affecting SSS provision.

2012 – Introduction of Stoptober Campaign (Public Health England)

- Annual mass quit attempt campaign using behavioural insights.
- Significant public engagement via media, mobile apps, and social support tools.

2013 – Transfer of Public Health to Local Authorities

- Resulted in variability in funding and delivery of SSSs across regions.
- Began a period of service fragmentation and budget cuts.

2016 – Tobacco Control Plan for England

- Aimed to reduce smoking prevalence to 12% by 2022.
- Supported a harm reduction approach including use of e-cigarettes.
- Smoking prevalence drops to ~14% of adults.
- Smoking becomes increasingly concentrated in disadvantaged communities.
- Research focuses on inequities in service access, medication uptake, and mistrust in healthcare.

2019 – NHS Long Term Plan (NHS England)

- Committed to embedding tobacco dependency treatment into secondary care, maternity, and mental health services.
- Marked shift toward integration of cessation within routine NHS care.

2020 – COVID-19 Pandemic

- Initial reports suggested increased quit attempts due to respiratory health concerns.
- Some smokers quit in fear of COVID risks; others relapse due to stress, isolation.
- Later data revealed complex patterns: increased stress-related smoking and widening health inequalities.
- 2020 – COVID-19 Pandemic and Medication Adherence

- Pandemic-related fear, disrupted healthcare access, and changing trust in institutions significantly influenced beliefs around medications.
- Trust in public health messaging becomes a key determinant of adherence.
- SSSs move online or pause altogether.
- Digital inequalities worsen disparities in access to smoking cessation.
- **2020–2022** – COVID-19 pandemic reshapes smoking behaviours; some quit due to health concerns, others relapse due to stress.
- **2021** – Studies show reduced engagement with SSSs during pandemic.
- **2023** – Qualitative studies highlight mistrust of pharmacotherapies and preference for e-cigarettes, especially among ethnic minorities.

2022 – Updated NICE Guidance on Smoking Cessation (NG209)

- Supported the use of e-cigarettes as cessation aids in service delivery.
- Promoted tailored behavioural support and offered structured pathways for hard-to-reach groups.
- 2022 – *Khan Review* (Making Smoking Obsolete) recommends:
    - Raising legal smoking age each year.
    - More investment in SSSs.
    - More funding for vaping as a cessation tool.

2023 – Varenicline withdrawn due to impurity concerns

- Increased reliance on NRT and e-cigarettes.
- Sparked debate about pharmaceutical availability and over-dependence on vaping as a cessation tool.
- Varenicline reintroduced for patients end of 2024.
- **2023–2024** – Focus on Mistrust, Cultural Values, and Polypharmacy in Minority Groups
    - New qualitative research explores mistrust in healthcare among ethnic minority populations, the impact of religious/spiritual beliefs, and cultural interpretations of medication use.
- **2023–24** – Mixed reactions to *Khan Review*; debates over:
    - E-cigarettes in youth.
    - Ethical tensions between harm reduction and regulation.
    - Return of mistrust narratives, especially in low-income and ethnic minority communities.

- **2024–2025** – Increasing focus on mixed-methods research combining RCT data with patient narratives to explore adherence, beliefs, and real-world medication use.
- **2022–2024: Polypharmacy, Vaping, and Digital Surveillance**
    - Research expands to multimorbidity, medication fatigue, and cultural mistrust.
    - Focus on adherence within populations who use e-cigarettes, self-manage chronic illness, or question "big pharma."

2024 – Rise of Digital Quit Tools and Equity-Focused Research

- Growing use of AI-based apps, SMS support, and digital therapeutics.
- Increased research focus on inequalities in medication adherence and access to cessation support, especially among ethnic minorities and low-income groups.

2025 – Moral Economies of Adherence and AI Integration

- Emerging concepts include:
    - *Moral ambivalence*: How patients navigate between personal responsibility and systemic pressure to adhere.
    - *AI-mediated adherence tools*: Ethical concerns around autonomy, surveillance, and patient agency (e.g., digital pills, smart dispensers).
    - *Post-pandemic distrust*: Ongoing influence of COVID-era misinformation and politicised health messaging.

