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Lifestyle Interventions in Primary Healthcare: A Path to Cardiometabolic Disease Prevention

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Abbreviations

BCTs	Behavior change techniques
CFIR	Consolidated Framework for Implementation Research
CPRD	Clinical Practice Research Datalink
DALYs	Disability-adjusted life-years
GBD	Global Burden of Disease
GP	General practitioner
NCDs	Non-communicable diseases
NCD-RisC	NCD Risk Factor Collaboration
NHS	National Health Service
NHS DPP	NHS Diabetes Prevention Programme
NICE	National Institute for Health and Care Excellence
QOF	Quality and Outcomes Framework
RCGP	Royal College of General Practitioners
RCTs	Randomized controlled trials
T2DM	Type 2 Diabetes Mellitus
WHO	World Health Organization

1 INTRODUCTION

> "The world is living dangerously, either because it has little choice or because it is making the wrong choices about consumption and activity." (Brundtland, 2002, p. 9)

With these words, Dr. Gro Harlem Brundtland, former Director General of the World Health Organization (WHO), aptly described the state of population health around the world in 2002. Today, statistics continue to confirm her observation as cardiometabolic diseases, including cardiovascular diseases, diabetes mellitus, and chronic kidney disease, remain the leading cause of premature death and disability globally (Allen et al., 2017). According to the Global Burden of Disease (GBD) estimates from 2019, cardiovascular diseases alone were responsible for 393 million disability-adjusted life-years (DALYs), accounting for 15.5 percent of all DALYs (Roth et al., 2020). Dr. Brundtland's words serve as a poignant reminder that unhealthy behaviors including poor diet, hazardous alcohol consumption, tobacco smoking, and physical inactivity are major risk factors for the development and progression of cardiometabolic diseases (D'Agostino Sr. et al., 2013; Murray et al., 2020).

In the second half of the 20th century, substantial reductions in mortality from cardiovascular diseases such as coronary heart disease and stroke were observed in the United States and many Western European countries (Centers for Disease Control and Prevention, 1999; Jones & Greene, 2013). This decline was attributed to risk factor control and advances in pharmacological and technological treatments for acute and long-term treatment (Dalen et al., 2014; Mensah et al., 2017). However, since the 1980s, there has been an increase in the prevalence of diabetes and obesity (Finucane et al., 2011; NCD Risk Factor Collaboration (NCD-RisC), 2016a, 2016b), and it appears that the previously declining rates of cardiovascular mortality have slowed down or plateaued (E. S. Ford & Capewell, 2007). In England, chronic heart disease deaths decreased consistently from 1995 to 2010, with an average annual reduction of 4.5%, but only for individuals without diabetes mentioned on their death certificate. Meanwhile, chronic heart disease mortality rates either remained constant or even slightly increased for those with a mention of diabetes on their death certificate (Ecclestone et al., 2015). Low- and middle-income countries have seen a considerable increase in cardiovascular disease mortality over the recent decades, with diabetes

prevalence rising even faster compared to high-income countries (Guariguata et al., 2014; NCD-RisC, 2016b). The rise of cardiometabolic diseases in low- and middle-income countries has been strongly linked to the increase in obesity and body mass index (Miranda et al., 2019; NCD-RisC – Africa Working Group et al., 2017). Given these observations, preventing and treating cardiometabolic diseases remains a substantial challenge for health care systems worldwide.

1.1 Preventive healthcare

Preventive measures can help to reduce the overall disease burden and limit health care spending by reducing the prevalence of risk factors, preventing cardiometabolic diseases from developing in an individual, or controlling early disease stages before complications become severe and require more intense and costly treatment (Ali et al., 2017; LeBlanc et al., 2018; O'Connor et al., 2018; World Health Organization, 2021). In particular lifestyle modifications or medication can improve risk factors and potentially even reverse early stages of the disease, such as impaired glucose tolerance, hypertension, and hyperlipidemia (Aburto et al., 2013; Galaviz et al., 2022; Rees et al., 2013; Valenzuela et al., 2021; Vetter et al., 2013; Wang et al., 2012).

Prevention may be conceptualized either temporally by distinguishing between primary, secondary, and tertiary prevention (Baumann & Ylinen, 2020), or with regard to its targeted health determinants such as socio-economic and environmental factors, living and employment conditions, social networks, or individual lifestyles (Dahlgren & Whitehead, 1991; Martin-Moreno et al., 2021). Different health determinants have been occasionally pitted against each other by dichotomizing between structural and behavioral approaches to prevention (Martin-Moreno et al., 2021). In particular behavioral interventions that aim to improve individual lifestyles through education have come under scrutiny for several reasons, including accusations of shifting responsibility to the individual and catering to industry stakeholders, as well as the perception that such interventions demand significant personal effort without a commensurate public health benefit (Hagger & Weed, 2019; Kelly & Barker, 2016; Martin-Moreno et al., 2021).

Indeed, recognizing that people's health does not depend solely on their individual choices has been vital in establishing a *Health in All Policies* approach as the guiding principle for health policy in many countries. This approach emphasizes that promoting health and health equity requires comprehensive policy-making in

various areas such as transport, housing and urban planning, the environment, education, agriculture, taxation, and economic development (McQueen et al., 2012). However, this does not imply that supporting individuals by informing, educating, and promoting healthy lifestyles in terms of consumption and activities should be disregarded in the prevention of cardiometabolic diseases. Unhealthy behaviors including poor diet, hazardous alcohol consumption, tobacco smoking, and physical inactivity are major risk factors for the development and progression of cardiometabolic diseases (D'Agostino Sr. et al., 2013; Murray et al., 2020). Specifically, the widespread adoption of these unhealthy behaviors has likely played a key role in the surge of excess weight and obesity, which in turn has contributed to an increase in the prevalence of diabetes and cardiovascular diseases in most regions of the world (NCD-RisC, 2016b). For example, maintaining a healthy lifestyle, including healthy diet and body weight, moderate to vigorous physical activity, and abstaining from tobacco smoking, is estimated to prevent a substantial proportion of cases of type 2 diabetes mellitus (T2DM), possibly up to 90 percent (Perry, 2002).

While health behaviors are multi-determined and often deeply ingrained in one's habits and social environments, they are in principle modifiable. Within a Health in All Policies approach, governments may consider introducing a sweetened beverage tax to discourage an unhealthy diet or planning new walking and cycling pathways to encourage physical activity (Goodman et al., 2014; Wang et al., 2012). At the same time, targeted lifestyle interventions (used as an umbrella term for interventions ranging from single-time brief advice to extensive behavioral, nutritional and psychological counseling) have been demonstrated to improve individual's risk factors and to subsequently reduce the incidence of cardiometabolic diseases in randomized controlled trials (Laaksonen et al., 2005; Rees et al., 2013; Sanchez et al., 2015). In particular, structured programs such as the US Diabetes Prevention Program can lead to reductions in risk factors and decrease the progression to T2DM compared to usual care (Diabetes Prevention Program Research Group, 2015). While there are concerns about the long-term effectiveness and the large variability in responses to lifestyle interventions, with some individuals being highly successful while others achieve very little lifestyle change (Aucott et al., 2009; Unick et al., 2014; Wadden et al., 2009), targeting lifestyle behavior changes is recommended as a first-line intervention for individuals diagnosed with conditions such as impaired glucose tolerance,

hypertension, hyperlipidemia, and obesity (Ferdinand & Nasser, 2017; Jonas et al., 2021; LeBlanc et al., 2018; O'Connor et al., 2018; Rippe, 2019).

1.2 Public Health Action Cycle for lifestyle interventions

The fact that behavioral lifestyle interventions do not achieve unequivocal success, in particular in routine practice, may be attributed to a lack of systematic development, implementation, and evaluation. In the 1980s, the US Institute of Medicine (2002) evaluated the country's public health activities initiatives, laying the groundwork for the *Public Health Action Cycle*, a four-phased model that was further developed by Rosenbrock (1995) and later adapted for preventive measures and health promotion activities by Ruckstuhl, Somaini and Twisselmann (1997). The model involves an assessment phase to investigate the status quo of the health issue in terms of medical, epidemiological, and social aspects; a development phase to weigh different strategies and interventions to address the issue; an assurance or implementation phase to put the resulting strategies and interventions into practice; and an evaluation phase to assess their effectiveness. The cycle starts anew with a reassessment of the original health issue and adaption of strategies and interventions, if necessary (Fig. 1).

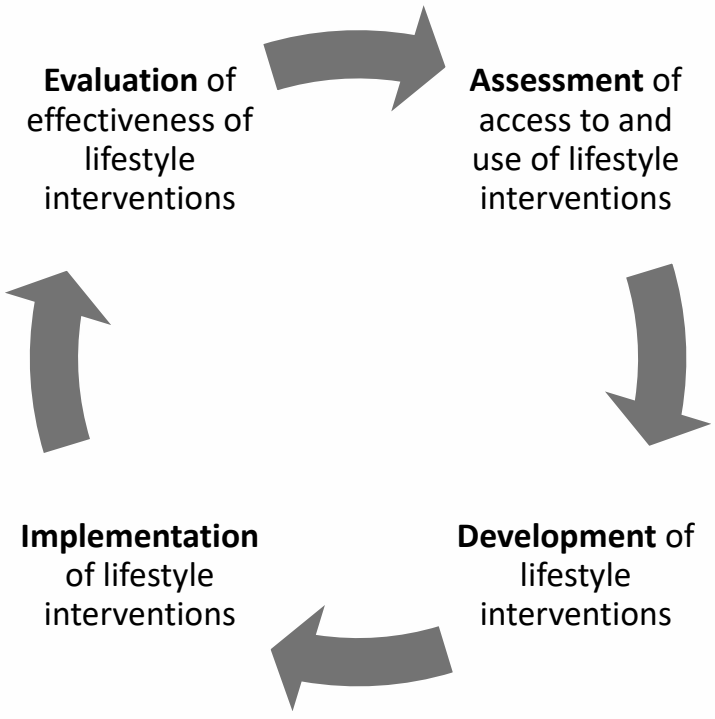

Fig. 1. Public Health Action Cycle for lifestyle interventions adapted from Ruckstuhl et al. (1997)

The Public Health Action Cycle highlights an important observation that there can be significant disparities between the conception and design of a health policy or intervention and its actual implementation in real-life contexts and practice, which could account for the limited success of certain behavioral lifestyle interventions. Recognizing that primary health care encounters present a crucial opportunity to engage with at-risk patients who have adopted unhealthy behaviors, lifestyle interventions have been identified as a potential tool for prevention and management of cardiometabolic diseases (Král et al., 2019; Piepoli et al., 2016). However, despite their potential large public health benefits, translating such interventions into routine practice remains challenging and underdeveloped (Sattar et al., 2020).

