Smoking and Smoking cessation interventions in the context of targeted lung cancer screening in the UK

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Thesis submitted for the degree of Doctor of Philosophy (PhD)

January 2024

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Declaration of originality

I declare that the work presented here is mine and or is correctly referenced, work carried out by me or in collaboration with others is clearly described. This is the first time this work has been submitted for a higher degree.

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Statement of contributions

I created the systematic review research question (Chapter 3) with support from Nicholas Hopkinson and Anthony Laverty. I conducted the MESH search terms, and search strategy with support from Georgina Wildman at Imperial College Library. The title and abstract search were conducted by me and Nicholas Hopkinson, and the full text screen was conducted by

myself, Keir Philip, Saeed Alghamdi and Alexis Perkins. I and Anthony Laverty assessed the risk of bias and quality of the evidence. I conducted the meta-analysis with support from Nicholas Hopkinson and Anthony Laverty.

The original Quit Smoking Lung Health Intervention Trial (QuLIT1) was designed by Nicholas Hopkinson and Rebecca Muswali, with the modification to conduct the intervention remotely or QuLIT2 designed by me and Nicholas Hopkinson (Chapter 4). To ensure appropriate masking of individuals, the recruitment and randomisation of participants was conducted by the respiratory nurses at the Royal Brompton Hospital (the Healthy Lung Project (HLP). The smoking cessation support was delivered by Navjot Gill, and Dee Flannery at the Royal Brompton hospital with support from me, and medical support from Nicholas Hopkinson and Keir Philip for pharmacotherapy prescriptions. I conducted both three and 12 month follow up (Chapters 4-5) in the QuLIT trials with support for holiday or illness from Sara Buttery and Keir Philip. I conducted the statistical analysis plan and analysis with support from Nicholas Hopkinson and Anthony Laverty.

Chapters 6 and 7, I had the original idea for the studies. Nicholas Hopkinson conducted the ethics amendments to conduct qualitative investigations to the original QuLIT ethics. I wrote all study protocols and interview guides, with support from Georgina Forden a trainee clinical psychologist. I recruited, conducted, recorded, and transcribed all interviews. For chapter 6 I led the thematic analysis with coding and theme development support from Keir Philip and Nicholas Hopkinson. Chapter 7 the thematic analysis was led by me with coding and theme development support from Sara Buttery and Nicholas Hopkinson.

Acknowledgments

Primarily, I would like to thank my supervisors Prof Nicholas Hopkinson and Dr Anthnoy Laverty for their inspiration, guidance, and support throughout my PhD. Nick has been an incredible primary supervisor, with his invaluable experience and guidance, throughout, he has encouraged me to develop as a researcher and inspired me to continue to fight the good fight within tobacco research. I'm so glad he answered that email in the middle of the pandemic asking for some research work experience. Anthony has provided me with a public health lens to my work, ensuring my statistical analysis models are correct and taking a wider look at the tobacco problem as a whole. He has provided the very best support and guidance towards my studies. Despite not providing any formal supervision Professor Mike Polkey has provided me with invaluable feedback, ensuring I take a deep analytical approach to my work, his support within the weekly Muscle Lab meetings have been vital. Many thanks also to On Min Con, Paul Cullinan, and Terry Tetley for doing my early and late-stage milestone assessments, which were extremely helpful.

I would like to thank all my colleagues and friends in the Muscle Lab. They are an inspiring bunch of physios, medics and physiologists who have provided me with laughter, support, and guidance throughout. A special mention to Sara Buttery, Keir Philip, Alexis Perkins, Lay Chan, Saeed Alghamdi, Lizzie Grillo, Anand Tana, Adam Lewis, and Zander Williams.

I would like to thank my colleagues at RM and Partners and the Healthy Lung Project, for their support in delivering the QuLIT interventional studies, a special thanks goes to Michelle Chen, Anand Devaraj, Jamie Addis, Jane Derbyshire and Sara Casanueva.

Finally, I would like to thank my friends and family for their continued patience, support and encouragement, Georgina Forden my oldest and dearest friend, Dilly and Sandra Dunk for

chats about the world and daily inspiration, Luke Williams my big brother and Suhaylah for their support, my cousin Josh Bland for chats over a takeaways, my friends Jen Harkness and Libby Roffe for chats, coffees and dinners and Emma Bailey for her support and inspiration, my coach and friend Gareth Pymm for his triathlon and life coaching, my running friends at Kent AC, with a special thanks to Richard Giles.

Funding

The research in this thesis was funded by RM Partners West Cancer Alliance and Royal Brompton and Harefield Charities.

Dedication

I dedicate this thesis to my parents Pete and Micheala who have given me a lifetime of support, encouragement, opportunity, and fun, and to my partner William for his patience, guidance, and inspiration.

First or Last author publications completed during my PhD

Buttery SC*, **Williams P*,** Mweseli R, Philip KEJ, Sadaka A, Bartlett EC, Devaraj A, Kemp SV, Addis J, Derbyshire J, Chen M, Morris K, Laverty A, and Hopkinson NS. Immediate smoking cessation support versus usual care in smokers attending a targeted lung health check: the QuLIT trial *BMJ Open Respiratory Research* 2022;**9:**e001030. doi: 10.1136/bmjresp-2021-001030** = joint first author*

Williams PJ, Cumella A, Philip KE, Laverty AA, Hopkinson NS. Smoking and socioeconomic factors linked to acute exacerbations of COPD: analysis from an Asthma+ Lung UK survey. BMJ Open Respiratory Research. 2022 Jul 1;9(1):e001290.

PJ Williams, Philip KEJ, Kaur-Gill N, Flannery D, Buttery, Bartlett EC, Devaraj A, Kemp SV, Addis J, Derbyshire J, Chen M, Morris K, Laverty A, and Hopkinson NS. Immediate, remote smoking cessation intervention in participants undergoing a targeted lung health check. The Quit Smoking Lung Health Intervention Trial. A randomized controlled trial (DOI: doi.org/10.1016/jChest.2022.06.048)

Williams PJ, Cheeseman H, Arnott D, Bunce L, Hopkinson NS, Laverty AA. Use of tobacco and e-cigarettes among youth in Great Britain in 2022: Analysis of a cross-sectional survey. Tobacco Induced Diseases. 2023;21

Williams PJ, Philip KE, Alghamdi SM, Perkins AM, Buttery SC, Polkey MI, Laverty AA, Hopkinson NS. Strategies to deliver smoking cessation interventions during targeted lung health screening - a systematic review and meta-analysis. *Chronic Respiratory Disease*. 2023;20

Williams PJ, Philip KEJ, Buttery SC, Perkins AM, Chan L, Bartlett EC, Devaraj A, Kemp SV, Addis J, Derbyshire J, Chen M, Polkey MI, Laverty AA, Hopkinson *NS.* Immediate smoking cessation support during lung cancer screening: long-term outcomes from two randomised controlled trials. *Thorax* Published Online First: 24 October 2023. doi: 10.1136/thorax-2023-220367

Williams PJ, Buttery SC, Laverty AA, Hopkinson NS. Being responsible for COPD- lung disease as a manifestation of structural violence medRxiv 2023.09.06.23295021; doi: https://doi.org/10.1101/2023.09.06.23295021. Pre-print, accepted for publication at American Journal of Respiratory Medicine and Critical Care.

Awards won from this thesis.

- Asthma+Lung UK ERS Travel Award 2022
- Royal Brompton and Harefield hospitals annual research showcase awards- early-stage career researcher 2023

Thesis Summary

Lung cancer screening (LCS) at risk people is a recently established intervention to reduce lung cancer mortality. However, an estimated 30-50% of attendees are likely to be current smokers, highlighting an opportunity to embed smoking cessation interventions.

This thesis aims to identify effective strategies for delivering smoking cessation support within LCS. I present five results chapters addressing the current research gaps within these areas.

First, I conducted a systematic review and meta-analysis. This revealed moderate certainty of evidence supporting smoking cessation interventions embedded within LCS [Odds Ratio (OR): 2.11, 95% CI 1.53-2.90, p<0.001] and high certainty of evidence supporting more intensive interventions delivered within LCS [OR: 2.40, 95% CI 1.64-3.51, p< 0.001].

Secondly, I conducted a randomised controlled trial and discovered significantly higher three-month quit rates among participants who were randomised to receive telephone smoking cessation intervention (TSI) after attending an LCS compared to usual care (UC) intervention, [TSI: 21.1% vs UC: 8.9%, OR: 2.83, 95% CI 1.44-5.60].

Thirdly, I analysed long term results from the two Quit Smoking Lung Health Intervention trials. I discovered significantly higher 12-month self-reported, and carbon monoxide (CO) verified quit rates among participants who were randomised to receive smoking cessation support (SCS) interventions compared to usual care [Self report: SCS: 20.0% vs UC: 12.8%, OR: 1.78, 95% CI 1.04-3.04], [CO verified: SCS: 12.0% vs UC: 4.7%, OR: 2.97, 95% CI 1.43-6.73].

In the fourth and fifth chapters I present a qualitative investigation into the participant experience of the intervention and barriers to accepting it. Patients reported they experienced supportive interventions, and how the LCS and past experiences influenced quit rates, as well as reporting several psychosocial barriers to accepting support.

These studies justify and highlight the importance of ensuring lung cancer screening services are delivering evidence-based smoking cessation support within their screening programmes.

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Abbreviations

QuLIT1	Quit Smoking Lung Health Intervention Trial, in clinic delivery of intervention
QuLIT2	Quit Smoking Lung Health Intervention Trial, telephone delivery of intervention
BC	Before Christ
AD	Anno Domini
RCP	Royal College of Physicians
US	United States
DALYs	Deaths and Disability Adjusted Life Years
GDP	Gross Domestic Product
WHO	World Health Organization
UK	United Kingdom
NHS	National Health Service
ASH	Action on Smoking and Health
NRT	Nicotine Replacement Therapies
NCSCT	National Centre for smoking Cessation and Training
COPD	Chronic Obstructive Pulmonary Disease
FEV_1	Forced Expiratory Volume
FVC	Forced Vital Capacity
ERS	European Respiratory Society
GP	General Practitioner
X-Ray	Electromagnetic Radiation
NICE	National Institute for Health Care Excellence
CT	Computed Tomography
NLST	National Lung Cancer Screening Trial
LDCT	Low Dose Computed-Tomography
NELSON	NEderlands Leuvens Screening ONderzoek
TLHC	Targeted Lung Health Check
HZ	Hazard Ratio
SUMMIT	Cancer Screening Study with or Without Low Dose Lung CT to Validate a Multi-cancer Early Detection Test
RCT	Randomised Controlled Trial
QALY	Quality Adjusted Life Years
HLP	Health Lung Project
PLCO	Prostate, Lung, Colorectal and Ovarian
LLP	Liverpool Lung Project
CO	Carbon Monoxide
Ppm	Parts per million
TA	Thematic Analysis
COM-B	Capability, Opportunity, Motivation-Behaviour
AECOPD	Acute Exacerbation of COPD
SSS	Specialist Smoking Cessation Services
COVID-19	Coronavirus Disease
OHID	Office for Health Improvement and Disparities
SES	Socioeconomic status
LCS	Lung Cancer Screening
ROB	Risk Of Bias
OR	Odds Ratio

AOR	Adjusted Odds Ratio
UC	Usual Care
VBA	Very Brief Advice
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
TSI	Telephone Smoking Intervention
IMD	Index of Multiple Deprivation
SD	Standard Deviation
MHRA	Medicines and Healthcare Products Regulatory Agency
SCS	Smoking Cessation Support
TM	Teachable Moment
SC	Smoking Cessation
YESS	Yorkshire Enhanced Stop Smoking Study
TB	Tuberculosis
FCTC	Framework Convention on Tobacco Control
NSC	National Screening Committee
SRR	Survival Risk Ratio

Chapter 1. Introduction

1.1 Tobacco

Tobacco is a natural substance derived from the leaves of the genus Nicotiana plant, indigenous to North and South Americas (Mishra 2013). The leaves are dried and cured, then inhaled via cigarettes, cigars, pipes, shishas, bidis, and more recently via heated tobacco products (Glantz 2018; Mishra 2013). Tobacco is also consumed orally via chewing tobacco, snus and snuff (Mishra 2013; Von Gernet 2014). Tobacco contains the highly addictive stimulant alkaloid nicotine and a group of alkaloids that stimulate the central nervous system named harmala alkaloids (Rose 2006).

1.1.1 History of Tobacco smoking

Previous archaeological studies estimate that the Maya people of Central America first smoked tobacco around the first century BC, for use in religious rituals. Due to the migration north of the Maya peoples around 470 - 630 AD, tobacco smoking was adopted by the first nation tribal populations in North American territories (Goodman 2005; Mishra 2013). Shamans of the first nation peoples used tobacco smoking not only in religious ceremonies but also to cure a multitude of illnesses such as headaches, depression, insect bites, stomach and topical ailments (Goodman 2005).

During the fifteenth and sixteenth centuries, European exploration and colonisation of the Americas occurred and tobacco smoking was appropriated by these settlers (Goodman 2005; Von Gernet 2014). Due to the economic success of tobacco plantations such as the English Virginia colony, “Tobacco Colonies” run by European colonists spread across North America and the use of tobacco spread across the Atlantic (Goodman 2005; Von Gernet 1988). By the late sixteenth century, tobacco was one of the most imported goods in the English and French trades, and remained so for a subsequent two centuries (Von Gernet 1988; Von Gernet 2014).

Today, tobacco use has spread worldwide. The most popular form of tobacco use is cigarette smoking (Mishra 2013; World Health Organization 2021). According to the World Health Organization (WHO) data in 2020, regions with the highest estimated use of tobacco in over 15-year-olds were the Southeast Asian regions (32.9%), European (27.2%) and Western Pacific Regions (26.1%) (World Health Organization 2021).

Four companies dominate global tobacco cultivation and supply, colloquially known as "Big Tobacco" These companies are Philip Morris International/Altria Group Inc, British American Tobacco Plc, Japan Tobacco Inc, and Imperial brands. China National Tobacco Corporation holds a large share of the market; however, it primarily caters to the Chinese domestic market (Expose Tobacco 2021). It is estimated that legal tobacco sales are worth £605 billion per year (Action on Smoking and Health 2023c).

1.1.2 Global burden of tobacco smoking

Tobacco smoking is a global public health epidemic, killing an estimated eight million people per year, accounting for 200 million disability adjusted life years (World Health Organization 2021; He 2022). Since the late 90s, there have been more than 200 million direct and indirect deaths attributable to tobacco use, despite prevalence reducing during the past 30 years (He 2022). These figures are projected to increase as recent numbers estimate more than one billion current smokers across the globe (Reitsma 2021). Smoking rates are particularly high among low and middle income countries, which currently account for 80% of global smokers (Reitsma 2021; World Health Organization 2021).

Data from the 2019 Global Burden of Disease study (GBDS) reported the global deaths attributable to tobacco (Institute for health metrics and evaluation 2020). He et al, 2022 used the GBDS data to explore deaths and disability adjusted life years (DALYs) attributed to

tobacco. The group reported the highest deaths and DALYs were within the Oceania region and lowest within the Andean Latin America region, attributed to Chronic Respiratory Diseases. Tobacco related neoplasm deaths and DALYs were highest in Central Europe and lowest in Western Sub-Saharan Africa. Eastern Europe and Central Asia had the highest tobacco related deaths and DALYs, attributed to cardiovascular disease (He 2022). The smoking of tobacco cigarettes caused most deaths and DALYs losses (88.29%), with the mortality rate at any year higher among males than females. Deaths and DALYs attributed to second-hand smoke were the highest tobacco related risk among young people, (≤24 years), due to lower respiratory tract infections and otitis media (middle ear infection) (He 2022).

The annual economic cost of tobacco smoking is upwards of $1400 billion (World Health Organization 2021). This is from both direct costs of healthcare expenditure and indirect costs such as productivity losses caused by excess levels of morbidity and mortality. These direct and indirect costs are estimated to be equivalent to 1.8% of the global gross domestic product (GPD), (Goodchild 2018). The economic burden is not spread evenly between countries. Estimates from Goodchild et al 2018, reported that 40% of the global cost of tobacco smoking occurred in developing countries, particularly within Brazil, Russia, India and China (Goodchild 2018). This study utilised 2012 data and conducted a costs of illness approach on 152 countries grouped into WHO region and World Bank income status. The strength of this analysis, including data from low and middle-income countries, highlights the huge economic burden of tobacco smoking on the global economy. This refutes the arguments made by tobacco companies that tobacco can provide a net benefit to a country's economy. These companies argue that the taxation and reductions in health and social care costs caused by tobacco induced premature death, bring a significant amount of money into the public purse (Ross 2004). These disputes are still at play today, with Imperial Brands responding and

disputing the UK Government's 2023 smokefree policies. Imperial Brands argued that tobacco companies bring £10 million into the public purse via taxation, and the projected smokefree policies would lead to a reduction in economic activities (Imperial Brands 2023; HM Revenue & Customs 2023).

1.1.3 The global response to the tobacco problem

In response to the global tobacco epidemic the WHO's launched its Framework Convention on Tobacco Control (FCTC). This international treaty launched in 2005, with the aim of reducing the supply and demand of tobacco. As of 2023 the FCTC has been ratified by 181 countries across the globe (WHO FCTC 2024). The FCTC has a set of specific measures that countries can implement either through legislative actions or regulatory processes, to enable countries in implementing evidence based and effective tobacco control measures. In 2008 the WHO created a set of measures titled MPOWER, to assist member states to adopt and implement effective tobacco control interventions (World Health Organization 2023b). Table 1.1 displays the list MPOWER measures, however I will elaborate on these below.

Table 1. 1 WHO's MPOWER measures

M	Monitor Tobacco use and prevention policies
P	Protect people from tobacco use
O	Offer help to quit smoking
W	Warn about the dangers of tobacco
E	Enforce bans on tobacco advertising, promotion, and sponsorship
R	Raise taxes on tobacco

1.1.3.1 Monitoring Tobacco use and prevention policies

Monitoring tobacco use and prevention policies is the first set of MPOWER measures. This requires all countries within the FCTC treaty to collect and share national data on tobacco use patterns, scale and consequences (World Health Organisation 2023a). Monitoring and

surveillance are key interventions used within public health science (Thacker 1988; Jamison 2006). In the case of tobacco control monitoring data is key for creating, implementing, and evaluating effective policies. This measure also includes the publication of the WHO's global report on prevalence and trends on tobacco use (World Health Organisation 2024d), the report publishes statistics on global tobacco use and can be utilised as a tool for member states to advocate for stronger tobacco control measures.

1.1.3.2 Protect people from tobacco use

The protecting people from tobacco use measure supports member states to create smoke-free legislation (World Health Organisation 2023b). It is widely established that inhalation of second hand smoke can cause a multitude of illnesses and premature mortality (Max 2012; Wipfli 2008). The aim of this measure is to protect people from second-hand smoke via creating smoke-free environments. The WHO has created a set of guidelines within Article 8 of the FCTC to assist counties in implementing smoke-free policies and places.

1.1.3.3 Offering help to quit smoking

Offering people the opportunity to quit smoking is the third MPOWER measure (World Health Organisation 2024b). The benefits of smoking cessation cannot be understated and will be explored in more detail within this chapter. Most adult smokers want to quit and if they can access support (counselling and pharmacotherapy), they are more likely to succeed (Royal College of Physicians 2018). However, not all member states provide comprehensive smoking cessation support to all tobacco users. There is a wealth of evidence supporting brief advice to quit within healthcare settings (Hartmann-Boyce 2021), as well as intensive formal cessation counselling (Hartmann-Boyce 2019b). The FCTC mandated that all participating countries must provide tobacco cessation services, whist providing technical resources to

help member states to adopt national smoking cessation policies and services (World Health Organisation 2024b).

1.1.3.4 Warning about the dangers of smoking

Warn about the dangers of tobacco. This measure highlights the importance of health warnings on tobacco packaging (World Health Organisation 2024c). Article 11 of the FCTC contains detailed guidelines on how warning messages should appear to enable member states to adopt this measure. Alongside health warnings, article 11 contains evidence and guidelines for plain tobacco packaging and anti-tobacco media campaigns (WHO FCTC 2013a).

1.1.3.5 Enforcing bans on tobacco advertising, promotion, and sponsorships

Enforcing bans on tobacco advertising promotion and sponsorships. Marketing and promotion campaigns are used by the tobacco industry to promote and glamorise their products. This is often targeted at younger people with the potential to addict millions of users. A Key tobacco control measure is to eliminate direct and indirect marketing of tobacco products to protect young people from misleading and dangerous advertising (World Health Organisation 2024a; Freeman 2022). Article 13 of the FCTC contains guidelines for member states on how to enforce total bans on tobacco marketing, promotion and sponsorship deals (WHO FCTC 2013b).

1.1.3.6 Raise taxes on tobacco

The final MPOWER measure focuses on enabling member states to raise taxes in tobacco products. This measure is arguably the most effective MPOWER measure as it influences the affordability of the product. Increasing taxes and reducing the affordability of tobacco makes the product less attractive, particularly for the youth (Peruga 2021). This is a relatively cheap measure for member states to implement, whilst generating revenue for the country. Article 6 of the FCTC contains guidelines for member states, the document states that tobacco excise taxes should amount to 75% of the retail price of a pack of cigarettes. (W. H. O. 2003).

1.1.3.7 Effectiveness of MPOWER

Effectiveness of the FCTC and MPOWER measures have been assessed and published. A 2020 investigation reported 43 member countries had implemented at least one MPOWER measure, between the years 2014-16. The report estimated that 14.6 million smoking attributable deaths had been averted due to the adoption of these measures (Levy 2020). There appears to be a dose response within countries that adopted more MPOWER measures earlier. Countries that implemented MPOWER measures early, saw larger declines in smoking prevalence, calculated as a decrease between 0.39 and 0.50 percentage point for each increase in MPOWER score. These data highlight the effectiveness and importance of early intervention and total adoption of measures (Husain 2021).

1.1.4 UK burden of tobacco smoking

Current UK statistics estimate around 12.9% of the adult population smokes, or one in eight adults. (Office for National Statistics 2023). Smoking rates are not spread evenly through the UK, and rates remain higher among people who were defined as unemployed (20.5%) or those who work in routine and manual occupations (22.5%) (Office for National Statistics 2023; Action on Smoking and Health 2023b).

In terms of smoking related mortality, in 2019 there were 74,600 deaths attributed to smoking, representing 15% of all deaths that year (NHS Digital 2020). Within this data, 35% of all deaths from respiratory diseases and 25% of all deaths from cancer were estimated to be attributable to smoking (NHS Digital 2020). Smoking causes a large strain on the NHS, in 2019 4% of hospital admissions were estimated to be attributed to smoking (506,100), a 10% increase over the past decade (NHS Digital 2020).

As with the global economy, tobacco smoking has a huge impact on England's economy. The lobbying charity Action on Smoking and Health (ASH) have created a calculator to quantify

the societal cost of smoking. The calculator uses data from a number of sources including, the 2021 Landman Economics report (Howard Reed 2021), ONS data on 2022 smoking habits (Office for National Statistics 2023), ONS 2021 population mid-year estimates (Office for National Statistics 2022), ONS 2008 General household survey data (Office for National Statistics 2008) and, 2009-2022 data from the United Kingdom Household Longitudinal study (University of Essex 2023). The tool has estimated that smoking costs England's economy £17.3 Billion per year (Action on Smoking and Health 2023a). This was broken down into £14 billion on productivity costs: £6.6 billion lost to smoking related unemployment (poor health, chronic disease) and £6.1 billion in smoking related lost earnings. In addition to health and social care costs: £1.3 billion in smoking related deaths, £1.9 billion in smoking related hospital admissions and primary care costs. The calculator also estimated charges of £1.1 billion for local authorities on social care costs. It is estimated that around £2.5 billion of these costs falls on the NHS (Action on Smoking and Health 2023a).

There is also a huge cost to the individual who has become addicted to smoking. Current smokers lose on average £2,451 a year on smoking attributable costs (Howard Reed 2021). It is established that smoking rates are higher among people within low socioeconomic positions (Kock 2022), and recent data suggesting that 400,000 adults and 180,000 children in the UK are living in tobacco adjusted poverty (Nyakutsikwa 2021). These figures demonstrate how tobacco smoking both causes and exacerbates the widening health and wealth inequalities in the UK. To put this into the wider context, in the financial year 2022-2023 tobacco companies operating in the UK made £10,004 million, or £1,563.12 per every smoker in the UK (HM Revenue & Customs 2023).

1.1.5 Tobacco smoking and lung health

Tobacco smoking has a devastating effect on lung health, the seminal work conducted by Doll and Hill in the 1950s characterised the first association between tobacco smoking and lung carcinoma (Doll 1950). The authors summarised "it must be concluded that there is a real association between carcinoma of the lung and smoking" (Doll 1950). This seminal paper was followed by the Hammond and Horn study four years later in the USA (Hammond 1954). Doll and Hill followed up their initial findings with the British Doctors study (Doll 2004; Doll 1956), this was a 50-year epidemiological prospective study of 34,439 male doctors in the UK. Smoking status, habits and cause specific mortality were collected in 1951 and followed up at 20, 40 and 50 years. The results reported an excess mortality rate among males who smoked compared to non-smokers, with smokers dying around ten years earlier. Lung neoplasms were not the sole cause of mortality, deaths attributable to vascular and respiratory diseases were also observed. This study demonstrated the importance of cessation, with the hazard ratio reducing by 50% among smokers who stopped at age 50. If cessation occurred earlier by age 30 the hazard was almost eliminated (Doll 2004).

These historical perspectives are still at pay today. Data from the GBD study indicated that in 2019 tobacco attributable deaths due to COPD and lung cancer were the second and third highest tobacco induced diseases globally [1.59 million and 1.31 million deaths respectively] (Reitsma 2021).

A meta-analysis conducted in 2012 highlighted current smokers had a risk eight times higher of developing lung cancer compared to never smokers [Risk Ratio (RR): 8.43, 95% CI 7.63-9.31], with ex-smokers displaying a fourfold greater risk vs never-smokers [RR: 4.30, 95% CI 3.93-4.71] (Lee 2012). This review included data on 287 lung cancer epidemiological studies and investigated a range of smoking tobacco products, including filtered cigarettes, unfiltered

cigarettes, and pipes. The authors conducted univariable and multivariable meta regression to adjust for heterogeneity within the included studies, which is a strength of the analysis.

SmokeHaz a systematic review conducted by the tobacco control committee of the European Respiratory Society (ERS). Explored the effect of tobacco smoking and respiratory health, including lung cancer and COPD. The review concluded there was an 11-fold increase in the risk of smokers developing lung cancer vs non-smokers [RR: 10.92, 95% CI 8.28-14.40] (Jayes 2016). Additionally, the review highlighted a pack years dose response risk relationship, which increased from a RR of three for smokers who had a <20 pack years to a RR of 12 among smokers who had >60 pack years (Jayes 2016). The authors highlighted the risk of passive smoke exposure for developing lung cancer. Non-smokers exposed to passive smoke had a 41% increase in lung cancer risk compared to unexposed non-smokers [RR: 1.41, 95% CI 1.21-1.65] (Jayes 2016). The review included COPD risk data, which demonstrated smokers had a higher risk for developing COPD compared to non-smokers [RR: 4.01, 95% CI 3.18-5.05]. Passive smoke exposure was also linked to the development of COPD [RR: 1.44, 95% CI 1.02-2.01] (Jayes 2016). The authors also found similar risk relationships among current smoking for the development of other respiratory conditions including asthma, sleep apnoea, tuberculous (TB) and childhood lower respiratory tract infections (Jayes 2016).

1.1.6 Additional tobacco induced diseases

The work conducted in the 1950s and subsequent years, highlighted the strong association between cigarette smoking and lung carcinoma (Doll 1956, 1950; Hammond 1954). Associations between cigarette smoking and chronic respiratory diseases, vascular diseases and other neoplasms were later discovered (Doll 2004). In 1962 the Royal College of Physicians (RCP) published their first report on smoking and health, their conclusion was that tobacco smoking caused chronic bronchitis, in addition to lung cancer and was highly likely to

contribute to upper airway cancers including mouth and throat. The report highlighted smoking related-cancers of the oesophagus and bladder, pulmonary tuberculosis, and low birth weight (Royal College of Physicians 1962).

Since this initial RCP report and the first US Surgeon General 1964 report (United States. Surgeon General's Advisory Committee on Smoking 1964), further studies and White papers have been published linking tobacco smoking with a multitude of negative health outcomes. The 2014 US Surgeon General's Report concluded that smoking causes 12 types of cancer across the body, alongside a wide range of other cardiorespiratory, ophthalmological, and metabolic diseases (US Department for health and Human Services 2014). The latest RCP report in 2018 "Hiding in Plain Sight, Treating Tobacco Dependency in the NHS" (Royal College of Physicians 2018), not only reaffirmed the strong association between tobacco smoking and lung cancer, chronic respiratory disease and cardiovascular disease, but reported on how smoking causes, and exacerbates a wide spectrum of diseases.

As with tobacco induced lung cancer and respiratory diseases, the GBD study indicated tobacco induced disease deaths were high within ischemic heart diseases, causing 1.68 million deaths worldwide (Reitsma 2021). A 2022 meta-analysis of Mendelian randomised studies concluded that smoking was associated with increased risk of several chronic diseases. This included 13 different cardiovascular diseases, neurological diseases such as epilepsy, endocrine disorders such as polycystic ovary syndrome, metabolic diseases such as type II diabetes, digestive system diseases such as gallstone and Crohn's disease and diseases of the eyes such as senile cataract. The review also highlighted the associations between smoking and numerous cancers such as cancers of the neck and head, pancreatic, bladder, ovaries and cervix (Larsson 2022). The strength of this review was the inclusion of studies using the

Mendelian randomisation method. This method determines the causal effect of an exposure in disease development, this is explored via the utilisation of genetic variants associated with the exposure, which in this case is smoking. This study design is thought to mitigate confounding as genetic alleles when passed from parent to child are allocated randomly (Davey Smith 2003).

It is not only one's physical health that can be worsened by tobacco smoking, the associations between smoking and risk for developing mental health conditions have been explored. A meta-analysis conducted in 2015 reported higher overall odds for the development of first episode psychosis within smokers compared to non-smokers [OR: 3.22, 95% CI 1.63-6.33), (Gurillo 2015). The authors also included prospective studies which further supported their findings [OR: 2.18, 95% CI 1.23-3.85) (Gurillo 2015). These associations were confirmed five years later, a 2020 meta-analysis of cohort and case control studies demonstrated compared to non-smokers, smokers had a significantly higher risk of developing schizophrenia [RR: 1.99, 95% CI 1.10%-3.61%], (Hunter 2020) The authors explored the effects of prenatal smoke exposure on schizophrenia risk, and again demonstrated a significant association [RR: 1.29, 95% CI 1.10%-1.51%] (Hunter 2020).

It is now almost universally acknowledged that tobacco smoking is harmful to both mental and physical health (particularly for lung cancer and respiratory diseases). Despite this, tobacco is still mass produced and sold globally, remaining a leading cause of premature death and disability worldwide (Reitsma 2021). Tobacco companies are effectively operating on a profit for death model, highlighting that the "Tobacco Problem" is far from over.

1.2 Smoking Cessation Support

Smoking cessation support is typically a combination of behavioural advice and pharmacological aids, targeted at supporting smokers through quitting (Bauld 2010). The aim of smoking cessation support is complete and continued abstinence from smoking. Depending on the country or location services will be offered in groups, outpatient settings, hospitals, pharmacies or dedicated one to one services (World Health Organization 2019). Delivering smoking cessation support is an effective intervention in reducing harms from the tobacco epidemic and is a key component in the WHO's tobacco control MPOWER measures (World Health Organization 2023b).

1.2.1 History of smoking cessation support in the UK

In 1999 the UK government published the first "Smoking Kills" White Paper on tobacco. Within this document the UK government outlined a plan to invest in NHS run smoking cessation services across all four UK nations (UK Government 1999). The paper stated that services would offer a combination of counselling support and a week's supply of Nicotine Replacement Therapies (NRT), which would be free for those on low income (UK Government 1999). The White Paper was guided in large part by the 1998 smoking cessation guidelines for health professionals (Raw 1998) and the findings of the Cochrane Tobacco Addiction Review Group. Both documents recommended that specialist stop smoking support should offer a combination of behavioural counselling and NRT to treat withdrawal symptoms (Silagy 1998; Silagy 2003). These services initially were piloted in areas with a high percentage of adult smokers and funded with a government protected grant of £10 million. Over three years the services expanded throughout the UK, with increased protected governmental funding of £30 million (UK Government 1999; West 2013).

1.2.2 Smoking cessation services in the UK today

Smoking cessation services in the UK have developed over the past two decades, particularly within the pharmacotherapy offered. Bupropion, which is an antidepressant tricyclic, was first offered as a medication to support smoking cessation in June 2001 (McNeill 2005) and has been available since. The introduction of Varenicline as a pharmacotherapy to support smoking cessation was a major change in service delivery since its inception. Due to successful phase III placebo-controlled trials, the nicotinic acetylcholine receptor (nAChR) partial agonist Varenicline was licensed as a smoking cessation medication (Lam 2007). Varenicline became available on NHS prescription in December of 2006 and was widely prescribed in the UK (Langley 2011). This remained so until Pfizer recalled the medication in the Summer of 2021 due to increased levels of nitrosamines within the medication (National Center for Smoking Cessation and Training 2021a). The use of e-cigarettes within NHS smoking cessation services has been a recent and controversial addition to smoking cessation services. Since Public Health England's e-cigarette report in 2015 (Public Health England 2015) and subsequent National Centre for Smoking Cessation and Training (NCSCT) e-cigarette guidance the following year (National Center for Smoking Cessation and Training 2016). Smoking cessation services across the UK now offer guidance for people wishing to quit using e-cigarettes, however, services are unable to directly prescribe e-cigarettes for their service users. The latest addition to smoking cessation pharmacotherapy in the UK has been the 2024 introduction of Cytisine. This medication was first developed in Bulgaria in the 1950s and has been primarily used within Eastern Europe and Canada as a cessation medication (West 2024). Cytisine is a selective partial agonist acting on the nicotinic acetylcholine receptors (Courtney 2021). There have been numerous studies reporting on its efficacy compared to NRT and varenicline (Ofori 2023; Courtney 2021). Due to the success of these studies and the

lack of available varenicline, in January 2024 the UK's Medicines and Healthcare Regulatory Authority (MHRA) licenced the drug to be used within UK smoking cessation services.

Smoking cessation services in the UK today will typically offer a combination of NRT/pharmacotherapy/e-cigarettes alongside behavioural counselling support. This is accessible in a range of settings from one to one, group and telephone/ remote options. However, provision of these services since the mid 2000's has drastically declined. Before 2013 smoking cessation services were commissioned and provided through primary care trusts (West 2013). Following the 2010 austerity measures and subsequent public service budget cuts, smoking cessation services switched to local authority direction and were funded by government public health grants (West 2013; Action on Smoking and Health 2019). A 2019 report produced by the lobbying charity Action on Smoking and Health in collaboration with Cancer Research UK, explored smoking cessation provision in the UK. The report highlighted how budget cuts from the central government to the local authorities and the reductions in public health grants given to these local authorities, have negatively affected smoking cessation service provision. Between 2015-2018 local authority spending on smoking cessation and tobacco control fell by £41.3million. This fall in central government funding resulted in only 56% of local authorities in England being able to offer smoking cessation services universally (Action on Smoking and Health 2019).