Emerging and Future Research Directions

1. **Structural Determinants of Adherence**
    - Poverty, racism, housing instability, and immigration status as key adherence disruptors.
    - Intersectional research will become central to understanding "adherence deserts" and health system disengagement.
2. **Medication Adherence and Identity Politics**
    - How gender, race, religion, and age intersect with medication use beliefs.
    - Resistance to medications as acts of autonomy or protest.
3. **Co-production of Knowledge with Marginalised Patients**
    - Rise of participatory qualitative methods: photovoice, ethnography, patient-led interviews.
    - Shift from research *on* to research *with* communities.

4. **Digital Divide and Algorithmic Bias in Adherence Monitoring**
    - Surveillance concerns with app-based or AI-driven adherence technologies.
    - Need for sociotechnical critique of digital health tools.
5. **Pharmacological Innovation and Adherence**
    - Renewed interest in medications like nortriptyline, combination NRT, and dual therapy models.
    - Focus on longitudinal qualitative research into beliefs, willpower, and scepticism about pharmacotherapy.
6. **Socio-cultural Factors in Cessation**
    - Research exploring how class, race, and identity intersect with smoking practices and treatment experiences.
    - Co-design of services with under-served communities.
7. **Vaping as a Cessation Tool**
    - Critical evaluations of vaping behaviours and their sociological meaning (e.g., habit substitution, moral framing).
    - Continued debates over medical licensing of e-cigarettes and regulation.
8. **Digital Health and Surveillance**
    - AI-enabled support tools (apps, trackers, online CBT) may aid cessation but raise ethical issues.
    - Unequal access and trust concerns among digitally excluded populations.
9. **Global and Comparative Research**
    - Comparative studies between the UK, New Zealand, and Scandinavian countries exploring tobacco endgame strategies.
10. **Endgame Policy Evaluation**
    - Evaluation of UK government efforts (e.g., raising legal smoking age).
    - Longitudinal studies on public perceptions of the "nanny state", autonomy, and state intervention in lifestyle choices.

9.2 Appendix 2 *Example Search Syntax*

MEDLINE (Ovid SP) was searched using the Ovid interface on 22/04/16 for the period 1946 to March week 3 2016

1. smoking.mp. (211575)
2. (smoking cessation or quit* or stop smoking or abstinence or success).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (304424)
3. tobacco dependence.mp. or "Tobacco Use Disorder"/ (9627)
4. (Medication adherence or medication compliance).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (13634)
5. (Adher* compl* or concord*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (44056)
6. (NRT or nicotine replacement therapy or bupropion or wellbutrin or zyban or voxa or budeprion or aplenzin or amfebutamone or nortriptyline or varenicline or chantix or champix).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (8890)
7. (belief* or attit* or view* or idea* or experien* or meaning* or percept* or misconcep*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1759265)

8. (pharmacology or medication or therapy or smoking cessation method or smoking cessation inter*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2057220)
9. (qual* or pheno* or survey or focus group or case study or quest* or diary).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2878804)
10. 1 or 2 or 3 (483489)
11. 4 or 5 (57498)
12. 10 and 11 (2274)
13. limit 12 to yr="1990 -Current" (2167)
14. limit 13 to humans (2063)
15. limit 14 to "all adult (19 plus years)" (1360)
16. 9 and 12 and 13 and 14 and 15 (549)

9.3 **Appendix 3:** *Standardised appraisal tools from the Joanna Briggs Institute (JBI) System for the Unified Management Assessment and Review of Information (SUMARI) package*