My dissertation aimed to identify and overcome key challenges in the translation of lifestyle intervention into routine primary health care settings under real-life conditions using a Public Health Action Cycle model. Specifically, I assessed the access to and use of lifestyle interventions in two different primary health care systems (England and Thailand), applied an evidence-based framework to the development and implementation of an innovative lifestyle intervention approach in Thailand, and evaluated the effectiveness of the English Diabetes Prevention Programme using rigorous quasi-experimental causal inference methods (Fig. 2).

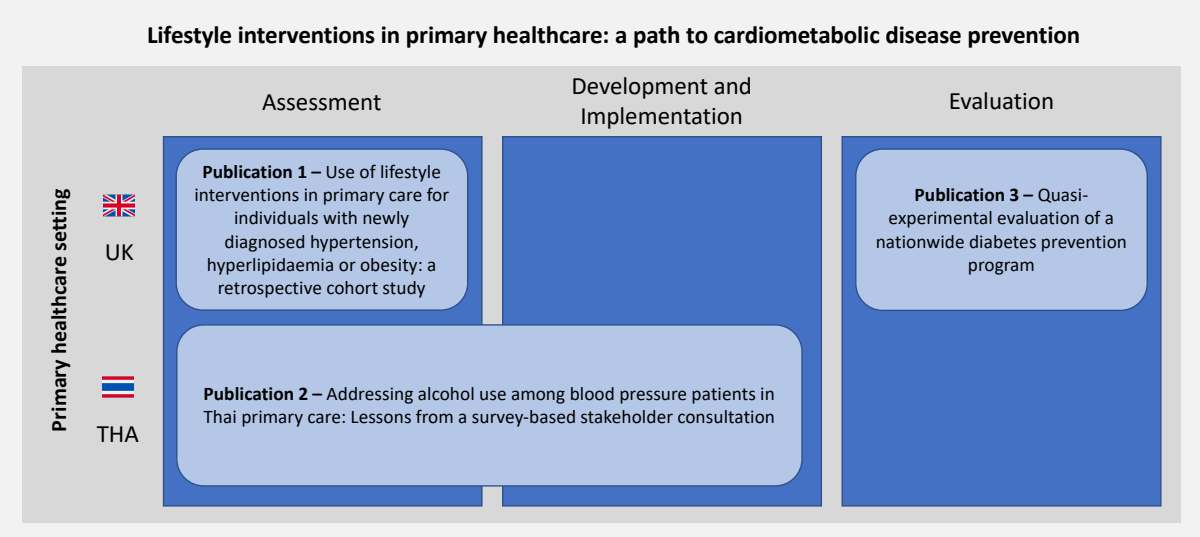

Fig. 2. Overview of my publications.

1.2.1 Assessment phase

In my dissertation, the assessment phase in the Public Health Action Cycle focused on understanding and clarifying the extent to which lifestyle interventions already exist in the primary health care settings in England (Publication 1) and Thailand (Publication 2), and whether and how individuals are assigned and referred to appropriate lifestyle interventions. Although it has been established that health behaviors and lifestyle choices have a strong influence on progression to cardiometabolic diseases and national guidelines often recommend lifestyle interventions as a first-line treatment for at-risk individuals diagnosed, structured referral pathways for lifestyle interventions that support individuals in improving unhealthy behaviors are frequently lacking. In both English and Thai primary health care settings, it remains unclear how the access to appropriate lifestyle interventions for individuals exhibiting risk factors for cardiometabolic diseases is realized in routine practice, despite being recommended by national public health guidance. Understanding the access to and use of lifestyle interventions is the first step to determine whether new strategies and interventions are necessary, how they can be embedded into existing structures, and what aspects may deserve particular attention in the subsequent development and implementation phases (Ruckstuhl et al., 1997).

In the UK, the National Institute for Health and Care Excellence (NICE) has recommended lifestyle interventions as a first-line treatment for individuals diagnosed with conditions such as T2DM, hypertension, hyperlipidemia, and obesity (NICE, 2011, 2014a, 2014b). While established lifestyle intervention programs like DESMOND (Diabetes Education and Self-Management for Ongoing and Newly Diagnosed) exist for individuals with T2DM, referral pathways for risk factors such as hypertension, hyperlipidemia, and obesity are not as well established in routine practice, despite being important risk factors for more severe cardiometabolic diseases and having a high prevalence in England. This may result in many missed opportunities for early support in managing these conditions by modifying lifestyle risk factors. **Therefore, the objective of publication 1 was to quantify the extent to which individuals with newly diagnosed hypertension, hyperlipidemia, or obesity were offered lifestyle interventions in English general practitioner (GP) practices**.

To this end, I used data from the Clinical Practice Research Datalink (CPRD) Aurum, a large primary care database of de-identified electronic health records (EHR) from a network of GP practices across the UK. The data cover approximately one-fifth of all GPs in England and are representative of the English population in terms of geographical spread, deprivation, age, and gender (Wolf et al., 2019). Working with EHR can have some methodological drawbacks such as high missingness for certain variables or inconsistent coding of diagnoses and procedures, which require meticulous data preparation to ensure the accuracy and reliability of the data. However, they offer valuable insights for research and quality improvement purposes and allowed me to study how patient cohorts with specific risk factors for cardiometabolic diseases pass through routine primary health care upon their initial diagnosis.

While the Thai health system differs substantially from the English National Health Service (NHS) in terms of structure, size, and funding, the Thai National Hypertension Guidelines likewise recommend lifestyle interventions as the first-line treatment for individuals with pre-hypertension and hypertension, specifying that all patients should receive lifestyle advice regardless of medication (Thai Hypertension Society, 2019). At the same time, a recent clinical audit revealed only partial compliance with the guidelines concerning medication regimes based on hypertension grade and cardiovascular disease risk, suggesting that guidelines may not be strictly followed (Angkurawaranon et al., 2021). Indeed, it is unclear whether practitioners adhere to recommendations for lifestyle interventions targeting hypertension risk factors and to what extent these interventions are implemented in Thailand. However, Thailand is a middle-income country, many of which have recently seen increases in hypertension. It was estimated that hypertension accounted for 8% of Thailand's disease burden in 2019, a 10% increase in the past decade (Institute for Health Metrics and Evaluation (IHME), 2023). A substantial proportion of this burden was from cardiometabolic diseases, with 40-50% of stroke, ischemic heart disease and chronic kidney disease prevalence in the adult Thai population being attributable to high blood pressure. According to the 2014 Thai National Health Examination Survey (NHES V), one in four Thais had hypertension, with 45% unaware and only 30% having their blood pressure under control (Roubsanthisuk et al., 2018). These numbers indicate an urgent need to improve prevention and treatment of hypertension. **Thus, the first objective of publication 2 was to identify the current practices for lifestyle**

interventions among patients with hypertension in Thai primary health care settings as the first phase in the Public Health Action Cycle.

To this end, I conducted a cross-sectional, mixed-method study as part of the wider project *'Improving Primary Care for Hypertension and Alcohol Problems in Thailand'*. This study involved three sets of respondents who comprise the external stakeholder advisory group for the project and whose perspectives are relevant to hypertension care in Thailand: a) policy- and decision-makers, members of educational institutions, and representatives from governing bodies of health care providers and advocacy groups, b) health care practitioners, particularly doctors and nurses working in hypertension outpatient clinics, and c) patients with hypertension. The questionnaires were designed to elicit information about current practices regarding lifestyle interventions among hypertensive patients and practical, social, economic, and cultural barriers to routine screening and lifestyle intervention in primary health care. The questionnaire included different question types including Likert-scaled statements to which the respondents could indicate their agreement as well as open-ended questions. The content was adapted to the perspective of each stakeholder group. Through this comprehensive approach, I aimed to gain a thorough understanding of the current access to and practices regarding lifestyle interventions for hypertension, including any existing and anticipated barriers and facilitators as perceived by stakeholders at different levels of the health care system in Thailand. Publication 2 also informed the second phase of the Public Health Action Cycle by applying a particular focus on hazardous and harmful alcohol use as a risk factor for hypertension.

1.2.2 Development and implementation phase

In my dissertation, the development and implementation phases in the Public Health Action Cycle focused on conceptualizing how synergies of addressing alcohol use and hypertension may be simultaneously leveraged in an intervention and what steps are necessary to ensure an equitable implementation given existing conditions and constraints in the Thai primary health care system (Publication 2).