1.2.3 Benefits of smoking cessation

The benefits of smoking cessation were first noted by Doll and Hill (Doll 2004) and have been investigated widely since. Given the wide range of tobacco induced diseases, the benefits of cessation are also wide reaching, both for the individual who smokes and for the healthcare system. The most recent 2020 US Surgeon General's smoking cessation report concluded that smoking cessation reduces the health risk of multiple chronic diseases, namely cardiovascular

disease, chronic lung diseases and cancers (U.S. Department of Health and Human Services 2020). The report highlights that these benefits of cessation occur at any age, increasing physical health and quality of life. In terms of mortality, the report concludes that cessation can add up to 10 years to life expectancy (U.S. Department of Health and Human Services 2020). These findings have been mirrored within the UK, the Royal College of Physicians 2018 report concluded that treating tobacco dependence within all areas in medicine will improve the patient's condition (Royal College of Physicians 2018). The report argues that smoking cessation is not solely a preventative intervention, but that for multiple diseases smoking cessation is as an effective evidence-based treatment. The report also comments on the cost effectiveness of smoking cessation and concluded that when compared to standard therapy interventions to treat smoking included diseases (such as brief advice and Quitline's), smoking cessation is by far the most cost-effective treatment (Royal College of Physicians 2018).

The focus of this thesis is the integration of smoking cessation interventions within lung cancer screening programs. The populations attending for lung cancer screening will be middle aged (55-80), and potentially have early-stage cancers. I will explore the current literature surrounding the benefits of smoking cessation within these two populations below.

1.2.3.1 Benefits of smoking cessation among middle and older aged adults

It is clear from the smoking cessation data, that the earlier cessation occurs, the greater the health benefits and mortality reductions (U.S. Department of Health and Human Services 2020; Royal College of Physicians 2018). However, the benefits of cessation among smokers quitting at middle and older age are demonstrated within the literature. Data from the US Cancer Prevention II study observed that smokers who quit at 65 years old gained between 1.4-2.0 years of life among men and 2.7-3.7 years among women (Taylor Jr 2002). A meta-

analysis conducted by the CHANCES consortium studied the impact of smoking and cessation on cardiovascular mortality among older adults (60 years +). The group observed higher cardiovascular mortality risk among current smokers (HR: 2.07, 95% CI 1.89-2.36) compared to former smokers (HR: 1.37 95%CI 1.25-1.49) (Mons 2015).

Quality of life and psychological health benefits have also been observed among middle and older adults who quit. Within a community subsample of middle-aged women, those who reported successful cessation for ≥1 year reported less financial stress (AOR: 0.50, 95% CI 0.25-1.00 and less life dissatisfaction (AOR: 0.51, 95% CI 0.24-1.09) compared to current smokers (Brook 2014). Data from the English Longitudinal Study of Ageing, highlighted within community dwelling adults aged 50 years and over, current smokers were more likely to be lonely (coef=0.111, 95% CI 0.025-0.196) and socially isolated compared to never or former smokers (Philip 2022).

These studies demonstrate how smoking cessation can increase physical health, social health, and quality of life within middle and older aged adults, highlighting the importance of cessation within this population. These studies, emphasise how healthcare and smoking cessation providers should encourage and promote cessation in middle aged and older ages, and not take a nihilist approach to cessation within this population.

1.2.3.2 Benefits of smoking cessation within lung cancer patients

The 2016 SmokeHaz systematic review, demonstrated that within patients with early-stage non-small cell lung cancer, all-cause mortality was significantly higher among patients who continued to smoke after diagnosis compared to those who stopped (HR: 2.94, 95% CI 1.15-7.54) (Jayes 2016). A similar effect was also observed among patients who continued to smoke with small cell cancer (HR: 1.86, 95% CI 1.33-2.56) (Jayes 2016). The researchers estimated that for 65-year-old patients diagnosed with non-small cell lung cancer, five year

survival for those who continued to smoke would be estimated at 33% and those who quit smoking estimated at 70% (Jayes 2016). A more recent 2024 systematic review and meta-analysis reported similar findings. Caini et al, 2022 concluded that lung cancer patients who quit smoking at or close to their diagnosis had a significantly improved survival rate (Survival Risk Ratio (SRR): 0.71, 95% CI 0.64-0.80). This was observed across patients that quit with non-small cell lung cancer (SRR: 0.77, 95% CI 0.66-0.90), and small cell lung cancer (SRR: 0.75, 95% CI 0.57-0.99) (Caini 2022). These reviews highlight the stark differences in mortality and survival between patients who quit and continue to smoke after a lung cancer diagnosis.

These reviews stress the importance of smoking cessation for patients newly diagnosed with lung cancer. This is illustrated within the conclusion of a review into the effects of tobacco smoking on cancer treatment. The authors state, attributed to the multiple benefits of smoking cessation, it needs to become an integral part of the cancer care pathway, through screening, diagnosis and treatment (Kassim 2020).

1.3 Lung Cancer

A malignant tumour that begins in the lungs is defined as a primary lung cancer. There are two main forms of primary lung cancer dependent on the cells in which the malignancy started growing in (Barta 2019; NHS 2022). Non-small-cell lung cancer, this is the most common form of lung cancer in the UK accounting for around 80% of lung cancers, categorised in three types, 1) squamous cell carcinoma, 2) adenocarcinoma or 3) large-cell carcinoma (Barta 2019). Small-cell lung cancer is the second most common form of lung malignancy and in the UK accounts for around 15% of lung cancer diagnoses (NHS 2022). Small-cell lung cancer has a quicker growing time than non-small-cell lung cancer, thus spreads throughout the body faster (American Cancer Society 2024,; NHS 2022).

The most common risk factor for lung cancer is inhalation of tobacco smoke (Jayes 2016). In the UK more that 70% of lung cancers are caused by smoking (Brown 2018), however, occupational exposures to chemicals, a family history of lung cancer, exposure to radon gas and other cancer treatments can also lead to a lung cancer diagnosis (Brown 2018; Shankar 2019)

1.3.1 Lung Cancer Statistics

The International Agency for Research on Cancer, estimated that 1.8 million deaths globally were attributable to lung cancer in 2020 (World Health Organization 2023a), presenting a global public health concern. In the UK lung cancer is the third most common form of lung cancer (Cancer Research UK 2023b) and the majority of patients (43%) will present with stage four disease. However, with advancements in screening and symptom awareness campaigning, in 2019 28% of patients presented with stage one-two disease, a marked increase since 2014 (Royal College of Physicians 2017). Despite these recent increases in early disease presentation, stage four disease presentation remains high, attributable common symptoms of lung cancer (persistent cough, dyspnoea and haemoptysis) often indicative of late stage of disease (Navani 2022). In terms of mortality, lung cancer is the deadliest cancer type, accounting for 21% of all deaths attributable to cancer (Navani 2022). As of 2018, one year survival from stage one disease was 83% and 17% for stage four disease (Royal College of Physicians 2017). Since 2014 lung cancer mortality rates have declined by an estimated 14%, however, there is a divergence between sexes, male mortality rates have decreased by 22% whereas female rates have only decreased by 5% (Royal College of Physicians 2017; Navani 2022).

1.4 Lung cancer screening

As previously mentioned, despite lung cancer mortality reducing in many western nations (Sung 2021; Cancer Research UK 2023a; Centers for Disease Control and Prevention 2022), a large proportion of lung cancer is still diagnosed at a late stage of disease. This leads to poor prognosis and survival for these patients (Navani 2022), which has led to the investigation and development of asymptomatic screening programmes (The National Lung Screening Trial Research Team 2011).

1.4.1. Background of lung cancer screening

Trials investigating asymptomatic screening for lung cancer began in the 1990s and the methods used were chest radiograph (X-ray), with or without sputum cytology screening (Bach 2003). These methods proved to be unsuccessful and were subsequently not recommended by national screening committees (Bach 2003; Humphrey 2004). Advancements in computed tomography (CT) technology in the mid-2000s, presented a new technique for lung cancer screening (Doria-Rose 2010). This CT procedure allowed high-resolution volumetric imaging to be possible with low radiation exposures (Doria-Rose 2010). Due to these low radiation exposures, this CT method presented a low-risk asymptotic screening tool, and resulted in several observational trials demonstrating its effectiveness over chest X-ray for nodule and early-stage cancer discovery (Doria-Rose 2010).

Thus, the USA conducted their National Lung Cancer Screening Trial (NLST). This Large randomised controlled trial enrolled 53,454 asymptomatic current or ex-smokers aged 55-74, with at least a 30-pack year smoking history. The participants received either three annual chest x-rays or three annual low dose CT (LDCT) scans and were followed up for seven years. The results demonstrated a 15-20% lower lung cancer mortality among patients who received the annual LDCT screening vs chest X-rays. (The National Lung Screening Trial Research Team

2011). The Dutch-Belgium NELSON trial, which had a similar study design to the NLST, demonstrated mortality reductions of 33% in women and 24% in men among participants who received LDCT screening (de Koning 2020). Annual asymptomatic screening using the LDCT method for high risk individuals is now recommended by the US Preventive Services Taskforce (US Preventive Services Taskforce 2021), and the European Respiratory Society (Kauczor 2020a).

1.4.2 The UK's Targeted Lung Health Check program

Due to the mortality reductions observed with lung cancer screening in the USA and Europe, in 2019 the NHS launched their targeted lung health check (TLHC) pilot project, within areas with high lung cancer mortality rates. The aim of the pilot was to investigate the feasibility and effectiveness of LDCT screening within the UK and NHS services (NHS England 2019). Several of these TLHC pilot services have now published preliminary findings, demonstrating that screening with LDCT is effective at identifying early-stage lung cancers and can be successfully implemented with the NHS framework (Crosbie 2018; Field 2015; Balata 2021). Longer follow up periods are required to assess if these TLHC pilot projects have been successful in reducing mortality rates for lung cancer. However, due to their success so far and the evidence from the USA and Europe, the UK government's National Screening Committee (NSC) in 2022 recommended that targeted lung health checks should be rolled out across the UKs four nations (National Screening Committee 2022).

Currently TLHCs are offered to people with an ever-smoking history, aged 55-74 and registered with a GP practice within the following areas East of England, London, Yorkshire and the Northeast, North West, Midlands, South East and the South West. The current service comprises of an initial consultation (in clinic or remotely) with a respiratory nurse, then a chest LDCT if clinically indicated via risk algorithms (NHS 2023).

1.4.3 Incidental findings within lung cancer screening

A symptomatic lung cancer screening with LDCT is effective at identifying nodule changes early, allowing curative treatment and reducing mortality from lung cancer. Alongside this, screening can also discover other non-cancerous abnormalities within the thorax (Pinsky 2022). Incidental findings detected within a LDCT lung cancer screen may include cardiovascular findings such as aortic disease and coronary artery calcification. Alongside incidental respiratory findings including, pulmonary fibrosis, pleural effusion, reticular opacities and emphysema (Tsai 2018; Yip 2021).

Within data from the USA NLST, researchers observed emphysema in 44% of participants at any scan. While only 10.6% of the 25,002 scanned participants reported a history of COPD/emphysema. Additionally, 36.8% of participants presented evidence of fibrosis, honeycombing or reticular/reticulonodular opacities on their scans. The researchers reported these participants with respiratory incidental findings had an elevated respiratory disease mortality of (HR: 2.27: 95% CI, 1.92-2.7) and (HR: 1.39; 95% CI 1.19-1.62) respectively (Pinsky 2022).

The UK data indicates similar findings. Within the SUMMIT screening study conducted in Central London, 33.4% of their screened participants displayed evidence of emphysema (Tisi 2023). The Manchester Lung Health Check Program found emphysema was present in 63.6% of their participants, however, it was unclear if this was reported by the participants at the initial health check consultation or indicated as an incidental finding after the LDCT (Bradley 2022). The West London screening program reported, within a sample of 1542, 3.6% of patients were referred to primary care for onward assessment of COPD. Of note the West London screening program included spirometry assessments as part of their initial lung health check consultation (Bartlett 2021).

It is clear from both the US and UK data, that lung cancer screening services can reduce lung cancer mortality, whilst identifying previously unknown respiratory diseases such as fibrosis and COPD. These recent studies into incidental findings demonstrate how the potential for lung cancer screening services reaches beyond early cancer detection.

1.4.4 Lung cancer screening and smoking cessation

Within these large screening RCTs, researchers have observed increased quit rates among current smokers who received screening. The Dutch-Belgium NELSON trial observed a quit rate of close to 17% among trial participants (van der Aalst 2010). A similar effect was also observed among current smokers within the UK lung cancer screening trial (UKLS). UKLS researchers observed increases in both two week and two year quit rates among patients who had received CT screening compared with control, 14% vs 8% and 24% vs 21% respectively (Brain 2017). These data suggested that attending a lung cancer screening programme may act as a "teachable moment" for smoking cessation (Iaccarino 2019). The teachable moment in healthcare theory illustrates when a healthcare cuing event elicits a positive health behaviour change (Lawson 2009). Within the lung cancer screening environment, it is likely that clinicians highlighting and reaffirming the dangerous effects of tobacco smoking may function as a cuing event, leading to an increased motivation to quit. The teachable moment for smoking cessation theory is described in detail in Chapter 2 of this thesis.

To take advantage of this teachable moment, several interventional trials embedding smoking cessation interventions within lung cancer screening services have been conducted. The results thus far have been varied, both in terms of smoking cessation delivery methods used and success. The systematic review and meta-analysis in Chapter 3, describes in detail the current literature, however I will provide a succinct summary in this section.

The earliest study was conducted within a lung cancer screening programme based in the USA. The participants were randomised to receive either written cessation materials or internet-based materials after they had undergone a LDCT screen. The current smokers were followed up at 12 months, and quit rates were not statistically higher within the intervention arm (Clark 2004a). Comparable studies using internet, audio or written materials as their smoking cessation interventions saw similar modest effect sizes (van der Aalst 2012; Marshall 2016). Later studies, using a combination of counselling support and pharmacotherapy (NRT and E-cigarettes) have seen larger effect sizes (Taylor 2022; Lucchiari 2020; Pistelli 2020).

A research group in Rotterdam conducted the most recent systematic review within this area. The authors concluded that lung cancer screening programs are opportune moments for smoking cessation, with high intensity smoking cessation interventions leading to greater quit rates, (Moldovanu 2021). The review is limited by its narrative design, however, stresses the need for high quality trials within this area to determine the most effective cessation modalities.

Alongside increases in smoking cessation rates, lung cancer screening programmes delivering smoking cessation may also improve the cost effectiveness of their screening services. Economic modelling conducted with the USA NLST, increased the cost effectiveness of the annual LDCT screening programme by 20% when smoking cessation was delivered alongside screening. The modelling also demonstrated that the cost effectiveness is increased further to around 45% when the intervention offered is a combination of NRT and multiple counselling sessions (Villanti 2013). This has been supported by a recent economic analysis comparing the Quality Adjusted Life Years (QALY) of a three week cessation intervention to

an eight weeks cessation intervention within a US lung cancer screening programme (Cao 2022).

Both economic and smoking abstinence modelling has been performed using UK data. Cost per quitter data within the Yorkshire Enhanced Stop Smoking Study (YESS) was calculated at £521.30 among smokers who received the intervention (Murray 2022). The same report included modelling data conducted by researchers at University College London (UCL), which concluded that embedding smoking cessation support within the UKs TLHC program would lead to a 2.23% reduction in smoking prevalence within the 55–74-year age group, equating to ~30,000 extra abstinent smokers in the UK (Beard 2022; Murray 2022).

Guidelines across the UK, USA, and Europe recommend that smoking cessation interventions be incorporated into lung cancer screening (UK National Screening Committee 2022b; Kathuria 2017; Kauczor 2020a). However, there is little guidance on how such interventions should be delivered and limited evidence on effectiveness to date (Iaccarino 2019). The current smoking populations presenting to lung cancer screening are likely to have long tobacco histories and be highly nicotine dependent, thus it is important to optimise the delivery of support for these individuals compared with services designed for the general smoking population (Kathuria 2017; de Koning 2020).

1.5.6 The rationale for embedding smoking cessation within lung cancer screening.

The public health benefit of embedding smoking cessation within lung cancer screening is potentially exceptionally large. Mass screening programs have the capacity to reach many current smokers, who may not otherwise interact with the healthcare system (Murray 2022). Given the eligibility criteria for screening, many of these current smokers may already have lung disease, further reducing their mortality. As previously stated, within the UK access to

specialist smoking cessation support has become increasingly difficult (Action on Smoking and Health 2019). However, the UK government has recently committed to doubling funding for smoking cessation services (Department of Health and Social Care 2023). Despite this announcement, access to community cessation support remains inadequate, with appropriate clinical NHS services presenting as opportunities to embed cessation services within them to expand access (Agrawal 2024)

Lung cancer screening presents as a good public health intervention. It is estimated that 1.1 million smokers in the UK meet screening criteria (Beard 2022), coupled with the individual health benefits and service cost savings. Lung cancer screening programmes may serve as an opportune environment to embed smoking cessation, however, to advocate widely for this combination of services, the evidence supporting effective smoking cessation approaches within this screening environment needs to be thoroughly evaluated and investigated.

Despite an emerging evidence base on strategies to combine smoking cessation support within the lung cancer screening setting. There is a lack of consensus on what the most effective modality or modalities are. The fundamental issues within the evidence are reflected in many national LCS guidelines, which mention that smoking cessation should be considered, but do not elaborate on how they should be delivered (National Screening Committee 2022; Kathuria 2017; Kauczor 2020a).

There is a framework of issues regarding the delivery of smoking cessation support within a LCS setting. The crucial questions which this thesis will aim to address are the following: will a comprehensive offer of smoking cessation support increase quit rates over a standard Very Brief Advice (VBA) approach, as suggested by the 2021 Moldovanu review and a recent policy review (O'Dowd 2023). What modality of cessation support is most effective, particularly

telephone-based support or traditional face to face delivery? Finally, as suggested by the latest ASH report proposing an opt out delivery approach should be adopted (Murray 2022), should Smoking Cessation Support (SCS) services provided within LCS settings follow an opt-out or opt-in service delivery model?

1.6 Aims and objectives.

1.6.1 Summary of thesis aims and objectives.

The main aim of this thesis is to identify effective strategies for delivering smoking cessation support within lung cancer screening services and investigate whether smoking cessation support delivered immediately after a TLHC, including the offer pharmacotherapy, is effective at increasing smoking abstinence.

To achieve this aim, this thesis has four objectives. The first is to identify the most effective smoking cessation delivery strategies within lung cancer screening programmes, achieved via a systematic review of the literature and meta-analysis. The second objective is to assess the impact of a telephone smoking cessation intervention delivered immediately post attendance to a TLHC. The third objective is to assess long term (12-month) quit rates among smokers who received smoking cessation interventions within a lung health check, including data from the first Quit Smoking Lung Health Intervention Trial (QuLIT1). The fourth and final objective is to investigate participant experience of these interventions and explore barriers, among participants who declined or dropped out of the smoking cessation interventions.

Chapter 2: Methods

2.1 Ethical Approval

For the studies in chapters 4-7 (QuLIT2 and further qualitative studies). Ethical approval was granted by the South Central – Oxford C Research Ethics Committee and the Health Research Authority (Ref:18/SC/0236). In QuLIT1 and QuLIT2 the requirement for individual participant consent was waived by the ethics committee, as obtaining this would itself have been an intervention and influenced outcomes in the control group. Formal verbal consent was gained by all participants prior to participating in interviews (Chapters 6-7).

2.2 Statistical analysis

Analyses were conducted using SPSS Statistics 27 (IBM Corporation, New York, USA). Specific analyses used in each study are described in more detail in the relevant chapters, a p-value <0.05 was taken to be significant for quantitative analysis. For the qualitative analysis NVivo 1.61 (QSR International) software was used to organise and support the thematic analysis.

2.3 Study Subjects

All the patients studied were recruited from the TLHC service at the Royal Brompton Hospitals (RBH) Healthy Lung Project (HLP). These participants were residing in either Hammersmith and Fulham, Sutton, or Hillingdon London boroughs, aged between 55-74 years old and had an ever-smoking history recorded on their medical records. For the purposes of the QuLIT trials only those patients who were recorded as current smokers were recruited into the study.

2.4 The Targeted Lung Health Check

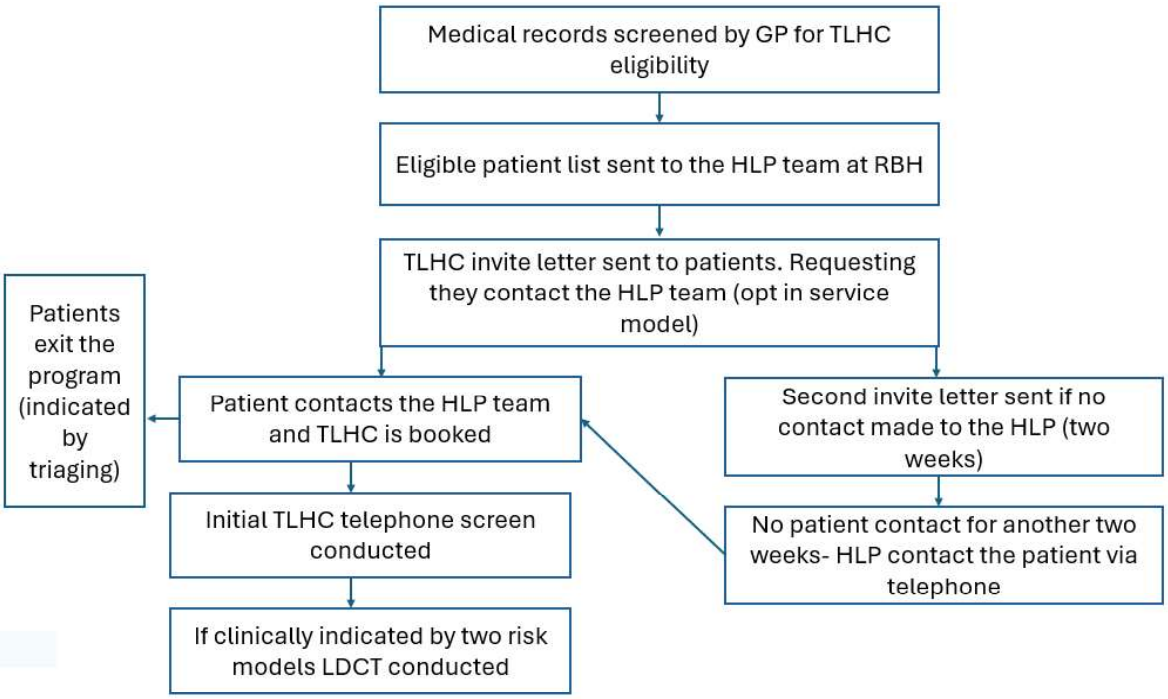
The TLHC service is an investigational lung cancer screening pilot project delivered by the Royal Brompton Hospital. The HLP service is supported by RM Partners, West London Cancer Alliance with NHS funding through the National Cancer Transformation Fund. The clinical

service comprises two stages: the first is an initial lung health check, the second is a CT scan if clinically indicated. The first stage includes discussion with specialist nurses of participants' current or historical smoking behaviour, medical history, familial cancer history and occupational history. If participants meet the risk threshold criteria according to the Prostate, Lung, Colorectal and Ovarian (section 2.5.1) or Liverpool Lung Project screening risk models (section 2.5.2) (Tammemägi 2013; Lebrett 2020), they were invited to attend a computed tomography (CT) scan, which is the second stage of the TLHC process.

2.4.1 Targeted Lung Health Check Recruitment

Patients whose GP surgeries were within the catchment boroughs and had opted to collaborate with the TLHC program were recruited by the HLP. The referral process for the HLP is as follows. Medical records were screened by the GP practice for eligibility (age 55-75 recorded as ever smokers and consent for records to be shared), this list was sent to the HLP team. Eligible participants were initially sent an invite letter to contact the TLHC program at the Royal Brompton Hospital to attend a lung health check. If no response had been received by the HLP team after two weeks, the administrators sent a second invite letter, if there was still no response after a further two weeks, participants received a reminder phone call asking if they'd like to take up the offer of a TLHC. Before any appointment was made, participants were asked several triage questions by an administrator to confirm GP practice, age, smoking history, if they had recent (<12 months) chest CT or were undergoing current treatment for cancer. Please see figure 2.1 for participant flow through the HLP.

Figure 2. 1 Patient flow through the HLP program at the Royal Brompton Hospital



2.5 Risk Models

2.5.1 Prostate, Lung, Colorectal and Ovarian (PLCO)

The Prostate, Lung, Colorectal and Ovarian ($PLCO_{M2012}$) model, determines a patient's risk of lung cancer using variables; age, body mass index, ethnicity/race, in depth tobacco smoking history (cigarettes per day, age started smoking, number of smoking years, and type e.g. cigarettes, cigars, cannabis), COPD status, history of cancer, family history of cancer and educational attainment (Tammemägi 2013). Patients were deemed high risk of lung cancer if they had a PLCOM2012 score of $\geq$1.51% and were eligible for a LDCT scan (Lebrett 2020). If patients did not meet the risk threshold of $\geq$1.51% they were assessed against the Liverpool Lung Project model.

2.5.2 Liverpool Lung Project (LLP model)

The Liverpool Lung Project (LLP) risk algorithm was used to identify individuals with $\geq$5% risk of developing lung cancer over five years (Field 2016; Cassidy 2008). Variables included in the model are age, gender, personal history of cancer, asbestos exposure, first degree relative with a lung cancer diagnosis, number of years smoked and history of lung infection/ diseases (pneumonia, emphysema, bronchitis, COPD, or tuberculosis). If participants were deemed according to the LLP model to have a $\geq$5% of developing lung cancer within five years, they were eligible for a CT scan.

2.6 Thorax Low Dose Computed Tomography Scan

Low dose computed Tomography scans (LDCT) were performed using either a 128 slice Siemens Edge CT scanner at the Royal Brompton Hospital or on a 128-slice GE Healthcare Optima CT660 scanner at a mobile unit. The scans were conducted using a low dose protocol with weight based scanning parameters, and maximum inspiration with breath hold manoeuvre was used to acquire images from apical to lung bases (Bartlett 2020).

2.7 Smoking Cessation programme

The smoking cessation programs were based upon the NCSCT, (NCSCT 2023) and Kick-IT programs (KickIt 2022). The program itself delivers a combination of behavioural counselling support in addition to pharmacotherapy prescription and advice.

2.7.1 Training of the smoking cessation advisors

The smoking cessation advisors who administered the intervention were registered research nurses. To ensure the gold standard smoking cessation delivery, the two nurses completed both the online NCSCT training course (NCSCT 2023) and a three-week part time smoking cessation advisor training. The training course was run by Kick-IT at the Royal Borough of Kensington and Chelsea local authority and covered how to deliver the six-week NHS cessation programme, cessation medications, motivational interviewing techniques and role-playing scenarios (KickIt 2022). The research nurses had to complete the three-week course and receive the certification as a smoking cessation practitioner before they were able to administer the intervention.

2.7.2 Behavioural Counselling

The behavioural counselling consisted of six weekly sessions, the counselling methods used were a combination of motivational behaviour change tools and support with withdrawal symptoms and cravings. The first session was an initial consultation, whereby the advisor would explain the program to the patient, and what is expected from them of complete abstinence after their last cigarette. In this first appointment the advisor would also assess the patient's current tobacco use and nicotine dependence, alongside past quit attempts. The advisor would then discuss with the patient options for pharmacotherapy, explain withdrawal symptoms, and clarify the importance of abstinence after the quit date. The first session would finish with the participant setting a quit date and a commitment to stay abstinent after

that date. The second appointment would occur after the participant had set their quit date. The advisor would ensure the participant had enough pharmacotherapy and discuss any withdrawal symptoms that the participant may be experiencing. In collaboration with the patient the advisor would action plan for any high-risk events in the upcoming week and look at changing the participants routine and address any smoking peers and the high-risk events. Again, the session would end with a commitment from the participant to stay abstinent. The remaining three-five sessions would follow this same pattern, unless the participant had relapsed in which case a new quit date would be set. The final session would include action planning in case of relapse, reaffirming the participants coping mechanisms for any high-risk situations and ensuring the participants had enough pharmacotherapy and knows the process for sourcing more. The last session would finish with the last commitment from the participant to stay abstinent (KickIt 2022; NCSCT 2023).

2.7.3 Pharmacotherapy

The pharmacotherapy made available to participants was either nicotine replacement therapies (NRT), offered as either a single item or double item (Hartmann-Boyce 2018) or the prescription medication varenicline (Garrison 2009).

2.7.4 Nicotine Replacement Therapy

Nicotine replacement therapy (NRT) reduces the physiological and psychomotor drivers to smoke. The mechanisms work by damping withdrawal symptoms, which are commonly experienced during a cessation attempt (West 2001; Hartmann-Boyce 2018). The method of action for NRT products acts through absorption via the skin (transdermal patch), oral or nasal mucosa (chewing gum, lozenge, inhalator), attributed to the fast-pass metabolism that nicotine undergoes in the liver (West 2001). The NRT available to patients undergoing the QuLIT2 (Chapter 4) are described below in table 2.1. Transdermal patches deliver a low dose

of nicotine throughout the the day and night passively. Oral and nasal delivery systems are faster acting, and often used for break-through cravings and in the case of the inhalator mimicking the behaviour of smoking (KickIt 2022; Hartmann-Boyce 2018; West 2001).

Table 2. 1 NRT used in in Chapter 4.

Transdermal Patches	Nicorette (INVISI) 25mg 16 hours Nicorette (INVISI) 15mg 16 hours Nicorette (INVISI) 10mg 16 hours Nicotinell (TSS10) 7mg 24 hours Nicotinell (TSS20) 14mg 24 hours Nicotinell (TSS30) 21mg 24 hours
Nasal Spray	Nicorette 0.5mg per metered dose
Oral Spray	Nicorette Quickmist 1mg per metered dose
Lozenges	Nicotine 2mg Nicotine 4mg
Inhalator	Nicotine 15mg cartridge
Chewing gum	Nicotinell 2mg Nicotinell 4mg

2.7.5. Varenicline

Varenicline of the brand name Champix, is a selective nicotine- receptor partial agonist. The medication interacts with the nicotine receptor agonist, reducing withdrawals and nicotine cravings. (Garrison 2009; National Institute for Health and Care Excellence 2023). The indication and dosing are as follows: 500 micrograms once daily for three days, increased to 500 micrograms twice daily, the patient would set their quit date in this period. The patient would then continue taking 1mg twice daily for 11 weeks, whilst staying abstinent from cigarettes (National Institute for Health and Care Excellence 2023). Caution was indicated for a prescription if a participant had a history of seizures, psychiatric illness, diabetes and kidney disease (National Institute for Health and Care Excellence 2023; Garrison 2009).

During the study trial period for QuLIT2 April-June 2021, (Chapter 4), Pfizer the manufacturer of varenicline paused the distribution of the drug in June due high levels of nitrosamines found in the medication (National Center for Smoking Cessation and Training 2021b). Several participants within the intervention arm in Chapter 4 had to switch from varenicline to NRT for the remainder of the study period.

2.7.6 Exhaled Carbon Monoxide verification

To biochemically confirm smoking cessation, exhaled breath carbon monoxide (CO) verification was used in Chapter 5. This is a common method of validating self-reported smoking cessation in clinical trials and stop smoking services (KickIt 2022; NCSCT 2023; Piper 2020).The MicroMedical Micro CO Smoke Monitor (CareFusion Limited) device was used to assess exhaled CO within the trial. Participants were asked to take a deep inhalation, place their mouth around the mouthpiece then exhale gently for 10 seconds. This was repeated three times and an exhaled CO of $\leq$ 5ppm indicated abstinence. The cutoff of $\leq$ 5ppm was used as it was indicated in the Kick-IT training undertaken by the smoking cessation advisors (KickIt 2022). The use of the $\geq$ 5ppm threshold has been indicated as a more sensitive measure of abstinence in research trials previously, compared to the use of $\leq$ 8ppm (Perkins 2013).

Figure 2. 2 Micro Medical CO Smoke Monitor (Care Fusion), device used in chapter 5.



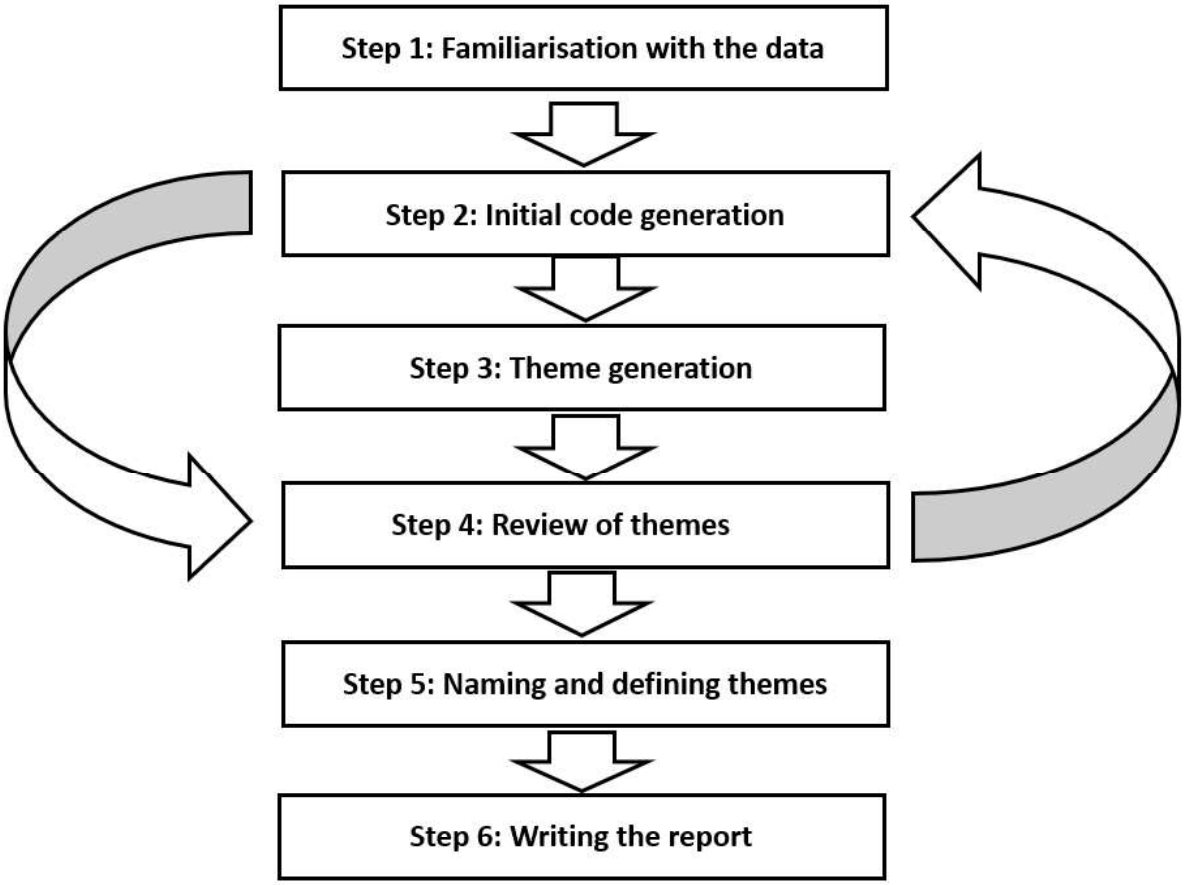
Table 2. 2 Exhaled CO breath test chart used in Chapter 5.

Carbon monoxide reading (ppm)	Indicates
0-5	Non-Smoker
6-10	Light Smoker/ heavy pollution
10-20	Heavy Smoker
20 +	Very heavy smoker

2.8 Thematic Analysis

Chapters 6 and 7 are qualitative studies. These studies are focused on understanding the patient experience of smoking cessation interventions within a screening context (chapter 6) and barriers to accepting the offer of cessation (chapter 7). The basis of qualitative analysis I used in this thesis is Reflective Thematic Analysis (TA). This method of analysis is based on the 2006 seminal paper by Braun and Clarke (Braun 2006), and further methodological iterations (Clarke 2015). The latest of which is the change in reference to include the word reflective in the title to allow for theoretical flexibility within the analytical process. Reflexive Thematic analysis (TA) is a qualitative analysis method which identifies, analyses and report's, themes, or patterns within qualitative data. Reflective TA is a flexible approach to qualitative analysis and can be used alongside a range of theoretical frameworks (Clarke 2015).