JBI QARI Critical Appraisal Checklist for Interpretive & Critical Research

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear
1. Is there congruity between the stated philosophical perspective and the research methodology?	☐	☐	☐
2. Is there congruity between the research methodology and the research question or objectives?	☐	☐	☐
3. Is there congruity between the research methodology and the methods used to collect data?	☐	☐	☐
4. Is there congruity between the research methodology and the representation and analysis of data?	☐	☐	☐
5. Is there congruity between the research methodology and the interpretation of results?	☐	☐	☐
6. Is there a statement locating the researcher culturally or theoretically?	☐	☐	☐
7. Is the influence of the researcher on the research, and vice-versa, addressed?	☐	☐	☐
8. Are participants, and their voices, adequately represented?	☐	☐	☐
9. Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?	☐	☐	☐
10. Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data?	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reasons for exclusion)

_____

_____

_____

_____

_____

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_____

9.4 Appendix 4: *Risk of bias summary: review authors judgements about each risk of bias item for each included interpretive study*

JBI checklist criteria for Qual studies	**White, 2006**	**Levinson, 2006**	**Burgess, 2007**	**Fu, 2007**	**Vogt, 2008**	**Carpenter, 2011**	**Tsang, 2014**
Is there congruity between the state philosophical perspective and the research methodology?	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Is there congruity between the research methodology and the research question or objectives?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is there congruity between the research methodology and the methods used to collect data?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is there congruity between the research methodology and the interpretation of results?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is there a statement locating the researcher culturally or theoretically?	Yes	Yes	No	Yes	Yes	No	Yes
Is the influence of the researcher on the	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

research, and vice versa, addressed?							
Are participants, and the voices, adequately represented?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is the research ethical according to current criteria or, for recent students, and is there evidence of ethical approval by an appropriate body?	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes
Do the conclusions drawn ion the research report flow from the analysis, or interpretation, of the data?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Summary of risk	**Unclear**	**Unclear**	**Unclear**	**Unclear**	**Unclear**	**Unclear**	**Unclear**

9.5 Appendix 5: *JBI Data Extraction for Interpretative & Critical Research*

JBI QARI Data Extraction Form for Interpretive & Critical Research

Reviewer _____ Date _____

Author _____ Year _____

Journal _____ Record Number _____

Study Description

Methodology _____

_____

Method _____

_____

Intervention _____

_____

Setting _____

_____

Geographical _____

_____

Cultural _____

_____

Participants _____

_____

Data analysis _____

_____

Authors Conclusions

_____

_____

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_____

Comments

_____

_____

9.6 Appendix 6: *qualitative study advertising poster*

UNIVERSITY OF BIRMINGHAM

School of Health & Population Sciences
Nursing & Physiotherapy

Adult volunteers required for a study

The study is interested in finding out what or who influences people's behaviour with smoking cessation (SC) medications (NRT, Zyban or Champix) especially how they follow prescription instructions.

This will require you to tell your story about using SC medications to the researcher (PhD student Mrs Carol J Sanders at The University of Birmingham). This will be tape recorded.
It will take approximately 1 to 1 and half hours and will be arranged at your convenience here at the stop smoking service.