The WHO Global Action Plan for the prevention and control of non-communicable diseases (NCDs) aims to reduce raised blood pressure and harmful alcohol use, which disproportionately affect low- and middle-income countries (Allen et al., 2017; World Health Organization, 2013). Notably, while both high blood pressure

and alcohol use are significant standalone contributors to the burden of disease and health care costs, accumulating evidence over the past decade has demonstrated a causal link between alcohol use and hypertension (Larsson, Burgess, et al., 2020; Roerecke et al., 2018; Santana et al., 2018). Two meta-analyses showed that there is a graded increase in the risk of hypertension in men, even at low levels of alcohol consumption (Jung et al., 2020; Roerecke et al., 2018). At the same time, alcohol brief interventions are effective at reducing hazardous or harmful alcohol consumption (Kaner et al., 2018). Addressing both risk factors simultaneously could have a greater impact on reducing morbidity, mortality, and health care costs from cardiometabolic diseases than addressing them separately (Rehm et al., 2017a; Roerecke et al., 2017). Following this evidence, screening for alcohol use and implementing brief interventions should be a priority in primary health care; yet only about half of the hypertension guidelines worldwide recommend reducing alcohol consumption as a strategy to reduce high blood pressure (Chalmers et al., 2013). While there is a need for more education and stigma reduction to increase implementation (Rehm, Prieto, et al., 2016), GPs in European countries have largely expressed favorable views about alcohol screening in hypertensive patients (Hanschmidt et al., 2017). However, there is limited evidence of attitudes and barriers in other regions such as South-East Asia, where alcohol use and high blood pressure are leading risk factors for NCDs (Murray et al., 2020).

In 2017, Thailand had an adult consumption of 8.8 liters of pure alcohol per capita, which is approximately double the regional average and sets the country apart from the rest of the South-East Asian region (Manthey et al., 2019; Sornpaisarn et al., 2020; World Health Organization, 2018). Despite comparatively low prevalence of current drinking in Thailand, with 55% among men and 28% among women, heavy episodic drinking, also known as “binge drinking”, is common among about 50% of male and 20% of female drinkers (World Health Organization, 2018). While the health risks related to alcohol use follow a dose-response continuum, heavy episodic drinking can increase the risk of ischemic heart disease even when usual alcohol consumption patterns are light or moderate (Rehm, Shield, et al., 2016). Given the substantial alcohol- and hypertension-attributable risks in the country, prioritizing hazardous and harmful alcohol use among hypertensive patients in Thailand could lead to considerable synergistic health gains and cost reductions by lowering the burden of cardiometabolic and other non-communicable diseases. Brief interventions can

effectively reduce alcohol consumption, making it an important focus for health professionals in Thailand. **Thus, the second objective of publication 2 was to map out a potential screening and brief intervention approach targeting lifestyle behaviors among Thai primary health care patients diagnosed with or at-risk of hypertension and with a focus on concomitant alcohol use.**

To this end, the study conceptualization and questionnaires were guided by the Consolidated Framework for Implementation Research (CFIR), a typology of constructs that have been associated with effective implementation (Damschroder et al., 2009; VanDevanter et al., 2017). This approach allowed me to identify constructs within the CFIR that are likely relevant for the successful implementation of lifestyle interventions among patients diagnosed with hypertension in Thailand. Lastly, based on stakeholders' favorable evaluation of a digital tool that supports resource-effective and culturally adapted delivery of alcohol screening, I illustrate a potential way forward for implementing and evaluating a digitally supported screening and brief intervention approach that integrates tailored advice for brief intervention and further treatment as a potential scalable solution.

1.2.3 Evaluation phase

Shifting the focus back to the primary health care setting in England, the evaluation phase in the Public Health Action Cycle focused on determining the effectiveness of the NHS Diabetes Prevention Programme (NHS DPP) (Publication 3).

The NHS DPP is a national behavior change program that has been implemented in three phases since June 2016. Commissioned local providers are responsible for delivering the program, which is designed to improve participants' diet, increase physical activity, and facilitate weight loss. The program is delivered in person to groups of 15-20 adults over at least 13 sessions, totaling 16 hours, with a minimum duration of 9 months. An NHS service description provides for the explicit use of behavior change theories and behavior change techniques (BCTs), which are observable, irreducible, and replicable components of an intervention that are assumed to produce behavior change based on existing evidence (Hawkes et al., 2021; Michie et al., 2013). BCTs applied in the program include, for example, goal setting and action planning, self-monitoring and behavioral rehearsal, or social support (Hawkes, Cameron, Bower, et al., 2020). Intervention features range from educational, group support, and visual activities to patient-led activities and knowledge testing

(Hawkes, Cameron, Cotterill, et al., 2020; Penn et al., 2018). Individuals who are eligible (having a recorded HbA1c measure between 42 and 47 mmol/mol in the past twelve months or a history of gestational diabetes) are identified and referred by their GP. To date, the NHS DPP is the largest diabetes prevention programme globally to achieve universal national coverage (Valabhji et al., 2020), making it a prime candidate to evaluate its impact in routine practice. If positively evaluated, the NHS DPP could serve as a valuable reference for other countries that are also implementing large-scale prevention programs.

Randomized controlled trials (RCTs) are considered the most reliable method for assessing the effectiveness of health care interventions (Sibbald & Roland, 1998). In RCTs, participants are randomly divided into two groups: the treatment group, which receives the intervention, and the control group, which does not. This random allocation accounts for both observable and unobservable confounding, ensuring that the two groups have similar characteristics. Comparing the outcomes of the treatment group to the control group allows estimation of the causal treatment effect. Various lifestyle interventions aimed at improving cardiovascular risk factors and reversing non-diabetic hyperglycemia have demonstrated efficacy in RCTs (Galaviz et al., 2018, 2022; Jonas et al., 2021; Pronk, 2016; Taheri et al., 2020). For example, the US Diabetes Prevention Program study (which serves as a model for numerous behavior change programs worldwide) has shown that targeting lifestyle behavior changes is more successful in preventing or delaying type 2 diabetes mellitus than metformin (Diabetes Prevention Program Research Group, 2015; Ramachandran et al., 2006). However, most studies, including the US Diabetes Prevention study, have mainly focused on efficacy, supplying proof of principle that the intervention worked when one-to-one sessions with specialists and a range of incentives are being provided (Brink, 2009). As this creates an artificial environment designed to maximize compliance with and benefits of the intervention (Gertler et al., 2016), it remains unclear to what extent the effects of behavioral lifestyle interventions in routine practice such as the NHS DPP compare to those observed in clinical trials.

It is crucial to establish the effectiveness of lifestyle interventions in routine care for several reasons. Firstly, behavioral advice and counseling are recommended as the first-line treatments for people with cardiovascular risk factors. However, health care providers tend to prescribe preventive medication instead due to limited time resources in primary care (Irving et al., 2017), inadequate knowledge and referral

options for promoting healthy lifestyles (Keyworth et al., 2019; Rubio-Valera et al., 2014), and a prevailing of the biomedical model that leaves clinicians uncertain about the effectiveness of counseling (Hébert et al., 2012; Rubio-Valera et al., 2014). Secondly, participants in clinical trials for behavior change programs may not represent the broader patient population. Patients enrolled in clinical cardiology trials have lower risk profiles compared to patients encountered in everyday practice. This is because they are typically younger, more likely to be male, and less likely to have comorbidities (Kennedy-Martin et al., 2015). In contrast, individuals drawn from an unselected, general population may respond differently due to lower health literacy, greater ethnic diversity, higher comorbidities, and differing levels of engagement (J. G. Ford et al., 2008; Rogers et al., 2021). **Therefore, the objective of publication 3 was to establish the transferability of behavior change programs to real-world settings by determining if routine referral to the NHS DPP leads to improvements in key cardiovascular risk factors such as HbA1c, excess weight, raised blood pressure, and serum lipid levels.**

To this end, I employed several quasi-experimental methods that allow for a causal interpretation of the treatment effect. Rather than relying on random assignment to treatment or control groups, quasi-experimental methods construct a comparison group, also known as the *counterfactual* (Morgan & Winship, 2014). If the assumptions of a quasi-experimental method are met, the counterfactual represents the outcome that would have occurred in the treatment group had they not received the intervention (Bärnighausen et al., 2017).

Quasi-experiments offer several advantages over RCTs: Firstly, quasi-experiments often use representative data from the population of interest, making their results more generalizable. Secondly, quasi-experiments evaluate interventions in real-world settings, reflecting the treatment effect under natural circumstances (Geldsetzer & Fawzi, 2017). Thirdly, quasi-experimental designs can provide a more practical and ethical option when an RCT is unfeasible or impractical, especially if withholding the intervention for an extended period of time would raise ethical or fairness concerns. Finally, quasi-experiments can be more cost-effective than RCTs since they do not require the same level of infrastructure and staffing (Gertler et al., 2016; Tollefson, 2015). Governments may also be hesitant to conduct RCTs due to their strict timelines, which may not align with policy cycles involving budgeting and elections, and the potential delay in observing effects (Gertler et al., 2016). In such

cases, alternative research designs and methods may be necessary to rigorously evaluate program effectiveness. However, conventional observational studies in health research are generally inadequate in providing causal interpretations as they do not account for confounding factors such as selection biases. Instead, I used three different quasi-experimental research designs: regression discontinuity design, difference-in-differences estimation, and instrumental variable estimation, which I will now briefly present.

Firstly, to implement a regression discontinuity design, I used the fact that the program is only open to patients above a prespecified threshold of HbA1c or fasting plasma glucose indicating non-diabetic hyperglycemia which draws a sudden distinction between the prediabetes and normal glycemia range. Intuitively, the regression discontinuity design exploits this distinction as patients within a narrow range around the eligibility threshold are similar to each other except for having a higher probability of receiving a referral to intensive lifestyle counseling if their HbA1c level crosses the threshold. Specifically, I compared patients lying closely on either side of the threshold using a local linear approach which allows for the interpretation of differences in clinical outcomes as causal (Imbens & Lemieux, 2008). Empirical evidence from numerous studies in the social sciences (Chaplin et al., 2018; Gleason et al., 2012; D. P. Green et al., 2009; Tang & Cook, 2018; Wing & Cook, 2013), and increasingly in clinical and epidemiological research (Maas et al., 2017; Oldenburg et al., 2018; Shoag et al., 2015; van Leeuwen et al., 2016, 2018), has demonstrated the validity of the regression discontinuity approach for causal effect estimation. In this analysis, I was therefore able to take advantage of the existing large-scale routine health data from CPRD while still obtaining causal effect estimates that are not vulnerable to confounding and measurement error (Cattaneo et al., 2019; Imbens & Lemieux, 2008).