Figure 2. 3 Flow diagram representing the reflective thematic analysis process, including its nonlinear approach between steps 2-4



2.8.1 Reflective Thematic analysis Approach

This analytic approach consists of six iterative steps, the purpose of which is to discover patterns of meaning or themes, within a qualitative data set to address a particular research question. The method consists of familiarisation with the data, coding of the data, initial code generation, theme development, theme revision, defining and naming of the themes and, final write up (Braun 2023; Clarke 2015). I led on each step of the analytical approach, with

secondary input from (KEJP, SB and NSH) at the coding and theme development stage to ensure quality analysis, as per guidelines (Braun 2023; Clarke 2015).

2.8.2 Step 1- Familiarisation with the data

This is the first step in the TA process and used to get an overall sense of the data while identifying anything important that may relate to the research questions (Clarke 2015; Byrne 2022). Familiarisation consisted primarily of manual transcription of the interviews, where MS Teams auto transcription was used for some interviews, detailed reading and manual correction was conducted on transcripts. The data was transcribed orthographically, noting breaks in speech and change in tones. Once the transcription was completed, each interview transcript was read thoroughly to ensure equal consideration across the whole data set, as per Bruan and Clarke guidelines (Braun 2023). I conducted this first step in the TA process for both chapters.

2.8.3 Step 2: Initial code generation

Generation of codes is the first step of theme development. The aim of this second step is to provide succinct interpretive or descriptive labels for items within the dataset, which appear to be important and relate to the research question (Clarke 2015; Byrne 2022). Despite being a brief description of the data, codes should provide enough detail to be able to highlight the underlying commonality among the data, in relation to the research question (Clarke 2015; Braun 2006). At this stage the data was uploaded into NVivo to support code generation and organisation, NVivo allowed me to highlight the data items and assign a code to it using the manual coding function. Once I had created a code, I then could highlight additional data items and assign it to that code, and coded any data item that might have been of use in answering the research questions. As this was an iterative analytical approach, codes were tracked using a codebook. The first iteration of the codebook was created in NVivo then

exported to excel, to allow the secondary coding researchers to monitor code progression and highlight potential themes. NVivo software enabled me to organise each of the coded data items into their respective codes and provided a coding hierarchy, in addition to keeping the manuscripts free from annotations to allow for regular review as per guidelines (Clarke 2015). In both chapters (6 and 7) I lead the analysis at this stage creating my own set of codes and the codebook. In the analysis for Chapter 6, KEJP coded 50% of the manuscripts separately and generated his own set of codes; we then met on multiple occasions to finalise and agree on the final codes and theme generation in step three. The same process was used to analyse the data in Chapter 7 with researcher SCB analysing 25% of the manuscripts and all researchers (SCB, NSH) meeting to discuss final codes.

2.8.4 Step 3: Theme generation

This step in the analysis begins only once all relevant data items have been assigned a code. The analysis focuses on the interpretation of meaningfulness across the entire dataset, not the analysis of single data points within the dataset. At this step codes are reviewed and organised into a hierarchy, with codes becoming themes themselves and the development of subthemes, or codes combining to develop themes and subthemes (Byrne 2022; Braun 2023; Clarke 2015). Multiple codes which have a shared meaning or narrative within the data will be organised into a single code at this stage. A code may also be promoted to a theme or sub-theme if it represents a relevant overarching narrative within the dataset. At this stage it was important that the pattern of codes and themes communicates meaningfulness which helps to answer the research question (Braun 2023; Clarke 2015).

At this stage of the analysis for both chapters 6 and 7, I met with the analysis team (KEJP- chapter 6) and (SCB, NSH- chapter 7) to discuss and review the codes. Then the analysis team

begin theme generation, once the research team had finalised on a set of preliminary themes, I created a thematic map of the data. The thematic map allowed the research team to visualise the meanings and relationships between the themes and subthemes, and how they interacted with the research question.

2.8.5 Step 4: Reviewing themes.

This analysis stage consists of a thorough review of the preliminary themes, whilst keeping an overview of the dataset as a whole and how it relates to the research question (Braun 2006; Clarke 2015). Byrne, 2022, proposed a set of questions that the researcher should ask at this stage of the analysis.

1- Is this a theme, or could it just be a code?
2- What is the quality of this theme? Does it tell us something useful about the data and research questions?
3- What are the boundaries of this theme?
4- Is there enough meaningful data to support this theme? Is it a thick or thin theme?
5- Is the theme too wide? Is the data too diverse or the theme lacks coherence?

(Byrne 2022)

The review was conducted in two stages, I led at this stage of the analysis, with support from other members of the research team. We first reviewed the relationship between the codes which were organised into subthemes and themes e.g. observing internal homogeneity. If these codes displayed a pattern and or revealed a logical argument, the analysis team agreed that this theme would contribute to answering the research question and accepted it. For the second stage, we judged the themes in terms of how well they represented the data set in relation to the research question (Braun 2006; Clarke 2015). I used thematic maps to guide

this stage of the analysis, annotating the maps used in step four to keep track of the changes before finally creating a clean map of the accepted themes.

2.8.6 Step 5: Naming and defining the themes.

This step consists of a deep analysis of the thematic map or framework. It was important to keep in mind how the individual themes and subthemes related to the research question and the dataset. As per guidelines, themes should provide an internally consistent account of the data that cannot be represented by another theme. However, all the themes must form a sound narrative that is representative of the dataset and addresses the research questions (Braun 2006; Byrne 2022; Clarke 2015). To define the themes, I identified chosen data extracts that best represented the sub themes and themes, at times using multiple extracts from the manuscripts. I conducted a deep analysis of the data extracts to ensure they provided a compelling account in respect to the theme, whilst also going beyond what the participant said and trying to interpret what they were meaning (Braun 2006; Clarke 2015). Once each theme and sub theme had relevant data extracts, I met with the research team (KEJP-Chapter 6), (SCB and NSH -Chapter 7) to finalise the naming of each theme and subthemes. The final thematic map was created, representing the final themes and subthemes, indicating the relationship between each theme and the research question.

2.8.7 Step 6: Writing the Report

This is the final step in the TA process and occurs at the end of the analysis and consists of writing up the TA process. The written reports included the descriptions of the themes and subthemes, data extracts pertaining to the representative themes and thematic map (Braun 2006; Clarke 2015). I conducted this step of the TA process and will form Chapters 6 and 7 of this thesis.

2.8.8 Analytical approaches within TA

The analysis approach used in Chapters 6 and 7 have both inductive and deductive elements. I predominantly took an inductive approach to coding and theme development, to ensure that the themes were developed directly from the participant's responses and experiences of the interventions, as opposed to using predefined codes to shape the analysis. However, grounding theories were used in relation to the deductive element of the analysis. These theories helped shape the interview questions, in addition to guiding elements of the analytical process.

2.9 Guiding Theories

2.9.1 Teachable Moment for Smoking Cessation

In Chapter 6, I used the teachable moment for smoking cessation as the grounding theory underpinning the analysis. McBride's Teachable Moment in healthcare for smoking cessation, was first proposed as a theory in 2003, as means of understanding when a cuing event within a healthcare setting elicits a smoking cessation behaviour change (McBride 2003). The theory is an extension on previous conceptual models in health psychology, particularly the health belief model (Hochbaum 1958). This conceptual theory proposes three conditions where a healthcare cueing event may be significant enough to result in a teachable moment for smoking cessation. The extent to which the cuing event 1) increases perceptions of personal risk and outcome expectations, 2) prompts strong affective or emotional responses, and 3) redefines a social role or self-concept (Lawson 2009; McBride 2003).

2.9.2 The COM-B Model

The COM-B (Capability, Opportunity, Motivation-Behaviour) model was used in chapter 7, as a means of understanding patients' barriers to engaging in smoking cessation (Michie 2011). The COM-B model, first proposed in the early 2010s, was an iteration on the traditional

behaviour change wheel used in health psychology (Michie 2011). This theoretical model proposes that behaviour and behaviour change must involve capability, opportunity and motivation, while motivation must be central to the behaviour, both capability and opportunity have an influence on the relationship between motivation and the behaviour. Over time these three elements interact so behaviour can be viewed as a dynamic system with both positive and negative feedback loops (West 2020; Michie 2011). Within the model capability is defined as one's physical and psychological capacity to engage within an activity, including having required skills and knowledge. Motivation is defined as the developments in the brain that direct and boost behaviour, including habits and emotional responses. Opportunity is defined as external factors that facilitate the behaviour (West 2020).

Chapter 3: Strategies to deliver smoking cessation interventions during targeted lung health screening - a systematic review and meta-analysis.

Published as: Williams PJ, Philip KE, Alghamdi SM, Perkins AM, Buttery SC, Polkey MI, Laverty AA, Hopkinson NS. Strategies to deliver smoking cessation interventions during targeted lung health screening-a systematic review and meta-analysis. Chronic Respiratory Disease. 2023 Jun 6; 20:14799731231183446

3.1 Introduction

In chapter 1 I introduced and discussed the success of targeted lung cancer screening (LCS) services, with a particular focus on how this complex intervention may be an opportunity to promote smoking cessation. As highlighted in section 1.4.4, within the introduction, large screening RCTs observed higher quit rates among participants who had received the screening intervention (van der Aalst 2010). Researchers proposed that LCS programmes may act as a "Teachable Moment" for smoking cessation (Brain 2017; Iaccarino 2019), and suggested that smoking cessation support should be delivered alongside screening (Moldovanu 2021).

Within the smoking cessation field in the UK, it is well known that a lack of funding has led to a decline in community service provision (Action on Smoking and Health 2019). Current inpatient smoking cessation guidelines in the UK now highlight the importance of NHS lead and integrated smoking cessation services (Agrawal 2024). Currently there is a disconnect between the inpatient delivery and outpatient delivery of smoking cessation within the UK, and an ongoing problem of lack of funding and complete coverage for smoking cessation services in the community (Action on Smoking and Health 2019).

Lung cancer screening services invite a-symptomatic patients who otherwise would have to access outpatient smoking cessation services, if so, it is highly likely they would struggle due to lack of service provision. Lung cancer screening services are prospective opportune moments to embed cessation within them, not only in terms of extending the possible teachable moment the LCS creates, but also as a way of expanding outpatient coverage for smoking cessation services within the NHS.

There have been multiple RCTs, interventional observational studies and systematic reviews to date exploring different modalities of smoking cessation support delivered within a LCS context. However, there has yet to be a consensus on what the most effective strategies are for smoking cessation support delivered within the LCS setting. To address this gap and explore the effectiveness of smoking cessation support delivered within LCS. In this chapter I present a systematic review and meta-analysis, exploring strategies to deliver smoking cessation interventions during lung cancer screening.

3.2 Background

Tobacco use remains a primary driver of global morbidity, mortality, and related economic and healthcare costs, responsible for more than 8 million deaths per year (Sung 2021; World Health Organisation 2022). Despite mortality rates declining for most cancers, lung cancer deaths have remained high, accounting for 21% of all cancer deaths in the UK (Cancer Research UK 2021). Patients typically present to healthcare services at a late stage, resulting in late diagnosis and a poorer prognosis (Cancer Research UK 2021), early diagnosis through lung cancer screening programmes has achieved success in the USA and Europe. The USA lead National Lung Cancer Screening trial observed a 20% reduction in lung cancer mortality among their populations who underwent screening (National Lung Screening Trial Research Team 2011). In 2019 the NHS rolled out their Targeted Lung Health Check (TLHC) pilot project,

with 77% of lung cancers successfully identified being stage 1 and 2 (NHS England 2022) and lung cancer screening is now recommended by the UK National Screening Committee (UK National Screening Committee 2022a).

Eligibility criteria for lung screening programmes vary slightly between countries. However, participants are typically: middle aged (55-80), a current or former smoker (quitting within the last 15 years), with a 30+ pack year history. Around 40-50% of people taking part in LCS still smoke (Joseph 2018) and are likely to be highly nicotine dependent creating a significant barrier for cessation (van der Aalst 2010). Attendance at screening programmes have been highlighted within the literature as a teachable moment for smoking cessation, with several RCTs that demonstrate increased quit rates among individuals taking part (Brain 2017; Field 2016; van der Aalst 2010; Pineiro 2016), however there is substantial scope to increase the modest quit rates observed (11-15%).

Increasing quit rates among this high-risk population has the potential to dramatically increase the impact and cost effectiveness of screening programmes, beyond their effect on early identification of lung cancers (Royal College of Physicians 2018; Villanti 2013). Identifying the most effective strategies for delivering cessation within a lung screening context is now recognised as a priority by multiple health organisations including the American Thoracic Society, NHS England, and the European Respiratory Society (Kathuria 2017; NHS England 2019; Kauczor 2020b). Studies investigating the effects of smoking cessation interventions in this context vary in terms of intervention type, frequency, and intensity of intervention.

A systematic review published in 2016 concluded that lung screening programmes were optimal environments to deliver smoking cessation. However, did not offer evidence on what type of smoking cessation delivery modality is most effective (Pineiro 2016). Additionally, a

more recent narrative review conducted in 2021, concluded that clinician delivered intensive smoking cessation support, delivered within LCS are successful at increasing quit rates (Moldovanu 2021). However, the review is limited by its narrative design, the authors suggested further research is needed to explore the optimal delivery smoking cessation type, timing, and modality for delivery within LCS settings (Moldovanu 2021).

This area of screening and smoking cessation medicine is rapidly evolving. Despite organisations across Europe and the US recommending that cessation support be incorporated into lung screening programmes, they do not provide exact guidelines on what form this should take. I therefore conducted a systematic review and meta-analysis to determine the most effective delivery strategies for smoking cessation interventions conducted during lung cancer screening programmes.

3.3. Methods

The Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines were used to complete and report this systematic review, which was registered prospectively on PROSPERO(CRD42021242431).

3.3.1 Inclusion criteria

1. Study type: randomised controlled trial (RCTs) and observational studies with a control group.
2. Population: current smokers enrolled in a lung health screening program, including any of the following interventions: Low Dose Computed Tomography (LDCT) scanning, thoracic radiograph, spirometry assessments, formal clinic visit with a physician specialising in respiratory health.

3. Intervention: a smoking cessation program (e-cigarette, behavioural therapy, pharmacological, motivational interviewing, group counselling, telephone counselling, online materials, and information leaflets).
4. Control: usual care or comparator as defined by the study.
5. Outcome measures: smoking quit rates, quit attempts and reductions in cigarettes smoked.

3.3.2 Exclusion criteria

1. Studies not published or translated into English.
2. Abstracts, conference posters, expert opinion, review articles, study protocols and student dissertations.

3.3.3 Search Strategy

I searched the following databases, MEDLINE, PsychINFO, CENTRAL, EMBASE, CINAHL and Scopus from 1950- 20th July 2022. The search strategy used exploded medical subject headings in the following: [smoking OR tobacco OR vape or vaping OR e-cigarette OR cigar OR nicotine] AND [cessation OR cease OR stop OR quit OR intervention OR abstain OR abstinence OR relapse OR reduce OR give up] AND [screen OR scan OR check OR early detection OR early diagnosis OR CT] ADJACENCY2 [lung OR thoracic OR pulmonary] AND [early detection of cancer OR tomography, emission- computed OR mass screening OR spirometry]. I also reviewed reference lists of included studies and two grey literature databases were searched, CORE and Grey Guide; however, I did not find any relevant articles.

3.3.4 Data extraction and quality assessment

I reviewed all titles and abstracts for eligibility, as did a second reviewer Nicholas Hopkinson. Four independent reviewers Keir Philip, Alexis Perkins and Saeed Alghamdi and I read full text studies to decide on final inclusion and exclusion (Figure 3.1), discrepancies were resolved by

discussion between all co-authors. I extracted the data as well as Anthony Laverty as a second reviewer using a predefined standardised form and COVIDENCE software, the data recorded included study design and setting, methodology, participant baseline characteristics, type and intensity of smoking cessation intervention used, definition of control group, primary and secondary endpoints, measurement of abstinence and follow up period. Quality of the evidence including the risk of bias (ROB) was measured by two independent reviewers myself and Athony Laverty using the Cochrane risk of bias assessment tool, as recommended in the GRADE handbook (Schünemann 2013; Higgins 2011). Studies were grouped by outcome assessment and intensity of the intervention. We defined intensive smoking cessation interventions as ≥3 behavioural counselling sessions and non-intensive interventions as those consisting of ≤2 behavioural counselling sessions or limited to online information audio take home materials such as pamphlets.

3.3.5 Outcome measures

3.3.5.1 Primary outcomes

We considered smoking abstinence at the end of the trial study period (acknowledging that this could vary from trial to trial) as our primary outcome. Smoking abstinence could be defined as; the self-reporting of abstinence of smoking cigarettes in the past seven days or more, following the cessation intervention, with or without biochemical verification. The measure of abstinence could include point prevalence, prolonged or continuous and biochemical verification could include exhaled carbon monoxide (CO) or urine cotinine. All these abstinence measures are recommended by a 2020 review for defining and measuring smoking abstinence in clinical trials (Piper 2020). To evaluate the effect of interventional intensity, we compared quit rate among studies that provided intensive interventions and

non-intensive interventions, compared with control. We also assessed quit rates among studies that provided pharmacotherapy (NRT, E-cigarettes or prescription medications).

3.3.5.2 Secondary outcomes

Secondary outcomes included changes in smoking behaviour in terms of number of quit attempts and reductions in tobacco usage (daily cigarette consumption). Quit attempts were defined as the number of individuals self-reporting a serious attempt to stop smoking that lasted for ≥24 hours and reduction in tobacco use was defined as a reduction in the number of self-reported daily cigarettes from baseline.

We searched for information on intervention impacts in terms of long-term mortality, exacerbations of respiratory diseases and patient experience, however none of the screened or included articles measured these as endpoints.

3.3.6 Data Analysis

A fixed effects meta-analysis was performed to estimate the pooled differences and 95% CI in quit rate and quit attempts between smoking cessation intervention groups and usual care. A Mantel-Haenszel fixed effects model was used to obtain estimates for dichotomous data, expressed as odds ratios (OR). To answer the primary and secondary questions I performed the following meta-analyses on data from included RCTs. Quit rate between smoking cessation interventions vs usual care, quit rate between intensive smoking cessation interventions vs usual care, quit rate between intensive smoking cessation interventions + pharmacotherapy vs usual care, quit rate between non-intensive smoking cessation interventions vs usual care, quit rate between intensive + pharmacotherapy smoking cessation interventions vs non-intensive interventions, and quit attempts between smoking cessation interventions vs usual care. Heterogeneity among included studies was assessed using the I^2 statistic, I contacted authors for missing primary and secondary endpoint data.

The statistical analyses were performed using the Cochrane Collaboration's Review Manager Software (RevMan V.5.2.0).

3.4 Results

Of 4084 initial studies, 3,826 titles and abstracts were excluded. The main reasons for exclusion were, smoking cessation not delivered in a lung screening setting or population (wrong setting and wrong population), or no comparator group. This left 258 studies included in the full text screen, of which thirteen studies were included (Figure 3.1). The reasons for exclusion were, no comparisons of cessation intervention, observational studies with no control group, abstracts, no smoking abstinence measures used as outcomes, review papers, study protocols and students' dissertations. I also searched clinicaltrials.gov and the ISRCTN registry for ongoing trials in this area. I found 12 investigational trials comparing different smoking cessation interventions to control groups within a lung screening setting (Clinical Trials.gov 2014, 2018a, 2021,, 2018b, 2017,-a, 2017,-b, 2022; Trials.gov 2025; Clinical Trials.gov 2018c, 2017, 2019; Murray 2020).

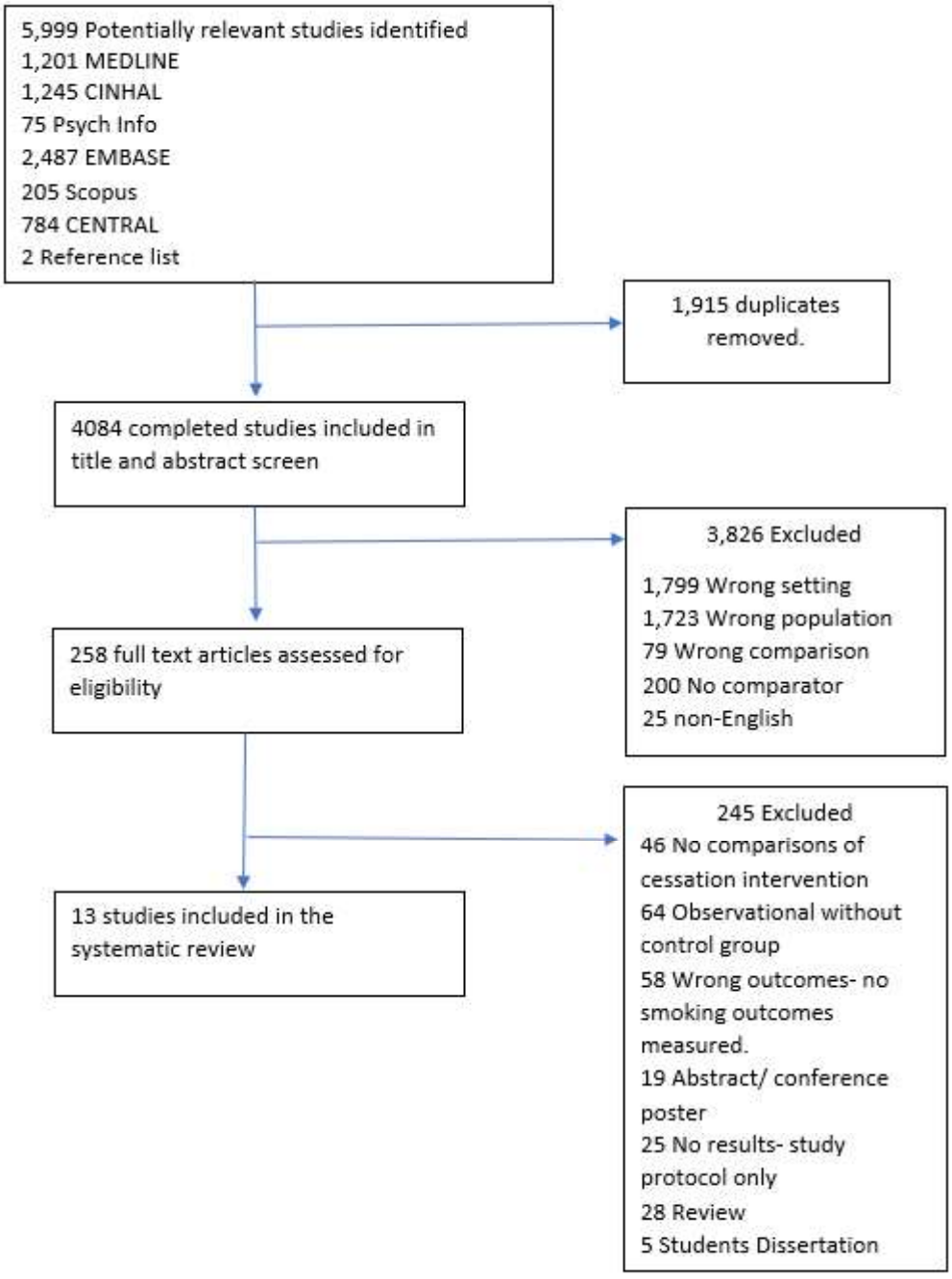
Table 3.1 Summary of included studies

Study (Design)	Setting	Smoking Cessation intervention	Intervention duration	Follow up	Control	Sample size	Results of Smoking Cessation group compared to control
Bade et al., 2016 (Observational with control)	Screened with LDCT for Lung Ca	Personal smoking cessation counselling session delivered on the day of screening	1 day	12 months	Routine screening clinical care	1236	Quit rate: Intervention: 14.6% (85/611) vs Control: 6.7% (41/625).
Buttery et al., 2022 (RCT)	Population attending for screening	6 sessions of smoking cessation counselling plus pharmacotherapy (F2F)	6 weeks	3 months	Signposting and very brief advice	115	Quit rate Intervention: 29.2% (14/48) vs Control: 11% (4/36). Quit attempts Intervention: 54.1% (26/48) vs Control 33% (12/36).
Clark et al., 2004 (RCT)	Attending LDCT lung Ca screening	Internet self-help materials including links to different cessation websites	1 day	12 months	Written take home materials	171	Quit rate intervention:13% (8/85) vs Control 7% (4/86). Quit attempts Intervention: 38% (23/85) vs Control 34% (20/86).
Ferketich et al., 2012 (RCT)	Patients eligible for LDCT	Before CT(BCT), 1 F2F with medic, 12 sessions of tobacco dependence with NRT and weekly calls.	12 weeks	4 and 6 months	The same intervention but delivered after the CT scan (ACT)	18	Quit rates at 4 months BCT 33% (3/9) vs ACT 22.2% (2/9). Quit rate at 6 months: BCT 22.2% (2/9) vs ACT 11.1% (1/9). Quit attempts at 4 months: BCT 88.9% (8/9) vs ACT 100% (9/9). Quit attempts at 6 months: BCT 66.7% (6/9) vs ACT 77.8% 7/8).
Lucchiari et al., 2020 (RCT)	Sub population of COSMOS II trial, large screening trial in Italy	Two Armed RCT Arm 1- E-cigarettes with nicotine Arm 2- Placebo (E-cigarettes without nicotine)	12 weeks	6 months	Arm 3: Behavioural counselling at weeks 1, 4, 8 and 12.	155	Quit rates: Arm 1: 16% (13/52), Arm 2: 19% (11/51), Control: 10% (7/52). Exhaled CO: Arm 1: 12.01 ± 8.1ppm, Arm 2: 15.28 ± 11.4ppm, Control: 16.52 ± 10.2ppm Reductions in cigarettes smoked per day Arm 1: 8.17± 6.5, Arm 2: 5.68 ± 7.9, Control: 5.82 ± 6.4.
Marshall et al., 2016 (RCT)	Population of the Queensland	One session of behavioural support after screening, plus	Missing	12 months	Standard written	55	Quit rate: Intervention: 14.3% (4/28) vs control: 18.5% (5/27)

	screening trial	audio take home materials.			materials with Quitline		Exhaled CO: Intervention 3.5% (1/28) vs control (11%) (3/27)
Pistelli et al., 2020 (Observational with control)	Population of the ITALIA lung screening trial (Pisa Centre)	Six clinic visits within 3-5 months including counselling and pharmacotherapy and follow up at 6 and 12 months.	5 months	4 years	Normal screening clinical care	425	Higher odds of quitting in those who choose to attend the smoking cessation support (OR:3.16 (95% CI 1.63, 6.12).
Taylor et al., 2017 (RCT) (Taylor 2017)	Population undergoing LDCT screening at Georgetown University Medical Centre	Six sessions of weekly behavioural support telephone calls.	6 weeks	3 months	Information booklet, website, and smartphone app links.	92	Self-reported quit rate: intervention: 21.7% (10/46) vs Control 19.6% (9/46) CO verified quit rates: Intervention: 17.4% (8/46) vs Control: 4.3% (2/46).
Taylor et al., 2022 (RCT)	Population undergoing LDCT screening at Georgetown University Medical Centre	Eight sessions of weekly behavioural support calls, plus 8-week supply of NRT patches.	8 weeks	3 months	Three behavioural support calls, plus 2-week supply of NRT patches.	818	Self-reported quit rates: Intervention 14.3% (58/409) vs control 9.7% (32/409). CO verified quits: Intervention: 9.1% (37/409) vs Control 3.9% (19/409).
Tremblay et al., 2019 (RCT)	LDCT Alberta screening trial.	Seven, weekly behavioural support telephone sessions.	7 weeks	12 months	Written information materials	345	Self-reported quit rates: Intervention: 14% (24/171) vs Control: 12.9% (22/174), CO verified quit rates: Intervention: 12.9% (22/171) vs Control: 10.9% (19/174)
van der Alast et al., 2011 (RCT)	NELSON LDCT screening trial.	Computer tailored behavioural support messages	Missing	24 months	Written information materials	1248	Self-reported quit rates Intervention: 12.5% (85/642) vs Control 15.6% (105/642).
Williams et al., 2022 (RCT)	Population of HLP. Clinic	Six sessions of smoking cessation	6 weeks	3 months	Signposting to local cessation	315	Quit rates: Intervention 21.1% (32/152) vs control 8.9% (14/163).

	visit and or LDCT	counselling plus pharmacotherapy, delivered via the telephone.			services and very brief advice to quit.		Quit attempts: Intervention: 37.5% (57/152) vs Control: 22% (36/163).
Zeliadt et al., 2017 (Observational)	Smokers offered LDCT screening	Two behavioural support calls, plus Quitline	2 weeks	1 month	Written information materials, plus Quitline	83	Quit rate: Intervention: 19% (5/27) vs Control: 7% (4/56) Quit attempts: Intervention: 52% (14/27) vs Control: 45% (26/56)

Figure 3. 1 Prisma diagram of search results and reasons for exclusion



3.4.1 Overview of included studies

Ten studies were RCT's (Buttery 2022; Williams 2022b; Clark 2004a; Ferketich 2012; Lucchiari 2020; Marshall 2016; Taylor 2017; Taylor 2022; Tremblay 2019; van der Aalst 2012) and three used an observational study design with control group (Zeliadt 2018; Pistelli 2020; Bade 2016a) (Table 3.1). The included studies were published between 2004 and 2022, involving a total of 5076 people who smoked, with sample sizes ranging from 18 to 1248. Median participant age ranged from 57 to 63 years, 61% of participants were male, mean number of cigarettes smoked per day by the population was 15.6±3.1 cigarettes.

Studies investigated effectiveness of smoking cessation interventions as follows: single, in clinic session of behavioural counselling (Bade 2016a). Single, in clinic session of behavioural counselling and audio materials (Marshall 2016). Single in clinic behavioural counselling, plus NRT and subsequent weekly telephone calls (Ferketich 2012). Internet self-help materials (Clark 2004b). Tailored information leaflet (van der Aalst 2012). Two behavioural support calls and Quitline (Zeliadt 2018). Multiple weekly behavioural support calls (Taylor 2017; Tremblay 2019). Multiple weekly behavioural support calls and pharmacotherapy (Taylor 2022; Williams 2022b). Multiple weekly behavioural support, in clinic plus pharmacotherapy (Buttery 2022; Pistelli 2020) or e-cigarettes (Lucchiari 2020). Timing of the intervention delivery varied across included studies from immediately on the day of the screening clinic to five- months after screening, average length of interventions was 13.2±13.6 weeks.

A variety of comparisons were used for usual care (UC) groups, including signposting to local cessation clinics, written information leaflets and standard behavioural counselling. In addition to the intervention delivered before the lung health screening appointment. Of note (Lucchiari 2020) used four sessions of behavioural counselling as their UC intervention, which is considerably more input compared to most UC interventions included.

All included studies used self-reported point prevalence smoking abstinence, either 30-day or seven-day. Additionally, five studies used exhaled carbon monoxide monitoring (Ferketich 2012; Marshall 2016; Taylor 2017; Taylor 2022; Tremblay 2019). Studies reported cessation outcomes at one month (Zeliadt 2018), three months (n=4) (Buttery 2022; Williams 2022b; Taylor 2022; Taylor 2017), four and six months (Ferketich 2012; Lucchiari 2020). Studies also observed longer term follow up, at 12 months (n=4) (Bade 2016a; Clark 2004a; Marshall 2016; Tremblay 2019), 24 months (van der Aalst 2012), and four years (Pistelli 2020). Five studies reported data on quit attempts (Buttery 2022; Williams 2022b; Clark 2004a; Ferketich 2012; Zeliadt 2018) and one study reported data on reductions in daily cigarettes smoked (Lucchiari 2020).

3.4.2 Description of included studies

Lucchiari et al, 2020 conducted a three-armed RCT, comparing the effect of behavioural counselling plus nicotine containing e-cigarettes, behavioural counselling plus nicotine free e-cigarettes (placebo) and behavioural counselling only (UC) and observed smoking behaviour in 155 smokers attending screening in Italy. Nine of the included studies used a two-armed RCT study design. Buttery et al, 2022 randomised 115 smokers attending a targeted lung health check to immediate support, which included six sessions of behavioural counselling plus pharmacotherapy or very brief advice (VBA) to quit and signposting to local cessation services (UC). Ferketich et al, 2012 used a similar intervention, 12-week tobacco cessation support, including pharmacotherapy, though this started a week after attending screening, rather than immediately. However, in this study the control group received the same smoking intervention delivered before the CT screening appointment, so it was not suitable for comparisons against “usual care”. Taylor et al 2017, randomised 92 smokers attending screening to receive six sessions of telephone behavioural counselling after participants had

attended screening and received results, or a written information booklet (UC). A subsequent paper from this same group randomised 818 smokers to receive intensive (eight telephone counselling sessions plus eight weeks of NRT patch) or less intensive (three counselling sessions, plus two weeks NRT patch), delivered 13 days post LDCT scan (Taylor 2022). Williams et al, 2022b randomised 315 smokers attending a TLHC to receive six sessions of telephone behavioural support starting immediately, pharmacotherapy prescriptions were provided within 48 hours of participating in the TLHC, or VBA to quit and signposting to local services (UC). A telephone intervention was also utilised by Tremblay et al 2019, who randomised 354 smokers attending LDCT screening to seven behavioural support calls delivered after participants had received screening results, or written information leaflets only (UC).

Three RCT's used low-intensity interventions; Clark et al 2004b, randomised 171 smokers attending screening to receive internet materials or standard written materials delivered on the day of screening (UC). Marshall et al, 2016 randomised 55 smokers attending screening to receive one session of behavioural support on the day of screening with audio take home materials, or written information plus Quitline (UC). Van der Aalst et al 2012, randomised 1248 male smokers who were in the screening arm of the large NELSON RCT, to receive computer tailored information leaflets or standard information leaflets after attendance to screening (UC).

The remaining three included studies used an observational with a control group study design. Bade et al 2016b, compared 12 month quit rates among 611 smokers attending screening who accepted the offer of one behavioural support session delivered before attendance to screening and 625 smokers who opted to receive standard screening care. Pistelli et al 2020, explored quit rate among smokers at the Pisa centre in the ITALIA lung screening trial.

Screened participants were offered six smoking cessation clinic visits within three-five months of screening, including counselling and pharmacotherapy (n=119), current smokers who did not accept the offer of cessation went onto routine clinical care (n=306). Lastly Zeliadt et al 2018, used a waitlist design and provided smokers who recently attended a LDCT scan but had not received their results (n=27), to receive two telephone behavioural counselling sessions plus Quitline and compared quit rates to recent attendees to a LDCT who had received their results (n=56).

3.4.3 Effect of stop smoking interventions on quit rate compared to usual care

To analyse the effectiveness of the smoking cessation interventions, I performed a meta-analysis on included RCTs which compared quit rate between smoking cessation and usual care groups. Meta-analysis of eight RCTs eligible for inclusion (Buttery 2022; Clark 2004a; Lucchiari 2020; Marshall 2016; Taylor 2017; Taylor 2022; Tremblay 2019; Williams 2022b) (n= 1,984). Demonstrated that providing a smoking cessation intervention improved quit rates among current smokers enrolled in screening programmes compared with usual care (OR: 2.01, 95% CI 1.49-2.72 p<0.001), figure 3.2. I included data from arm one (e-cigarette with nicotine) and arm three (usual care) from the Lucchiari study, as this best answered the research question. Measures to assess quit rate varied between included studies, three studies used exhaled CO to measure quits (Taylor 2022; Taylor 2017; Tremblay 2019) and the remaining five studies used self-reported point prevalence smoking abstinence to assess quit rate (Buttery 2022; Williams 2022b; Marshall 2016; Clark 2004a; Lucchiari 2020). Data from two RCTs were excluded from the meta-analysis, (Ferketich 2012) did not use a usual care group, rather explored the effect of timing of the same intervention and (van der Aalst 2012), their intervention group was too similar to their UC group (two types of information leaflet).