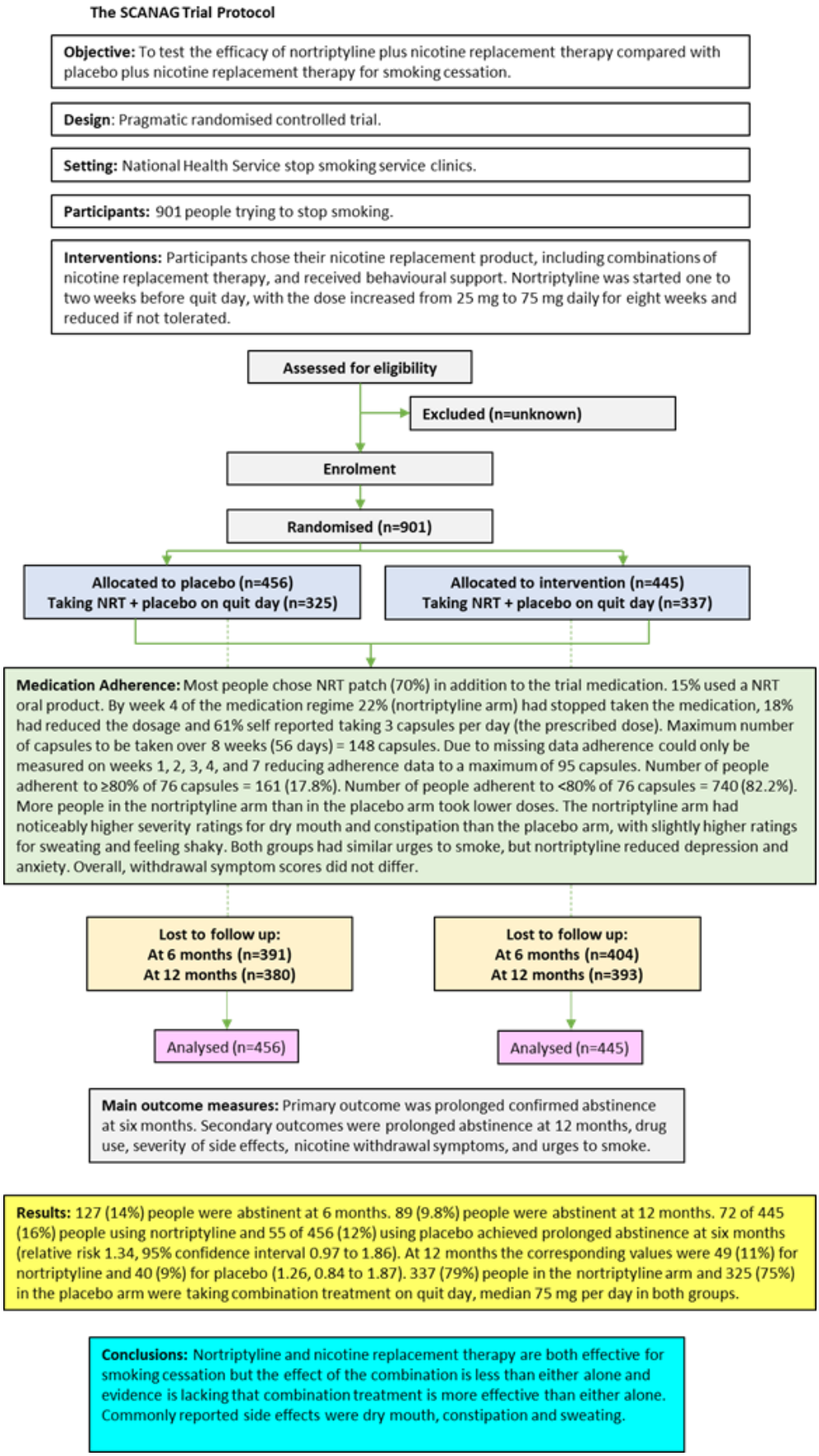
Your participation is voluntary and you are free to withdraw at any time. You should only participate if you want to; choosing not to take part will not disadvantage you in any way.

If you would like to take part please let a SC adviser know this; he/she will inform Carol. Carol will then arrange to meet with you to talk about the study and answer your questions and if you agree Carol will then arrange an appointment with you.

9.7 Appendix 7: *qualitative study interview guide*

- What is your view on the medication methods for people trying to quit?
- What kind of support do you need and/or prefer in dealing with your experiences and symptoms of quitting smoking?
- Could you please tell me about your experiences with medications to help you stop smoking?
- Do you think it is necessary to use TDMs to help you stop smoking? Do you think
- it is safe? Do you think it is effective?
- Please tell me about the support you have had regarding using TDMs.
- Could you please tell me in your own words what did you do to help adhere (stick to) your TDM prescription?
- How have your experiences of using TDMs changed your views of them?
- Do you adhere (stick to) to other medication differently to TDMs?
- Can you tell me more about situations that affected how you took your medication?
- What are the most important things that helped you take your medication?
- Do you have suggestions for health professionals about providing support to help people adhere (stick to) talking their TDMs?