Secondly, I performed a difference-in-differences analysis, an established quasi-experimental method originating from social sciences (Bärnighausen et al., 2017; Card & Krueger, 1994). Specifically, I used the fact that the NHS DPP was rolled out nationally in three waves (first wave start date: 1st June 2016, second wave start state: 1st April 2017, and third wave start date: 1st April 2018). In a difference-in-differences analysis the estimate of interest represents how much the average outcome of the treatment group has changed in the period after the treatment, compared to what would have happened in the absence of the intervention. Thus, this analysis

essentially compares patients from practices belonging to different NHS DPP roll-out phases under the assumption that, in the absence of NHS DPP implementation, the outcome trends would have been the same in the treatment group as in the comparison (Bärnighausen et al., 2017). This assumption can be verified by examining whether outcome trends are parallel in the period before the NHS DPP introduction. If this assumption holds, any difference in the changes in the outcome variable between the treatment and control groups after the program is introduced can be interpreted as the treatment effect.

Thirdly, I used the time-variant regional differences in NHS DPP coverage as an instrument for actual referral to the program to conduct an instrumental variable estimation. Instrumental variable estimation is a statistical technique used to address endogeneity in regression analysis, where the independent variable (in this case, being referred to the NHS DPP) is correlated with the error term, e.g., due to selection bias in treatment assignment (Angrist et al., 1996; Bärnighausen et al., 2017). Specifically, I estimated the effect of NHS DPP referral on glycemic control from comparing those who changed from not being referred to being referred due to a change in program coverage in their region. The instrumental variable approach relies on two key assumptions, namely that the instrument must be correlated with the treatment (*relevance*) and that the instrument must not be directly related to the outcome variable, except through its effect on the treatment variable (*exclusion*) (Bärnighausen et al., 2017). If these assumptions hold, then the instrumental variable approach can provide unbiased estimates of the causal effect of the treatment variable on the outcome variable.

1.3 Aim and objectives

The following studies aimed to identify and overcome key challenges in the translation of lifestyle intervention into routine primary health care settings under real-life conditions using a Public Health Action Cycle model (Fig. 1). To achieve my overarching aim, the studies had four specific objectives:

I. Quantify the extent to which individuals with newly diagnosed hypertension, hyperlipidemia, or obesity were offered lifestyle interventions in English GP practices (Publication 1)
II. Identify the current practices for lifestyle interventions among patients with hypertension in Thai primary health care settings (Publication 2)

III. Map out a potential screening and brief intervention approach targeting lifestyle behaviors among Thai primary health care patients diagnosed with or at-risk of hypertension and with a focus on concomitant alcohol use (Publication 2)

IV. Establish the transferability of behavior change programs to real-world settings by determining if routine referral to the NHS DPP leads to improvements in key cardiovascular risk factors (Publication 3)

In the following, the original publications are presented in the clockwise direction of the Public Health Action Cycle, starting with the assessment phase. While each publication is linked with specific phases of the Public Health Action Cycle (Fig. 2), there may be some intersections such as that Publication 3 includes information about the access to the NHS DPP.

2 PUBLICATION 1: LIFESTYLE INTERVENTIONS FOR HYPERTENSION, HYPERLIPIDAEMIA OR OBESITY

Lemp, J. M., Nuthanapati, M. P., Bärnighausen, T. W., Vollmer, S., Geldsetzer, P., & Jani, A. (2022). Use of lifestyle interventions in primary care for individuals with newly diagnosed hypertension, hyperlipidaemia or obesity: A retrospective cohort study. *Journal of the Royal Society of Medicine*, *115*(8), 289–299. https://doi.org/10.1177/01410768221077381

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Use of lifestyle interventions in primary care for individuals with newly diagnosed hypertension, hyperlipidaemia or obesity: a retrospective cohort study

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Abstract

Objective: Lifestyle interventions can be efficacious in reducing cardiovascular disease risk factors and are recommended as first-line interventions in England. However, recent information on the use of these interventions in primary care is lacking. We investigated for how many patients with newly diagnosed hypertension, hyperlipidaemia or obesity, lifestyle interventions were recorded in their primary care electronic health record.

Design: A retrospective cohort study.

Setting: English primary care, using UK Clinical Practice Research Datalink.

Participants: A total of 770,711 patients who were aged 18 years or older and received a new diagnosis of hypertension, hyperlipidaemia or obesity between 2010 and 2019.

Main outcome measures: Record of lifestyle intervention and/or medication in 12 months before to 12 months after initial diagnosis (2-year timeframe).

Results: Analyses show varying results across conditions: While 55.6% (95% CI 54.9–56.4) of individuals with an initial diagnosis of hypertension were recorded as having lifestyle support (lifestyle intervention or signposting) within the 2-year timeframe, this number was reduced to 45.2% (95% CI 43.8–46.6) for hyperlipidaemia and 52.6% (95% CI 51.1–54.1) for obesity. For substantial proportions of individuals neither lifestyle support nor medication (hypertension: 12.2%, 95% CI 11.9–12.5; hyperlipidaemia: 32.2%, 95% CI 31.2–33.3; obesity: 43.9%, 95% CI 42.3–45.4) were recorded. Sensitivity analyses confirm that limited proportions of patients had lifestyle support recorded in their electronic health record before they were first prescribed medication (diagnosed and undiagnosed), ranging from 12.1% for hypertension to 19.7% for hyperlipidaemia, and 19.5% for obesity (23.4% if restricted to Orlistat).

Conclusions: Limited evidence of lifestyle support for individuals with cardiovascular risk factors (hypertension, hyperlipidaemia, obesity) recommended by national guidelines in England may stem from poor recording in electronic health records but may also represent missed opportunities. Given the link between progression to cardiovascular disease and modifiable lifestyle factors, early support for patients to manage their conditions through non-pharmaceutical interventions by establishing lifestyle modification as first-line treatment is crucial.

Keywords

Disease prevention, cardiovascular disease, primary care, lifestyle intervention

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Introduction

Despite the decrease of cardiovascular disease seen in many Western countries in recent decades, it continues to be a major health problem.[1] The most recent Global Burden of Disease study estimated that, in 2019, cardiovascular disease accounted for 2.4 million disability-adjusted life years and over 150,000 deaths in England, representing over 14% of total disability-adjusted life years and 30% of all deaths in England, with a large proportion of this mortality being attributable to high systolic blood pressure (42.9%), high low-density lipoprotein cholesterol (25.3%) and high body mass index (16.4%).[2]

Several well-established risk factors predispose individuals to developing cardiovascular disease including age, gender, high systolic blood pressure, high total cholesterol, elevated low-density lipoprotein cholesterol, smoking behaviour and diabetes

status.[3] Several of these risk factors are directly linked to lifestyle-related behaviours which can be modified through interventions that support individuals to, for example, maintain a healthy diet and body weight,[4] engage in physical activity,[5] reduce sodium intake[6] and alcohol consumption,[7] and abstain from tobacco smoking.[8] General practitioners can play a particularly important role on this by recommending and monitoring lifestyle-related changes for reduction in cardiovascular disease risk.[9]

Lifestyle interventions are generally seen to be successful in controlled clinical trials.[4,5,10–12] While there are concerns about the long-term effectiveness[13] and the large variability in responses to these interventions, with some individuals being highly successful while others achieve very little lifestyle change,[14,15] in the UK, the National Institute for Health and Care Excellence have recommended addressing lifestyle behaviours as a first-line intervention for individuals diagnosed with conditions such as type 2 diabetes, hypertension, hyperlipidaemia and obesity.[16–18] In line with their recommendations, several lifestyle intervention programmes are used through England's National Health Service to support individuals in changing their lifestyle, and they include more formal programmes like DESMOND for individuals with type 2 diabetes[19] as well as programmes that target behaviours related to diet and/or physical activity. While more formal programmes like DESMOND have specific referral pathways, the pathways for hypertension, hyperlipidaemia and obesity are not as well established despite these conditions having a high prevalence in England. Hypertension is estimated to affect 12.5 million adults, over 20% of the population, in the UK[20] and was associated with about 30% of deaths in the UK Biobank study.[21] Dyslipidaemias come in various forms with the most common being raised cholesterol. In 2017, it was reported that the prevalence of raised cholesterol in UK adults was 48%.[22] Obesity, another common risk factor for cardiovascular disease, has a prevalence of 28% in the UK.[23]

To better understand how cardiovascular disease risk is managed in primary care in England, this study aimed to quantify use of lifestyle interventions for individuals with an initial diagnosis of hypertension, hyperlipidaemia or obesity. We use a well-established primary care dataset from England, and the results have important implications for policy and practice to ensure that individuals with modifiable risk factors linked to cardiovascular disease can benefit from interventions that can help to improve their health, prevent disease and, most importantly, put their health back in their hands.

Materials and methods

Data source and ethics

This retrospective observational study used data from Clinical Practice Research Datalink Aurum, an ongoing database of pseudonymised routine primary care records from general practitioners in the UK. The data are representative of the population in England with respect to geographical spread, deprivation, age and gender.[24] Data were extracted from the Clinical Practice Research Datalink Aurum database in July 2020, containing electronic health records from 35.9 million patients and 1296 currently contributing practices in England. In this release, over 93% of permanent registrations were deemed to have research quality data based on Clinical Practice Research Datalink metrics derived from internal consistency of key variables including date of birth, practice registration date and transfer out date.[24] The Clinical Practice Research Datalink Independent Scientific Advisory Committee approved study protocols for each condition (20_000180, 20_000181 and 20_000182) in accordance with the Declaration of Helsinki.