Figure 3. 2 ***Effect of smoking cessation interventions vs usual care on quit rates***

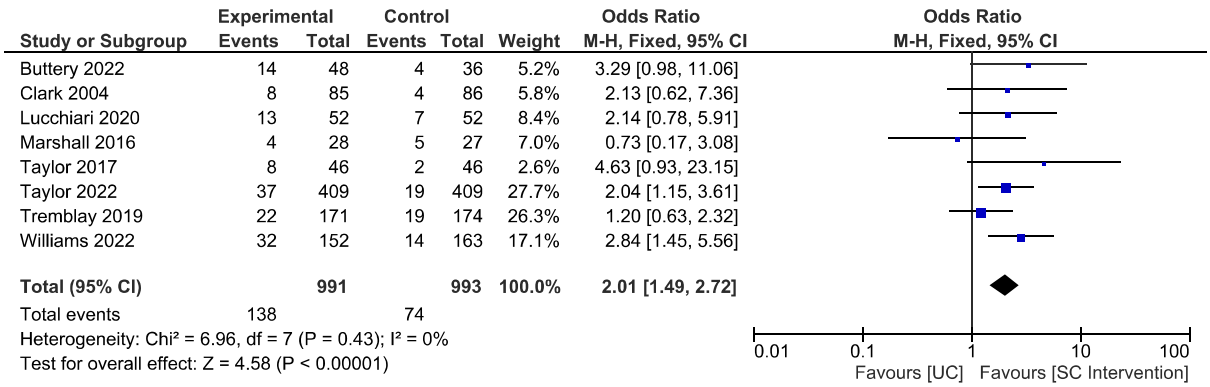


Figure 3. 2. Forest plot comparing quit rate among participants randomised to SC intervention compared with UC. Quit rates measured via self-reported (30-day or 7-day pp) or CO verification at follow up time periods ranging from 3 months to 12 months post intervention. Data from Arm 1 (E-cigarette with nicotine) and Arm 3 (UC) from Lucchiari et al's 3 armed RCT was included in this analysis.

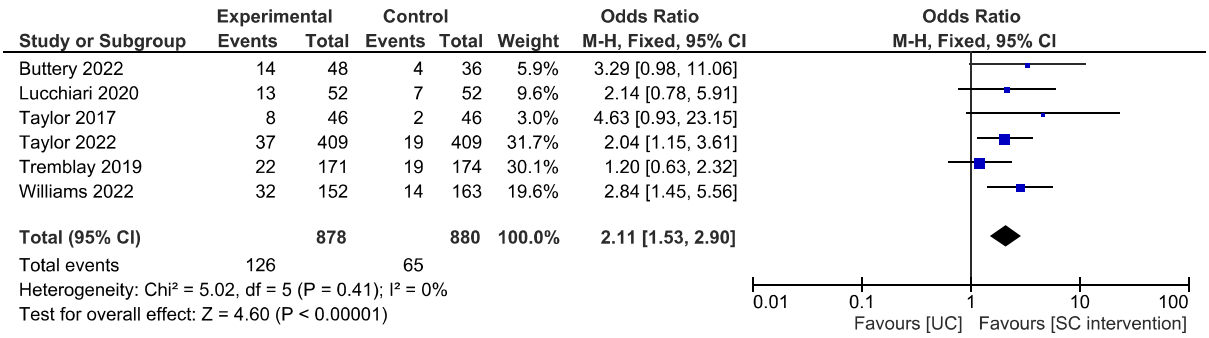
UC- Usual Care

SI- Smoking Cessation

3.4.4 Effect of intensive cessation interventions on quit rates

Meta-analysis of the six RCTs (Taylor 2017; Taylor 2022; Buttery 2022; Williams 2022b; Lucchiari 2020; Tremblay 2019) (n=1,758). That provided an intensive smoking cessation intervention, defined as ≥3 sessions with a smoking cessation advisor, nurse, or councillor+/- pharmacotherapies. Demonstrated that intensive smoking cessation interventions yield greater quit rates compared to UC (OR: 2.11, 95% CI 1.53-2.90, p<0.001), figure 3.3.

Figure 3. 3 Effect of intensive cessation interventions on quit rates



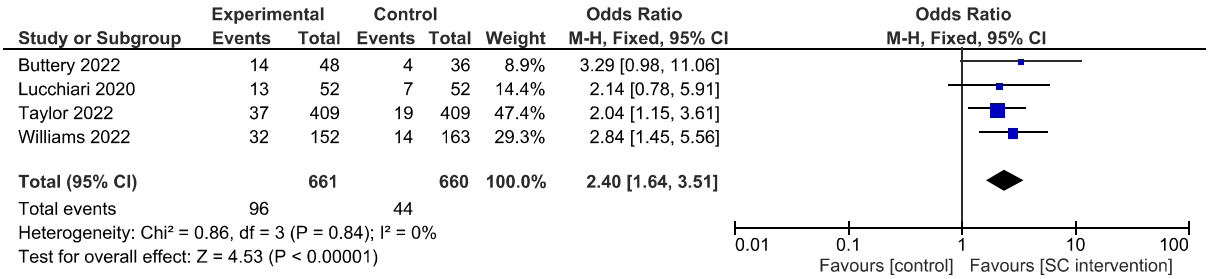
Forest plot comparing quit rates in studies that randomised participants to intensive SC interventions (≥3 behavioural counselling sessions compared with UC. Quit rates measured via self-reported (30-day or 7-day pp) or CO verification at follow up time periods ranging from 3 months to 12 months post intervention. Data from Arm 1 (E-cigarette with nicotine) and Arm 3 (UC) from Lucchiari et al's 3 armed RCT was included in this analysis.

UC- Usual Care

SI- Smoking Cessation

I also conducted a meta-analysis among studies that provided pharmacotherapy (NRT, varenicline, e-Cigarettes), alongside behavioural counselling. Of note, only studies that were defined as providing intensive support were also studies that provided pharmacotherapy. A meta-analysis of four RCTs (Taylor 2022; Lucchiari 2020; Buttery 2022; Williams 2022b) (n=1,321), demonstrated that intensive smoking cessation support plus pharmacotherapy, yields higher quit rates compared to control among a screening population (OR: 2.40 95% CI 1.64-3.51, p <0.001) (Figure 3.4).

Figure 3. 4 Effect of intensive smoking cessation with pharmacotherapy vs usual care on quit rates



Forest plot comparing quit rates in studies that randomised participants to intensive SC interventions (≥3 behavioural counselling sessions and pharmacotherapy compared with UC. Quit rates measured via self-reported (30-day or seven-day pp) or CO verification at follow up time periods ranging from 3 months to 6 months post intervention. Data from Arm 1 (E-cigarette with nicotine) and Arm 3 (UC) from Lucchiari et al's 3 armed RCT was included in this analysis

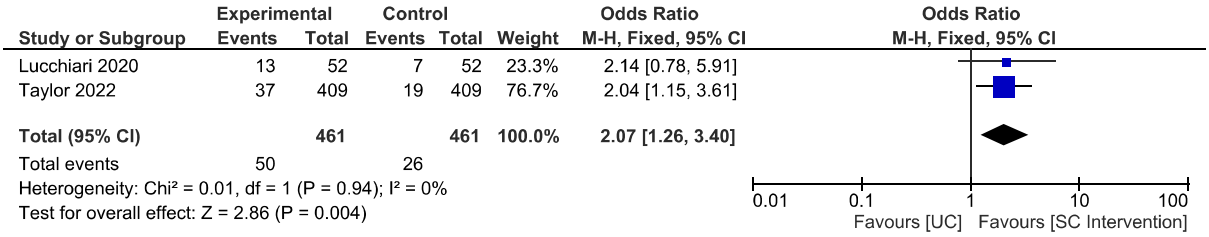
UC- Usual Care

SI- Smoking Cessation

3.4.5 Effect of intensive interventions compared to non-intensive interventions on quit rate.

A meta-analysis of two RCTs (Taylor 2022; Lucchiari 2020), (n=922), investigating the effect of intensive interventions compared to non-intensive interventions. In the case of these two studies their UC interventions would be classed as a non-intensive smoking cessation intervention itself. Results from the analysis demonstrated that intensive smoking cessation interventions compared to non-intensive smoking cessation interventions, results in higher quit rates (OR: 2.07, 95% CI 1.26-3.40 p=0.004), Figure 3.5.

Figure 3. 5 Effect of intensive vs non-intensive smoking cessation interventions on quit rates



Forest plot of self-reported quit rates in two studies that randomised participants intensive SC interventions compared with non- intensive SC interventions Quit rates measured via self-reported pp at six month follow up, and CO verification at 3 month follow up. Data from Arm 1 (E-cigarette with nicotine) and Arm 3 (UC) from Lucchiari et al's 3 armed RCT was included in this analysis.

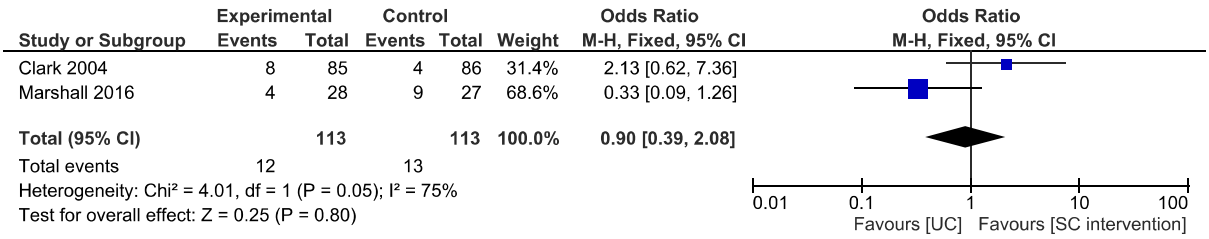
UC- Usual Care

SI- Smoking Cessation

3.4.6 Effect of non-intensive interventions on quit rate

A meta-analysis of two RCTs (Clark 2004a; Marshall 2016) (n= 226), investigating non-intensive smoking cessation interventions (≤2 behavioural counselling sessions), did not find higher quit rates compared to UC, (OR: 0.90, 95% CI 0.39-2.08 p=0.80), Figure 3.6.

Figure 3. 6 Effect of non-intensive smoking cessation intervention vs usual care on quit rate

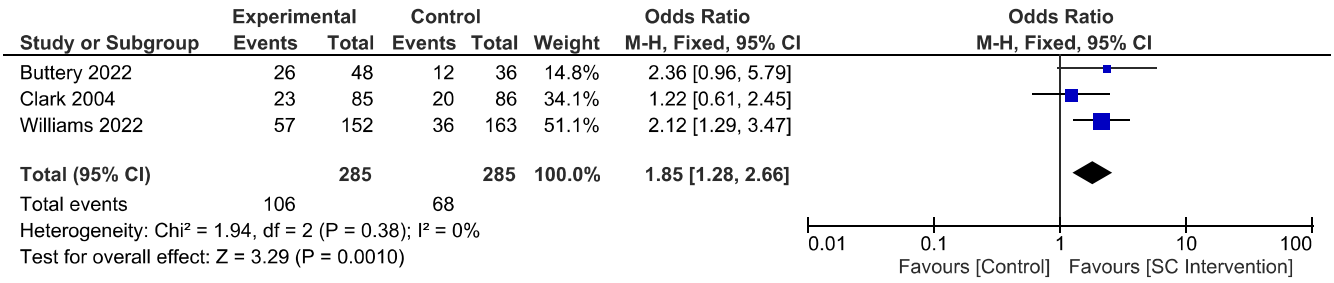


Forest plot of self-reported quit rates in two studies that randomised participants to non- intensive SC interventions compared with UC (≤2 counselling sessions, online materials, audio self-help materials). Quit rates measured via self-reported pp at 12 month follow up.
UC- Usual Care
SI- Smoking Cessation

3.4.7 Effect of smoking cessation interventions on quit attempts

The impact of smoking cessation interventions on participants reporting quit attempts was compared in three RCTs (Buttery 2022; Williams 2022b; Clark 2004a) (n=570). Pooled analysis demonstrated that smoking cessation interventions produce significantly higher quit attempts compared to UC interventions (OR: 1.85, 95% CI 1.28-2.66, p<0.001) (Figure 3.7).

Figure 3. 7 Effect of smoking cessation intervention vs usual care on quit attempts

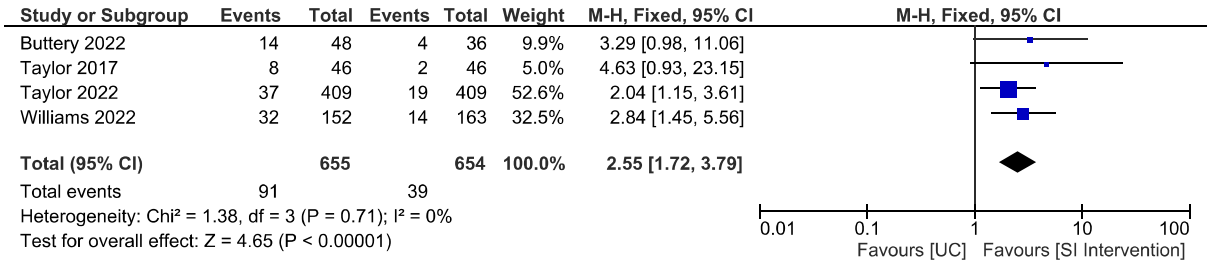


Forest plot comparing quit attempts between smoking cessation interventions versus control. Quit attempts measured by self-reported data, follow up time periods ranging from 3- 12 months post intervention.
UC- Usual Care
SI- Smoking Cessation

3.4.8 Effect of smoking cessation interventions vs usual care among short term quit rate.

The impact of smoking cessation interventions on quit rates measured in the short term (three months post randomisation), was measured by four RCT's (Taylor 2017; Taylor 2022; Buttery 2022; Williams 2022b) (n= 1,309). Meta- analysis demonstrated that smoking cessation interventions delivered in a screening setting increase quit rates measured in the short term (OR: 2.55, 95% CI 1.72-3.79, p<0.001), figure 3.8.

Figure 3. 8 Effect of smoking cessation interventions on short term quit rate



Forest plot comparing quit rate between smoking cessation interventions versus control measured 3 months post intervention (short term). Quit rates measured by self-reported and CO verified data.

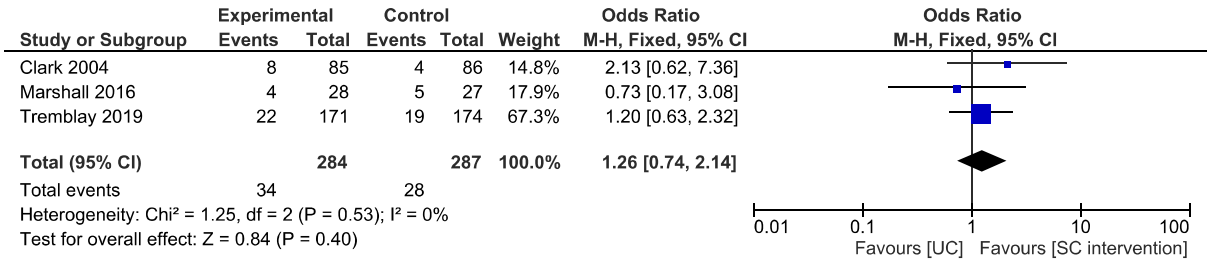
UC- Usual Care

SI- Smoking Cessation

3.4.9 Effect of smoking cessation interventions vs usual care among long term quit rate.

A meta-analysis of three RCT's (Clark 2004a; Marshall 2016; Tremblay 2019), (n= 571), investigating quit rates in the long term (12 months post randomisation) did not discover higher quit rates within the intervention groups compared to UC groups (OR: 1.26, 95% CI 0.74-2.14, p= 0.40), figure 3.9.

Figure 3. 9 Effect of smoking cessation interventions on long term quit rate



Forest plot comparing quit rate between smoking cessation interventions versus control measured 12 months post intervention (long term). Quit rates measured by self-reported and CO verified data.
UC- Usual Care
SI- Smoking Cessation

3.4.10 Risk of bias and evidence quality

Risk of bias (ROB) and evidence quality was judged using the Cochrane risk-of-bias assessment tool (Higgins 2011). There was wide variation in the risk of bias among included studies, illustrated in table 3.2. Four studies were assessed as having low risk of bias (Buttery 2022; Williams 2022b; Lucchiari 2020; Taylor 2022). Reviewers assessed four studies as having an unclear risk of bias (Clark 2004a; Tremblay 2019; Taylor 2017; van der Aalst 2012), mainly attributed to unclear methods of blinding of outcome assessors and unclear methods of randomisation. The remaining five studies were deemed high risk of bias, attributed to the observational study design in three of the studies, (Bade 2016a; Pistelli 2020; Zeliadt 2018) with no attempt to blind outcome assessors and poor allocation concealment, selective reporting and low sample sizes seen in two of the studies (Zeliadt 2018; Marshall 2016). A more detailed description of risk of bias domains and scoring can be found in table 3.3.

Using the GRADE criteria (Atkins 2004), reviewers found moderate quality evidence to support inclusion of smoking cessation interventions into lung cancer screening. This was attributed to strong association of results, directness of the evidence in terms of assessing our primary endpoint (quit attempts) and the precision of results (large sample size of included participants) (Table 3.4). For intensive smoking cessation interventions, the GRADE criteria found high quality evidence supporting embedding intensive smoking cessation interventions into lung screening. This was attributed to strong association of results, directness of the evidence in terms of assessing primary endpoint (quit attempts), the precision of results (large sample size) and moderate inconsistency (heterogeneity) (Table 3.5). In terms of non-intensive smoking cessation interventions, the GRADE criteria found low certainty evidence for non-intensive interventions, attributed to low and unclear risk of bias,

large heterogeneity across included studies and the low sample sizes of (Marshall 2016) (Zeliadt 2018) (Table 3.6).

Table 3. 2 Risk of Bias assessment

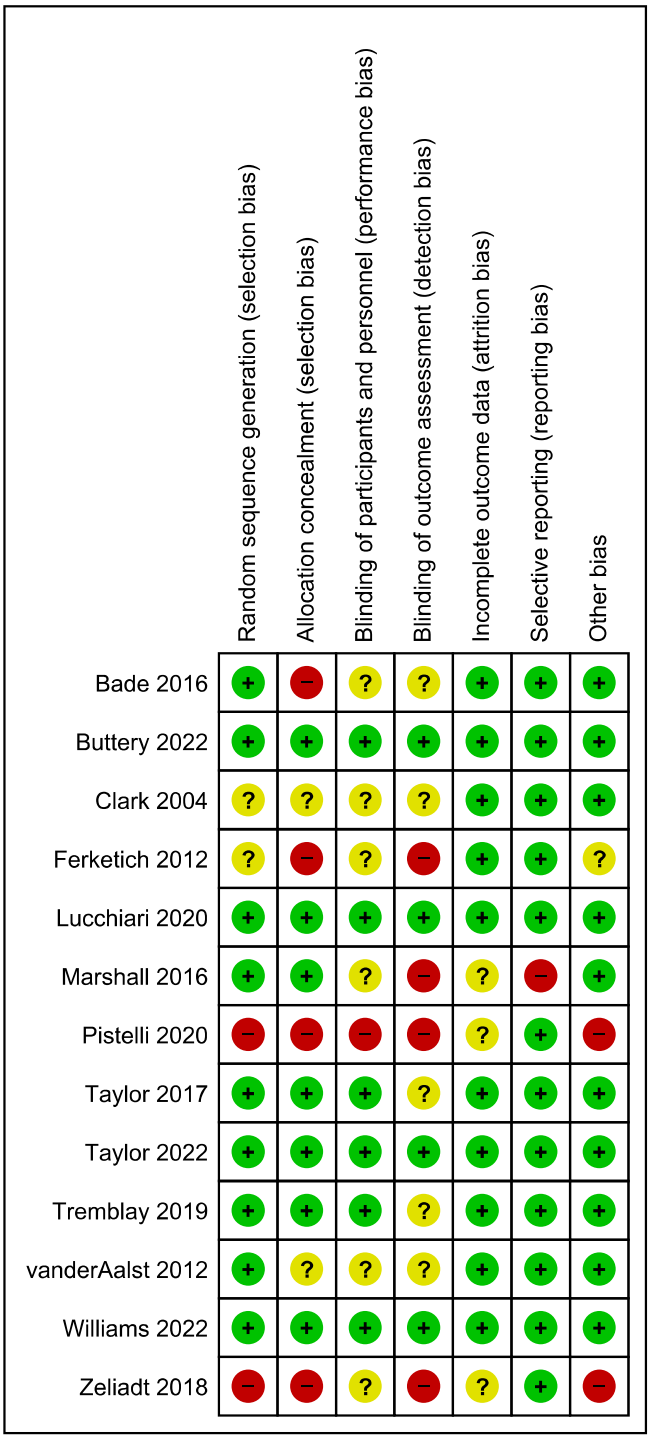


Table 3. 3 Risk of bias domains and scoring

	Random Sequence generation	Allocation Concealment	Blinding- Participants & Personnel	Blinding of outcome assessors	Incomplete outcome data	Selective reporting	Other	Overall Score
Bade et al, 2016 (Observational with control)	Low: Use of electronic randomisation system in 2012 study	High: Participants opted into the intervention group	Unclear: Not stated if study personnel were blinded to outcome	Unclear not clear if outcome or assessors were blinded.	Low: Use of multiple imputations for missing data	Low: Both primary and secondary outcomes reported	Low: None	High
Buttery et al, 2022, (RCT)	Low: Use of sealed envelope, randomised by day of the week	Low: Only nurses delivering intervention, participants and nurses delivering TLHC aware of group allocation.	Low: Study personnel conducting follow up unaware of group allocation.	Low: All outcome assessors blinded.	Low: use of ITT, those who were lost to follow up recorded as current smokers	Low: Both primary and secondary outcomes reported	Low: None	Low
Clark et al, 2004, (RCT)	Unclear: Not stated how randomisation occurred.	Unclear: Not stated how allocation concealment occurred.	Unclear: Not stated if blinding of personnel occurred.	Unclear: not stated if outcome assessors/ analysts were blinded	Low: use of ITT, those who were lost to follow up recorded as current smokers	Low: Both primary and secondary outcomes reported	Low: None	Unclear
Ferketich et al, 2012, (RCT),	Unclear: stated randomisation occurred but not how was conducted	High: No allocation concealment occurred	Unclear: blinding of personnel occurred.	High: No blinding of outcome assessors/ analysts	Low: No missing data (small sample size)	Low: Both primary and secondary outcomes reported	Unclear Small sample size but stated as a pilot study.	High

Lucchiari et al, 2020, (RCT)	Low: Permuted block design 40 blocks of 6 subjects.	Low: Use of placebo group	Low: Participants in Arms 1,2 blinded alongside study personnel.	Low: Stated as double blind	Low: use of ITT, those who were lost to follow up recorded as current smokers	Low: Both primary and secondary outcomes reported	Low: None	Low
Marshall et al, 2016, (RCT)	Low: 1:1 randomisation method	Low: Group allocation concealment	Unclear: not stated if personnel blinded	High: No blinding of outcome assessors/ analysts	Unclear: not stated if any data was missing	High: They did not report CO verified quit data	Low: None	High
Pistelli et al, 2020, (observational with control)	High: No sequence generation occurred	High: No allocation concealment occurred	High: No blinding occurred	High: No blinding occurred	Unclear: Use of ITT but not stated how missing data was handled.	Low: Both primary and secondary outcomes reported	High: Potential risk of social desirability bias	High
Taylor et al, 2017, (RCT)	Low: Permuted block design, blocks of 4 stratified by site.	Low: use of computer allocator	Low: Study personnel blinded	Unclear: not stated if outcome assessors/ analysts were blinded	Low: Use of ITT, those who were lost to follow up recorded as current smokers	Low: Both primary and secondary outcomes reported	Low: None	Unclear
Taylor et al, 2022, (RCT)	Low: Permuted block design, blocks of 4 stratified by site.	Low: use of computer allocator	Low: Study personnel blinded	Low: outcome assessors blinded	Low: Use of ITT, those who were lost to follow up recorded as current smokers	Low: Both primary and secondary outcomes reported	Low: None	Low
Tremblay et al, 2019, (RCT)	Low: 1:1 stratified by CT result and intention to quit	Low: use of computer allocator	Low: Study personnel blinded	Unclear: not stated if outcome assessors/ analysts were blinded	Low: Use of ITT, those who were lost to follow up recorded as current smokers	Low: Both primary and secondary outcomes reported	Low: None	Unclear

van der Alast et al, 2012, (RCT)	Low: 1:1 randomisation method	Unclear: Not stated how allocation concealment occurred.	Unclear: not stated if personnel blinded	Unclear: not stated if outcome assessors/ analysts were blinded	Low: Use of ITT, those who were lost to follow up recorded as current smokers	Low: Both primary and secondary outcomes reported	Low: None	Unclear
Williams et al, 2022, (RCT),	Low: Use of sealed envelope, randomised by day of the week	Low: Only nurses delivering intervention, participants and nurses delivering TLHC aware of group allocation.	Low: Study personnel conducting follow up unaware of group allocation.	Low: All outcome assessors blinded.	Low: use of ITT, those who were lost to follow up recorded as current smokers	Low: Both primary and secondary outcomes reported	Low: None	Low
Zeliait et al, 2017, (Observational with control)	High: No sequence generation occurred	High: No allocation concealment occurred	Unclear: not stated if personnel blinded	High: No blinding out outcome assessors	Unclear: not stated how missing data was handled	Low: Both primary and secondary outcomes reported	High: probable recruitment bias	High

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Table 3. 4 Grade assessment: Smoking cessation interventions vs control for self-reported quit rates.

Participants (Studies)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Overall Certainty
5,079 (10 RCT's & 3 Observational)	Serious: Majority of studies had either unclear or high risk of bias	Serious: Heterogeneity between studies, variation in quit rates.	Not Serious: All studies directly answer the healthcare question	Not Serious: Large sample size, with large number of events	Minimal publication bias, strong association of results	Moderate

Table 3. 5 Grade Assessment: Intensive smoking cessation interventions vs control for self-reported quit rate

Participants (Studies)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Overall Certainty
1,910 (7 RCT's)	Serious: Some of the studies had either unclear or high risk of bias	Not Serious: low Heterogeneity between studies, majority of studies reported increases in quit rates.	Not Serious: All studies directly answer the healthcare question	Not Serious: Large sample size, with large number of events	Minimal publication, Strong association of results.	High

Table 3. 6 Grade Assessment: Non-intensive smoking cessation interventions vs control for self-reported quit rate

Participants (Studies)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Overall Certainty
2,829 (3 RCT's & 2 Observational)	Serious: Majority of the studies had either unclear or high risk of bias	Serious: large heterogeneity between studies, variations in quit rate success	Not Serious: All studies directly answer the healthcare question	Not Serious: Large sample size, with large number of events	Publication bias detected in 3 of the studies, weaker association of results.	Low

Table 3.7 Table of ongoing trials

Trial	Primary Investigator	Intervention	Comparison	Primary Outcomes	Secondary Outcomes	Expected Completion date
Program for lung cancer screening and tobacco cessation (PULTO) Sequential, multiple assignment, randomized trial (SMART) design. NCT02597491 (USA). https://clinicaltrials.gov/ct2/show/NCT02597491)	Joseph, A	Arm 2: Telephone tobacco longitudinal care (TLC) Arm 3: TLC plus pharmacotherapy	Arm 1: 8 weeks of tobacco cessation	6 months continued tobacco abstinence at 18 months post randomisation	Intensiveness of TLC on abstinence (monthly vs quarterly follow up) How CT results moderate smoking outcomes.	30/11/2022 (Results not published)
Capitalizing on a teachable moment to promote smoking cessation, RCT. NCT02276664 (USA). (https://clinicaltrials.gov/ct2/show/study/NCT02276664)	Brandon, T	Behavioural self-help booklet intervention (developed via focus groups)	Standard information booklet	7-day point prevalence abstinence 9 months post randomisation		21/06/2019 (Results not published)
Personalized Smoking Cessation Tool Based on Patient Lung CT Image, RCT. NCT03087617 (USA). (https://clinicaltrials.gov/ct2/show/NCT03087617)	McEvoy, C	Arm 1: Usual care + smoking cessation report that includes data analysis from a CT lung cancer screening exam. Arm 2: Usual care plus behavioural counselling. Arm 3: Usual care + smoking cessation report + behavioural counselling.	Usual care for lung cancer screening patients and Quitline	Reports impact on participants calling Quitline number (3 weeks are treatment).	Number of quit attempts (3 weeks after treatment)	23/08/2021 (Results not published)

Yorkshire Enhanced Stop Smoking study (YESS), RCT. NCT03750110. (UK). (https://clinicaltrials.gov/ct2/show/NCT03750110)	Murray, R	Standard smoking cessation support in line with NICE guidelines plus personalised feedback from CT result.	Standard smoking cessation support in line with NICE guidelines	7-day point prevalent CO validated smoking cessation (3 months post CT scan).	Continuous smoking abstinence at three months. Smoking abstinence measures at 4 weeks and 12 months post CT. Changes in perceived lung cancer risk, motivation to quit smoking, confidence, and efficacy beliefs of stopping smoking, Self - reported changes in health at 4 weeks, 3 months, and 12 months post CT.	21/03/2022 (Results not published)
Implementing Tobacco Treatment in Low Dose CT Lung Cancer Screening Sites, RCT. NCT03315910 (USA). (https://clinicaltrials.gov/ct2/show/NCT03315910)	Ostroff, J	Arm 1: 2 motivational interviewing sessions (telephone or face to face) Arm 2: Nicotine Lozenge, 6 cartons of 2 mg lozenges. Arm 3: Nicotine patch, 6 weeks.	Enhanced standard care: education and follow-up cessation counselling during their first session within 1 month of	Smoking abstinence (self-reported and Bio verified 6 months post randomisation .	Quit attempts and reductions in cigarettes per day.	October 2024

		Arm 4: Message framing, participants receive a standardised message that emphasises either the benefits of quitting (gain-framed) or the risks of continuing to smoke (loss-framed).	randomization or during the shared decision-making discussion + self-help materials and Quitline			
Implementation of Smoking Cessation Within NCI Community Oncology Research Program (NCORP) Sites (OaSiS), RCT. NCT03291587 (USA) (https://clinicaltrials.gov/ct2/show/NCT03291587)	Foley, K	Tobacco coaching sessions, 6 sessions every 4-6 weeks over 8 months	Usual screening clinical care	7-day sustained smoking abstinence 6 months after treatment	Bio verified smoking abstinence (6 months follow up) Short term smoking abstinence (3 month follow up).	25/07/2022 (Results not published)
Smoking Cessation Intervention During Low Dose CT (LDCT) Screening for Lung Cancer, RCT. NCT03059940 (USA). (https://clinicaltrials.gov/ct2/show/NCT03059940)	Cinciripini, P	Quitline + Rx (Arm1): LDCT provider and patient discuss options for pharmacotherapy Quitline referral. 5 smoking cessation counselling sessions over the next 12 weeks. Integrated Care (IC) Group (Arm2): Participant referred to Tobacco Treatment Program (TTP). TTP provides 4-8 counselling sessions and	Quitline group: Referral to Quitline for counselling +NRT for at least 5 sessions	Smoking abstinence at 6 months		01/06/2023

		pharmacotherapy over a 10–12-week period,				
Promoting Smoking Cessation in Lung Cancer Screening Through Proactive Treatment (PROACT), RCT NCT03612804 (USA). (https://clinicaltrials.gov/ct2/show/NCT03612804)	Zeliadt, S	Two sessions of proactive cessation care, including cessation medications and behavioural telephone counselling	Standard clinical screening care	Self-reported abstinence from smoking 12 months post randomisation		30/04/2023
CONNECT Smoking cessation and lung cancer screening, RCT, NCT04149249 (USA). (https://clinicaltrials.gov/ct2/show/NCT04149249)	Walsh, J	View and participate in the interactive Video Doctor about Smoking Cessation before LCS appointment	Standard information leaflet about smoking cessation.	30-day abstinence, Self-reported quit attempts, percentage of participants who attend cessation clinics.	Change in participation rate	31/05/2023
Comparing smoking cessation interventions among underserved patients referred for lung cancer screening, RCT NCT04798664 (USA) (https://clinicaltrials.gov/ct2/show/NCT04798664)	Scott D Halpern	Arm 1: free access to nicotine replacement therapy (NRT) and/or reimbursement of up to $300 for any smoking cessation medications (varenicline/Chantix or bupropion/Zyban) Arm 2: Arm 1 plus an incentive plan in which participants will be informed of their eligibility to earn $100, $200, and $300 if they	Standard cessation care, Ask, Advise, Refer	Biochemically confirmed smoking abstinence sustained for 6 months	Self -report smoking abstinence and Bio confirmed at 2 weeks, 3 months, 6 months, 12 months	December 2024

		submit negative tests for nicotine metabolites at 2 weeks, 3 month and 6 months following their quit date, respectively. Arm 3: Participants receive all aspects of Arm 2 plus an intervention to promote episodic future thinking (EFT), Patients will practise using EFT cues to envision the "future is now" between the time of enrolment and the quit date and will then receive cues from the quit date through the end of the intervention period, 6 months later.				
Tobacco treatment in the context of lung cancer screening, RCT NCT03927989, (USA). (https://clinicaltrials.gov/ct2/show/NCT03927989)	Rojewski, A	Advice to quit and brief discussion of tobacco use plus dual nicotine replacement therapy plus 8 weeks of gain-framed text messages tailored to lung screening	Brief advice to quit smoking prior to Lung screening	Self-reported 7-day PP smoking abstinence 8 weeks after treatment	End of Study Abstinence Rates 3 months follow up	August 2023
Assessing the integration of Tobacco Cessation Treatment into Lung Cancer Screening (LCS), (ScreenASSIST), RCT (NCT03611881), (USA). https://clinicaltrials.gov/ct2/show/NCT03611881)	Park, E	Arm 1: 4 weeks of counselling + 2 weeks of NRT + local referral Arm 2: 4 weeks of counselling + 8 weeks of NRT + local referral	No control	Self-reported past 7-day smoking abstinence (6 months post treatment)	Reduction in cigarettes per day, intention to quit.	01/02/2023

		Arm 3: 8 weeks of counselling + 2 weeks of NRT + local referral Arm 4: 8 weeks of counselling + 8 weeks of NRT + local referral Arm 5: 4 weeks of counselling + 2 weeks of NRT + no referral Arm 6: 4 weeks of counselling + 8 weeks of NRT + no referral Arm 7: weeks of counselling + 2 weeks of NRT + no referral Arm 8: 8 weeks of counselling + 8 weeks of NRT + no referral				

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3.5 Discussion

3.5.1 Main findings

This systematic review addressed the effectiveness of smoking cessation intervention strategies delivered as a component of lung health screening programmes. Moderate quality evidence supports the embedding of smoking cessation interventions within screening programmes. Intensive interventions and those including pharmacotherapy support (NRT, varenicline or E-cigarettes) were supported by high quality evidence and appeared to be more effective at increasing quit rates. Where smoking cessation intervention intensity was low, the evidence supporting the recommendation of these strategies was low, suggesting a minimum intervention threshold needed to have an effect.

3.5.2 Findings in context

The health, social and economic harms from smoking have been well established (Goodchild 2018; Larsson 2022). The value of lung cancer screening programmes will be enhanced by embedding smoking cessation interventions into them (Murray 2022), modelling suggests that providing behavioural cessation advice, plus pharmacotherapy can reduce the cost per quality adjusted life year (QALY) of a lung screening programme by up to 50% (Villanti 2013). The economic evaluation of the (Taylor 2022) study, comparing eight-week intensive intervention to two-week minimal intervention, estimated greater lifetime cost savings with cessation support, and the incremental costs per QALY gained were projected to be larger with the eight-week intensive counselling (Cao 2022).

Results from the current review suggest that providing more support (multiple counselling sessions and pharmacotherapy) compared with less-intensive approaches may be more favourable for a screening population. However, there were only two studies using direct comparison data, leading to only a recommendation of moderate certainty. Two RCTs found

increases in quit rates with more intensive smoking cessation support compared with less intensive support, (Lucchiari 2020) found that nicotine e-cigarettes combined with four sessions of behavioural counselling was more effective than behavioural support alone. Taylor et al, 2020 demonstrated self-reported and CO verified quit rates were significantly higher among smokers who received eight counselling sessions plus eight weeks of NRT patch, compared to three sessions plus two-week supply of NRT. This further supports the argument that smoking cessation interventions delivered in a screening context should provide multiple sessions and offer pharmacotherapy provision. I also note that all the intensive interventions included pharmacotherapy, so, it is not possible from the available data to disentangle these two effects.