9.8 Appendix 8: *The SCANAG Trial*



9.9 Appendix 9: *Critical Appraisal of SCANAG RCT*

CASP Randomised Controlled Trial Standard Checklist:

11 questions to help you make sense of a randomised controlled trial (RCT)

Main issues for consideration: Several aspects need to be considered when appraising a randomised controlled trial:

- Is the basic study design valid for a randomised controlled trial? (Section A)
- Was the study methodologically sound? (Section B)
- What are the results? (Section C)
- Will the results help locally? (Section D)

The 11 questions in the checklist are designed to help you think about these aspects systematically.

How to use this appraisal tool: The first three questions (Section A) are screening questions about the validity of the basic study design and can be answered quickly. If, in light of your responses to Section A, you think the study design is valid, continue to Section B to assess whether the study was methodologically sound and if it is worth continuing with the appraisal by answering the remaining questions in Sections C and D.

Record 'Yes', 'No' or 'Can't tell' in response to the questions. Prompts below all but one of the questions highlight the issues it is important to consider. Record the reasons for your answers in the space provided. As CASP checklists were designed to be used as educational/teaching tools in a workshop setting, we do not recommend using a scoring system.

About CASP Checklists: The CASP RCT checklist was originally based on JAMA Users' guides to the medical literature 1994 (adapted from Guyatt GH, Sackett DL and Cook DJ), and piloted with healthcare practitioners. This version has been updated taking into account the CONSORT 2010 guideline (http://www.consort-statement.org/consort-2010, accessed 16 September 2020).

Citation: CASP recommends using the Harvard style, i.e., *Critical Appraisal Skills Programme (2021). CASP (insert name of checklist i.e. Randomised Controlled Trial) Checklist. [online] Available at: insert URL. Accessed: insert date accessed.*

Study and citation: (Aveyard et al., 2008)

Nortriptyline plus nicotine replacement versus placebo plus nicotine replacement for smoking cessation: pragmatic randomised controlled trial

Section A: Is the basic study design valid for a randomised controlled trial?	

1. Did the study address a clearly focused research question?
CONSIDER:
• *Was the study designed to assess the outcomes of an intervention?*
• *Is the research question 'focused' in terms of:*
  • *Population studied*
  • *Intervention given*
  • *Comparator chosen*
  • *Outcomes measured?*
	Yes No Can't tell
	√
	
	RCT objective To test the efficacy of nortriptyline plus nicotine replacement therapy compared with placebo plus nicotine replacement therapy for smoking cessation.
	Setting National Health Service stop smoking service clinics.
	Participants 901 adults trying to stop smoking.
	Interventions Nortriptyline and placebo were provided in 25 mg capsules, maximum daily dose 75 mg. One to two weeks before quit day participants used 25 mg of either drug for three days, 50 mg for four days, and 75 mg thereafter, a dose found effective in previous trials. Participants chose their nicotine replacement product, including combinations of nicotine replacement therapy, and received behavioural support. Nortriptyline was started one to two weeks before quit day, with the dose increased from 25 mg to 75 mg daily for eight weeks and reduced if not tolerated.
	The **primary outcome** was prolonged abstinence at six months—defined, as is usual, as no smoking at all between day 15 after quit day and the six-month follow-up, confirmed by cotinine concentration in saliva or exhaled carbon monoxide concentration.
	The **secondary outcomes** were confirmed seven-day point prevalence abstinence at 26 weeks and 52 weeks, and prolonged abstinence at 52 weeks. We also measured prolonged abstinence at four weeks; seven-day point prevalence abstinence; nicotine withdrawal symptoms; urges to smoke, using the mood and physical symptoms scale severity rating of known side effects of nortriptyline; and quality of life using the EQ-5D.