Study period

The study period spans from 2010 to 2019. For hypertension, it spans from 2011 to 2019, as we were only interested in periods during which clinical guidelines by the National Institute for Health and Care Excellence specifically recommended lifestyle interventions as a first-line treatment option for the condition.

Study population

The eligible population had an initial diagnosis of hypertension, hyperlipidaemia or obesity at adult age during the study period, at least 12 months of continuous registration after said initial diagnosis and was deemed as research quality based on Clinical Practice Research Datalink metrics. The diagnosis had to be clearly indicated by the presence of an electronic health record code entered by the general practitioner, whereas a physical measurement or laboratory test result exceeding commonly applied disease thresholds (e.g. a systolic blood pressure measurement above 140 mmHg) did not qualify as a diagnosis (Supplementary Table 1). In addition, patients that received any condition-specific medication (e.g. statins for hyperlipidaemia) during the 15 years before their initial electronic health record recorded diagnosis or had any record indicating genetic

causes for the condition (e.g. familial hypercholesterolemia) were excluded. Code lists for medication and exclusion diagnoses are provided in the Supplementary Data (Supplementary Tables 2–3). Follow-up ended at the last data collection from the general practitioner practice, practice deregistration or death.

Outcomes

We were interested in the course of treatment of patients who had an initial diagnosis of hypertension, hyperlipidaemia or obesity. The primary outcome was thus the presence of any record of signposting to, performance of or referral to lifestyle intervention appropriate for each condition before and after a patient's initial diagnosis. We identified relevant electronic health record codes based on a string-based term search which was performed independently by two members of our research team (Supplementary Box 1, Supplementary Table 4). For lifestyle support, we distinguished between codes that indicated signposting (i.e. signposting such as 'Physical activity opportunity signposted', brief advice such as 'Diet leaflet given' or 'Advice about exercise') and codes that indicated an offer, referral or performance of a lifestyle intervention on-site or off-site (i.e. counselling such as 'Dietary management education, guidance, and counselling' or referrals such as 'Referral to community dietician' or 'Exercise on prescription'). When presenting what proportion of patients received lifestyle support, we distinguished by signposting (including brief advice) and lifestyle intervention, with the latter being less susceptible to underreporting as general practitioners often act as gatekeepers for referrals to lifestyle intervention services and programmes. In addition, we determined whether patients received any prescription of condition-specific medication. We identified medication prescriptions using British National Formulary terms (Supplementary Table 3). Presence and absence of relevant codes were determined for different time periods in relation to the initial diagnosis – within 12 months or 6 months before the initial diagnosis; at time of diagnosis, for which we allowed the records to be entered 1 week before to 1 week after the initial diagnosis; and within 1 month, 2 months, 3 months, 4 months, and 12 months after the initial diagnosis.

Statistical analysis

R Version 4.0.3 was used to conduct the analyses. Baseline characteristics were described for all patients with an initial diagnosis of hypertension, hyperlipidaemia or obesity that fulfilled our inclusion criteria. We calculated the proportion and number of patients among those with an initial diagnosis that had an electronically recorded lifestyle intervention and/or medication for each condition. Confidence intervals were computed with standard errors using a variance-stabilising transformation for the binomial distribution and are clustered at the general practitioner practice level. We compared the proportion of patients that had these interventions recorded in their electronic health record before and after their initial diagnosis as well as the cumulative proportion of patients that had these interventions recorded in their electronic health record at any point in time from 12 months before to 12 months after their initial diagnosis.

Sensitivity analysis

While there is evidence that correctness of diagnosis codes in Clinical Practice Research Datalink Aurum is high,[25] Persson et al. report that half of patients who had either high cholesterol values or medication had no hyperlipidaemia diagnosis codes. The authors concluded that there may be a substantial number of patients with hyperlipidaemia treated by their general practitioner but with no diagnosis code in their electronic health record. Thus, as sensitivity analysis, we created an alternative cohort, where we used the first recorded condition-specific medication as the index date instead of the initial recorded diagnosis and determined what proportion of patients (diagnosed and undiagnosed) had a lifestyle intervention recorded in their electronic health record in the 12 months before said prescription.

Results

After excluding patients who had receipt of medication recorded in their electronic health record before their initial recorded diagnosis (n = 223,414 for hypertension, n = 38,221 for hyperlipidaemia and n = 32,296 for obesity), the full sample consisted of 770,711 patients who met our inclusion criteria and received an initial diagnosis of hypertension, hyperlipidaemia or obesity during our study period. Table 1 provides the baseline characteristics for all newly diagnosed patients stratified by condition.

Hypertension

Among newly diagnosed hypertension patients between 2011 and 2019 (N = 403, 129), 86.8% (95% confidence interval [CI] 86.5–87.1) had a combination

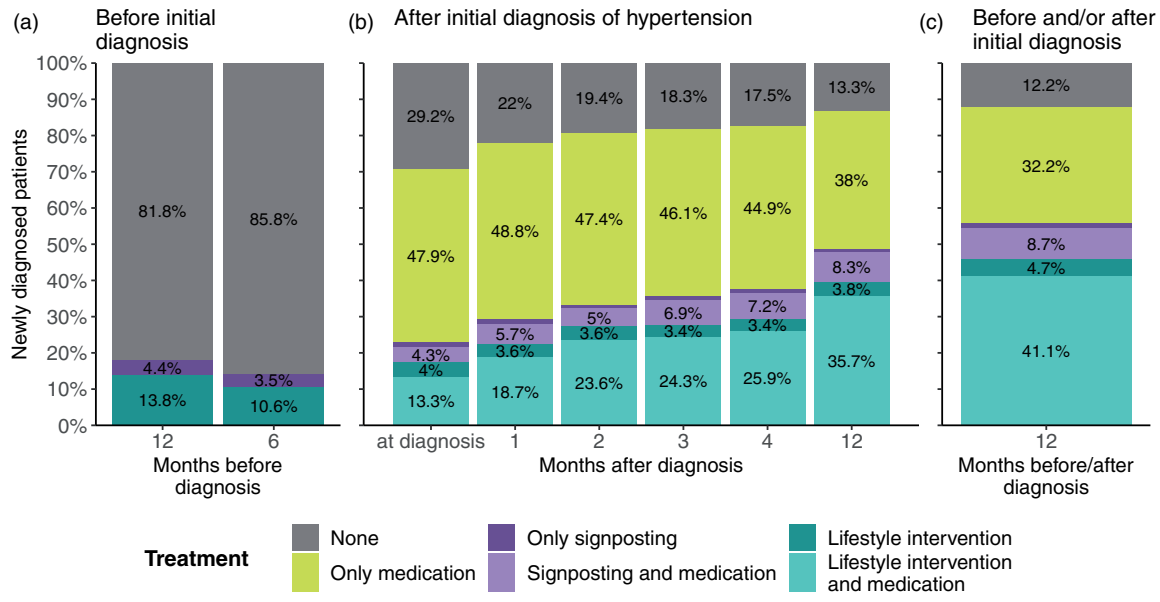
Table 1. Characteristics of patients by condition.

Variable	Hypertension (n = 403,129)		Hyperlipidaemia (n = 105,900)		Obesity (n = 261,682)	
	Median	IQR	Median	IQR	Median	IQR
Year of diagnosis	2014	2012–2017	2015	2013–2017	2014	2012–2017
Age[a]	57	48–67	55	46–65	48	34–61
Follow-up time (in months)	55.6	32.5–82.0	51.8	31.2–80.0	54.4	31.4–84.3
	%	n	%	n	%	n
Gender						
Female	44.3	178,746	49.8	52,697	57.2	149,809
Male	55.7	224,380	50.2	53,203	42.8	111,868
Non-binary	0.0	3	0.0	0	0.0	5
Region						
North East	3.3	13,254	2.0	2,144	8,829	3.4
North West	16.1	64,794	20.6	21,827	43,739	16.7
Yorkshire and the Humber	3.2	12,929	2.0	2,134	8,317	3.2
East Midlands	2.5	9,898	2.0	2,115	5,468	2.1
West Midlands	17.2	69,284	19.2	20,286	41,838	16.0
East of England	4.3	17,237	3.7	3,894	8,240	3.1
South West	12.1	48,950	5.9	6,282	40,612	15.5
South Central	12.7	51,377	8.6	9,088	31,257	11.9
London	19.6	78,922	26.2	27,719	52,311	20.0
South East Coast	8.9	35,680	9.4	9,992	20,799	7.9
Unknown	0.2	804	0.4	419	272	0.1

Table shows characteristics of patients who met all inclusion criteria.
[a]Age in years at time of the initial diagnosis.
IQR; interquartile range.

of medication, signposting for lifestyle-related support, and/or lifestyle intervention recorded in their electronic health record within 12 months after their initial diagnosis (Figure 1(b) – all coloured bars except for grey). This number increases to 87.8% (95% CI 87.5–88.1) if we also take lifestyle intervention up to 12 months before the initial diagnosis into account (Table 2: 'All patients with medication and/or lifestyle support record'). While 82.0% (95% CI 81.6–82.5) of diagnosed patients were recorded in their electronic health record as having been prescribed medication within 12 months after their diagnosis (either alone or in combination with signposting and/or lifestyle intervention), only about half of newly diagnosed patients (55.6%, 95% CI 54.9–56.4) had any lifestyle intervention or signposting recorded in their electronic health record in a window from up to 12 months before to within 12 months after their diagnosis (Figure 1(c) – dark and light purple and dark and light teal bars; Table 2). The percentage of patients who had any lifestyle intervention or signposting recorded in their electronic health

Figure 1. Prescribed medications and recorded lifestyle interventions for patients with an initial diagnosis of hypertension. Proportions of patients by hypertension treatment (hypertension medication, signposting to lifestyle intervention and lifestyle intervention) 12 months before to 12 months after an initial recorded diagnosis of hypertension. Patients with a prescription of hypertension medication before any initial diagnosis of hypertension are excluded. Grey bars – no intervention; yellow bars – only medication; dark purple bars – only signposting; light purple bars – signposting and medication; dark blue bars – only lifestyle intervention; light blue bars – lifestyle intervention and medication.



record after their initial diagnosis rose from 22.9% (95% CI 22.4–23.4) at the time of diagnosis to 48.7% (95% CI 48.0–49.4) within 12 months after their diagnosis (Figure 1(b) – dark and light purple and dark and light teal bars).