Data from the broader smoking cessation literature supports the use of intensive smoking cessation support. A 2022 systematic review and meta-analysis compared four sessions of behavioural counselling to brief face to face cessation advice, continuous abstinence was significantly higher within the intensive arm [RR: 2.60, 95% CI 1.71-3.97) (Rasmussen 2022). When comparing study quit rates, the short-term pp quit rates seen within the Rasmussen review are numerically higher compared to the present review, [intensive smoking cessation 26.9% non-intensive 20.9%] and [intensive smoking cessation 10.8% vs non intensive 5.6%]. This is likely attributed to the difference in number of included studies (Rasmussen 2022) included nine studies in their meta-analysis, while the present study only included two. A Scoping review focused on effective smoking cessation interventions among populations with COPD, highlighted the importance of combining pharmacotherapy and multiple counselling sessions. The authors suggested mobile-health (m-heath) counselling sessions may be effective for a COPD population, however, the evidence was limited by low certainty (Feng 2022). Intensive smoking cessation interventions within cancer patients have been explored

within the literature. A 2020 RCT, demonstrated a higher six month quit rate among patients who received four biweekly, three monthly telephone counselling sessions and pharmacotherapy prescriptions, compared to four biweekly telephone counselling sessions (34.5% intensive vs 21.5% in control) (Park 2020). Of note, the quit rates demonstrated in the Park trial are numerically higher than many of the included studies within the present review. It is likely that patient motivation to quit smoking may be higher among those with a confirmed cancer diagnosis compared with patients undergoing asymptomatic screening.

Not only does the academic literature support the use of intensive smoking cessation interventions, but smoking cessation programs also available in multiple counties utilize intensive methods. This includes the UK's specialist smoking cessation support program which comprises of six sessions of behavioural counselling plus pharmacotherapy (West 2013). The USA also describe intensive smoking cessation programmes as gold standard in their clinical practice guidelines (Fiore 2009). European countries such as Denmark and Sweden both recommend intensive cessation programmes as their standard tobacco dependency treatment (Rasmussen 2022; Rasmussen 2017).

E-cigarettes have been supported as a stop smoking aid by a recent UK NIHR Health technology assessment (Thomas 2021). As well as used successfully within smoking cessation interventions delivered during LCS programmes (Lucchiari 2020; Murray 2024). A living Cochrane review finds high certainty evidence that nicotine containing e-cigarette use increases quit rates compared to NRT (Lindson 2024). However, this may in part be due to the typically longer duration of use of e-cigarettes compared to medicinal forms of NRT and other pharmacological agents. This probably reduces the risk of relapse to smoking, but longer-term

use of e-cigarettes is itself likely to cause some health harms. Individuals should be advised to quit vaping in due course if they can, though not at the expense of going back to smoking.

To date there have been previous systematic reviews aimed at investigating effective smoking cessation interventions delivered during LDCT screening (Iaccarino 2019; Moldovanu 2021). The reviews conducted 2019 and 2020, both used a narrative systematic review format, despite both reviews concluding that LCS are opportune moments to deliver cessation services (Iaccarino 2019), as well as suggesting that intensive interventions yield greater quit rates (Moldovanu 2021). Both reviews concluded that the data was insufficient to recommend one type of smoking cessation intervention over another. The current review presented contains statistical pooled analyses of included studies enabling us to draw firmer conclusions from the data.

This review demonstrates that providing smoking cessation within lung health screening programmes increases quit rates. Given that smoking cessation is arguably the most successful and cost-effective intervention for reducing tobacco induced diseases (Royal College of Physicians 2018), it is vital that smokers who attend screening clinics are offered support. This not only reduces risk for the individual but potentially increases the cost effectiveness of the screening intervention (Villanti 2013; Cao 2022). The population who attend lung screening clinics will typically have a high degree of nicotine dependence and addiction (Brain 2017), in addition to a higher risk of ill health and frequent exacerbations (Williams 2022a). Given that the current and previous reviews on this topic supports the use of intensive counselling with pharmacotherapy support (Moldovanu 2021), coupled with the wider cessation literature and national gold standard cessation guidelines from multiple countries. Offering pharmacotherapy alongside multiple behavioural counselling support,

should be mandated when designing pathways to support smoking cessation within lung cancer screening environments. Finally, it is apparent that more research is needed within this area, particularly aimed at intensiveness and timing of the interventions, which potentially could be addressed through a second systematic review, including the ongoing trials highlighted in table 3.7.

3.5.3 Methodological Considerations

This review has certain limitations that must be addressed. The primary endpoint of smoking cessation was assessed at a range of time points among the studies included. The immediacy of intervention also varied and what was usual care. This led to a high variation between the studies included in the meta-analysis, however, this is to an extent addressed in the different analyses presented, comparing both any additional smoking cessation intervention vs usual care, more intense intervention vs less and short-long term follow up data. Additionally, heterogeneity was measured within the meta-analyses using the I^2 statistic. In all but one of the meta-analyses conducted the I^2 statistic was at 0%, indicating a low level of heterogeneity between the pooled studies. The only outlier was the meta-analysis conducted among the two studies that used non-intensive cessation interventions. In this analysis the I^2 statistic was 75%, indicating a high level of heterogeneity between the two studies.

Despite having no search limitations based on location, all included studies were conducted in high income countries, so generalisability to middle and low-income countries need to be considered. Additionally, tobacco use habits are changing and will be influenced by the social and cultural factors, as the studies included in this analysis were all conducted in Europe/USA, the extent to which these findings can be applied globally is unclear. Although not included in the meta-analysis, the findings of observational studies also support the conclusion that smoking cessation is effective in this context.

3.6 Conclusion

Lung health screening settings are a key environment for delivering smoking cessation. All screening programmes should provide evidence-based smoking cessation alongside screening, and efforts should be made to ensure sustained counselling support alongside pharmacotherapy is provided.

Chapter 4: Immediate, remote smoking cessation intervention in participants undergoing a targeted lung health check: QuLIT-2 a randomised controlled trial.

Published as: Williams PJ, Philip KE, Gill NK, Flannery D, Buttery S, Bartlett EC, Devaraj A, Kemp SV, Addis J, Derbyshire J, Chen M. Immediate, remote smoking cessation intervention in participants undergoing a Targeted Lung Health Check: Quit Smoking Lung Health Intervention Trial, a randomized controlled trial. Chest. 2023 Feb 1;163(2):455-63.

4.1 Introduction

There is an increasing interest within the lung cancer screening field as to whether attendance to a LCS may function as a teachable moment for smoking cessation. The evidence is summarised in section 1.5 of this thesis, with results from large RCTs, demonstrating increased quit rates among smokers who received annual CT screening (van der Aalst 2010; Brain 2017). Due to these results, there has been increased attention in, and how comprehensive smoking cessation interventions should be delivered within lung cancer screening programs. The previous chapter addresses this question, highlighting the importance of intensive interventions for this population and setting.

The present study aims to also address this question, the COVID-19 pandemic allowed me to modify and adapt the previous QuLIT1 trial study design (Buttery 2022). The research presented here is a clinical RCT, investigating the effectiveness of six sessions of telephone smoking cessation support, with pharmacotherapy offered immediately after attendance to a TLHC. This is compared to usual care, consisting of signposting and very brief advice, to smokers attending a lung health check within West London.

4.2 Background

The original Quit Smoking Lung Health intervention Trial (QuLIT1) was an RCT investigating the effect of immediate in clinic smoking cessation support compared to usual care (UC) in patients attending a TLHC in West London (Buttery 2022). This trial demonstrated significantly higher quit rates among participants who received the intervention (29.9% vs 11%) and forms the basis for the current and subsequent chapters. Variations within the literature suggest that testing the effectiveness of different smoking cessation approaches, which maximises the impact and effectiveness of the lung health check remains a key question (Clark 2004a; Taylor 2017; Tremblay 2019; Marshall 2016). The systematic review in the previous chapter attempted to address this gap and suggested the more intensive the intervention is, the more successful it would be (Williams 2023a).

The QuLIT1 trial ran before the COVID-19 pandemic (Jan-Mar 2020). As with most healthcare services at the time, the TLHC switched to a hybrid delivery model. The initial consultation with the respiratory nurse was conducted over the phone, then Low Dose CT (LDCT) scan in clinic if clinically indicated. I then developed the QuLIT2 trial, adjusting the delivery of the smoking cessation intervention to a telephone service to align with the TLHC. Here I present three month follow up data from the immediate remote smoking cessation intervention or QuLIT2 trial.

4.3 Methods

4.3.1 Study design

QuLIT2 was a single-blind RCT, comparing the effectiveness of an immediate, intensive telephone smoking cessation intervention (TSI), compared to Very Brief Advice (VBA) and signposting (UC), delivered in the context of a TLHC.

4.3.2 Participants

People living in the London boroughs of Sutton, Hillingdon, and Hammersmith and Fulham, aged 55-75, with a recorded history of smoking, were invited for a TLHC assessment as described in more detail in chapter 2. All current smokers who took part in the TLHC were included in the study (current smokers were defined as any person self-reporting smoking tobacco including cigarettes, pipes and cigars at the time of the TLHC). All participants who smoked were included in the study population, regardless of readiness or motivation to quit.

4.3.3 The Targeted Lung Health Check Setting.

The Healthy Lung Project is described in greater detail in Chapter 2, due to the COVID-19 pandemic in 2021 all initial pre-scan TLHC appointments were changed to a remote telephone delivery model. If participants met the risk threshold criteria according to the models described in Chapter 2, then they were invited to attend the Royal Brompton Hospital or mobile unit for a LDCT scan.

4.3.4 Trial Registration

The initial QuLIT study (QuLIT1) and the amended study reported here (QuLIT2) were registered prospectively online (ISRCTN12455871).

4.3.5 Randomisation

Participants in the trial attended their TLHC appointment between 1st April and 31st June 2021, half the days during that period were allocated by random number generation as TSI days and half as UC. The appointments for the TLHC were allocated by an administrator who was unaware of which study arm days had been allocated to.

4.3.6 Interventions

4.3.6.1 Telephone Smoking Cessation.

Participants in the TSI group received a telephone call from the smoking cessation practitioner after their initial TLHC appointment. To capitalise on this "teachable moment," the smoking cessation practitioners attempted to call the participants the same day they received their TLHC. If they were unable to get through, the practitioners would call the participant the next day. Participants randomised to the TSI arm were offered six sessions of telephone behavioural counselling support, in addition to pharmacotherapy (varenicline or nicotine replacement therapies), which was mailed out to participants after their first session within the first 48 hours. A more detailed description on the content of the counselling sessions and pharmacotherapy available is described in chapter 2.

4.3.6.2 Usual Care

Those attending on usual care days received VBA to quit ("Stopping smoking is the most important thing that you can do to improve your health now and reduce the risk of health problems in the future") as outlined by the NCSCT. They were also directed to the London Stop Smoking portal which provides information to smokers about how to engage with local stop smoking services and a Quitline service. Participants living in the London borough of Sutton were advised to contact their GP for stop smoking support. As there was no specialist smoking cessation support available in this borough. The usual care intervention was delivered by the specialist respiratory nurses who administered the TLHC clinics and occurred at the end of their appointment.

4.3.7 Three Month Follow up

Three months following the TLHC appointment, all participants were called by Keir EJ Philip or myself who were blind to study allocation. The content of the call was structured on a set of short- predefined questions, including the primary outcome measure which was self-

reported seven-day point prevalence smoking abstinence, successful quitting was defined as no smoking or other tobacco product use within the last seven days. Data relating to secondary outcome measures was also collected, this Included quit attempts made and pharmacotherapy used. Quit attempts were defined as a serious attempt to stop smoking that lasted for ≥24 hours and was presented as the number of individuals who made at least one quit attempt during the previous three-month period. I deemed quit attempts as unsuccessful, if patients reported current smoking at the time of three month follow up but had made a serious attempt to stop smoking within the three-month period.

If participants did not pick up on the first call, two more calls were made at different times of the day. If the participant did not pick up on the third call, a voicemail was left requesting a call back. If the participant did not call back within the week (or had no voicemail facility) they were classed as lost to follow up.

4.3.8 Statistical analysis

The primary outcome was self-reported seven-day point prevalence abstinence from smoking, three months post randomisation compared between groups. Randomisation occurred at the date of participants' TLHC appointment. The sample size was calculated using the findings of two studies; the EAGLES trial (Anthenelli 2016) which found a 38% quit rate in the pharmacology arm and the UK Lung Cancer Screening Study (Brain 2017), which found a 14% quit rate in the arm undergoing CT screening. Based on these rates, a superiority study (1:1 randomisation) with 90% power at a 5% significance level would require 136 participants. Simple logistic regression analysis (unadjusted) was used to assess primary and secondary endpoints. To explore the effect of selected covariates on quit rate, two adjusted logistic regression models were conducted, model one adjusted for sex, age and CT result and model two adjusted for sex, age, and baseline demographics (age, sex, smoking characteristics).

Intervention arm, age and sex were retained in both models. Analysis was based on intention to treat principle, and I assumed that participants lost to follow up were current smokers. A p value of <0.05 accepted as statistically significant, all data were analysed using SPSS V27.

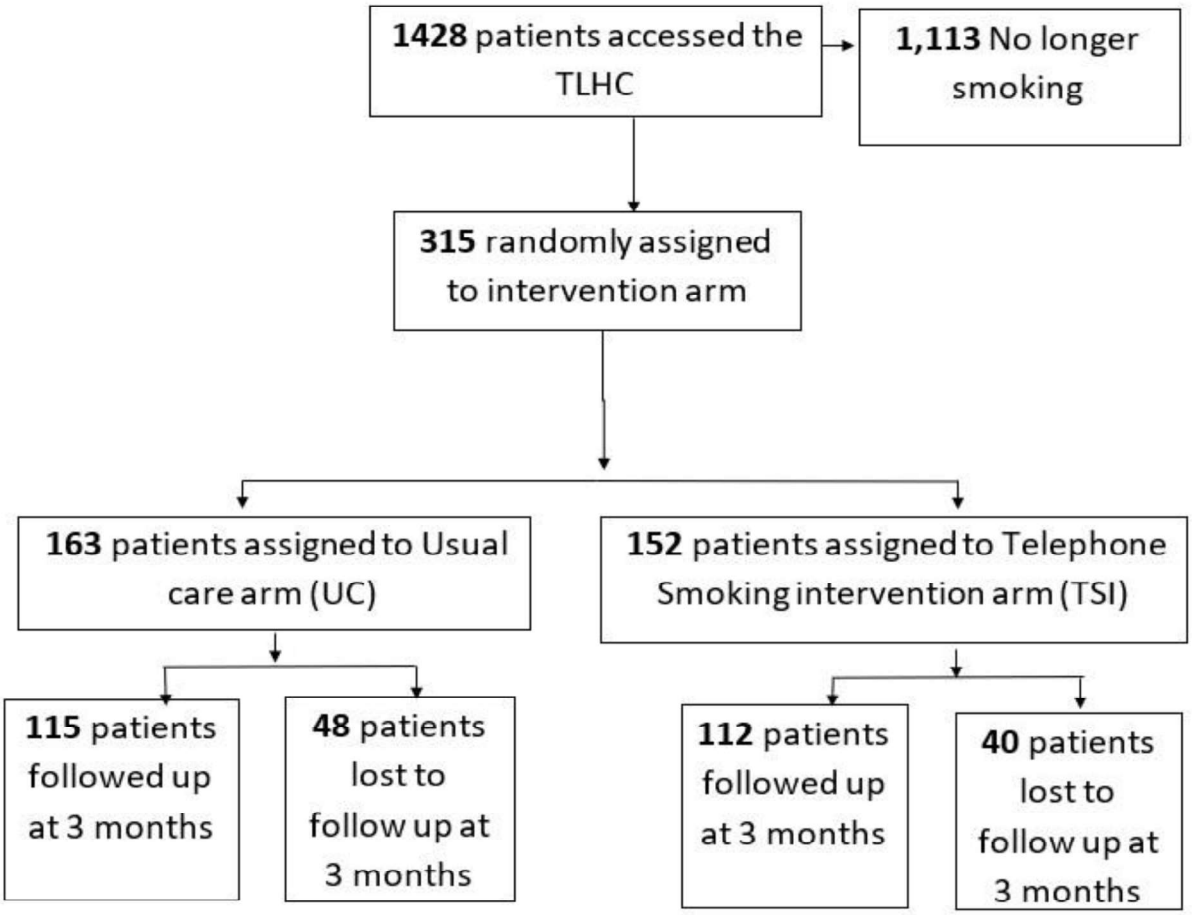
4.4 Results

Baseline participant characteristics at the time of enrolment were well matched (Table 6.1). A total of 315 individuals who smoke, underwent a TLHC during the study period and were enrolled onto the study, 163 attended on days allocated to UC and 152 on TSI days. Figure 4.1 represents patient flow through the trial. The justification for enrolling 315 participants into the study, which is higher than the estimated sample size was to allow for subgroup analysis, this was outlined in the ethics application and trial registration.

4.4.1 Engagement with smoking cessation

Of the 152 participants attending on days randomised to TSI, 80 (52%) declined to engage with the smoking cessation support. These participants explicitly asked not to be contacted by our cessation nurses. Of the remaining 72 participants in the TSI arm, 57/72 (79%) were enrolled onto the full cessation program and 16/72 (21%) dropped out after the initial session. Reasons given for dropping out were being unable to commit to the "not a puff" rule, or not being ready to commit to the program, both are important components of the SCS programme as set out by the NCSCT and KickIt (NCSCT 2023; KickIt 2022). The average number of sessions completed by the participants was 5.1, with 61% of participants completing the full six sessions, average length of time for the telephone counselling sessions was 27 minutes.

Figure 4. 1. Patient flow through the trial



Targeted Lung Health Check (TLHC)

Table 4. 1 Baseline Demographics

Characteristics	Usual Care (n=163)	Intervention (n= 152)
Age, mean years (SD)	63.0 (5.4)	61.3 (4.8)
Sex		
Female, n (%)	84 (51.5)	68 (44.7)
Male, n (%)	79 (48.5)	84 (55.3)
Ethnicity, n (%)		
White	138 (84.6)	131 (86)
Black	9 (5.6)	6 (4.0)
Asian	12 (7.3)	9 (6.0)
Other	3 (1.9)	5 (3.3)
Prefer not to say	1 (0.6)	1 (0.7)
Education, n (%)		
< GCSE Level	64 (39.3)	59 (38.9)
GCSE Level	63 (38.7)	49 (32.2)
A Level	23 (14.2)	17 (11.1)
Some University	2 (1.3)	7 (4.6)
Degree + Postgrad	11 (6.5)	20 (17.2)
IMD quintile n (%)		
1 (Most deprived)	9 (5.5)	15 (9.9)
2	19 (11.7)	19 (12.5)
3	40 (24.5)	26 (17.1)
4	65 (39.9)	52(34.2)
5 (Least Deprived)	30 (18.4)	40 (26.3)
Baseline Smoking Characteristics		
Age started years smoking, mean (SD)	18.1 (6.3)	18.0 (5.9)
Average number of cigarettes per day, mean (SD)	12.6 (7.9)	12.5 (7.7)
Number of smoking years, mean (SD)	42.5 (9.5)	40.9 (9.0)
CT Result		
No Scan needed, n (%)	59 (36.2)	52 (34.2)
CT negative, n (%)	55 (33.7)	60 (39.4)
CT positive, n (%)	49 (30.1)	40 (26.4)

Ethnicity groupings as recommended by the Prostate, Lung Colorectal and Ovarian Screening Trial (PLCO).

Index of multiple deprivation quantile (IMD), quantile 1= most deprived areas in England quantile 5= least deprived areas in England (IMD) (Ministry of Housing 2019).

Computed Tomography (CT)

CT positive = nodules requiring 3, 6 or 12 month follow up scan, suspicious lesions, nodular consolidation, or incidental findings.

CT negative = CT result was clear, no evidence of nodules or incidental findings.

No Scan needed = participant did not meet CT scan criteria according to the PLOC and LLP risk models(Cassidy 2008; Ten Haaf 2017).

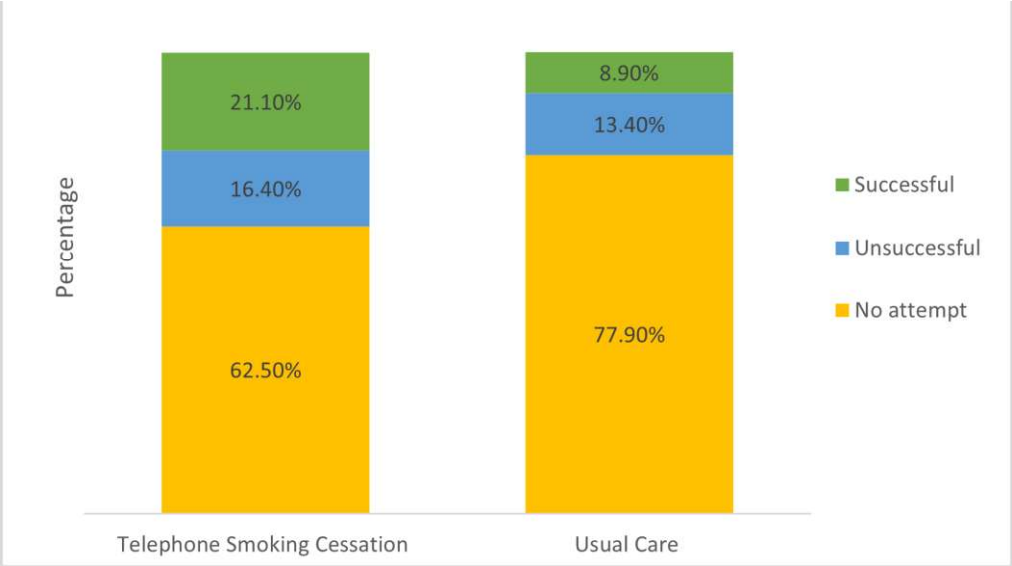
4.4.2 Smoking Cessation Outcomes

Three month follow up data were available for 227/315 (72%) participants (UC: 115/163 (70%), TSI: 112/152 (73%). However, I present results here based on the intention to treat principle and assuming participants lost to follow up are current smokers. Quit rates were higher in the intervention arm [(21.1% vs 8.9%), (OR: 2.83, 95% CI 1.44-5.60, p=0.002)] (table 4.2). The numbers reporting quit attempts, including successful and unsuccessful attempts was also higher in the TSI group [(57/152 37.5% vs 36/163 22.0%), (OR: 2.11, 95% CI 1.29-3.47 p=0.003)], (Table 4.2, Figure 4.2).

4.4.3 Influence of CT result on quit rates

I explored if receiving the CT scan itself influenced quit rates among the study arms, within the UC arm receiving a CT scan did not influence quit rates [UC no CT (4/59 6.7%) vs UC and CT (10/104 9.5%) (AOR: 0.68, 95% CI 0.20-2.28, p= 0.53)]. Post Hoc analysis comparing quit rates among participants in the UC arm that had a positive CT (n=49) compared to negative CT (n=55), demonstrated numerically higher CT negative quit rates, but this had no statistical significance, [CT negative 6/55 (10.9%) vs CT positive 4/49 (8.2%), (AOR: 0.72, 95% CI 0.19-2.74)]. All models adjusted for sex and age. Exploring the effect of CT scan vs no CT on quit rates was also explored within the TSI study arm, [No CT 14/52 (26.9%) vs received CT 18/100 (18%), (AOR: 1.67, 95% CI 0.75- 3.72, p= 0.23)]. Post Hoc analysis comparing quit rates among participants in the TSI arm that had a positive CT (n=40) compared to negative CT (n=60), demonstrated numerically higher quit rates within participants who received a negative CT. However, this had no statistical significance [CT negative 14/60 (23.3%) vs CT positive 4/40 (10.0%), (AOR: 2.73, 95% CI 0.83-9.03, p=0.98)]. All models were adjusted for sex and age.

Figure 4. 2 Bar chart representing quit rates and attempts in the trial



Bar graph displaying the percentage of smoking cessation in the intervention and usual care arms. Successful cessation is defined as no smoking or other tobacco product use within the last 7 days, unsuccessful cessation defined as attempt to stop smoking that lasted for ≥24 hours and no attempt defined as no attempt to stop smoking.

4.4.4 Pharmacotherapy use

The use of all types of pharmacotherapies (varenicline, single item NRT and dual item NRT) during quit attempts was more common in the TSI group (OR: 20.90, 95% CI 6.98- 62.55, p=<0.001) (Table 4.2). By contrast, participants in the UC group were more likely to report use of e-cigarettes to aid quit attempt (TSI: 14.0% vs UC: 30.5%). Of note, in the UC arm only 3/36 participants attempting to quit accessed behavioural support via their local service, two quit successfully and one used the NHS stop smoking smartphone app.

Table 4. 2 Smoking cessation and quit attempts at 3-months

	Telephone Smoking Intervention (TSI) (n=152)	**Usual care (UC) (n=163)**	**Odds Ratio (95% CI)**	**P Value**
Seven-day smoking abstinence	Yes 32 (21%) No 120 (79%)	Yes 14 (8.9%) No 149 (91.1%)	2.83 (1.44-5.61)	0.002
Individuals reporting a quit attempt*	Yes 57 (37.5%) No 95 (62.5%)	Yes 36 (22.0%) No 127 (78.0%)	2.11 (1.29-3.47)	0.003
Pharmacotherapy Aids used to support quit attempts				
• Varenicline	16 (28.0%)	1 (2.7%)	13.65 (1.72-108.24)	0.01
• Single item NRT	12 (21.0%)	2 (5.5%)	4.53 (0.95- 21.61)	0.05
• Dual item NRT	21 (37.0%)	3 (3.8%)	6.41 (1.75-23.51)	0.005
• E-cigarette	8 (14.0%)	11 (30.5%)	0.37 (0.13-1.04)	0.05
• Nil	0 (0%)	19 (57.5%)	0.06 (0.0-0.27)	0.004

NRT nicotine replacement therapy (NRT)
CI, Confidence interval
****Quit attempt includes both successful and unsuccessful quit attempts.***

4.4.5 Influence of covariates on quit rates

Results from the two logistic regression models are displayed in Table 4.3, data from participants who did not receive a CT scan were excluded from model two. Person demographics (sex, age), CT scan result (positive, negative) and smoking characterises (average number of cigarettes per day, age started smoking and number of years smoking) had no effect on quit rates at three months within our cohort.

Table 4. 3 Logistic Regression Models of covariates associated with smoking abstinence at 3 months.

	Model 1: Sex, age, CT result (n=315)	**Model 2: Sex, age, baseline smoking characteristics (n=315)**
Intervention	**2.80 (1.42-5.53)**	**2.62 (1.32-5.24)**
Sex (men vs. women)	1.00 (0.581-1.44)	1.00 (0.57-1.43)
Age (continuous)	1.00 (0.90-0.98)	1.01 (0.90-1.01)
CT Negative	1.46 (0.77-2.72)	-
CT Positive	.990 (0.50-1.61)	-
Average Number of cigarettes per day	-	0.995 (0.97-1.04)
Age started Smoking	-	1.02 (0.95-1.07)
Number of years Smoking	-	.977 (0.94-1.03)

Bold type indicates p< 0.05

Data presented as: Adjusted odds ratio (95% CI)

CI, Confidence Interval

CT positive = nodules requiring 3, 6 or 12 month follow up scan, suspicious lesions, nodular consolidation, or incidental findings.

4.5 Discussion

4.5.1 Main findings

The main finding of this randomised controlled trial, is that the provision of smoking cessation consisting of counselling support and pharmacotherapy, delivered by telephone immediately following attendance at a targeted lung health check significantly increased seven-day point prevalence smoking abstinence at three months. This was compared to an offer of usual care of very brief advice to quit and signposting to smoking cessation services.

4.5.2 Findings in context

These results support the hypothesis that the immediate provision of remote, intensive smoking cessation support for high-risk people who smoke undergoing TLHC, is more effective (21.1% vs 8.9%) for increasing quit rates within this cohort than usual care.

These findings extend those from the previous trial QuLIT1 which found immediate face-to-face support can increase quit rates compared to usual care (29.2% vs 11%) in the context of TLHC (Buttery 2022). Comparing the two trials, the quit rates in the usual care groups in both studies were numerically similar, whereas quit rates in the face-to-face intervention were higher. The number of quit attempts was also higher in the intervention group (37.5%) and similar between both QuLIT1 and QuLIT2 interventions (QuLIT1: 35.3%). The increased quit rates seen with the QuLIT1 in clinic delivery may be attributable to the COVID-19 pandemic. The data is somewhat suggestive that the pandemic led to an increase in quit attempts and abstinence (Jackson 2021). This effect is also indicated within the qualitative analysis of the QuLIT1 data, whereby participants stated they quit due to the COVID-19 pandemic (Buttery 2022).

The wider literature is contradictory when comparing face to face and remote cessation services. A Japanese trial demonstrated similar continuous absence rates at 6-12-weeks among smokers who received either an internet telemedicine intervention or standard face to face intervention (81% vs 78.9%) (Nomura 2019). In compassion, a study conducted within the midst of the COVID-19 pandemic observed significantly lower 12-week quit rates among participants who received tele counselling compared to face to face (face to face: 30.5% vs tele 19.7%) (Naja 2023). In the case of the present study and QuLIT1, the two approaches were not directly compared, so future studies will be required to confirm which approach is more effective.

Several trials, including the initial QuLIT1 study have investigated the impact of smoking cessation support within lung cancer screening pathways. These studies report mixed results, limited by factors including statistical power and the nature, intensity, duration, and immediacy of intervention (Clark 2004a; Taylor 2017; Marshall 2016; Buttery 2022; Zeliadt 2018). The 21.1% three-month quit rate observed in the QuLIT2 intervention arm is comparable with other studies where quit rates ranged from 10-25%. Interestingly, the two studies which reported lower interventional quit rates than our current study conducted their cessation remotely (telephone and online) however, did not offer any pharmacotherapy (Clark 2004a; Zeliadt 2018).

Other studies have also investigated which factors might be associated with successful smoking cessation within TLHC settings. Tremblay et al, 2019 found that current smokers who reported a cancer history, smoked at work, and consumed alcohol once a week or more were more likely to be still smoking at 12 months (Tremblay 2019). In the NELSON screening trial, individuals who smoke with higher educational attainment and higher motivation to quit

were more likely to have quit at two year follow up (van der Aalst 2012). By contrast, I found no associations between participant characteristics and successful smoking abstinence, this may be due to a lack of statistical power, the NELSON trial investigated quit rates in 1,248 smokers.

The effect of receiving a CT scan vs not having a CT as part of a TLHC did not significantly alter quit rates within our population (CT: 13.7% vs No CT: 16.2%). This finding is contradictory to much of the wider screening literature; data from the UKLS demonstrated significantly higher quit rates among smokers whose CT scan indicated a clinical investigation compared to smokers who received a negative CT result (16% vs 11%) (Brain 2017). Data from the US NLST, also observed higher quit rates among smokers that had a major non-cancerous CT finding (OR: 0.81, 95% CI 0.72- 0.91), suspicious lung cancer finding but stable from previous scan (OR: 0.78, 95% CI 0.70-0.87), or suspicious lung cancer finding that had changed or was new compared to previous findings (OR: 0.66, 95% 0.67-0.72), compared to smokers with a clear CT result. The group observed that these quit rates were sustained up to five years (Tammemägi 2014). However, when observing the effect of CT result on quit rates among some of the smoking cessation and LCS interventional trials, a similar effect to the present study is observed. (Clark 2004a; Taylor 2017; Pistelli 2020), did not observe higher quit rates among smokers that received a positive CT compared to negative. This is attributed to the smaller sample sizes seen within these smoking cessation interventional trials and the larger lung cancer screening studies. It must be noted, the present study is an outlier as it included smokers who did not receive a CT scan but attended the initial TLHC. This supports the offer of smoking cessation support to everyone taking part in targeted lung health screening, not only those whose risk score means that they qualify for low dose CT scanning.

When compared among the study arms and within participants who received a positive or a negative CT. Smokers randomised to the TSI arm, who received a negative CT demonstrated higher quit rates compared to those who received a positive CT result (23.3% vs 10%), however, this had no statistical significance. A similar, but significant effect was observed within the later Taylor trial, which observed higher quit rates among those with a normal CT within the intensive cessation arm of the trial compared to control (8.6% vs 3.8%) (Taylor 2022). This may suggest that the present study was underpowered to detect change within this secondary outcome. A sample size of around 952 has been calculated to be sufficient to detect change within this secondary outcome of CT result.

Pharmacological cessation aids were accessed by people trying to quit in both study arms, however participants in the TSI group were around twenty times more likely to use pharmacological aids including NRT and varenicline. This is unsurprising as the combination of pharmacological aids and behavioural support were the main components of our intervention. Yet the pharmacotherapy usage within the UC arm was remarkably low, only 6/36 (16%) participants who attempted to quit used pharmacotherapy and only three participants in the UC arm accessed cessation support from their local services, despite advice and signposting to do so. E-cigarette usage to support quit attempts was significantly higher in the UC arm of our study [TSI: (8/57 14.0%) vs UC: (11/36 30.5%)]. Indicating that in the absence of organised support and pharmacotherapy, individuals who smoke are more likely to adopt this approach. There are data to support the effectiveness of e-cigarettes in the context of lung cancer screening, with observed significantly higher three month abstinence among both nicotine e-cigarettes (25.4%) and nicotine free e-cigarettes (23.4%) compared to control (10.34%) (Masiero 2019). These findings coupled with the announcement from the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) that it will support the

medicinal licensing of e-cigarettes for smoking cessation (Agency 2021) and the recent 2023 UK Government swap to stop campaign (Gov.UK 2023). Indicate that providers of cessation interventions within a screening context in the UK should be prepared to support people using e-cigarettes to support quit attempts.

These results have the potential to inform future service delivery of TLHC programs, through optimisation of smoking cessation support delivery in this population. Both QuLIT1 and QuLIT2 suggest improved quit rates with early intervention delivery, utilising either face-to-face or remote modalities. While face-to-face approaches might be more effective for those able to attend in person, remotely delivered interventions could expand access in general. This is particularly important for people living in remote and low-income areas and are of particular interest during the COVID-19 pandemic where limitations have been placed on face-to-face activities. These results also suggest that providing pharmacotherapy within the smoking cessation support, is a critical component of the intervention, contributing to successful abstinence. It is likely that a combination of delivery modality options and pharmacotherapy will be most appropriate for a population with varying needs and preferences.

I recognise the multiple organisational, personnel and financial barriers that lung screening clinics face when considering embedding smoking cessation into their service. A 2016 qualitative study of healthcare professionals providing lung cancer screening in the US reported that healthcare providers did not have enough time to devote to smoking cessation discussions (Kanodra 2016). Given these constraints, particularly time and personnel, recommendations to employ specific smoking cessation advisors to work exclusively within these screening clinics may be appropriate. These dedicated advisors could provide tailored

in person and telephone support which would include both behavioural counselling and pharmacotherapy provision, all of which will eliminate workload constraints from clinical teams, in addition to increasing the cost effectiveness of the interventions (Solberg 2006).

4.5.3 Methodological Considerations

I conducted the study in the context of a clinical lung cancer service, without deviation from the standard pathway or change in patient experience. This was apart from the provision of the smoking cessation support on TSI days, which increases the generalisability of the findings. The inclusion of all current smokers enrolled in the healthy lung project, regardless of their current readiness or motivation to quit, allows the trial to assess the impact of the approach within the whole screened population, not just those immediately motivated to stop smoking.