2. Was the assignment of participants to interventions randomised? *CONSIDER:* • *How was randomisation carried out? Was the method appropriate?* • *Was randomisation sufficient to eliminate systematic bias?* • *Was the allocation sequence concealed from investigators and participants?*	Yes No Can't tell √ An independent statistician generated the randomisation schedule in Stata. Block randomisation, with randomly ordered block sizes of two, four, and six, stratified by stop smoking adviser. Study nurses recruited participants, and the study administrator (who had not met the participants) allocated participants in sequence against the list for each adviser. Only the administrator and the pharmacist knew the allocation. Advisers, participants, and study staff carrying out follow-up were blind to allocation. Nortriptyline tablets were encapsulated, and identical powder filled capsules provided the placebos.
3. Were all participants who entered the study accounted for at its conclusion? *CONSIDER:* • *Were losses to follow-up and exclusions after randomisation accounted for?* • *Were participants analysed in the study groups to which they were randomised (intention-to-treat analysis)?*	Yes No Can't tell √ The Russell standard, including as smokers those lost to follow-up, was followed. The researchers calculated the proportion of people using each possible combination of drug as a proportion of all still attempting to quit at each of the four weeks of clinic follow-up, calculating χ^2 statistics for the differences. The study was not stopped early. Participants were analysed in the study groups to which they were randomised (intention-to-treat analysis).

• *Was the study stopped early? If so, what was the reason?*	

Section B: Was the study methodologically sound?

4. • **Were the participants 'blind' to intervention they were given?** • **Were the investigators 'blind' to the intervention they were giving to participants?** • **Were the people assessing/analysing outcome/s 'blinded'?**	Yes No Can't tell √ √ √
5. Were the study groups similar at the start of the randomised controlled trial? *CONSIDER:* • *Were the baseline characteristics of each study group (e.g. age, sex, socio-economic group) clearly set out?* • *Were there any differences between the study groups that could affect the outcome/s?*	Yes No Can't tell √ Anyone aged 18 years or older attending a stop smoking service and smoking 10 or more cigarettes a day was eligible. People were excluded with a contraindication or caution to nortriptyline or contraindication to nicotine replacement therapy and those taking a drug that interacted with nortriptyline. A research nurse attended stop smoking groups and briefly introduced the trial. Interested people were then interviewed individually. Researchers were therefore unable to count the number of people who were eligible and declined participation or were ineligible. About one third of participants in the group were interviewed, however, and about one fifth of those were excluded, mainly because they were taking other antidepressants. Baseline characteristics of each study were clearly tabulated and there were no differences between the study groups that could affect the outcomes.

6.	**Apart from the experimental intervention, did each study group receive the same level of care (that is, were they treated equally)?** *CONSIDER:* • *Was there a clearly defined study protocol?* • *If any additional interventions were given (e.g. tests or treatments), were they similar between the study groups?* • *Were the follow-up intervals the same for each study group?*	Yes No Can't tell √ There was a clearly defined study protocol. Interventions ewer similar between the study groups and the follow-up intervals were the same for both study groups.

Section C: What are the results?		
7.	**Were the effects of intervention reported comprehensively?** *CONSIDER:* • *Was a power calculation undertaken?* • *What outcomes were measured, and were they clearly specified?* • *How were the results expressed? For binary outcomes, were relative and absolute effects reported?* • *Were the results reported for each outcome in each study group at each follow-up interval?* • *Was there any missing or incomplete data?* • *Was there differential drop-out between the study groups that could affect the results?* • *Were potential sources of bias identified?* • *Which statistical tests were used?* • *Were p values reported?*	Yes √ No Can't tell The power calculation was based on assumptions informed by previous nortriptyline plus NRT versus NRT alone trails. The power calculation: 430 participants would be needed in each arm to give a type 1 error rate of 5% and 80% power for continuous abstinence at 6 months. Therefore 860 participants were determined as needed for the test of nortriptyline efficacy. Results were reported for each outcome in each study group at each follow up interval. The lost to follow up rates were not different between study groups. Missing data: By four weeks no data on smoking status were available for 12 (3%) people in the nortriptyline arm and 18 (4%) in the placebo arm. By six months the corresponding values were 41 (9%) and 65 (14%) and by 12 months were 52 (12%) and 76 (17%). At six months, however, 89% of those lost after four weeks had not achieved prolonged abstinence at four weeks so were by definition treatment failures at six months. Researchers calculated the proportion of people using each possible combination of drug as a proportion of all still attempting to quit at each of the four weeks of clinic follow-up, calculating χ^2 statistics for the differences. They calculated the median number of capsules taken per day, testing differences with a Mann-Whitney U test. For abstinence they used the intention to treat approach, calculating risk differences and 95% confidence intervals and relative risks and 95% confidence intervals using the Mantel Haenszel approach for stratified analyses. The analysis of differences in the occurrence of side effects and withdrawal symptoms was done only on those who took nortriptyline and nicotine replacement therapy for all four weeks of clinical follow-up to examine whether side effects or withdrawal symptoms changed over time, as expected. Those with intolerable symptoms, however, could stop treatment and such people would be excluded. Researchers used a Mann-Whitney U test to examine whether initial severity of side effects was worse in those who stopped treatment than those who continued. Researchers accommodated the repeated weekly measures of side effects, withdrawal symptoms, and quality of life by random effects regression of observations nested within individuals, assuming a normal distribution for the error function for means and using ordered proportional odds models