Among patients who had a recorded medication prescription in their electronic health record within 12 months of their initial diagnosis (n = 330, 606; Table 2: 'Medication total'), 60.7% (95% CI 60.0–61.5) also had any lifestyle intervention or signposting recorded in their EHR during 12 months prior to 12 months after their diagnosis (200,785 out of 330,606 patients; Table 2: 'Medication w/signposting' and 'Medication w/lifestyle intervention' divided by 'Medication total'). 5.8% (95% CI 5.5–6.1) of patients had any lifestyle intervention or signposting recorded in their electronic health record up to 12 months before to within 12 months after their initial diagnosis without being prescribed any medication within 12 months after their diagnosis (23,484 out of 403,129 patients; Table 2: 'Lifestyle intervention only' and 'Signposting only' divided by 'Total').

Hyperlipidaemia

Among newly diagnosed hyperlipidaemia patients between 2010 and 2019, 61.9% (95% CI 60.8–62.9) had a combination of medication, signposting for lifestyle-related support, and/or lifestyle intervention recorded in their electronic health record within 12 months after their initial diagnosis (Figure 2(b) – all coloured bars except for grey). This number increases to 67.8% (95% CI 66.7–68.8) if we also take lifestyle intervention up to 12 months before the initial diagnosis into account (Table 2: 'All patients with medication and/or lifestyle support record). While 44.2% (95% CI 42.8–45.6) of diagnosed patients were recorded as having received a medication prescription within 12 months after their diagnosis (either alone or in combination with signposting and/or lifestyle intervention), 45.2% (95% CI 43.8–46.6) had any record in their electronic health record of lifestyle intervention or signposting in a window from up to 12 months before, to within 12 months after their diagnosis (Figure 2(c) – dark and light purple and dark and light teal bars; Table 2). The percentage of patients who had any record of lifestyle intervention or signposting in their electronic health record after their initial diagnosis rose from 17.7 (95% CI 16.8–18.7) at the time of diagnosis to 33.0% (95% CI 31.7–34.3) within 12 months after their diagnosis (Figure 2(b) – dark and light purple and dark and light teal bars).

Among patients who had a record of receiving a medication prescription within 12 months of their

Table 2. Proportion of patients with electronic health records of medication prescription and/or lifestyle support in a period of 12 months before to 12 months after initial diagnosis for each condition.

Treatment	Hypertension (N = 403,129)		Hyperlipidaemia (N = 105,900)		Obesity (N = 261,682)	
	Per cent (95% CI)	n	Per cent (95% CI)	n	Per cent (95% CI)	n
None	12.2 (11.9–12.5)	49,039	32.2 (31.2–33.3)	34,144	43.9 (42.3–45.4)	114,789
Medication						
Medication only	32.2 (31.5–32.9)	129,821	22.5 (21.6–23.5)	23,858	3.5 (3.3–3.7)	9231
Medication w/signposting	8.7 (8.4–9.1)	35,210	4.1 (3.8–4.4)	4,355	0.9 (0.8–1.0)	2364
Medication w/ lifestyle intervention	41.1 (40.3–41.8)	165,575	17.6 (16.9–18.3)	18,623	3.7 (3.5–3.9)	9769
Lifestyle support						
Lifestyle Intervention only	4.7 (4.4–5.0)	18,917	17.8 (16.6–19.0)	18,834	38.4 (37.0–39.7)	100,441
Signposting only	1.1 (1.0–1.2)	4,567	5.7 (5.3–6.2)	6,086	9.6 (9.0–10.3)	25,088
Total	100	403,129	100	105,900	100	261,682
	Prop. (95% CI)	n	Prop. (95% CI)	n	Prop. (95% CI)	n
All patients with medication record	82.0 (81.6–82.4)	330,606	44.2 (42.8–45.6)	46,836	8.2 (7.7–8.6)	21,364
All patients with lifestyle support record	55.6 (54.9–56.4)	224,269	45.2 (43.8–46.6)	47,898	52.6 (51.1–54.1)	137,662
All patients with medication and/or lifestyle support record	87.8 (87.5–88.1)	354,090	67.8 (66.7–68.8)	71,756	56.1 (54.6–57.7)	146,893

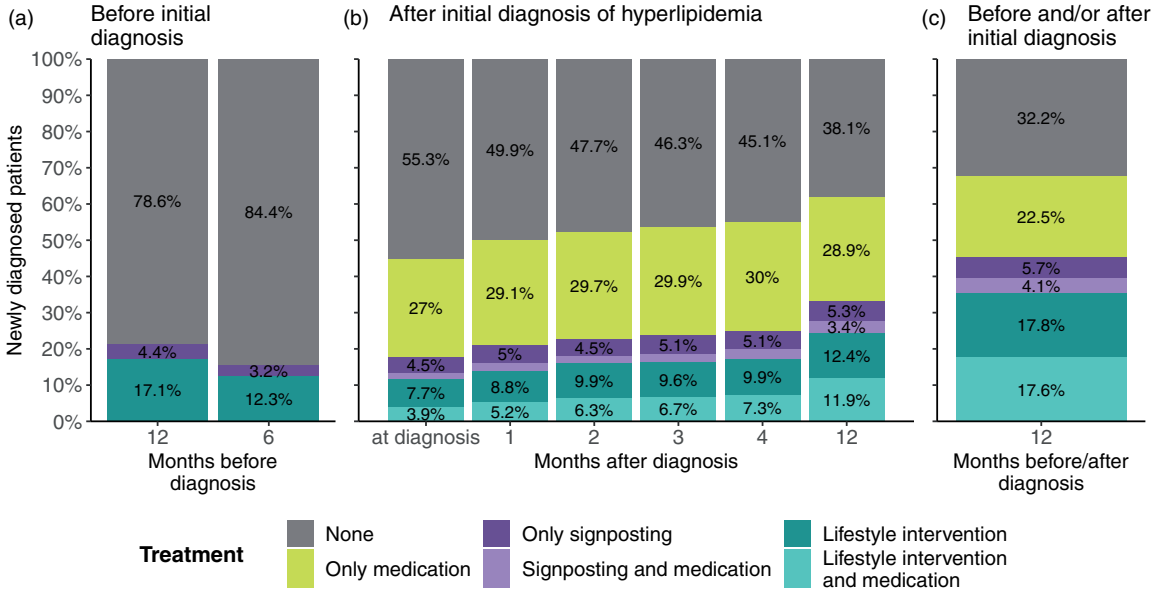
CI: confidence interval. Table shows the proportions of patients by treatment group and condition. The patient must have a record of a given treatment at any point between 12 months prior to and/or 12 months after their initial diagnosis. Confidence intervals were computed with standard errors using a variance-stabilising transformation for the binomial distribution and are clustered at the practice level. Patients that have received a lifestyle intervention may have also concurrently received signposting.

initial diagnosis (n = 46 836; Table 2: 'Medication total'), 49.1% (95% CI 47.8–50.3) also had any lifestyle intervention or signposting recorded in their electronic health record during 12 months prior to 12 months after their diagnosis (22,978 out of 46, 836 patients; Table 2: 'Medication w/signposting' and 'Medication w/lifestyle intervention' divided by 'Medication total'). Of patients, 23.5% (95% CI 22.2–24.9) had any lifestyle intervention or signposting recorded in their electronic health record within 12 months before to 12 months after their initial diagnosis without being prescribed any medication up to 12 months after their diagnosis (24,920 out of 105,900 patients; Table 2: 'Lifestyle intervention only' and 'Signposting only' divided by 'Total').

Obesity

Among newly diagnosed obesity patients between 2010 and 2019, 49.5% (95% CI 47.9–51.1) had combination of medication, signposting for lifestyle-related support and/or lifestyle intervention recorded in their electronic health record within 12 months after their initial diagnosis (Figure 3(b) – all coloured bars except for grey). This number increases to 56.1% (95% CI 54.6–57.7) if we also take lifestyle intervention up to 12 months before the initial diagnosis into account (Table 2: 'All patients receiving medication and/or lifestyle intervention'). Given the lack of approved anti-obesity medicines, only 8.2% (95% CI 7.7–8.6) had receipt of medication commonly

Figure 2. Prescribed medications and recorded lifestyle interventions for patients with an initial diagnosis of hyperlipidaemia. Proportions of patients by hyperlipidaemia treatment (hypertension medication, signposting to lifestyle intervention and lifestyle intervention) 12 months before to 12 months after an initial recorded diagnosis of hypertension. Patients with a prescription of hyperlipidaemia medication before any initial diagnosis of hyperlipidaemia are excluded. Grey bars – no intervention; yellow bars – only medication; dark purple bars – only signposting; light purple bars – signposting and medication; dark blue bars – only lifestyle intervention; light blue bars – lifestyle intervention and medication.