Certain limitations and considerations should be discussed. The first limitation, being that I used self-reported seven-day point smoking prevalence as the primary endpoint rather than biochemically confirmed quit rates to keep study costs and participant burden low. Although point prevalence self-reported data is a known valid abstinence measure within clinical trials (Piper 2020), and often used in other cessation screening trials as an outcome measure (Taylor 2017; Brain 2017; Tremblay 2019). The use of exhaled CO monitoring would increase the rigour of the study outcome and is addressed with the 12 month follow up outcomes in Chapter 5. The second limitation was generalisability of the sample population. The ethnicity of our sample population is predominantly white (85%) which is higher than the proportion of people identifying as white in the catchment areas, Hammersmith and Fulham (58%), (London Borough of Hammersmith and Fulham 2018) Hillingdon (41.7%) (London Borough of Hillingdon 2018) and Sutton (61.1%) (London Borough of Sutton 2020). When compared to other TLHC trials within the UK which observed a more ethnically diverse sample population,

including the Yorkshire Lung Screening trial which observed 40.8% population as mixed ethnicity (Crosbie 2022). As did the SUMMIT trial which observed 64% of their population that accepted the TLHC invite as white ethnicity (Dickson 2023). The detail that all participants resided within areas of Southwest and West London needs to be addressed. It is established that health and particular smoking behaviours are influenced by the social, cultural and policy environment (Calo 2013), with differences both between and within countries. So, some caution is needed when extrapolating the results from the present analysis to areas within the UK and other countries. Finally, the loss to follow up observed (28%) within the study population was slightly higher than anticipated, though like other studies (Clark 2004a; Masiero 2019). Importantly, intention to treat analysis, taking the cautious assumption that all those lost to follow up continued to smoke was used.

4.6 Conclusion

Immediate, intensive telephone-based smoking cessation support with pharmacotherapy, delivered within a TLHC setting increased three month quit rate. This suggests that this approach is appropriate and effective for this population and that access to specialist smoking cessation support should be embedded within the delivery of lung cancer screening.

Chapter 5: Immediate smoking cessation support during lung cancer screening: long term outcomes from two randomised controlled trials.

Published as: Williams PJ, Philip KEJ, Buttery SC, Perkins A, Bartlett EC, Devaraj A, Kemp SV, Addis J, Derbyshire J, Chen M, Polkey MI, Laverty AA, and Hopkinson NS. Immediate smoking cessation support during lung cancer screening: long-term outcomes from two randomised controlled trials Thorax Published Online First: 24 October 2023. doi: 10.1136/thorax-2023-220367

5.1 Introduction

The two randomised controlled trials QuLIT1 (Buttery 2022) and QuLIT2 (Chapter 4) (Williams 2023b), compared the effectiveness of offering immediate smoking cessation support, with pharmacotherapy at the time of participation in TLHC against usual care. Outcomes within both trials observed significantly higher quit rates within the intervention arms; QuLIT1 (29.2% vs 11%), QuLIT2 (21.1% vs 8.9%), three months after randomisation. However, three month follow up in cessation trials is relatively short, particularly to address whether, in the context of TLHCs, the benefit of providing immediate smoking cessation compared to only signposting to smoking cessation services is sustained longer term. One year smoking cessation outcomes have been investigated among many of the smoking cessation and LCS interventional trials, demonstrating varied success (Bade 2016a; Clark 2004a; Marshall 2016; Tremblay 2019). Within this chapter I present 12-month follow-up data from participants who were enrolled into both QuLIT trials. The aim of this study was to strengthen the data by establishing biochemical confirmation of smoking cessation, with the underlying premise that

strengthening the evidence base might lead to more widespread incorporation of smoking cessation support into the THLC service.

5.2 Background

It has been established that lung cancer screening clinical services provide a teachable moment for smoking cessation (Iaccarino 2019; Moldovanu 2021). If screening services provide smoking cessation services within them, this teachable moment is likely extended, increasing quit rates among smokers who receive them (Williams 2023a). This was demonstrated clearly by the three-month smoking cessation outcomes from the two QuLIT trials, whereby quit rates were almost doubled among smokers who received intervention (Buttery 2022; Williams 2023b). A recent policy review focused on lung cancer screening in the UK, stated that smoking cessation interventions that diverges from the standard cessation approach (VBA and signposting), needs to be supported by health economic assessments (O'Dowd 2023). Thus, it is essential that long term data is provided on the cessation outcomes of these interventions.

This same policy review also recommends an opt-out based approach (O'Dowd 2023), which has been supported by recent data from the YESS trial (Murray 2024). In the context of the QuLIT trials, QuLIT1 smokers were directed to the SCP after their TLHC, and QuLIT2 all smokers got a telephone call after their TLHC if they attended on an intervention day. In both trials the smoking cessation was an opt-out approach, with participants having to explicitly state they did not want advice. Given that recommendations suggest this approach, it is vital that long term data, proving its effectiveness is provided.

The UK's national screening committee in September of 2022 recommended that TLHC's be rolled out throughout the UK, with projections that lung health checks will be available to all

eligible populations by 2029 (Gov.UK 2022). Effective interventions to tackle tobacco dependence in this context therefore have the potential to have a significant impact on public health, moreover, modelling suggests that integrating smoking cessation support into lung cancer screening could halve the cost per quality adjusted life year (QALY) (Villanti 2013; Cao 2022) of a THLC intervention. Therefore, it is essential long-term data is collected to strengthen the position that cessation services must be delivered alongside TLHC's in the UK.

5.3 Methods

The one year follow up reported here was a pre-specified secondary endpoint of both QuLIT1 and QuLIT2 trials, as outlined on the trial registry. Chapters 2 and 4 contain detailed descriptions of the methods, including study design, randomisation methods and interventions.

5.3.1 Study outcomes

Twelve month follow up was conducted via a telephone interview conducted by two blinded assessors (SCB and me). The content of the call was structured, with predefined questions exploring 1) self-reported seven-day point prevalence smoking abstinence (Primary endpoint), 2) pharmacotherapy used to quit, 3) quit attempts (defined as an attempt to stop smoking that lasted for 1 day), 4) pharmacotherapy used for the quit attempt.

If the assessors were unable to contact participants on three separate occasions, a voicemail was left requesting a call back. If the participant failed to contact the team within two weeks of the voicemail, the participant was recorded as lost to follow up.

All participants who reported continued smoking at 12 month follow up were offered referral to a local cessation service. If participants reported a successful quit, they were invited to attend either their local scanning mobile unit or the Royal Brompton Hospital for exhaled

breath carbon monoxide (CO) test to verify their reported quit. Due to COVID-19 restrictions on face-to-face appointments we were unable to CO verify self-reported quits from the QULIT1 cohort at the time of their initial 12 month follow up period (January-March 2021). I instead invited all those who self-reported a quit at 12 months to attend CO verification at the same time as the QuLIT2 cohort (April-July 2022), which would equate to 28 month follow up.

Exhaled CO was measured using MicroMedical Micro CO Smoke Monitor (CareFusion Limited), a level of ≤5ppm or below as confirming smoking cessation, described in greater detail in Chapter 2.

5.3.4 Statistical analysis

All analyses were conducted on the intention to treat principle, based on whether the day of attending the TLHC had been allocated to SCS intervention or not, regardless of whether they accepted the offer of support. The participants that were lost to follow up were assumed to be continuing smokers and included in the analysis. The primary outcome was self-reported seven-day point prevalence (pp) abstinence from smoking 12 months after randomisation. The secondary endpoints were CO-verified quitting and number of reported quit attempts, as with the previous chapter, quit attempts were defined as a serious attempt to stop smoking that lasted ≥24 hours. Quit attempts were either classed as successful if they reported a quit at 12 months, or unsuccessful if they reported current smoking at 12 months. I used three logistic regression models to assess study arm on primary (seven-day self-reported pp smoking abstinence) and secondary endpoints (CO verified abstinence and quit attempts). In addition to exploring the impact of having a CT scan or CT scan results on primary and secondary endpoints. All models were adjusted for age, which we grouped into three (55-60, 61-65 and 66-75), sex, deprivation quintile and study cohort (QuLIT1 or 2), unsuccessful quit

attempt data reported at three month follow ups were included in the analysis. Data were analysed using SPSS version 27 software.

5.4 Results

Baseline participant characteristics are displayed in Table 5.1; 430 current smokers were enrolled in the QuLIT studies (QuLIT1 115, QuLIT2 315) with 217 participants attending on days randomised to SCS intervention and 213 to UC. Mean age was 62.1±5.3 years, 48% were female and participants smoked an average of 12.9±8.0 cigarettes per day.

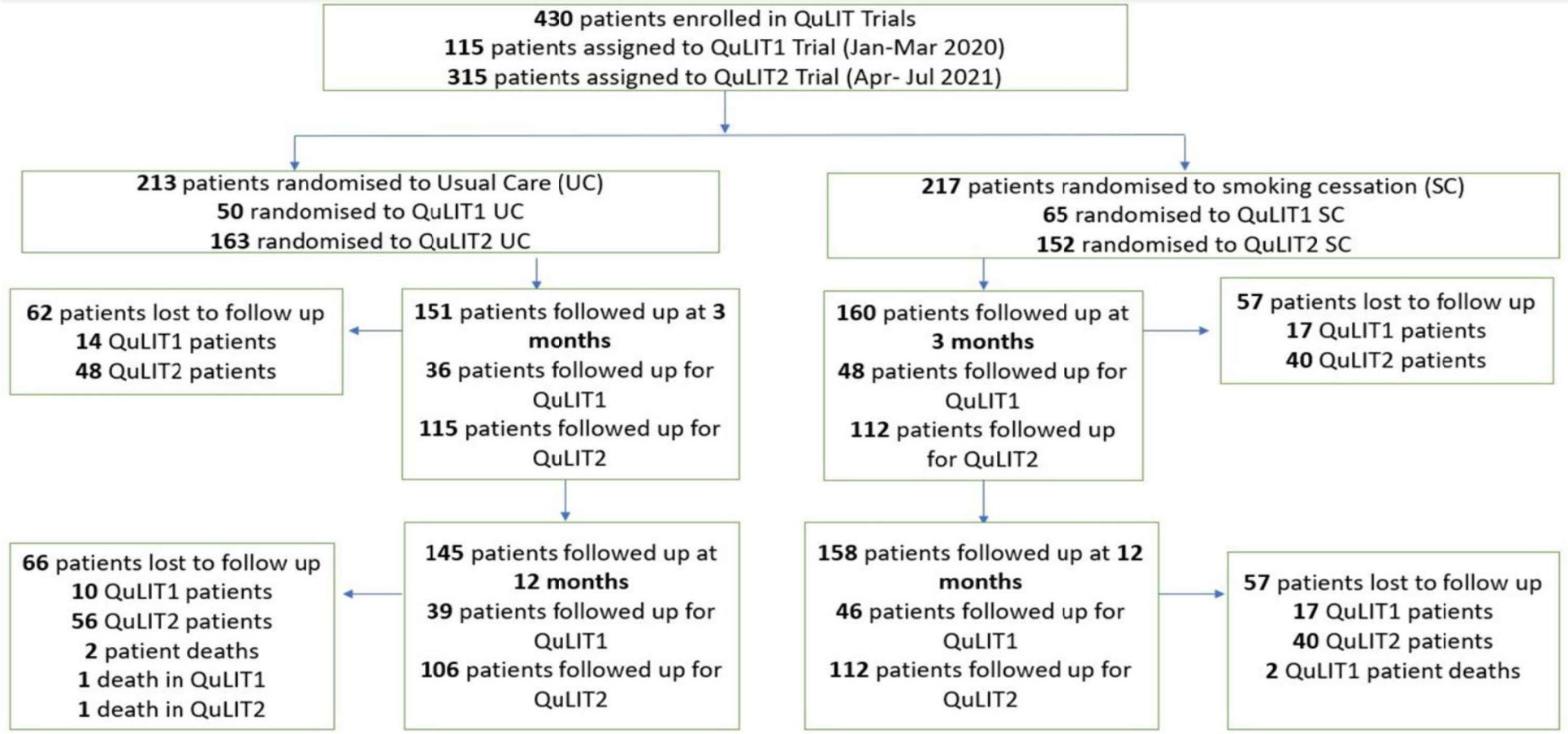
I was able to follow up 303 (77%) trial participants at 12 months, 152/151 in the SCS and UC arms respectively, mean follow up from TLHC attendance was 56.4 weeks for the QuLIT1 cohort and 60.8 for the QuLIT2 cohort. During the 12 month follow up period four deaths occurred: two in each study arm, three of the deaths were among the initial QuLIT1 face to face population and one in the second trial population (QuLIT2), their data have been excluded from the analysis (Figure 5.1).

Table 5. 1 Participant characteristics

	Smoking cessation support (SCS) (n=217)	**Usual Care (UC) (n=213)**	**Total Population (n=430)**
Age, mean years (SD)	61.91 (4.8)	62.34 (5.45)	62.1 (5.2)
Females, n (%) Males, n (%)	98 (45%) 119 (55%)	110 (51%) 103 (49%)	208 (48%) 222 (52%)
Cigarettes per day, mean years (SD)	12.69 (7.75)	13.22 (8.25)	12.9 (8.0)
Index of Multiple Deprivation Quintiles, n (%) * IMD 1 (Most deprived) IMD 2 IMD 3 IMD 4 IMD 5 (Least deprived)	 15 (7%) 45 (21%) 54 (25%) 63 (29%) 40 (18%)	 9 (5%) 39 (18%) 60 (28%) 75 (35%) 30 (14%)	 24 (6%) 84 (20%) 114 (26%) 138 (32%) 70 (16%)
Baseline CT results			
No scan needed*	69 (31%)	76 (36%)	145 (38%)
CT negative	101 (47%)	82 (38%)	183 (42%)
CT positive *	47 (22%)	55 (26%)	102 (20%)

Data are presented as number (%) or mean ± Standard deviation.
****Index: quantile 1 = most deprived areas in England, quantile 5 = least deprived areas in England***
****Participant didn't meet CT scan risk criteria according to the Prostate, Lung Colorectal and Ovarian Screening Trial and the Liverpool Lung Project models***
****Results were clear, did not show evidence of nodules or incidental findings***
****Nodules requiring 3,6, or 12 month follow up scan, suspicious lesions, nodular consolidation, or incidental findings***

Figure 5. 1 Participant flow through the QuLIT trials



flow diagram representing flow through the trials. QuLIT1- the smoking cessation intervention was delivered in clinic, QuLIT2 the smoking cessation intervention was delivered remotely over the telephone.

5.4.1 Smoking cessation in entire QuLIT population

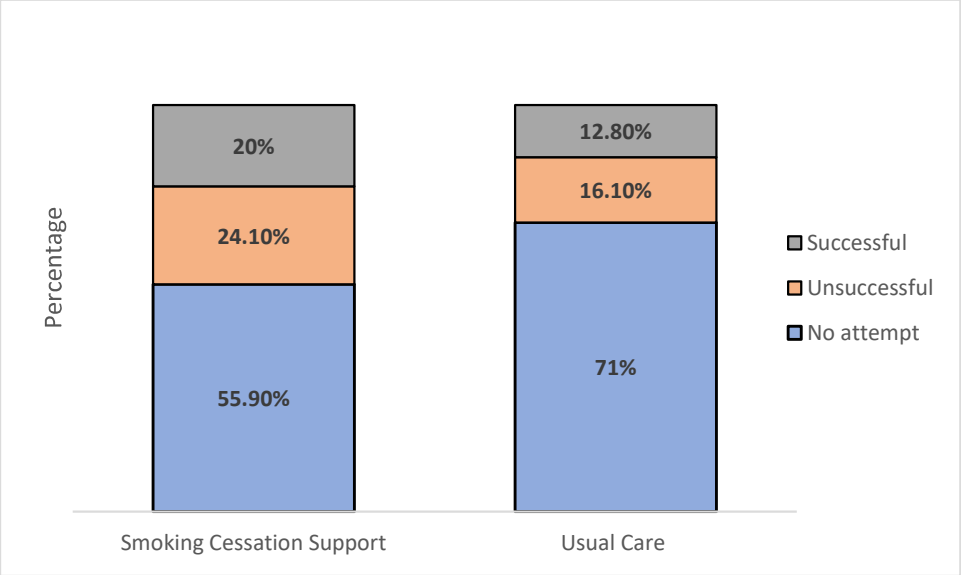
Participants in the SCS arm had higher quit rates compared to UC both for self-reported seven-day pp [(20.0% vs 12.8% AOR: 1.78 95% CI, 1.04-2.89)] and CO verified quits [(12.1% vs 4.7%; AOR: 2.97, 95% CI 1.38-6.90)], (Table 5.2). Of note participants in the QuLIT1 arm attending CO verification, attended this at 28- month follow up. Among those still smoking at 12 months, participants in the SCS intervention arm were more likely to report having made a quit attempt during the subsequent year than smokers who received the UC intervention [(SCS 30.2% vs UC 18.5%; AOR: 1.90, 95% CI 1.15-3.15)], table 5.2, figure 5.2. Quit rates did not differ between those who were or were not eligible for a CT scan based on their initial assessment, nor between those with a normal or abnormal scan (Table 5.3).

Table 5. 2 Impact of smoking cessation intervention

Smoking abstinence for all randomised participants (ITT)	Smoking Cessation Support (SCS) (n=215)	Usual Care (UC) (n=211)	AOR (95% CI)
7-day self-reported cessation	43/215 (20.0%)	27/ 211 (12.8%)	**1.78 (1.04-3.04)**
CO verified cessation	26/215 (12.0%)	10/211 (4.7%)	**2.97 (1.43- 6.73)**
Smoking quit attempts for all randomised participants who are still smoking	(n=172)	(n=184)	
Unsuccessful	52/172 (30.2%)	34/184 (18.5%)	**1.98 (1.20-3.25)**
No attempt	120/172 (69.8%)	150/184 (81.4%)	-

AOR= Adjusted Odds Ratio (adjusted for age, sex, IMDQ and QuLIT trial) CI= Confidence Interval
Bold Type = Statistically significant at 0.05
CO Verified = Self-reported quit verified using exhaled carbon monoxide monitor
ITT= intention to treat principle all those lost to follow up assumed as still smoking
Quit attempts = attempt to stop smoking that lasted for one day, data is presented as the number of individuals who made at least one quit attempt during the previous 12-month period.

Figure 5. 2 Smoking Cessation in the intervention and control arms



Bar graph displaying the percentage of self reported smoking cessation in the intervention and usual care arms, successful cessation is defined as no smoking or other tobacco product use within the last 7 days, unsuccessful cessation defined as attempt to stop smoking that lasted for one day, and no attempt defined as no attempt to stop smoking.

Table 5. 3 Effect of CT result on smoking abstinence in the entire population

	Smoking Abstinence per CT Result (%)	**AOR (95%, CI)**
Entire Cohort (n=426)		
No CT (n=128)	20/128 (15.6%)	- Ref
CT Negative (n=186)	36/186 (19.4%)	1.02 (0.53- 1.96)
CT Positive (n=112)	14 (12.5%)	0.66 (0.30-1.46)
Entire Cohort SCS arm (n=215)		
No CT (n=69)	12/69 (17.4%)	- Ref
CT Negative (n=102)	22/102 (21.6%)	0.95 (0.40-2.23)
CT Positive (n=44)	9/44 (20.5%)	0.94 (0.33-2.74)
Entire Cohort UC arm (n=211)		
No CT (n=59)	8/59 (13.8%)	- Ref
CT Negative (n=84)	14/84 (16.7%)	1.02 (0.35-2.90)
CT Positive (n=44)	5/68 (7.4%)	0.40 (0.11-1.46)

AOR= Adjusted Odds Ratio (adjusted for age, sex, IMDQ and QuLIT trial) CI= Confidence Interval
No CT= Participant didn't meet CT scan risk criteria according to the Prostate, Lung Colorectal and Ovarian Screening Trial and the Liverpool Lung Project models
CT Negative= Results were clear, did not show evidence of nodules or incidental findings
CT Positive =Nodules requiring 3,6, or 12 month follow up scan, suspicious lesions, nodular consolidation, or incidental findings

5.4.2 Individual study outcomes

5.4.2.1 QuLIT1 12 and 28-month study outcomes

In QuLIT1 (face to face) both seven day self-reported and (28-month) CO verified smoking abstinence were numerically higher in the intervention arm, but the difference was not significant; [(seven-day self-reported cessation, SCS: 16/63 (25.4%) vs UC: 8/49 (16.3%), (AOR: 1.66, 95% CI 0.64-4.29)] 28-month CO verified cessation, [(SCS: 4/63 (6.3%) vs UC: 1/49 (2.0%), (AOR: 3.13, 95% CI 0.33-28.92)]. Results were similar for quit attempts [SCS: 11/47 (23.5%) vs UC: 8/41 (19.5%), (AOR: 1.41, 95% CI 0.51-3.89)].

Table 5. 4 Smoking cessation in QuLIT1 cohort

Smoking abstinence for all randomised participants (ITT) (n=112)	**Smoking Cessation intervention (n=63)**	**Usual Care intervention (n=49)**	**AOR, 95% CI**
7-day self-reported Cessation	16/63 (25.4%)	8/49 (16.3%)	1.66 (0.64-4.29)
CO Verified Cessation (28-month)	4/63 (6.3%)	1/49 (2.0%)	3.13 (0.33- 28.92)
Smoking quit attempts for all randomised participants who are still smoking	**(n=47)**	**(n=41)**	
Unsuccessful	11/47 (23.5%)	8/41 (19.5%)	1.41 (0.51-3.89)
No attempt	36/47 (76.5%)	33/41 (80.5%)	-

AOR= Adjusted Odds Ratio (adjusted for age, sex and IMDQ), CI= Confidence Interval
Quit attempts = attempt to stop smoking that lasted for one day, data is presented as the number of individuals who made at least one quit attempt during the previous 12-month period.

5.4.2.2 QuLIT2 12-month study outcomes

In QuLIT2 (telephone support) population, self-reported cessation was again numerically higher within the intervention arm [SCS: 27/152 (17.8%) vs UC: 19/162 (11.7%), (AOR: 1.62, 95% CI 0.86-3.06)], but this difference was not significant. However, CO verified quit rates were significantly higher in the SCS arm; [SCS: 22/152 (14.5%) vs UC: 9/162 (5.6%), (AOR: 2.87, 95% CI 1.28-6.46)], as were quit attempts [SCS: 41/125 (32.8%) vs UC: 12/143 (18.1%), (AOR: 2.19, 95% CI, 1.24-3.86)], table 5.5.

Table 5. 5 Smoking cessation in QuLIT2 population

Smoking abstinence for all randomised participants (ITT) (n=314)	**Smoking Cessation intervention (N=152)**	**Usual Care (N=162)**	**AOR, 95% CI**
7-day Self-Reported Cessation	27/152 (17.8%)	19/162 (11.7%)	1.62 (0.86-3.06)
CO Verified Cessation	22/ 152 (14.5%)	9/162 (5.6%)	**2.87 (1.28-6.46)**
Smoking quit attempts for all randomiesd participants who are still smoking	**(n=125)**	**(N=143)**	
Unsuccessful	41/125 (32.8%)	26/143 (18.1%)	**2.19 (1.24-3.86)**
No Attempt	84/125 (67.2%)	117/143 (81.9%)	-

AOR= Adjusted Odds Ratio (adjusted for age, sex and IMDQ), CI= Confidence Interval
Bold Type= statistically significant at 0.05
Quit attempts = attempt to stop smoking that lasted for 1 day. Data is presented as the number of individuals who made at least one quit attempt during the previous 12-month period.

5.4.3 Effect of CT result on smoking cessation among QuLIT1 and QuLIT2 cohorts separately

As in the main analysis, quit rates did not differ in QuLIT1 or QuLIT2 between those who were or were not eligible for a CT scan based on their initial assessment, nor between those with a normal or abnormal scan, table 5.6.

Table 5. 6 Effect of CT result on smoking abstinence in QuLIT1 and QuLIT2 cohorts separately.

	Smoking Abstinence per CT Result (%)	**AOR (95%, CI)**
QuLIT1 (n=112)		
No CT (n=17)	3/17 (17.6%)	- Ref
CT Negative (n=71)	19/71 (26.8%)	1.96 (0.45- 8.48)
CT Positive (n=24)	2/24 (8.3%)	0.58 (0.07-4.72)
QuLIT2 (n=214)		
No CT (n=111)	17/111 (15.3%)	- Ref
CT Negative (n=115)	17/115 (14.8%)	0.78 (0.36-1.69)
CT Positive (n=88)	12/88 (13.6%)	0.65 (0.27-1.57)

AOR= Odds Ratio (adjusted for age, sex and IMDQ), CI= Confidence Interval
CT= Computed Tomography
No CT= participant did not meet the risk eligibility criteria
CT Negative = no evidence of nodules or incidental findings
CT Positive= evidence of nodules requiring 3, 6, or 12 month follow up scan, suspicious lesions, nodular consolidation, or incidental findings

5.5 Discussion

5.5.1 Main findings

The main finding of this study is that offering immediate enrolment into smoking cessation support, including the provision of pharmacotherapy as appropriate, is associated with a sustained increase in biochemically confirmed quit rates at twelve months. This is when compared to usual care provision of VBA to quit and signposting to smoking cessation services.

5.5.2 Findings in context

It was apparent from the findings of the QuLIT1 and QuLIT2 trials that smoking cessation support interventions delivered during TLHC increase quit rates in the short term (Buttery 2022; Williams 2023b). However, a criticism was that the intervention might only be bringing forward quits and that the usual care arm would catch up over time, meaning that the overall health effect was modest. The data presented here do not support this criticism, instead they show clearly that the difference in quit rates is sustained in this population out to at least a year.

The systematic review and meta-analysis in Chapter 3 concluded that providing smoking cessation support interventions in the context of lung cancer screening may increase quit rates compared to UC and suggest that more intensive smoking cessation interventions are likely to be more effective (Williams 2023a). However, there are several issues related to these conclusions which the present study addresses. The QuLIT trials are distinct from other interventional studies to date; firstly, all people who attended an initial TLHC were included, not just those who met the criteria for LDCT. The TLHC itself is a complex intervention, the initial consultation includes a review of smoking history which may provoke behaviour change contemplation in some participants even if they do not meet the risk threshold for CT

scanning. Secondly, the studies provided the cessation intervention immediately after attendance at a TLHC. In the case of QuLIT1, the participants were directed to the smoking cessation advisors after they had seen the TLHC nurses. In QuLIT2, smoking cessation advisors called the participants as soon as they had finished their telephone TLHC consultation. In other studies, the intervention has been delayed which may have reduced the immediacy of the teachable moment (Taylor 2022; Taylor 2017; Tremblay 2019; Masiero 2019). Among studies included in the review in chapter 3 (Bade 2016b; Pistelli 2020) compared quit rates in people who took up an offer of smoking cessation with those who did not, which represent two distinct populations.

I did not find any difference in effect based on eligibility for CT scanning or CT scan result, as reported among previous trials (Clark 2004a; Taylor 2017; Pistelli 2020). This may suggest that the comprehensive approach that we adopted, offering support to all TLHC participants, is justified. However, I did observe numerically higher quits among smokers who received a negative CT result. This was observed across the entire cohort (19%), entire cohort SCS arm (21%), entire cohort UC arm (16%) and QuLIT1 population (26.8%). As discussed in the previous chapter, smokers reporting increased quit rates with negative CT results have been observed (Taylor 2022). However, many of the large screening trails did observe increased quitting behaviour among smokers who had to attend for follow up scans or incidental findings (Tammemägi 2014; Brain 2017). As the present study explored longer term smoking outcomes (12-28 month), with 26% of the study population receiving a positive CT result. Finding no effect based on CT results is surprising, and contradictory to the qualitative findings in the subsequent chapters. Nonetheless, as highlighted in the discussion section in chapter 4, the current study may have been underpowered to detect change between CT outcomes.

The data from this analysis is suggestive that telephone smoking cessation support delivered within a lung screening setting may be a more effective intervention, compared to the more traditional in-clinic intervention. It should be noted that there was no direct comparison of the two QuLIT trials and both QuLIT1 and QuLIT2 observed numerically higher quit rates at 12 months within their intervention arms compared to usual care. However, QuLIT2 CO verified quit rates demonstrated statistical significance. The use of telephone delivery models for smoking cessation in a screening context have been explored previously. Taylor et al, 2017 randomised 92 smokers who had attended a LCS to either six sessions of telephone cessation support or usual care. The researchers observed significantly higher three month biochemically quit rates within their intervention arm (UC: 4.3% vs. SCS: 17.4%) (Taylor 2017). The same research group examined the intensiveness of a telephone-based cessation intervention in a screening context. Their intervention consisted of eight 20-minute phone sessions and eight weeks of NRT, compared to their minimal arm which was three 20- minute phone sessions and two-week supply of NRT. Three month quit rates were significantly higher with the intensive arm compared to minimal arm, for both self-reported (14.3% vs 7.9%) and bio-verified quit rates (9.1% vs. 3.9%) (Taylor 2022). The authors however, found no significant difference between study arms with quit rates measured at 12 months. Suggesting that in the case of lung cancer screening, telephone-based cessation modalities prove effective in the short term. I have discussed within the previous chapter, the wider cessation literature comparing remote to face to face interventions (Naja 2023; Nomura 2019), with many studies reporting comparable quit rates and uptake between face to face and telephone-based interventions (Berndt 2017; Berndt 2014). While face-to-face approaches will remain to be effective and should be offered to participants, the effectiveness of remote telephone-based interventions should be noted. Particularly for participants who may live in

rural areas or may have limitations on access to transport or mobility (Nomura 2019). It may be the case that offering a tailored approach, with both face to face and remote options for smoking cessation, may be most effective for delivery within a LCS setting. As conducted successfully within the YESS trial in Northern England (Murray 2024).

5.5.3 Methodological considerations

In both QuLIT trials I enrolled all current smokers who attended their initial TLHC appointment, regardless of motivation to quit and CT eligibility. This allowed me to assess the intervention's impact among the entire screened population, not only those who met the CT risk criteria and/or motivated to quit smoking. The study was designed as such to provide as little divergence from the normal TLHC clinic process, or patient experience as possible (apart from providing the SCS), which increases the generalisability of the findings. Randomisation was by day of attendance, and the requirement for individual consent was waived because the consent process itself would have constituted an intervention and introducing selection bias reducing confidence in the results. Finally, I was able to perform biochemical verification of self-reported quitting, which increases the validity of the results.

There are, however, specific limitations that need to be addressed. First, there was loss to follow up (29%), though this was similar in magnitude to other studies within the field (Clark 2004a; Masiero 2019). However, by using a conservative approach, i.e. if all participants lost to follow up were continuing to smoke. I may have underestimated the impact of the intervention. Second, there are possible effects of the COVID-19 pandemic which might impact on generalisability. However, quit rates in the usual care arm were similar in QuLIT1 (pre-pandemic) and QuLIT2 suggesting that standard care was not impacted. Third, considering the two trials separately, the impact of the intervention at 12 months appeared to be greater for telephone than for face-to-face delivery. This seems unexpected, but caution

is needed as the two approaches were not directly compared and the sample size in the telephone study was almost three times larger, reducing the effect of chance. Fourthly, the longer term follow up (28-month) among the QuLIT1 population. As stated in the methods section due to pandemic restrictions on face-to-face clinics, CO verification in this case equated to 28-month follow up. This method may have missed participants who may have quit between 12 and 28 months, underrepresenting the true number of successful quitters. Alongside making it harder to directly compare the CO verified quit rates between the two QuLIT studies. Finally, the most deprived quintile of deprivation in the sample was under-represented. This may impact on generalisability but also highlights the need to support this group to engage with lung health screening.

5.6 Conclusion

Providing immediate SCS, in the context of a targeted lung health check appointment, with pharmacotherapy is successful at increasing longer term (12-month) self-reported and CO confirmed smoking quit rates among this high-risk population. Providers of TLHCs should ensure smoking cessation provision is integrated into the service, tailoring options for delivering this systematically to the population they serve. Future research should focus on the direct comparison between face to face and remote smoking cessation delivered within a LCS context, to best answer the question of most effective modality.

Chapter 6: Exploring patient experiences of smoking cessation support during targeted lung health checks: a qualitative study.

6.1 Introduction

Previous chapters in this thesis have investigated the effectiveness of delivering immediate smoking cessation support within lung cancer screening programmes. These studies suggest that offering comprehensive smoking cessation support within a lung screening clinic at least doubles the quit rate compared to very brief advice to quit and signposting to local services (Buttery 2022; Williams 2023b). However, little is known about the participant experience of these interventions, particularly their views and experiences of combining cessation support with the TLHC screening programme. In this Chapter I present a qualitative analysis of the participant experience of smoking cessation support within a TLHC setting, using the McBride TM in smoking cessation as the grounding theory.

6.2 Background

The QuLIT1 trial, utilised a mixed methods approach and investigated the effectiveness of smoking cessation support within a TLHC in West London. Alongside increased quit rates among smokers who were randomised to receive cessation support, the researchers conducted a qualitative analysis on participant quotes. The qualitative data was collected during the three month follow up telephone call, this qualitative analysis primarily focused on the patient experience of the study and their opinions on combining cessation support within the TLHC service, alongside if they would recommend these services (Buttery 2022). The researchers discovered four main themes in the qualitative data. The first theme focused on the patient reported barriers to cessation in this context. Patients cited they were unable to quit or stay abstinent due to psychological barriers including stress and anxiety. The second

theme was the influence of the COVID-19 pandemic on the patient experience. This included how patients cited they quit because of the pandemic, some were unable to source their smoking cessation medication due to the lockdown, alongside COVID-19 barriers to quitting such as isolation due to the lockdowns. The third theme relates to the TLHC itself and how the CT scan influenced smoking behaviour. Patients cited that going for the CT scan made them reevaluate their smoking behaviour, reporting they quit due to their CT result being positive or negative. The final theme focused on how the participant's individual beliefs about how to quit smoking influenced their experience of the study. This included how some patients believed they could only quit if this was unassisted, or it wasn't the correct time to quit. However, patients also reported how they believed smoking cessation support provided within the TLHC setting was useful and they would recommend it (Buttery 2022).

There have been several qualitative studies within lung cancer screening, however these trials focus primarily on patient and clinician acceptability of integrating smoking cessation into screening programmes (Groves 2022; Golden 2020). As opposed to exploring the participants' experiences of attending smoking cessation with lung cancer screening. There has been a recent qualitative study exploring the patient facilitators and barriers of engaging with smoking cessation support in the YESS trial (Smith 2023).

The qualitative findings reported in the QuLIT1 trial are useful in beginning to understand the participant experience, however, these were collected from participant quotes gathered during the short 5–10-minute interview to collect primary endpoint data limiting the depth of the thematic analysis. Given the gap in the qualitative literature focused on the participant experience, I undertook the current qualitative investigation. The aim of the present study was to explore the participant experience of receiving smoking cessation interventions within

a TLHC. I also wanted to explore to what extent the smoking cessation interventions act as and utilise a teachable moment for smoking cessation. The grounding theory underpinning this analysis is the McBride's 2003 Teachable Moment in healthcare theory, (McBride 2003) which has been described in greater detail in Chapter 2.

6.3 Methods

6.3.1 Study Design

I conducted a qualitative sub study among participants who were enrolled in the QuLIT2 trial, see chapter 4 for detailed description of the QuLIT2 trial. Inclusion criteria were 55-75 years of age, current smoker, had undergone a TLHC and were enrolled in the QuLIT2 trial. I recruited participants from both study arms of the QuLIT2 trial, as receiving VBA is an established smoking cessation intervention. All participants completed a verbal informed consent process before any interviews were conducted as per research ethics approval.

6.3.2 Participant recruitment

From July 2021- November 2021 all participants who were enrolled into the QuLIT2 trial were followed up three months post randomisation. The telephone consultations were primarily to collect data on current smoking status and quit attempts, (primary and secondary endpoints of QuLIT2). At the end of each follow up call the participants would be invited to attend a longer more in-depth interview. The participants were informed this would be about their experience and opinions of the interventions (convenience sampling). If patients expressed interest in participating in the interview, a participant information sheet was sent, and verbal consent was gained before the interviews were conducted. I initially recruited ten participants and conducted a primary analysis, as this had not reached saturation, a further six participants were recruited until saturation was achieved.