		for individual symptoms measured on Likert-type scales. They entered time as days and days squared and tested whether the change in symptoms over time differed between users of nortriptyline and users of placebo using multiplicative interaction terms.
8.	**Was the precision of the estimate of the intervention or treatment effect reported?** *CONSIDER:* • *Were confidence intervals (CIs) reported?*	Yes √ No Can't tell
9.	**Do the benefits of the experimental intervention outweigh the harms and costs?** *CONSIDER:* • *What was the size of the intervention or treatment effect?* • *Were harms or unintended effects reported for each study group?* • *Was a cost-effectiveness analysis undertaken? (Cost-effectiveness analysis allows a comparison to be made between different interventions used in the care of the same condition or problem.)*	Yes √ No Can't tell Nortriptyline plus NRT compared with NRT alone led to a modest increase in prolonged abstinence from smoking at six months, but this was not statistically significant. 72 of 445 (16%) people using nortriptyline and 55 of 456 (12%) using placebo achieved prolonged abstinence at six months (relative risk 1.34, 95% confidence interval 0.97 to 1.86). At 12 months the corresponding values were 49 (11%) for nortriptyline and 40 (9%) for placebo (1.26, 0.84 to 1.87). 337 (79%) people in the nortriptyline arm and 325 (75%) in the placebo arm were taking combination treatment on quit day, median 75 mg per day in both groups. Harms or unintended effects were reported for each study group. The nortriptyline arm had noticeably higher severity ratings for dry mouth and constipation than the placebo arm, with slightly higher ratings for sweating and feeling shaky. Both groups had similar urges to smoke, but nortriptyline reduced depression and anxiety. Overall, withdrawal symptom scores did not differ. A cost-effectiveness analysis was not undertaken. For the intention to treat analysis, people using nortriptyline plus nicotine replacement therapy were slightly more likely to stop smoking on every measure at every follow-up than those using placebo plus nicotine replacement therapy, but the differences were small and not statistically significant. For the per protocol analysis, the effects in those using nortriptyline plus nicotine replacement therapy or placebo plus nicotine replacement therapy on quit day were similar

Section D: Will the results help locally?

10.	**Can the results be applied to your local population/in your context?** *CONSIDER:*	Yes √ No Can't tell