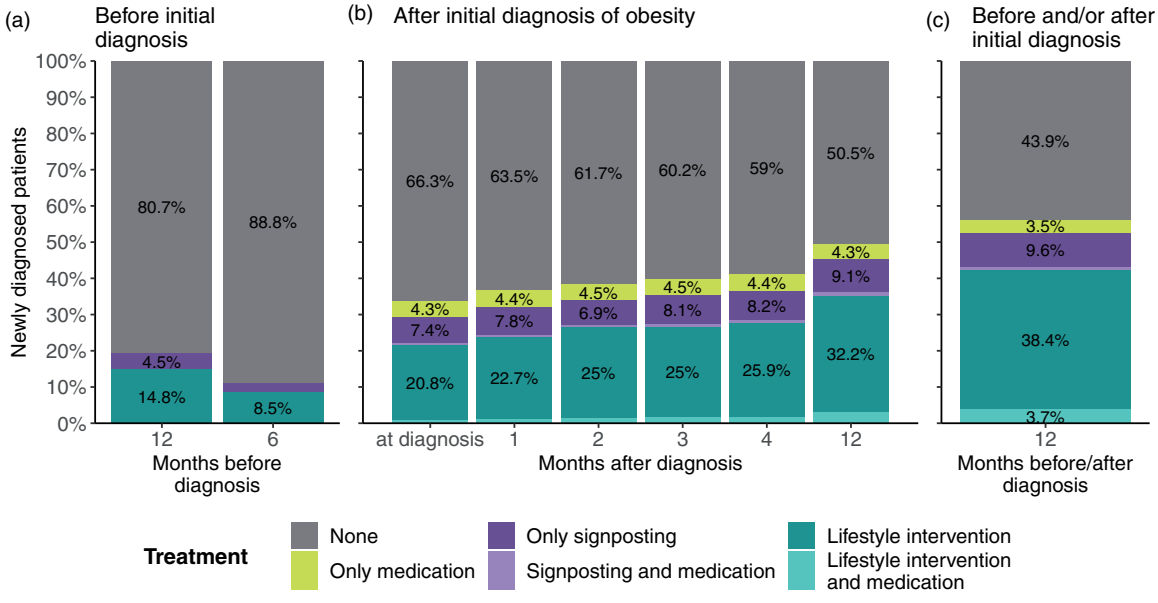


used to target obesity recorded in their electronic health record (including gastro intestinal anti-obesity drugs such as Orlistat, appetite suppressants and bulk-forming laxatives, see Supplementary Table 3; Table 2: 'All patients with medication record'). The percentage of patients who had any record in their electronic health record of lifestyle intervention or signposting after their initial diagnosis rose from 29.4% (95% CI 27.9–31.0) at the time of diagnosis to 45.2% (95% CI 43.7–46.7) within 12 months after their diagnosis (Figure 3(b) – dark and light purple and dark and light teal bars). If we also take lifestyle intervention up to 12 months before their diagnosis into account, this number increases by 7.4 percentage points, resulting in 52.6% (95% CI 51.1–54.1) of patients that had any record of lifestyle intervention or signposting in a window from up to 12 months before to within 12 months after their diagnosis (Figure 3(c) – dark and light purple and dark and light teal bars).

Sensitivity analyses

Given that a substantial number of patients were already recorded as having been prescribed medication before their initial recorded diagnosis, we performed additional analyses where we explored the recorded use of lifestyle interventions before an initial prescription of medication rather than using the initial diagnosis as an index date (Supplementary Table 6). The proportion of individuals (diagnosed and undiagnosed) who had any record in their electronic health record of lifestyle support up to 12 months before their initial prescription ranges from 12.1% (95% CI 11.8–12.5) for antihypertensive medication to 19.7% (95% CI 19.2–20.3) for lipid-lowering medication and 19.5% (95% CI 19.0–20.0) for anti-obesity medication, respectively. If we restrict anti-obesity medication to Orlistat, which is the only medication singularly used for obesity treatment, the number slightly increases to 23.4% (95% CI 22.8–24.1). If we restrict this sample further to those that have been diagnosed at the time they had their first recorded medication prescription, the numbers increase slightly: The proportion of individuals (diagnosed) who had any record of lifestyle support up to 12 months before their initial prescription then ranges from 21.6% (95% CI 21.0–22.2) for antihypertensive medication to 26.7% (95% CI 25.7–27.8) for lipid-lowering medication and 33.1% (95% CI 32.3–34.0) for anti-obesity medication, respectively. We present figures for these analyses in the Supplementary Data (Supplementary Figures 1–4).

Figure 3. Prescribed medications and recorded lifestyle interventions for patients with an initial diagnosis of obesity. Proportions of patients by obesity treatment (anti-obesity medication, signposting to lifestyle intervention and lifestyle intervention) 12 months before to 12 months after an initial recorded diagnosis of obesity. Patients with a prescription of anti-obesity medication before any initial diagnosis of obesity are excluded. Grey bars – no intervention; yellow bars – only medication; dark purple bars – only signposting; light purple bars – signposting and medication; dark blue bars – only lifestyle intervention; light blue bars – lifestyle intervention and medication.



Discussion

Summary

Based on the primary care eletronic health records in our analysis, the main finding of our study points to a general lack of adherence to guidelines by the National Institute for Health and Care Excellence on the recommended use of lifestyle interventions for individuals with an initial diagnosis of hypertension, hyperlipidaemia or obesity. Given that these conditions are often linked to modifiable lifestyle factors, it is a missed opportunity to fail to support these individuals to manage their conditions through non-pharmaceutical routes.

Through our analyses we also find heterogeneity in the recorded use of lifestyle interventions across conditions with 45.8% of individuals with an initial diagnosis of hypertension having a electronic health record of some sort of lifestyle intervention (55.6% if signposting is included), going down to about 35.4% (45.2% if signposting is included) for those with an initial diagnosis of hyperlipidaemia. There are also substantial proportions of individuals not having any recorded support (medication, lifestyle intervention and/or signposting) at all within 12 months of diagnosis – ranging from only 12% of people with an initial diagnosis of hypertension to 44% for people with an initial diagnosis of obesity. In addition, our results suggest that only a small proportion of patients had a recorded lifestyle intervention before they were first prescribed medication for hypertension, hyperlipidaemia or obesity, raising the question why not more individuals receive a lifestyle intervention as first-line intervention.

Limitations

Our study used a large population-based primary care dataset that is representative of the adult population of England. However, this study also has several limitations. First, there are alternative explanations pertaining to the lack of recorded lifestyle interventions that could be related to our findings. Given that our analyses only capture what is recorded in primary care electronic health records, it is possible that interventions are being given but are not recorded. Brief advice, in particular, may be given to patients but not recorded by general practitioners, which could have led to an underestimation of lifestyle intervention rates. It may also be

that patients are offered lifestyle interventions but decline this, or that there is a lack of services in the area that provide lifestyle interventions.

Second, our primary analysis sample only includes patients for which an initial diagnosis was recorded in their electronic health record, excluding patients who had any medication prescription prior to their initial diagnosis. Sensitivity analyses revealed low recorded lifestyle intervention rates for patients prior to their initial medication prescription (independent of their diagnosis status), substantiating a generally low recorded use of lifestyle intervention as first-line treatment.

Third, our analyses do not capture all details related to the diagnosis (e.g. exact lipid profile) and health status of the individual. However, this should not reflect a lack of general practitioners utilising lifestyle interventions. Given the importance of lifestyle-related factors in perpetuating cardiovascular disease risk, even patients who are given medications because of advanced disease at their initial diagnosis should receive lifestyle support to help them better manage their condition and, ideally, bring it into remission.[26]

Fourth, in these analyses, we did not distinguish lifestyle interventions by content, duration or intensity and we also did not determine whether patients actually received or completed a given lifestyle intervention. While even brief advice by physicians can help patients change their health behaviours in the short term,[27] oftentimes more intensive lifestyle and maintenance programmes are needed to induce the long-term lifestyle modification needed for cardiovascular disease risk reduction.[28] Thus, our results reflect the proportion of patients that can potentially access lifestyle interventions through general practices rather than the proportions of patients eventually benefitting from lifestyle interventions. This information is still valuable, however, in guiding future modifications to primary care pathways to improve care and outcomes for patients with these conditions.

Fifth, comparisons across conditions cannot be made without important limitations as it is unknown whether accuracy of and type of recorded lifestyle intervention information varies systematically across conditions.

Comparison with existing literature

While several studies have evaluated the effectiveness of primary care lifestyle interventions,[5,11,12] few studies have investigated how patients access lifestyle intervention in primary care. Booth et al. evaluated the use of weight management interventions among overweight and obese patients (based on body mass index) in English primary care and found that the proportion of patients that received a weight management intervention ranged from 8.7% to 28.1%, depending on their body mass index category.[29] Similarly, Sheppard et al. reported that in a cohort of patients with mild hypertension, only 12% received lifestyle advice.[30] We identified a higher proportion of patients receiving lifestyle interventions. Differences between the present study and these other studies include a more recent study period for our study, an inclusion of lifestyle interventions pertaining not only to weight management but also to general lifestyle and physical activity, and a cohort identification based on clinical diagnosis codes rather than body mass index categories.

Implications for research and/or practice

The results of this study suggest that lifestyle interventions to reduce cardiovascular disease risk are underutilised in English primary care. Given the strong link between modifiable lifestyle factors and progression to cardiovascular disease, establishing early support for lifestyle modification as a first-line intervention is crucial. It is possible that intervention rates have been underestimated through a lack of formal recording in medical records and it is important that our study outcomes are interpreted as recorded lifestyle interventions by general practitioners rather than interventions received. However, given the large burden of cardiovascular disease on primary healthcare services and lack of long-term follow-up on the effectiveness and equity of access to lifestyle interventions for conditions predisposing patients to cardiovascular disease, the use of electronic health records will be indispensable to better understand their use and impact. Thus, as a starting point, improvements in formal recording of lifestyle interventions in routine medical records are needed. Furthermore, though unpicking the factors that contribute to our results will take additional study, our results have important implications for policy and practice to ensure we can create more efficient and effective mechanisms for primary care to utilise and refer individuals with risk factors linked to cardiovascular disease to lifestyle interventions to promote health and prevent further exacerbations of cardiovascular disease.