6.3.3 Data Collection

Interviews were conducted by me using a semi- structured interview guide which I created with support from Georgina Forden, a trainee clinical psychologist. (Appendix 1). The interview questions were guided by the four themes from QuLIT1 qualitative analysis and the desire to get a deeper understanding of the patient experience, as well as McBride's 2003 Teachable moment theory. The questions primarily focused on the participant experience of receiving either the immediate remote smoking cessation intervention or VBA and signposting (UC) and the TLHC process. We also included questions focused on understanding broader opinions of smoking cessation to give us a deeper context and understanding.

6.3.4 Data Analysis

The Interviews were conducted remotely either via the telephone or video conferencing software (Microsoft Teams or Zoom), recorded and then transcribed. The data was analysed using a reflective thematic analysis method, according to guidelines (Braun 2019) and conducted using NVivo 2.1 software. To ensure familiarisation and accuracy of the data I listened back to all audio recordings before coding was started. I led the analysis with assistance from Keir EJ Philip. Firstly, we used an open inductive coding approach, once the preliminary codes were created, I then created a codebook to organise the data which was shared. We then reviewed the codebook together and organised the codes into meaningful themes, we then met on several occasions to review the themes, thematic maps and agree upon the final themes that best represented the data (Bradley 2007). At each stage of the analysis, Keir EJ Philip and I compared the results, resolved discrepancies through discussion and collaboratively agreed upon the final themes within each content area.

6.4 Results

6.4.1 Sample Population

A total of 30 participants consented to be interviewed, however due to scheduling issues and drop out 16 participants were included in the final analysis. The average age 62.6 ± 5.6, 9 (56%) were male, 10 (62%) were randomised to the TSI arm, and 11 (68%) participants self-reported quit at three months. Please see table 6.1 for full participant demographics. Two of the participants who were randomised to receive the TSI intervention, declined that offer.

Table 6. 1 Participant Demographics

Age (mean ±SD)	62.6 (5.6)
Sex (%)	
Male	9 (56%)
Female	7 (44%)
Education	
Degree & Postgrad	5 (31%)
Some University	3 (18%)
A-Level or equivalent	2 (12%)
GCSE	1 (8%)
<GCSE	5 (31%)
Index of Multiple deprivation quintiles (IMDQ)	
IMDQ1- Most Deprived	3 (18%)
IMDQ2	3 (18%)
IMDQ3	3 (18%)
IMDQ4	3 (18%)
IMDQ5 -Least Deprived	4 (28%)
QuLIT intervention arm	
Telephone smoking intervention (TSI)	10 (62%)
Usual Care (UC)	6 (38%)
3-month smoking status	
7-day self-reported cessation	11 (68%)
Current smoking	5 (32%)

Data are presented as number (%) or mean ± Standard deviation.
****Index: quantile 1 = most deprived areas in England, quantile 5 = least deprived areas in England***
GCSE=General certificate of secondary education

6.4.2 Thematic Analysis Results

Three main themes were constructed from the thematic analysis. The themes relate to the participant experience of the combination of services and how their personal factors shape and influence their experience. Theme 1) Supportive and motivating smoking cessation support. This first theme focuses on the experience of the smoking cessation support. Theme 2) The synergistic interaction between the smoking cessation support and the TLHC. This theme focuses on how participants experienced and viewed the combination of services. Theme 3) Modulating effect of past experiences and promoters shaping the experience. This final theme focuses on how individual factors shape the participant experience. The themes are described in greater detail below, including participant quotes identified by participant age bracket, trial arm and smoking status, to ensure anonymity. Figure 6.1 represents the thematic map containing the three main themes and sub themes within the data.

6.4.2 Theme 1: Supportive and motivating smoking cessation support

The first theme in this analysis focuses on the supportive and motivating environment the cessation support created. Patients cited that the supportive and motivating nature of the support directly led to successful quitting, increasing their motivation to quit and continue with support. When viewed in relation to the McBride model, these positive experiences elicited positive emotional responses (McBride 2003), thus increasing motivation to quit.

"The smoking nurse was so supportive, and I felt like I could talk to her about when I was finding things hard, and she would support me through it all" (50s, TSI arm, quit smoking).

Participants reported that the cessation support acted as a guide through their personal journey from smoker to non-smoker. This was in relation to the initial decision-making

process, aiding with pharmacotherapy choices and providing continual motivation for behaviour change.

"I think the talk is quite important because we did discuss various options and spoke about behaviours" (50s, TSI arm, quit smoking)

"Every week she and she made an appointment that you know I will call you at 10:00 o'clock on next Thursday or whatever we agreed that time and then she'd spend that time and she was persistent in a sense that she followed through on everything" (60s, TSI arm, quit smoking).

The participants also highlighted how they felt the smoking cessation support was very person centred, that the information and support they received was tailored to their specific needs, which was important to them.

"That worked really well and also having lots of choices with the different aids to help quitting and being able to have the telephone calls when I wasn't busy, It all worked around what I wanted to do and when I could do it" (60s, TSI arm, quit smoking).

Participants reported that the combination of supportive behavioural support and pharmacotherapy such as varenicline or NRT increased their motivation to quit and stay abstinent.

"so I went at that time with the patches on as the same time as the phone calls, yeh and I did all that and I've never looked back, I've been smoke free for well over three months now (60s TSI arm, quit smoking).

The participants reported that the cessation support was delivered in such a way that wasn't stigmatising. Participants stated that they didn't feel they were getting scolded too, which they had previously experienced from healthcare services.

"one thing I appreciate as well. It was never lecturing, you know? Yeah, get too much lecturing. And frankly, smokers don't need lecturing because there's no one who smokes doesn't realise it's bad for you". (50s, TSI arm, quit smoking)

Supportive and I would say a mature approach cause there's there's so many doctors and dentists, they're the worst. (60s, TSI arm, quit smoking)

However, some participants had critiques of the intervention and suggestions for improvements. Some of those interviewed participants suggested a more aligned approach with the lung health check itself.

"I think having the smoking nurse talk though a bit more about the CT scan and what that means would be good" (60s, TSI arm, quit smoking).

Participants who were randomised to the usual care intervention, which consisted of very brief advice to quit and signposting to local cessation services, reported difficulties in accessing their local cessation services, despite a desire to quit. This is reflected in the three month follow up data from the QuLIT2 study whereby only three participants accessed local support in the UC arm.

"Well, yeh they gave me the spiel about how smoking is bad for my health and that, but I kinda tuned out cause I know what I need to do" (60s, UC arm, still smoking)

They gave me the NHS smoking website links and referred me to the local place, but when I called them, they said they don't offer quit smoking help no more which was really disappointing" (50s, UC arm, still smoking).

6.4.3 Theme 2: Synergistic interaction between the smoking cessation support and the TLHC.

The second theme reflected in the data was how patients viewed and experienced the combination of services, including participants' views and opinions about embedding of smoking cessation support within lung cancer screening services. This is alongside how these services alone or combined influenced quitting behaviour and influenced the teachable moment. When viewed in relation to the McBride TM theory this theme is likely to increase perceptions of personal risk and prompting strong emotional responses (McBride 2003).

Participants cited that they thought the combination of the smoking cessation support and the lung health check setting was a good environment for people wanting to quit.

"I think getting the scan then the support is excellent really. I wasn't thinking about quitting at all before having the appointment. It was just at that point when the nurse said would you like to get some help to quit." (60s, TSI arm, quit smoking)

The timing of the intervention was a key factor for many participants. Many of the interviewees highlighted the importance of receiving the cessation support immediately after their TLHC appointment was a contributing factor to their successful quit, mirroring what previous data has suggested that the TLHC appointment may act as a teachable moment for cessation support.

"The call came at the right time really as just having the chat to the nurses the day before about your lungs and smoking, it does make you think about your smoking and that you

should quit, so getting the call the day after is good cos you are kind of thinking about stopping" (50s, TSI arm, quit smoking).

"I think the immediacy after a lung check of being vulnerable is a very good, good thing" (70s, TSI arm, quit smoking).

Patients who received the intervention cited how they preferred the remote option; both for the initial TLHC call and the cessation intervention. This was particularly important for participants, considering many healthcare services had stopped in this period because of the pandemic.

"I thought that was good as covid has stopped so many things and this was something they haven't stopped" (60s TSI arm, quit smoking)

Patients also highlighted how they liked the remote delivery of the pharmacotherapy, that the service was quick, free and made it easy for them to quit.

"So yeh, I went for the gum and patches actually and that was good as the lady sent them in the post and they came pretty quickly. I think it's great that you get all these things delivered in the post for free and that" (60s TSI arm, quit smoking).

For some participants the TLHC appointment itself elicited an emotional response, causing them to think more deeply about their smoking behaviours, leading to possible behaviour change, which is consistent with McBride's TM in smoking cessation model (Lawson 2009; McBride 2003).

"Yeah, it did make me think about it, as I said I have cut down and switching to the roll ups" (60s, UC arm, still smoking).

"On the way back from the scan really made me think that I need to quit. I was sitting in the car thinking it is really stupid that I still smoke." (50s, UC arm, still smoking).

Results from the LDCT also had a direct impact on our participants' smoking behaviours, with participants reporting they quit or reduced the amount they smoked due to their CT result. This suggests that the CT result itself may act as a teachable moment for smoking cessation.

"getting those results, I guess it was a trigger and then I just gave up like" (50s UC arm, quit smoking).

Participants cited they were glad they received the cessation support alongside receiving their result, that the results reaffirmed their decision and motivation to quit smoking.

"Well, it really just confirmed what I was already thinking about, that I needed to quit, and this was the best time to do it really," (50s, TSI arm, quit smoking).

For some participant's the negative emotions they experienced whilst waiting for their CT results, acted as a cue or motivator for smoking behaviour change. They cited these concerns were mediated by receiving the smoking cessation support, again reaffirming their decision.

"But actually waiting for the results made me feel a bit worried because of all the smoking, so it was a good thing I'd decided to quit with the help offered" (60s TSI arm, quit smoking).

A few participants, however, reported that these feelings of anxiety had the opposite effect causing them to smoke.

"And leaving the appointment you have that bit of worry about what the scan might show up and then that can make you reach for the cigarettes" (60s UC arm, still smoking).

Among participants who attended their TLHC and offered onward cessation support were unable to quit smoking, there was an overall impression that even though the TLHC made them think about their smoking behaviours, they were still unable to quit.

"***Yeh, you know it make me think about my smoking and that, after the phone call before the scan and the nurse actually referred me for it the smoking therapy near me, but I just never went for it, it's silly really but quitting you know, it's just so hard" (50s, UC arm, still smoking")***

6.4.4 Theme 3: The modulating effect of past experiences and personal promoters shape experiences.

The final theme in the analysis centres on how participants past experiences and personal promoters influence their experiences of smoking cessation support within TLHCs. This theme focuses on how the participants past experiences and their motivation may shape how they respond to the cessation support and the TLHC, alongside focusing on how participants self-motivation and reported barriers influences a smoking cessation behaviour change.

Patients reported on previous quit attempts, which in this context was used as either a facilitator or barrier for smoking behaviour change.

"I have done it before, I quit for 11 years so I know how to do it and what it feels like" (50s TSI arm, still smoking).

"Thought I might as well, go for it you know, I'd tried to quit a few times before and I quit for a few weeks then just started again" (60s, TSI arm, quit smoking)

Patients cited both internal and external motivators that aided their cessation experience, which were not a direct consequence of the cessation support or TLHC.

"I just really want to live a little bit longer, that's what it really comes down to you know" (50s, UC arm, quit smoking).

"I dunno really, I think money wise really" (60s, TSI arm, Quit Smoking)

Patients also highlighted how the process of quitting with the support and then receiving the scan increased their internal motivation to stay abstinent.

"Then also getting the scan results after I'd quit it's like an extra bit of motivation" (60s, TSI arm, quit smoking).

It was evident that some participants had a high perception of risk regarding smoking behaviour. There was an understanding that participants were aware of the dangers of smoking and their risk of lung cancer and for some participants this acted as a promotor to quit and accept cessation support.

"That little thing in the back of your head saying you should quit, and how stupid it is. Then the next day you get a call, and someone is going to help you quit it all kind of works together" (50s, TSI arm, quit smoking)

However, for some participants despite a high perception of risk, this did not always translate to changes in smoking behaviours.

"I know it's bad but tried to quit before and put on weight. I'd rather just risk the 5 fags" (60s, UC arm, still smoking).

Alongside patient identified promoters to quit smoking, many of the participants also identified barriers to quitting. These barriers included the perceived difficulty in quitting as well as psychological barriers.

"But then aahgh it's just so hard to stop it's like a block" (60s, UC arm, still smoking).

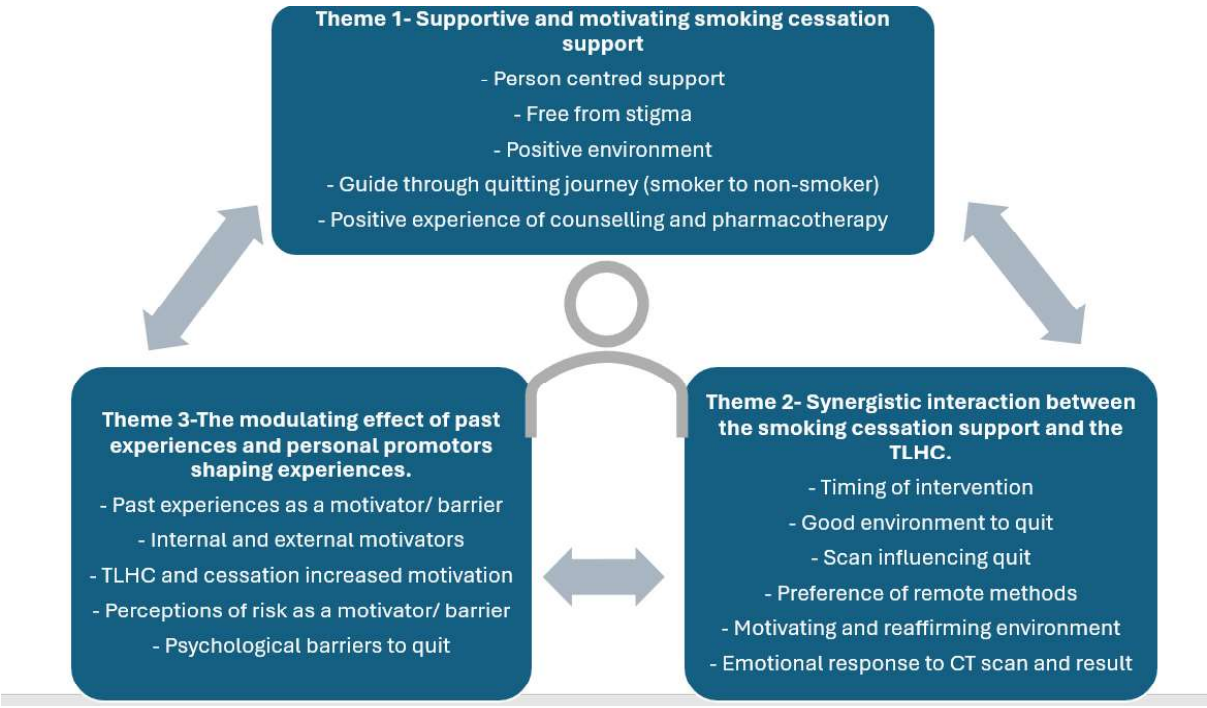
"But I think most smokers actually do want to give up smoking. It's just the difficulty of doing it" (60s, TSI arm, quit smoking)

Psychological barriers were also cited by our participants, in particular anxiety and depression. Often these participants stated they used smoking as a coping mechanism to help with unpleasant feelings.

***"Next day you have a difficult moment and you're like you know what I'm going to go out and have a cigarette"* (50s, UC arm, still smoking).**

***I feel depressed then I go for the cigarettes and then I do try and then I might be okay for a day or something* (60s, UC arm, still smoking).**

Figure 6. 1 Thematic Map



6.5 Discussion

6.5.1 Main findings

The main findings of this qualitative analysis were that participants who received the intervention reported that the support was both supportive and motivating. Participants reported on the synergistic interaction between the cessation support and TLHC and how this increased motivation to quit. Finally, the data also highlighted how the individuals past experiences and promoters influenced their experience of smoking cessation support within a TLHC.

6.5.2 Findings in context

These findings are consistent with other lung cancer screening qualitative analysis, particularly the first QuLIT trial (Buttery 2022), which note the influence of the CT scan on smoking behaviours, and multiple external and internal barriers regarding cessation in this setting.

Groves and colleagues, interviewed 31 lung cancer eligible patients about their views on integrating smoking cessation into screening clinics, reported positive views regarding the embedding of smoking cessation into lung cancer screening (Groves 2022). As within the current study and within much of the qualitative research within smoking cessation, barriers and facilitators to uptake have been reported. These barriers to cessation have been observed within a wide range of populations from prenatal and neonatal women, people from deprived areas and within patients accessing clinical cancer care (Flemming 2015; Murray 2009; Roddy 2006; Quinn-Scoggins 2022; Wells 2017). The recent qualitative analysis of participants in the YESS trial report significant barriers to accepting smoking cessation support within LCS, particularly physical and psychological barriers and perceived effectiveness of cessation support (Smith 2023). These data alongside the current study, highlight there are significant

specific barriers to cessation among smokers attending LCS, which need to be examined further, chapter 7 in this thesis will address this issue.

Understanding and designing smoking cessation interventions within a screening context, using the teachable moment as a grounding theory was utilised by (Meltzer 2019). They conducted focus groups with 15 current smokers who recently attended lung cancer screening. The aim of which was to develop a smoking cessation intervention within lung cancer screening in the US, their key findings also mirror the current analysis. Among the interviewed participants, they cited a change in perceived risk after the CT scan eliciting change in smoking behaviour. Additionally, there was an emotional response with regards to the screening appointment, including relief after getting negative results or feelings of anxiety while waiting for scan results. Of note, several of their participants identified getting a negative CT scan as a licence to continue smoking, which has been discovered within the wider literature (Golden 2020), but not identified within this data. Their data also reported significant benefits and barriers to smoking cessation within a screening context, as echoed in the current and previous analyses. Interestingly (Hagerman, 2015) observed a divergence within their focus group participants in terms of the licence to smoke effect, some participants cited that a clear CT or positive CT would encourage cessation. However, several participants stated that they would continue to smoke after receiving a clear CT result (Hagerman 2015), illustrating the complexities of both the benefits and harms of screening.

Qualitative data from the current analysis and previous QuLIT1 paper describes how participants quit due to positive or incidental findings (Buttery 2022). However, this was not reflected within both three and twelve-month outcome data from the two trials. Numerically higher quit rates were observed among participants who had recived a negative CT scan, both

within the short and long term follow up periods (Williams 2023b; Williams 2024). Within the discussion sections in chapters 4 and 5, discuss in depth why these findings may have occurred, possibly due to the studies lack of statistical power to detect change within this secondary outcome. However, given the qualitative data suggests that smoking behaviour is changing attributed to CT result, it is important not to disregard this effect.

6.5.3 Relation to the TM Theory

McBride's TM for smoking cessation proposes three conditions occur for a healthcare cueing event to elicit a smoking behaviour change. The first condition occurs when a healthcare event increases the risk perception and outcome expectations. The theory suggests that to prompt increases in motivation for cessation, individuals have to experience a direct increase of risk which overrides their optimistic biases related to smoking (McBride 2003). This condition also relates to the participants' expectation of the health outcomes. Either that quitting will lead to positive health outcomes or that continuing to smoke will lead to negative health outcomes (McBride 2003; Lawson 2009). The qualitative data from the present study demonstrated that patients reported their risk was increased through attending the lung health check. This was seen within theme two of the TA, patients cited they thought the cessation intervention occurring after they experienced the TLHC increased their motivation to quit, as the initial consultation made them more aware of their smoking risk. Patients also mentioned how the CT results and waiting for them increased their perception of risk leading to increased motivation to quit. Within theme three, patients' perception of risk was also highlighted as a motivation to quit and utilise the support.

The second condition in the TM theory occurs when the healthcare event elicits a strong effective or emotional response (Lawson 2009; McBride 2003). The model proposes that both negative emotional responses (fear, worry) or positive emotional responses (joyful, hopeful)

can elicit a smoking cessation behaviour change. Within theme one patients cited they experienced positive and supportive cessation support, likely eliciting a positive emotional response. This positive emotional response may have served as a strong cue to action, increasing motivation to quit. On the other hand, within theme two patients cited feelings of worry whilst waiting for their CT results. Fear has been suggested as a negative, but impactful emotion for behaviour change (Frijda 1986). Fear was also observed within theme three, as an internal motivator to quit among some of the interviewed participants.

The final TM condition focuses on how a change in social role and self-concept can influence cessation. The TM model suggests that healthcare events that trigger changes in the perceived norms, that decrease self-esteem related to smoking or make smoking incompatible with a social role, may be an optimal condition for smoking cessation behaviour change (McBride 2003). This was illustrated within theme one of the TA. Patients cited the supportive cessation supported and guided their journey from smoker to ex-smoker. The support directly influenced a change in social role and patients viewed themselves as non- or ex-smokers. Within theme two, patients also highlighted positive results influencing their decision to quit. Demonstrating that a positive scan may increase these patients' view that smoking is unacceptable for someone with a positive CT result, and thus increase motivation to quit as to limit any stigma.

Data from this qualitative analysis demonstrates that TLHC settings are likely teachable moments for smoking cessation and if cessation support is offered alongside TLHC's this may extend the impact of this teachable moment. This extension of the teachable moment may increase motivation for smoking cessation and acceptability of cessation support within this setting.

Contrary to this, a qualitative investigation into both clinicians and patients' perspectives on the initial lung cancer screening decision assessment, as a teachable moment for smoking cessation, concluded that the lung cancer decision assessment discussions were not teachable moments for smoking behaviour change (Golden 2020). This is likely attributed to the differences between the US based LCS assessment discussion and the UKs TLHC programme. The current USPSTF recommend screening for 50–80-year-olds with at least a 20-pack year history, which is slightly different to the UK TLHC criteria (55–75-year-olds, ever smoking on medical records). The US guidelines also state that if patients meet the above criteria and consent to be screened, a shared decision discussion regarding the benefits and harms of screening should occur (US Preventive Services Taskforce 2021). The US guidelines also indicate that smokers should receive cessation, however this only occurs for smokers who meet the above criteria for scanning (US Preventive Services Taskforce 2021). Again, which differs from the TLHC model whereby all smokers who attend the initial lung health check consultation should get smoking cessation input. In addition, the researchers observed that the standard smoking cessation delivery in the USA; (the 5 As for smoking cessation) was not conducted systematically within their lung cancer screening services.

6.5.4 Reflective statement

The thematic analysis approach used for the analysis was Bruan and Clarke's reflective thematic analysis. As per guidelines a reflective statement is necessary to ensure that the research judgments, beliefs and practices have been examined throughout the analysis (Braun 2023). I have worked within the NHS in respiratory medicine for over seven years, and previously within health and fitness. Due to my background, I have never smoked myself and have always had the view that smoking is bad for one's health. As this analysis is focused of

ex and current smokers' views of cessation support, it is important to be aware of how my personal background, beliefs and biases may have influenced the thematic analysis.

6.5.5 Methodological considerations

This study has multiple strengths. To our knowledge this is the first study exploring in depth the participant experience of smoking cessation interventions during a TLHC service, extending the previous findings within the QuLIT1 cohort. Much of the qualitative data within this area is focused on participants views and opinions on smoking cessation within LCS, but not their personal 'real-world' experience. Secondly, the use of semi-structured interviews enabled an inductive exploration of the data, whilst allowing the TM theory to ground the analysis. Thirdly, I was able to recruit a larger proportion of male's which is often lacking within healthcare qualitative research. The lack of participating males in qualitative research has been attributed to a possible lack of emotional expression and verbal communication skills among male participants (Affleck 2013). Despite this, the male participants interviewed within the current study provided insight and depth within their interviews. There are several limitations that must be addressed, the relatively small sample size needs to be highlighted. Despite reaching saturation of the data, I was unable to recruit more participants who had signposting and VBA (UC) intervention, and participants who were still smoking. This may have proved more varied experiences and insights, in addition to affecting the transferability of the findings. Secondly, there is likely to be an element of selection bias, participants who had a positive experience of the services may have been more willing to participate in research and share their experiences. It would have been interesting to interview participants who declined the cessation intervention or dropped out to explore their experiences.

6.6 Conclusion

It is apparent from the present analysis that embedding smoking cessation support within lung cancer screening extends the teachable moment for smoking cessation and is a positive experience as reported by many of the participants. However, providers need to be aware of the multiple personal beliefs and past experiences which may act as barriers to smoking cessation. Therefore, it is vital that smoking cessation support delivered within this setting is person centred, supportive and free from stigma to have the best chance of success.

Chapter 7: Exploring the barriers to accepting smoking cessation support within targeted lung health screening programmes: a mixed method approach.

7.1 Introduction

Throughout this thesis I have argued that smoking cessation support should be an integral part of the UK's TLHC program and that the support offered should be comprehensive, including both multiple counselling cessations alongside pharmacotherapy options. The use of intensive smoking cessation interventions, within a LCS setting is supported by data presented in this thesis, alongside published literature within the field (Taylor 2022; Murray 2024; Williams 2023a).

Data from the QuLIT1 qualitative analysis reported patient barriers to smoking cessation support, primarily psychological barriers and barriers attributed to COVID-19 (Buttery 2022). The qualitative analysis in the previous chapter, also mirrors these findings, specifically psychological barriers to quitting and past negative experiences affecting motivation to quit. Alongside patient reported barriers to quitting in this population, uptake of cessation support within LCS remains to be an issue. Data from the QuLIT2 trial highlighted that 52% of the 152 participants randomised to receive the smoking intervention, declined the offer and further 15 participants dropped out of the intervention. (Williams 2023b). This data, coupled with the qualitative data, suggest there are likely significant and specific barriers to accepting and continuing cessation support within a screening population.

The report into embedding cessation support into TLHCs highlighted the cost effectiveness of these interventions, and the large public health benefit (Beard 2022; Murray 2022). To ensure these services are as cost effective as possible, they need to be providing cessation support

to as many smokers attending TLHC's as possible. Therefore, it is vital that we understand why participants are declining cessation support in this setting, alongside recognising the demographics of these participants. In this chapter I present a mixed methods analysis, to understand the demographic predictors of accepting cessation support during LCS and exploring in depth, the patient reported barriers of accepting cessation support. I focused this analysis on the participants who were randomised to receive the intervention, but who declined at the initial TLHC or dropped out of the intervention.

7.2 Background

It is well established that attendance to smoking cessation increases the likelihood of quitting successfully (West 2013), despite this, smokers are not accessing this support. In 2011 the proportion of smokers in the UK attending smoking cessation services was around 5% (West and Brown 2012) currently it is around 0.8% of smokers (NHS England 2023). Barriers to accessing and accepting smoking cessation support have been widely cited within smoking cessation literature, particularly physical, psychological, and perceived effectiveness barriers (Murray 2009; Flemming 2015; Roddy 2006). Given that the smoking population eligible for LCS differ from the general smoking population, one can assume that their barriers to accepting cessation support likely differ.

The original QuLIT1 intervention, which used a mixed methods approach to investigate the effectiveness of smoking cessation support within the UKs LCS setting. Observed that participants cited psychological barriers such as stress and anxieties, and the influence of the COVID-19 pandemic as barriers to quitting smoking post lung cancer screening. A recent study, exploring the facilitators and barriers to accepting smoking cessation support within LCS, also discovered patient reported psychological barriers. As well as highlighting past

experiences and low self-efficacy as reasons why participants may have declined cessation support (Smith 2023).

As previously stated, over half of the QuLIT2 smokers randomised to receive the cessation intervention declined, thus, an in-depth analysis is warranted to explore why. Therefore, the aim of the present study is twofold, first to investigate demographic predictors among smokers who are more likely to accept smoking cessation support vs those who decline. Secondly, to explore, in depth the barriers and reasons why participants declined the smoking cessation intervention offered.

The theoretical model underlying this qualitative analysis is the COM-B model of behaviour change. The Capability, Opportunity, Motivation and Behaviour model is a framework of understanding behaviour as a system (Michie 2011). This model has been used extensively in health behaviour and smoking cessation research (Fulton 2016; Vijayaraghavan 2023). The model views behaviour as a system, with motivation at the centre, but both capability and opportunity constantly interacting with motivation to bring about a behaviour change (Michie 2011). I have described the model in greater detail in chapter 2. In the case of the present study, the COM-B model was chosen to guide the analysis and help to guide and understand the barriers in relation to behaviour change. This will enable clinicians to provide recommendations and adjustments on how to overcome these barriers and to aid in the design of interventions offered.

7.3 Methods

7.3.1 Study design

I used a mixed methods approach, firstly, using logistic regression models to determine demographic predictors of accepting the offer of smoking cessation support in the context of

lung cancer screening. Secondly, conducting a qualitative study to explore participant barriers to accepting smoking cessation support within the smokers who declined the intervention in the QuLIT2 study (chapter 4).

7.3.2 Participant recruitment

From April 2022 to August 2022 all participants who were randomised into the QuLIT2 interventional trial (Chapter 4) were followed up 12 months post randomisation. This 12 month follow up data is presented in chapter 5 of this thesis. At this follow up, participants who were randomised to receive the TSI intervention, but who had declined the intervention were invited to attend an interview. Only participants who had declined at the initial invite after their TLHC consultation or declined/ dropped out of the intervention were recruited, a participant information sheet was sent to all participants who expressed interest, verbal consent was gained before any interviews were conducted.

7.3.3 Data Collection

7.3.3.1 Quantitative analysis

The demographic data used in the models was collected during the participants initial targeted lung health check consultation. I used the data that was collected from participants who were recruited into the QuLIT2 trial within chapter 4 of this thesis.

7.3.3.2 Qualitative analysis

Interviews were conducted using a semi-structured interview guide (Appendix 2). The interview questions were focused on understanding participants' reasons for not accepting smoking cessation support, alongside their views and opinions on smoking cessation support more broadly. The interviews were conducted remotely either via telephone interview or video conferencing software (MS Teams) and lasted for an average of 45 minutes. I initially interviewed 10 participants and conducted preliminary analysis, as this had not reached

saturation. I then recruited and interviewed a further five participants, until saturation of the data was reached.

7.3.4 Data Analysis

7.3.4.1 Quantitative analysis

Five binary logistic regression models were performed to determine demographic predictors of accepting the offer of smoking cessation support in the context of lung cancer screening. To conduct the analysis the data was split into two groups, the participants that accepted and were enrolled onto the smoking cessation intervention (responders=1) and those who declined the offer of support or dropped out of the intervention (non-responders=2). Model one observed the effect of sex and age on intervention uptake, male was used as the reference category and age was a continuous variable. Model two observed the effect of education attainment, using <GCSE as the reference category. Model three observed the effect of index of multiple deprivation, using IMDQ 1 as the reference category. Model four observed the effect of smoking covariates, cigarettes per day, age started and smoking years (all continuous variables). Model 5 observed the effect of CT outcome, using no CT needed as the reference category. Age and sex variables were retained in all five models.

7.3.4.2 Thematic Analysis

The Interviews were conducted remotely, recorded, and then transcribed. Data were analysed using a reflective thematic analysis method. According to guidelines (Braun 2019), and conducted using NVivo 2.1 software. To ensure familiarisation and accuracy of the data I listened back to all audio recordings before coding was started. I lead the analysis with assistance from Sara Buttery and Nicholas Hopkinson. Firstly, we used an open inductive coding approach. Once the preliminary codes were created, I then created a codebook to organise the data which was shared. I then met with Sara Buttery to review the codebook together and organised the codes into meaningful themes and the second iteration of the

codebook was shared with the analysis team. Then all three researchers met on several occasions to review the themes, then finally to agree upon the final themes and sub themes that best represented the data (Bradley 2007).

7.4 Results

7.4.1 Predictors of acceptance of cessation support- Sample population

Demographic data from the TSI intervention arm in chapter 4 (QuLIT2) was used in the model. This included a total of 152 participants, average age 61.3 years, 58% male, majority white ethnicity and smoked an average of 12.5 cigarettes per day and is displayed in table 7.1.

Table 7. 1 Participant demographics used in regression models.

Characteristic	All Participants (n=152)	Accepted intervention (n=57)	Declined intervention. (n=95)
Age, y	61.3 (4.8)	60.1 (4.3)	62.0 (5.1)
Sex			
Female	68 (44%)	30 (52%)	38 (40%)
Male	84 (58%)	27 (48%)	57 (60%)
Ethnicity			
White	131 (86%)	45 (78%)	86 (90%)
Black	6 (4%)	3 (6%)	3 (3%)
Asian	9 (6%)	3 (6%)	6 (7%)
Other	6 (4%)	6 (10%)	0 (0%)
Education			
<GCSE	59 (38%)	19 (33%)	40 (42%)
GCSE	49 (32%)	18 (31%)	31 (32%)
A Level	17 (11%)	8 (15%)	9 (9%)
Some Uni	7 (4%)	3 (6%)	4 (4%)
Degree/ postgrad	20 (15%)	8 (15%)	12 (13%)
IMDQ			
1 (Most Deprived)	27 (21%)	6 (10%)	21 (22%)
2	56 (36%)	20 (36%)	36 (37%)
3	29 (19%)	15 (27%)	14 (15%)
4	21 (14%)	5 (9%)	16 (17%)
5 (Least Deprived)	19 (10%)	10 (18%)	9 (9%)
Smoking behaviours			
Average number of cigarettes per day	12.5 (7.7)	13.6 (7.9)	12.0 (7.6)
Age Started	18.0 (5.9)	18.5 (6.8)	17.6 (5.3)
Number of smoking years	40.9 (9.0)	39.4 (8.5)	41.9 (8.8)
CT result			
No CT needed	52 (34%)	23 (40%)	29 (30%)
CT Negative	60 (39%)	20 (35%)	40 (42%)
CT Positive	40 (27%)	14 (25%)	26 (28%)

Ethnicity groupings as recommended by the Prostate, Lung Colorectal and Ovarian Screening Trial (PLCO).

Index of multiple deprivation quantile (IMD), quantile 1= most deprived areas in England quantile 5= least deprived areas in England (IMD) (Ministry of Housing 2019).

Computed Tomography (CT)

CT positive = nodules requiring 3, 6 or 12 month follow up scan, suspicious lesions, nodular consolidation, or incidental findings.

CT negative = CT result was clear, no evidence of nodules or incidental findings.

No Scan needed = participant did not meet CT scan criteria according to the PLOC and LLP risk models

7.4.2 Predictors of acceptance of cessation support

Participants who accepted the offer of the smoking cessation intervention were more likely to be female [Accepted: 53% vs declined 40% AOR: 3.30, 95% CI 1.47-7.48]. Younger [AOR: 0.90, 95% CI 0.80-0.98], and more likely to live in areas of medium or low deprivation, [IMDQ3: Accepted 26% vs Declined 14% AOR: 3.79, 95% CI 1.17-13.47], [IMDQ5: Accepted 17%vs Declined 9%, AOR: 4.26, 95% CI 1.11-16.33]. Attaining education at A Level was also associated with accepting the offer of the cessation intervention compared to <GCSE level however this was not statistically significant, (table 7.2).

Table 7. 2 Demographic predictors of accepting cessation support

Variable	AOR	95%CI
Sex Female	**2.16**	**1.08-4.34**
Sex Male	Ref	Ref
Age	**0.90**	**0.80- 0.98**
IMDQ 1 most deprived	Ref	Ref
IMDQ 2	1.42	0.47- 4.31
IMDQ 3	**3.97**	**1.17- 13.47**
IMDQ 4	1.06	0.25-4.41
IMDQ 5	**4.26**	**1.11-16.33**
Cigarettes per day	1.03	0.99-1.08
Age Started	1.04	0.93-1.10
Smoking years	0.99	0.91-1.07
Education <GCSE	Ref	Ref
GCSE level	0.89	0.38-2.07
A Level	2.26	0.71-7.21
Some university	1.57	0.28-8.84
Degree/Postgrad	1.71	0.56-5.21
No CT	Ref	Ref
CT Negative	0.72	0.33-1.55
CT Positive	0.71	0.20-2.47

***Bold type denotes significance at the 0.05 level**

Index of multiple deprivation quantile (IMD), quantile 1= most deprived areas in England quantile 5= least deprived areas in England (IMD) (Ministry of Housing 2019).