• *Are the study participants similar to the people in your care?* • *Would any differences between your population and the study participants alter the outcomes reported in the study?* • *Are the outcomes important to your population?* • *Are there any outcomes you would have wanted information on that have not been studied or reported?* • *Are there any limitations of the study that would affect your decision?*	The main choice of drug at all treatment follow-up periods was combination nortriptyline plus nicotine replacement therapy or placebo plus nicotine replacement therapy, although the proportion of people using the combinations decreased from 77% on quit day to 57% by week 4. At week 4, 44 (22%) of those in the nortriptyline arm were not using nortriptyline, 15 (8%) were taking one capsule daily, 20 (10%) were taking two capsules daily, and 121 (61%) were taking three capsules daily. Adherence to medication in both study groups was not considered at the protocol; development stage, it was limited to a single question in the trial questionnaire pack, it's effect was under investigated, analysed and reported. Baseline characteristics did not include the Beliefs about Medicines Questionnaire (BMQ) and the Modified Morisky Scale® (MMS®) and were not part of the eligibility screening process. A definition of adherence was not included in the protocol or in the trial publication. Participation or declining to participate to the RCT was not an independent variable in this trial. Adherence to medication and the beliefs about medication were not dependent variables. Measures of medication adherence were not undertaken by this trial. Information about the beliefs, perceived necessity and concerns the participant may have had regarding their tobacco dependency, quit attempt and prescribed medication were not measured. The trial was not able to report differences (or not) in medication adherence between participants and non-participants prior to the inclusion of the trial. Interventions for improving medication adherence were not clearly reported and may have had effect or not on the trial outcomes and would have been useful to the interpretation of trial outcomes. At the time of the trial (2008) there was no systematic approach to medication adherence measurement, analyses, interpretation, or reporting. Given the importance of adherence within clinical trials, there is a pressing need for a standardised approach or framework.

11.	**Would the experimental intervention provide greater value to the people in your care than any of the existing interventions?** *CONSIDER:* • *What resources are needed to introduce this intervention taking into account time, finances, and skills development or training needs?* • *Are you able to disinvest resources in one or more existing interventions in order to be able to re-invest in the new intervention?*	Not applicable

APPRAISAL SUMMARY: *Record key points from your critical appraisal in this box. What is your conclusion about the paper? Would you use it to change your practice or to recommend changes to care/interventions used by your organisation? Could you judiciously implement this intervention without delay?*

The trial was a high quality RCT and methodically sound, the results found that Nortriptyline and nicotine replacement therapy are both effective for smoking cessation but the effect of the combination is less than either alone and evidence is lacking that combination treatment is more effective than either alone. For clinical practice although nortriptyline alone has a place in smoking cessation clinics the data show that the efficacy of combination treatment is slight and should not be used routinely. Adherence is a critical mediator of treatment outcome across health conditions and low rates of adherence undermine success in smoking cessation treatment. More understanding about the medication adherence of participants as well as non-participants before the start of tobacco dependency RCT's, during and after the trial may have contributed to a better understanding of why studies show no improvement in medication adherence in this patient group and would also provide additional insight into the efficacy of the trial intervention(s).

One possible explanatory determinant for (non) adherent behaviour is medication beliefs. Personal beliefs about need for treatment (necessity beliefs) and concerns about several potential adverse consequences (concern beliefs) could explain a large part of (non) adherent behaviour. If tobacco dependant adults seeking to quit perceive that the need for medication outweighs the concerns, they are more likely to be adherent to their medication(s). While randomised controlled trials (RCTs) remain the optimal study design for evaluating the effectiveness of an intervention; research to understand and improve the design, delivery, and analysis of RCTs is required in tandem. This includes the concept of adherence, or the extent to which participants receive their allocated intervention as intended. Trials should plan and implement robust processes for monitoring adherence and describe these in the protocol. This may include the measurement of adherence and how this will be collected, whether there is a defined acceptable minimum adherence level, and a rationale for these decisions. Standardised published guidelines to enhance the quality of measuring and reporting adherence is now available the Medication Adherence Reporting Guideline (EMERGE) was published in 2018.

https://www.espacomp.eu/project/emerge-guidelines/

Adherence monitoring and optimisation should be a standard component of smoking cessation treatment research. While optimising and tracking adherence are important in clinical trials, the effectiveness of a medication can be challenged by the likelihood that similar measures to promote adherence may not be in place in real world settings.

CHAPTER 10
CHAPTER 11
CHAPTER 12

CHAPTER 13 REFERENCES

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