Computed Tomography (CT)

CT positive = nodules requiring 3, 6 or 12 month follow up scan, suspicious lesions, nodular consolidation, or incidental findings.

CT negative = CT result was clear, no evidence of nodules or incidental findings.

No Scan needed = participant did not meet CT scan criteria according to the PLOC and LLP risk models

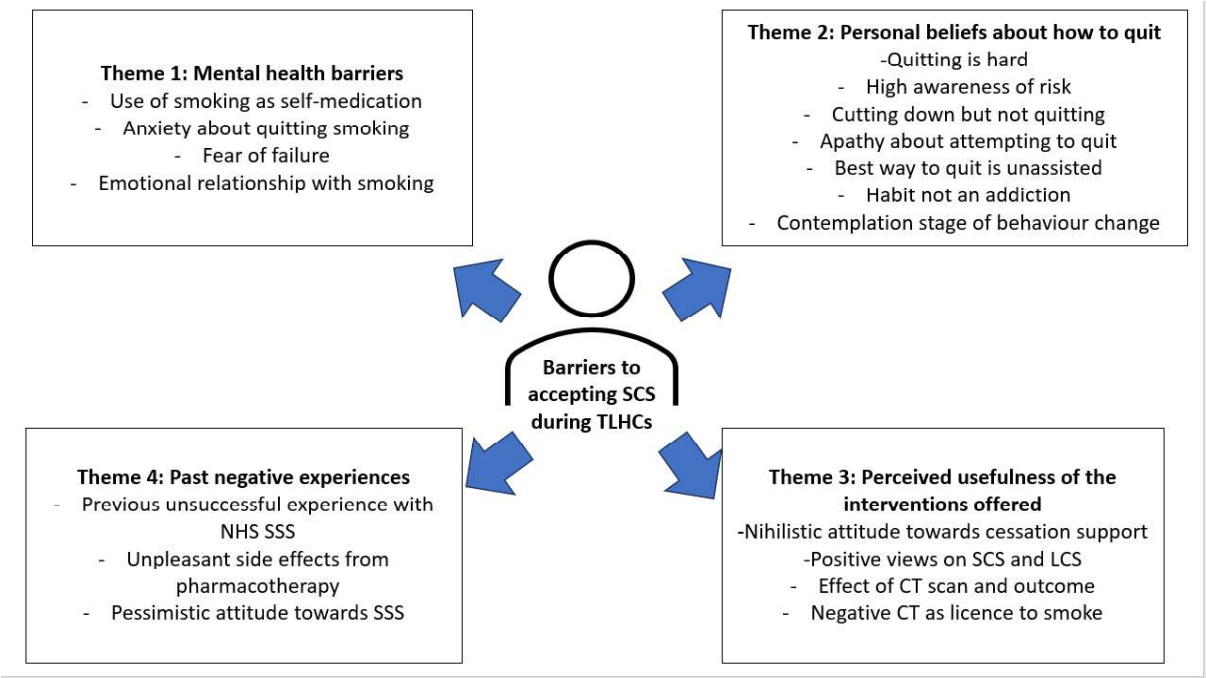
7.4.3 Thematic Analysis- Sample population

A total of 83 participants were invited to participate in the interviews as this was the number of participant's who either declined the intervention or dropped out and were not lost to follow up at 12 months. At the initial invite to participate in the qualitative study 50 participants declined to participate, 33 participants expressed interest and were sent the PIS, however due to scheduling and video conferencing software issues 18 of these participants dropped out. This left 15 full participant interviews that were recorded and analysed. Average age of the sample interviewed was 62.9 ±5.3 years, 53% male and smoked on average 16.0 ± 4.6 cigarettes per day; one participant had quit smoking within the 12 months since QuLIT2 recruitment.

7.4.4 Barriers to accepting smoking cessation support within lung cancer screening.

Four main themes were constructed from the thematic analysis, representing barriers to smoking cessation within a screening context. Theme 1: Mental health as a barrier, Theme 2 personal beliefs about quitting smoking, Theme 3: Perceived usefulness of the interventions offered and Theme 4: Past negative experiences of smoking cessation support. The themes are described in greater detail below, with participant quotes identified by participant age bracket and gender to ensure anonymity. Figure 7.2 represents the thematic map containing the three main themes and sub themes within the data.

Figure 7. 1 Thematic Map



7.4.5 Theme 1 Mental Health aspects as barriers

Mental health as a barrier to quitting and accepting the offer of support was highly cited by the participants interviewed. When we view this in relation to the COM-B model, it is apparent that mental health, in particular stress and anxiety, impacts both capability and motivation domains of behaviour change.

Many participants reported using smoking as a form of self-medication. This was to help them deal with life stressors, with many participants believing smoking is good for their mental health.

"It's the stress and then that effects the motivation to quit. I do know that I need to stop, but it's quite difficult to when you a feeling stressed, you can't really think about anything else. It's the one thing that helps me" (Female, 50s)

"because of my depression smoking helps me deal with things, it gives me a release when something upsets me or stresses me out" (Male, 50s)

Participants highlighted that when asked about quitting smoking these induced feelings of anxiety. The participants cited that they had either attempted to quit previously and started again due to their anxiety or felt anxious about the idea of stopping and never smoking again.

"But it causes a bit of worry giving up as I won't have the crutch anymore, and it just really helps me when things get hard" (Female, 60s)

"Yeh, I did quit for quite a long time actually before Covid and that, then everything just got worse with the depression and stress, so yeh I started again" (Male, 60s)

Within this theme, participants stated that if they tried a quit attempt, but failed this would elicit negative emotions. This may suggest that a fear of failure may be acting as a barrier to trying a quit attempt within these participants.

"I don't want to try and attempt something that won't work. You get used to failing and then it becomes commonplace, so why try." (Male, 60s)

The last sub-theme within the data, was that many of the participants appeared to have an emotional relationship with smoking, and this was a reason why they didn't want to accept the support offered.

"it's just more or less a comfort thing, it's the thing I reach for when things make me sad or happy." (Female, 60s)

7.4.6 Theme 2: Personal beliefs about quitting smoking.

This second theme focuses on how the individuals' personal beliefs and experiences impacts the decision to decline the smoking cessation support. This theme reflects and represents on

how an individual's beliefs and emotions likely influence both the motivation and capability domains of the COM-B model, resulting in behaviour change unlikely.

All participants interviewed reported on how they believed that quitting smoking is a hard and difficult process, particularly for people like them.

"But you've got to make sure they want the help coz quitting is hard for us and you have to want to stop" (Female, 60s).

"That it's just hell giving up, every day is hell" (Female, 60s).

Participants also reported that despite having a high awareness of risk from smoking and knowing the dangers to their health they continued to smoke and are unable to stop.

"I don't know what it is about smoking, and you know people have terrible problems with drinking and everything else. And I know the end result is not going to be good, and yet that doesn't seem to come into it somehow, it's just ridiculous really" (Female, 50s).

"Well, I have been diagnosed with COPD and I do cough quite a lot, certainly from a health point of view, my coughing would probably better if it stopped" (Male, 60s).

Several participants reported that they were using "natural cigarettes" or cutting down, as opposed to quitting and this was perceived as better for their health.

"I've got it all under control now, I've cut right down to 1 or 2 a day" (Male 60s).

Within the data, there was an overall sense of apathy from the participants about quitting or starting a quit journey, that they are either too old, or suck in their current behaviours to even attempt to quit.

"I just think it's not gonna work for me, I'm too much of a wuss to give it up" (Female, 60s).

"I'm in my 60s now, too old, too long in the tooth to try all that" (Male, 60s)

The participants also stressed the importance of being ready to quit, and this had to be cold turkey without any assistance. They believed that they would have to change their mindset and the way they thought about smoking to quit and that this was their responsibility.

"it's all about the willpower and mindset, I will quit and when I do, I will do it on my own terms, it's just about thinking of yourself as a non-smoker" (Male, 60s)

"I'm fairly idiosyncratic about it. I need to do it in my way, not someone telling me what I can and can't do" (Male, 50s)

Interestingly, many of the participants viewed their smoking as a habit as opposed to an addiction, and this may have contributed to their decisions not to accept the support offered.

"I think it's, it's more at a habit type thing where you associate smoking with day-to-day things, like I just go on the phone, light a cigarette, get in the car light a cigarette It's just this awful habit." (Female, 60s)

Finally, within this theme there were contradictions between the participants actions in terms of smoking, but they also stated they wanted to stop. Participants reported that they were just unable to quit smoking despite a desire to, or they would go as far as thinking about stopping, but that didn't translate into motivation for behaviour change.

"I do want to stop, and I do think I should, but that's it really that's all I do is think about it. I think that's it no more that's it and then I sit down and have a cigarette, it's like I block or something I just can't seem to stop." (Female 60s)

"I swear each time I go and buy a packet I say this will be my last pack, but it's like I don't

know" it just can't pack it in." (Female, 50s)

7.3.6 Theme 3: Perceived usefulness of the interventions offered.

The third theme focuses on how useful the participants viewed the smoking cessation support that was offered. Participants reported how they experienced both the TLHC appointment and how they viewed the combination of cessation support and LCS. The data included in this theme relates to the opportunity, and motivation domains within the COM-B model, particularly how participants viewed the cessation support as an opportunity to help them quit smoking.

It was apparent among the data, that despite many of the participants suggesting they thought cessation support is good and worked for some people, it wasn't useful or doesn't work for them. It was observed within the data that many participants displayed a nihilistic attitude towards cessation support.

"I think it kind of depends on the individual, for some people that's gonna, you know that's gonna work really well, but it just wouldn't for me." (Male, 50s)

"Well, I think if they work for you, they work, for me it just didn't get on with it all." (Male, 50s)

This was also apparent within how participants viewed the combination of smoking cessation and lung cancer screening. Many of the participants reported they thought the combination of services was a good idea, a good opportunity to quit, but it wasn't enough to motivate them to quit.

"Tell you the truth, at first yeah it did make me think about it, after the first telephone call, so yea of course it is a good idea to start the stop smoking stuff after that, and as I said I have cut down and switching to the roll ups." (Female, 60s)

Participants cited that the experience of the CT scan and receiving results, did make them rethink their smoking behaviour, however, this wasn't enough of a motivation to evoke a behaviour change. This was despite in some cases participants reporting a positive CT result.

"But it was really when they said I needed a second scan that I thought I really need to stop the cigarettes, but that's as far as it goes. I just think about how I should stop. I don't actually go as far as stopping or even trying to." (Male, 60s).

Worryingly, a few participants reporting that receiving a negative CT result, allowed them the opportunity to continue smoking, highlighting the licence to smoke effect, which was not discovered within the previous qualitative analysis in chapter 6.

"It was nice to know everything was okay and I thought well I can carry on doing that now, which is totally the wrong way round, you know it's, as I say mad mad." (Female, 60s).

7.4.7 Theme 4: Past negative experiences of smoking cessation support

The final theme within this analysis relates to how the participants past and mainly negative experiences of smoking cessation services influenced their decision to decline the support offered. Again, as with the first two themes, this final theme is likely influencing both the capability and motivation domains of the COM-B framework.

Each one of the participants interviewed reported previous quit attempts, with the majority reporting previous negative experiences of NHS stop smoking services as a reason for

declining the offer of cessation support during the trial.

"I think the problem I found with service was, yes okay I got some patches, which is just kind of like a small nicotine drip if you like, it didn't really help with stopping the habit, cause really effectively you feel like you are going cold turkey really. So, when the nurses were talking about the patches and that again over the phone, I just said no thanks cause it didn't work last time." (Female, 60s)

Participants also reported experiencing negative side effects from stop smoking pharmacotherapy, previously and they did not want to experience this again.

"And they gave me those patches to help me stop but they didn't work, and I just felt sick and was still smoking so it didn't work for me at all." (Male 60s)

Finally, as within the theme two, participants believed that smoking cessation services, didn't or don't work for them, highlighting a pessimistic attitude towards the smoking cessation services offered.

"That group thing just didn't and doesn't work for me, were to do it again, I would just do it my own way like I did before, cold turkey with no nicotine replacement." (Male, 60s)

7.5 Discussion

7.5.1 Main findings

The main findings from this analysis highlights that there are significant barriers to accepting smoking cessation support among smokers who attend TLHCs. These are mental health concerns, personal beliefs surrounding smoking, the perceived usefulness of the interventions offered and negative past experiences of smoking cessation support. This study also highlighted how female participants were more likely to accept the offer of SCS within a TLHC context as well as younger participants and those who live in areas with less deprivation.

7.5.2 Findings in context

Exploring facilitators and barriers to smoking cessation uptake in the Yorkshire lung cancer screening program have been explored. These findings mirror the current study and wider cessation literature, the authors observed smoking as a coping mechanism for psychological symptoms, past negative experiences of smoking cessation services, and fatalistic attitudes towards quitting as barriers to accepting smoking cessation support within a TLHC setting (Smith 2023).

Psychological barriers to smoking cessation, such as anxiety and depression for accessing smoking cessation services, have been previously reported in the qualitative analysis in the first QuLIT paper(Buttery 2022), within the previous chapter and within the wider literature. Psychological barriers such as stress and emotional events were reported among female smokers in the Netherlands and smokers with type II diabetes (Dieleman 2021; Georges 2019). The use of smoking as a coping mechanism and as a way to self-medicate have been reported as barriers for cessation, however this was among populations with serious mental health conditions (Keller-Hamilton 2019).

The desire for smokers to quit on their own way, and the belief that the best way to quit is unassisted has been explored and reported on previously. The belief that smokers should quit unassisted, cold turkey, as well as nihilism, previous negative experiences and views of smoking cessation pharmacotherapy were prevalent barriers to accessing smoking cessation support in the UK and Australia (Kale 2019; Morphett 2015). The barriers cited in this current analysis, and wider literature suggest that smokers may have a lack of knowledge or awareness about the benefits of specialist smoking cessation support, thus, underestimate the benefits of such programmes. The underestimation of the benefits of stop smoking support has been corroborated in earlier qualitative studies (Hammond 2004). Contrary to this, many of the interview participants had previous experiences of NHS specialist smoking cessation support and would have firsthand knowledge of the services but may have not experienced the benefits.

Sex differences in the uptake of smoking cessation services, is not uncommon. There have been previous studies reporting female smokers are more likely to access formal cessation support such as Quitline, healthcare counselling services and pharmacotherapy, compared with their male counterparts (Jayakumar 2020). This is also somewhat reflected in NHS England's smoking cessations statistics, whereby 53% of the people who set a quit date (accessed support) in 2023 were women (NHS England 2023). Lower smoking cessation success and uptake rates among populations living in less affluent areas have also been mirrored across the wider literature (Murray 2009; Brose 2016). This remains an important issue when it comes to both smoking cessation and LCS provision in the UK. It should be noted that the differences between the demographic predictors of accepting support in the analysis of this chapter were numerically quite small, so these results should be interpreted with some caution.

7.5.3 Relation to the COM-B model

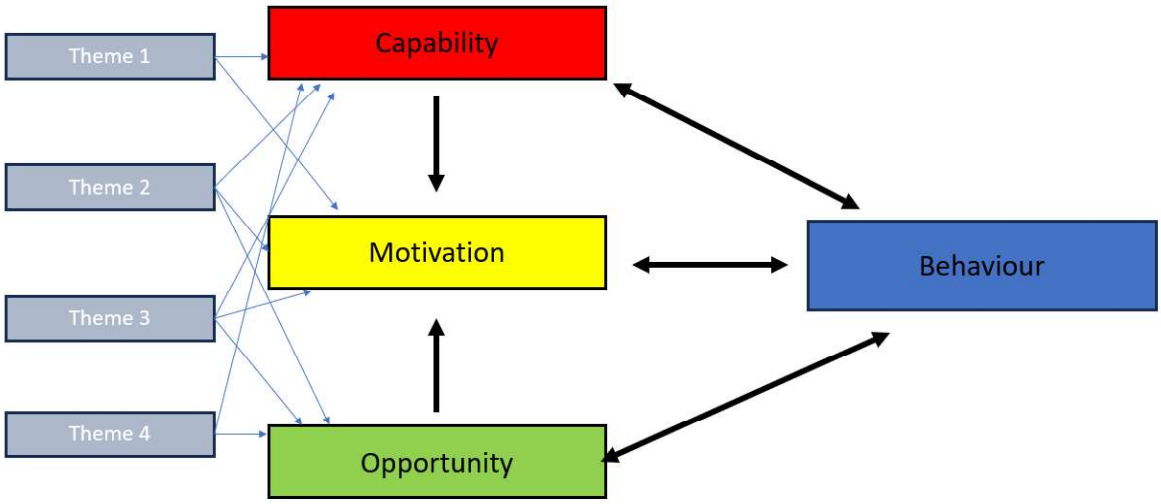
As previously stated, the COM-B model views behaviour and behaviour change as a continuous system, with motivation at the centre, needed to enact any behaviour change. However, both capability and opportunity is also needed to influence one's motivation. (Michie 2011). Viewing the model in relation to the present study, will enable a greater understanding of why people decline cessation support, alongside guiding and informing interventions to overcome these barriers. Figure 7.3 illustrates how the four themes generated via the thematic analysis interact with the domains of the COM-B model.

The first theme within the analysis interacts with both the capability and motivation domains of the COM-B model. It has been well cited that psychological issues such as depression and anxieties can affect a person's motivation (McGraw 2012; Kastaun 2022). In the case of the participants in the present study patients reported feelings of anxiety or a fear of failure surrounding quitting smoking. This highlights that patients may lack self-esteem and self-efficacy, which are intrinsic factors needed for one's capability to enact a behaviour change (West 2020; Michie 2011). The same interaction is observed within the second theme of the analysis. Patients reported that they know and perceive that quitting is hard, particularly for them, again, suggesting a lack of self-esteem when it concerns quitting interacting with the capability and motivation COM-B domains. Within theme two the data highlighted participants believed if they were to quit it should be unassisted and that this was important to them. This data may demonstrate that participants may be truly unaware of the benefits of smoking cessation support, this underestimation of the benefits will likely influence the opportunity domain of the COM-B model. Within theme three, participants indicated that despite positive views of smoking cessation support in LCS, they believed it wouldn't work for them, again highlighting a lack of self-efficacy influencing the capability and motivation

domains. The opportunity domain is also interacted with here, as patients reported they did not perceive the cessation support as being useful for them or a good opportunity for them to quit smoking. Within the final theme, patients reported negative past experiences which acted as a barrier. These negative experiences and previous unsuccessful attempts may have negatively affected the self-efficacy of participants, interfering with one's capability and motivation to enact a smoking behaviour change (Michie 2011).

This study highlights that all domains of the COM-B model need to be addressed for encouraging uptake of SCS within a screening setting. Both physical and psychological capabilities are needed to enact any behaviour change (Michie 2011). In the case of the TLHC setting the physical capabilities have been met, provided participants attend screening. However, efforts could be made to ensure that participants have a choice of face to face or remote smoking cessation support, increasing the physical opportunities for support. Regarding addressing psychological capabilities, previous research suggests that the use of diverse educational materials about smoking cessation support offered should be available (Fulton 2016). This is to inform participants about the service and what is expected of them, these educational materials should be delivered alongside the offer of cessation support. Finally, the use of success stories, again delivered alongside the offer of cessation support may increase participants' confidence and self-efficacy regarding a smoking behaviour change. These recommendations for smoking cessation services have been suggested by Fulton et al 2016, whose research group designed a mobile app based on the elements of the COM-B and behaviour change wheel to increase uptake of NHS cessation services (Fulton 2016).

Figure 7. 2 Interplay between the four themes and the COM-B model



7.5.4 Reflective statement

As stated in the chapter above. I have worked within the NHS in respiratory medicine for over seven years, and previously within health and fitness. Due to my background. I have never smoked myself and have always held the view that smoking is bad for one's health. As this analysis is focused on reasons why participants declined cessation support, despite their high risk of lung cancer and respiratory disease. It is important to reflect how my own judgements and basis may have been reflected within the data analysis.

7.5.5 Methodological considerations

To my knowledge this study is among some of the first studies exploring the barriers for declining cessation support in this population and setting, which provides insight for future TLHC when designing and planning services. The use of semi-structured interviews enabled an inductive exploration of the data, whilst using the COM-B model theory to ground the

analysis and shape the understanding of the difficulties in accepting cessation support in this population. There are several limitations that must be addressed, generalisability of the findings to the wider population, as the study population all reside within North and North-West London. Secondly, as with any qualitative analysis there is likely to be an element of selection bias. Finally, it would have been interesting to assess baseline psychological health status at initial TLHC, as this is a prevalent barrier to cessation support.

7.5.6 Implications for service delivery

This mixed methods analysis has implications for current and future screening services that either deliver or wish to deliver smoking cessation interventions. Smoking cessation advisors within this environment must be aware of the psychological barriers this population may have. The SCP must provide a supportive service, that is free from any stigma and provide easy to digest, diverse educational materials which have been previously recommended (Fulton 2016). To tackle the previous negative experiences of cessation support, it has been recommended that the intervention offered has multiple options, of both location (in clinic/ telephone/online) and a variety of NRT/ pharmacotherapy options, potentially including the use of e-cigarettes as used in the YESS study (Murray 2020; Fulton 2016). It should also be recommended that alongside providing a supportive cessation environment, practitioners need to be aware and challenge incorrect beliefs about smoking, such as that the best way to quit is unassisted and that it is good for their mental health. It is well established that statistically these smokers are more likely to quit with support (Royal College of Physicians 2018), and that smoking can exacerbate mental health symptoms (Taylor 2021). Is it, therefore, the duty of healthcare professionals to challenge this thinking, albeit in a supportive manner to ensure participants are aware of the harms of smoking on mental health and the benefits of support. Due to the high disease and cancer risk among smokers

attending screening, the benefits of specialist smoking cessation support should be provided immediately, particularly if they decline formal support as a way of challenging their refusal. Finally, as with all smoking cessation services, and lung cancer screening programs the service needs to be aware of populations who are least likely to attend, people with a low socioeconomic status, older people, and males.

7.6 Conclusion

There are specific barriers to accepting smoking support within a high-risk smoking population, particularly psychological barriers and past negative experiences. Efforts need to be made by cessation services embedded within TLHC's to design interventions that meet the needs of this specialist population. Including, providing varied educational materials and modality of services (remote/ in clinic), whilst also challenging rigid beliefs about quitting smoking and smoking behaviour more generally.

Chapter 8: Discussion and Future work

8.1 Summary of thesis aims and objectives.

The aim of this thesis was to identify effective strategies for delivering smoking cessation support within lung cancer screening services. This was alongside, investigating if smoking cessation support delivered immediately after attendance to a TLHC, with an offer of pharmacotherapy is effective at increasing abstinence rates. To achieve this aim, this thesis had four objectives. The first objective was to identify effective smoking cessation delivery strategies within lung cancer screening programmes via a systematic review of the literature and meta-analysis. The second objective was to assess the impact of a telephone smoking cessation intervention delivered immediately post attendance to a TLHC on quit rates. The third objective was to assess long term (12-month) quit rates among smokers who received smoking cessation interventions within a lung health check. The fourth and final objective was to observe participant experience of these smoking cessation interventions and investigate the barriers among participants who declined or dropped out of the interventions.

8.2 Summary of the main findings

The rationale for this thesis within chapter 1 section 1.5.6, outlined the current framework of issues surrounding SCS delivered within the screening context. I focused on three issues that this thesis could address, the main findings of this thesis in relation to the framework of issues are discussed below.

The first issue the framework highlighted was if a comprehensive smoking cessation intervention should be delivered within LCS, over the standard VBA approach. This thesis provides a strong and varied evidence base supporting the use of intensive or comprehensive

smoking cessation interventions within LCS settings. The systematic review and meta-analysis within chapter 3, supports this finding. The review demonstrated high certainty of evidence supporting the use of intensive smoking cessation support, with pharmacotherapy compared to less intensive smoking cessation support. The data presented within chapter 4, further supports the use of intensive smoking cessation support compared to VBA approaches. The QuLIT2 RCT confirmed significantly higher three month quit rates among smokers who were randomised to receive six sessions of telephone cessation support with pharmacotherapy compared to VBA and signposting services. Again, this issue is addressed and further supported within long term follow up data presented in chapter 5. Which observed significantly higher quit rates among smokers who received intensive cessation support compared to VBA and signposting. However, when observing long term (12-month) follow up data on the different QuLIT modalities (face to face or telephone), the telephone delivery approach appears to be more effective. Finally, the first qualitative investigation also supports the use of an intensive based approach. Participants cited how the combination of support SCS and pharmacotherapy lead to successful quitting, alongside reporting favourably on the combination of both SCS and LCS, and the timing of the interventions. The use of intensive cessation approaches have been widely cited and recommended within the literature both within LCS settings (Taylor 2022; Murray 2024; Lucchiari 2020) and the broader cessation literature (Rasmussen 2022; Park 2020; Feng 2022). The use of intensive smoking cessation interventions with pharmacotherapy must be recommended for lung cancer screening services embedding smoking cessation support within them.

The second issue within the framework focused on the delivery modalities of SCS within a LCS setting, particularly if remote interventions were as effective or more effective compared to traditional face to face approaches. This issue has been somewhat addressed and discussed

throughout this thesis. As previously highlighted chapter 4, contains favourable data on telephone cessation support within this context. However, there was no direct comparison between face to face and telephone modalities. Data from chapter 5, observed statistically higher 12-month bio-verified quit rates and quit attempts among the smokers who received telephone-based cessation. This statistical effect was not observed among the smokers who received face to face cessation support. Does this data, however, provide enough evidence to directly recommend telephone-based cessation support over in clinic support within a screening context. Previous smoking cessation and LCS interventional trials have observed large effect sizes using telephone delivery modalities (Taylor 2022; Taylor 2017; Zeliadt 2018). However, the cessation literature remains divided when directly comparing the effectiveness of remote cessation interventions to face to face interventions (Nomura 2019; Berndt 2017; Naja 2023). The most recent Cochrane review concluded that telephone-based cessation counselling yielded moderate- certainty evidence for increasing quit rates (Hartmann-Boyce 2019a). However, telephone counselling was less effective when provided alongside intensive face to face counselling support (Hartmann-Boyce 2019a). The authors concluded the results were limited due to an insufficient number of studies within the area. Highlighting a need for more high quality RCTs and interventional studies comparing the effectiveness of telephone and in clinic cessation. Within a LCS context, the evidence is also varied, and firm conclusions cannot be drawn recommending telephone-based support over face-to-face support. It ought to be recommended that a combination of support should be offered to smokers attending LCS, offering both telephone and face to face options. As demonstrated by the YESS trial, which observed high patient uptake (75%) and a 15% quit rate, with a combination of initial face to face cessation and the option for remote or face to face follow up (Murray 2024). The variation of access to cessation has been recommended for increasing the opportunities for

smoking cessation, and as an intervention to increase the uptake of cessation services (Fulton 2016).

The final issue highlighted in the framework, focused on whether SCS embedded within LCS should utilise an opt-out or opt-in approach. Within chapter 4, all patients who attended the TLHC on the allocated intervention day received a telephone call from the cessation advisors and classed as an opt-out approach, the smokers had to explicitly decline the intervention at this first telephone contact. This approach yielded both increased quit rates at three and twelve month follow up. Within QuLIT1 the patients who attended on intervention days were directed to the cessation advisor after their TLHC, again an opt-out approach. Within the QuLIT1 population this was successful at increasing short and long term quit rates (Buttery 2022). As previously discussed, opt-out smoking cessation interventions have been recommended when SCS are delivered within a screening context (Murray 2022), with recent data from the YESS trial supporting this recommendation (Murray 2024). The wider cessation data also supports this approach in pregnancy and inpatient care settings (Campbell 2017; Murray 2013). It has been suggested that opt out interventions can increase the uptake and referral rate, whilst limiting opportunities for participants declining (Campbell 2017; Agrawal 2024). Opt-out smoking cessation is the most recent recommendation within the latest BTS guidelines for treating tobacco dependency within NHS inpatient services. The recommendations state all current smokers should receive NRT as soon as their tobacco dependency status has been confirmed and recorded (Agrawal 2024). Data from this thesis, alongside the wider literature and clinical guidelines support the use of an opt-out method for smoking cessation. All smoking cessation interventions designed to be embedded within LCS must now utilise this opt-out method.

The main findings of this thesis support previous work, but also build on current findings within this specialist area of cessation research. The results from the systematic review were the first of its kind to quantify and collate the effects combining smoking cessation within lung cancer screening, supporting the use of intensive smoking cessation interventions over usual care interventions. The QuLIT2 intervention builds on the previous QuLIT1 intervention but also supports the wider findings that intensive, opt-out cessation interventions should be used within LCS settings. Alongside adding to the ongoing discussion covering telephone vs face to face support. Finally, the qualitative investigations give a richer understanding of how this smoking population views and experiences smoking cessation within lung screening services. Alongside providing qualitative data supporting the use of immediate access to counselling and pharmacotherapy and a telephone delivery modality. The qualitative data also sheds light on the barriers to accepting these interventions, which is essential information for services providing and designing future interventions.

8.3 Summary of main limitations

The systematic review and meta-analysis (Chapter 3) presented results with a high-level heterogeneity, attributed to the differences in primary endpoint, follow up periods and what the studies defined as usual care. In addition, all the studies were conducted in western countries (Europe, USA & Australia), despite having no geographical limitations within the search strategy.

The three month follow up of the QuLIT2 study (Chapter 4), used self-reported seven-day point prevalence as the primary endpoint smoking abstinence, and is the main limitation of this study, however this was rectified in the 12 month follow up (Chapter 5). As the same population was followed up in Chapters 4 and 5, the main limitations are as follows. The largely white study population, the West London catchment area, and the

underrepresentation of participants from the lowest areas of deprivation within the population may have influenced the generalisability of the findings. Finally, the relatively high loss to follow up at both three and 12 month follow up, however like previous remote follow up studies within the literature and mediated using the intention to treat analysis.

The main limitation of the qualitative investigation exploring participants experiences of the QuLIT2 study (Chapter 6). Is the underestimation of participants interviewed who were randomised to the usual care arm of the trial. Finally, the main limitations of the second qualitative investigation are again the generalisability given that the population is from West London only, and previous experiences of cessation services and smoking behaviour is likely to be influenced somewhat by their environment.

8.4 Implications of the findings for future research

The public health and clinical implications of the remaining chapters are huge in terms of designing and implementing lung cancer screening services. The results of these studies are clear in that embedding smoking cessation services within lung cancer screening services increases quit rates over brief advice or standard clinical care. This model of service delivery recommends that cessation services delivered within LCS should be intensive (multiple counselling sessions with pharmacotherapy), opt-out interventions offering both remote and face to face options. Quit rates within the QuLIT2 trial and long term follow up studies increased to almost a third among smokers receiving interventions and patients are drastically decreasing their cancer, cardiovascular and respiratory disease risk. As previously highlighted within this thesis, the UKs TLHC is to be expanded throughout all four UK nations, meaning 1.1 million smokers or 15% of the current smoking population in the UK meet the age criteria (Beard 2022). Evidence based smoking cessation services should be embedded within these screening services, not only to expand access of cessation to these high-risk

smokers, increasing their health, but also, to increase the cost effectiveness of the screening services. All efforts now must be made to ensure policy and guideline documentation within this area includes this important aspect of the lung health check programme. It must be noted however, research trials focused on increasing both the attendance of smokers to lung cancer screening and increasing the uptake of cessation services within screening is a noticeable gap within the literature.

8.5 Future research

Future research should include the results from the ongoing randomised controlled trials within smoking cessation delivery in LCS. As displayed in Table 3.7 in this thesis into an updated meta-analysis. It would be interesting to observe if the inclusion of additional good quality randomised controlled trials within this area strengthens the findings of the meta-analysis conducted in chapter 3, whilst also adding data to the ongoing discussion surrounding the effectiveness of telephone vs face to face delivery.

Future interventional research should examine different approaches to increase the uptake of lung cancer screening services, particularly in the comparison between face to face and remote cessation delivery options. Alongside, exploring effective interventions for at-risk and underrepresented populations, such as ethnic minorities, those living in areas of deprivation and the homeless. These populations are most at risk of lung cancer, respiratory disease, with high smoking rates and will likely benefit hugely from attending a combination of screening and cessation programs. The trials should investigate different methods of communication and messaging, considering behaviour science theories, and input from patient and public representatives from these populations to inform and create interventions.

As highlighted and addressed in chapter 7, a proportion of smokers who attend screening and are offed cessation interventions refuse the offer. Future research should be conducted into approaches on how to increase the quit rates among these smokers; it would be interesting to observe the effect of an e-cigarette intervention among this population given the effectiveness of e-cigarettes in previous trials among smokers with little or no quit intentions (Lindson 2024).

Finally, it would be exciting for future research to extend the reach of the teachable moment that lung cancer screening creates. This would be either through continued follow-up, digital messaging, or utilisation of mobile applications. This could be used to not only increase and encourage smoking cessation but also promote additional health behaviours such as physical activity.

8.6 Thesis conclusion

Smoking cessation interventions delivered immediately after attendance to a lung health check are successful at increasing quit rates among high-risk smokers. These cessation interventions provided must be intensive, provide pharmacotherapy, use an opt-out service, and offer remote and face to face options. Lung cancer screening services are opportune clinical settings to embed smoking cessation interventions within them, it is essential that lung cancer screening policy and guideline documentation include recommendations that screening providers must incorporate evidence-based smoking cessation interventions within the clinical screening service.

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Chapter 11: Appendix

Appendix 1- Interview guide used in Chapter 7

ALL

Can you tell me about your experience of the lung health check process? (What happened from the beginning, scan no scan)

At the telephone lung health check appointment where you offered any smoking cessation sessions?

Received SI

Can you tell me a bit more of your experience of this? Did you accept the sessions? If you didn't why didn't you?

How did the sessions make you feel about your smoking?

What do you think about receiving smoking cessation at the same time getting the LCS appointment?

What are your thoughts on stop smoking services in general?

Have you got any experiences of stop smoking services?

If did not receive SI

Can you explain how the nurses spoke to you about your smoking?

Can you explain how the nurses spoke to you about onward referrals?

What do you think about receiving stop smoking support at the same time as LCS?

Did the lung health check process change the amount you are smoking or change your plans to cut back / quit?

What are your thoughts of stop smoking services in general?

What are your experiences of stop smoking services?

ALL

Did the lung health check process effect any other health behaviours?

(Prompt question for example Exercise/ Diet)

What, if anything, should be done differently during the health check process?

Would you recommend the lung health check to others at risk of lung cancer?

Did these questions cover the areas that you expected?

Appendix 2- Interview guide used in Chapter 8

1) How long have you been smoking for?
2) Have you ever tried to quit? And if so, what method did you use and how long did you quit for?
3) Positives of smoking
    a. What does smoking bring you
    b. Why do you smoke
4) Negatives of smoking
    a. Consequences
    b. Risk to heath
5) Did attending the lung heath screening program make you think about your smoking?
    a. Quitting/ smoking more
6) Why did you not decide to take part in the smoking cessation program?
    a. Tried before?
    b. Setting?
    c. Not ready to quit?
7) Was there anything stopping your from accepting the offer of smoking cessation?
    a. Time?
    b. Cost
    c. Stress/ anxieties
8) When/ if you think about quitting what feelings occur?
    a. Sense of dread?
    b. Hard journey
    c. Do not think about it
9) What are your general thoughts/ feelings/ opinions around offering smoking cessation alongside lung health screening programmes?
    a. Good/ bad
    b. Too much
10) What would you like to see from smoking cessation services in the future?
    a. More choice?
    b. Different settings?
    c. Focus on psychological aspects of addiction
    d. E-cigs?