Declarations

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Ethics approval: Permission for data usage was obtained from the Clinical Practice Research Datalink Independent Scientific Advisory Committee (protocol numbers 20_000180, 20_000181, and 20_000182). Linked pseudonymised data were provided by Clinical Practice Research Datalink. Analysis of pseudonymised data (i.e. data that could not be linked to individuals without additional information that was not available to the analysts) was considered exempt for nonhuman subjects research by the institutional review board of the Heidelberg University Medical Faculty.

Guarantor: AJ.

Contributorship: JML, PG and AJ contributed to the idea generation and protocol development. JML and MPN prepared the data for analysis, and JML performed the statistical analyses. JML, SV, PG, and AJ interpreted study results, and JML, MPN, and AJ had primary responsibility in writing the manuscript. TWB, SV and PG also contributed to manuscript writing. All authors critically reviewed the manuscript.

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3 PUBLICATION 2: ALCOHOL AND BLOOD PRESSURE IN THAILAND

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Addressing alcohol use among blood pressure patients in Thai primary care: Lessons from a survey-based stakeholder consultation

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ABSTRACT

Alcohol use is a major risk factor for noncommunicable diseases in Thailand, and one of its pathways is high blood pressure. Given that brief intervention can effectively reduce hazardous alcohol consumption, this study aimed to investigate how hypertensive patients with concomitant alcohol use are identified and treated in Thai primary care settings and what this may mean for screening and lifestyle intervention strategies. In a cross-sectional, mixed-method design, we surveyed 91 participants from three different groups of Thai stakeholders: policy- and decisionmakers; healthcare practitioners; and patients diagnosed with hypertension. Data was collected between December 2020 and May 2021. Responses were analyzed descriptively and using open coding tools to identify current practices, barriers, facilitators, and implications for interventions. All stakeholder groups regarded alcohol use as an important driver of hypertension. While lifestyle interventions among hypertensive patients were perceived as beneficial, current lifestyle support was limited. Barriers included limited resources in primary healthcare facilities, lack of continuous monitoring or follow-up, missing tools or procedures for risk assessment and lifestyle intervention, and stigmatization of alcohol use. Our results suggest that although screening for lifestyle risk factors (including alcohol use) and lifestyle interventions are not yet sufficiently established, a wide range of stakeholders still recognize the potential of interventions targeted at hazardous alcohol use among hypertensive patients. Future interventions may establish standardized assessment tools, be tailored to high-risk groups, and include electronic or remote elements.

1. Introduction

High blood pressure (hypertension) and alcohol use are both major risk factors for noncommunicable diseases (NCDs), placing a significant burden on patients, healthcare systems, and society as a whole (Murray et al., 2020). Globally, one in four men and one in five women were estimated to have hypertension (at least 140/90 mm Hg) in 2015 (NCD Risk Factor Collaboration, 2017), and the most recent Global Burden of

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Disease (GBD) estimates (2019) showed that high systolic blood pressure was the most impactful risk factor for mortality and disability-adjusted life-years (Murray et al., 2020). While the prevalence of hypertension is decreasing in high-income countries, it is rapidly increasing in low- and middle-income countries (Mills et al., 2016; NCD Risk Factor Collaboration, 2017).

Importantly, alcohol use and hypertension are causally linked in a dose–response fashion (Taylor et al., 2009; O'Keefe et al., 2014; Briasoulis et al., 2012; Roerecke et al., 2018), making heavy alcohol use one of the most common causes of reversible hypertension. Interventions to reduce alcohol consumption could be a feasible and effective approach for reducing the prevalence of hypertension and related NCD burden (Roerecke et al., 2017). Results from several trials suggest a comparable reduction in patients' blood pressure can be achieved through either lowering alcohol intake or other interventions that focus on lifestyle risk factors such as weight loss, diet and physical activity (Roerecke et al., 2017; Semlitsch et al., 2016; Lin et al., 2014). This is promising since alcohol brief interventions (defined as a conversation comprising five or fewer sessions of brief advice or brief lifestyle counselling and a total duration of fewer than 60 min) can reduce hazardous or harmful alcohol consumption and may be as effective as extended interventions (Beyer et al., 2019; O'Connor et al., 2018; Kaner et al., 2018). Currently, though overall implementation is low and there is a need for further education and stigma reduction (Rehm et al., 2016), evidence from Europe shows that alcohol screening in hypertensive patients was largely accepted by general practitioners (Hanschmidt et al., 2017). However, as of yet, there is limited evidence of attitudes and barriers elsewhere, such as South-East Asia, where alcohol use and hypertension are among the leading risk factors for NCDs (Murray et al., 2020).

For instance, it was estimated that hypertension accounted for about 8 % of the total disease burden in Thailand in 2019, with a 10 % increase over the past 10 years (Institute for Health Metrics and Evaluation, 2021). According to the Thai National Health Examination Survey (NHES V) conducted in 2014, one in four Thais had hypertension. Of those with hypertension, 45 % were unaware of it and only 30 % had their blood pressure under control (Roubsanthisuk et al., 2018). At the same time, with an estimated 8.8 liters of pure alcohol per capita in 2017, alcohol consumption in Thailand is nearly double the average consumption of the WHO South-East Asia Region overall (World Health Organization, 2018; Manthey et al., 2019; Sornpaisarn et al., 2020). While the prevalence of current drinking is comparatively low in Thailand with 55 % among men and 28 % among women, about 50 % (men) and 20 % (women) of the current drinkers engage in heavy episodic drinking (World Health Organization, 2018). While national clinical guidelines recommend lifestyle counselling for patients with hypertension (Thai Hypertension Society, 2019), it remains unclear to which extent alcohol brief interventions and lifestyle interventions that focus on other lifestyle risk factors are currently implemented in Thailand. We henceforth refer to all interventions focused on lifestyle risk factors – including but not limited to alcohol use – as lifestyle interventions.

In this study, we aimed to identify (i) current practices regarding alcohol use and lifestyle interventions among hypertensive patients, (ii) practical, social, economic, and cultural barriers to routine screening and lifestyle intervention targeted at hypertensive patients, particularly at those with hazardous alcohol use, and (iii) implications for targeted interventions in Thai primary care.

2. Methods

This study is a cross-sectional, mixed-method assessment based on surveys among three sets of respondents whose perspectives are relevant to hypertension care in Thailand: a) policy- and decisionmakers, members of educational institutions, and representatives from governing bodies of healthcare providers and advocacy groups (henceforth referred to as policymakers), b) healthcare practitioners (henceforth referred to as practitioners), and c) patients with hypertension (henceforth referred to as patients).

2.1. Study setting

The district health system, consisting of a district hospital together with several Community Health Promoting Hospitals (CHPHs) at sub-district level, is the backbone of Thailand's primary healthcare system. Practitioners and patients in our study were recruited in the province of Nakhon-Pathom, situated in a semi-urban setting about 50 kms outside-Bangkok. All six district hospitals of the province (providing primary and secondary care), the provincial hospital (providing tertiary care in addition to primary and secondary care), and one community hospital (limited to providing primary care and basic secondary care) were included in the study. Each district hospital serves a population of 30,000–50,000 and has inpatient facilities as well as outpatient clinics. With some variation, each district hospital is linked with 8–12 CHPH, which are the first point of contact for the population for preventive and basic curative services. While newly diagnosed hypertension cases may be identified through community-based or opportunistic screening during regular services, ongoing hypertension management primarily takes place in district hospitals' NCD outpatient clinics (World Health Organization, 2019). According to National Hypertension Guidelines, while patients with hypertension wait their turn to see the doctor in NCD outpatient clinics, nurses, counsellors, or pharmacists provide group education on treatment adherence and healthy lifestyles (Thai Hypertension Society, 2019). At CHPH, hypertension management services are generally limited to prescription refills by nurses.

2.2. Inclusion criteria, sampling strategy, and recruitment

We purposely identified policymakers as established, national experts in either hypertension care or alcohol use through consultations, desktop and internet search, and review of policy and strategy documents. Policymakers were invited to participate in our study via e-mail or phone.

Practitioners were medical doctors and nurses working at outpatient clinics of the eight hospitals included in our study. With permission from the Provincial Health Administrative office, each hospital's study coordinator invited all doctors and nurses working in the hypertension outpatient clinic (usually 1–3 per profession) to participate in our survey and distributed the questionnaires. Nurses may have simultaneously worked in alcohol clinics. Responses of those who returned the questionnaire to the hospital study coordinator were included in our study.

To ensure that patients had undergone all aspects of hypertension care (and not just diagnostics), patients must have had a recorded hypertension diagnosis made at least 6 months ago. We chose 35 years as the minimum age requirement as this is the threshold to be eligible for organized hypertension screening activities, and hypertension prevalence is notably higher compared to adult patients aged below 35 years (Thai Hypertension Society, 2019; Charoendee et al., 2018). Half of the patients were purposely selected by the hospital study coordinator based on their prior medical records indicating alcohol use, while the other half constituted a convenience sample of patients diagnosed with hypertension. Nurses and village health volunteers supported the recruitment of all patients and arranged appointments at their nearest health facility. Respondents provided informed consent and were compensated for their time.

2.3. Study materials, data collection, and analysis

Questionnaires elicited information regarding current practices and feasibility of interventions targeted at concomitant hypertension and alcohol use (Fig. 1). The content was adapted to the perspective of each stakeholder group. Questionnaire sections generally included a set of statements for which participants indicated their response on a Likert

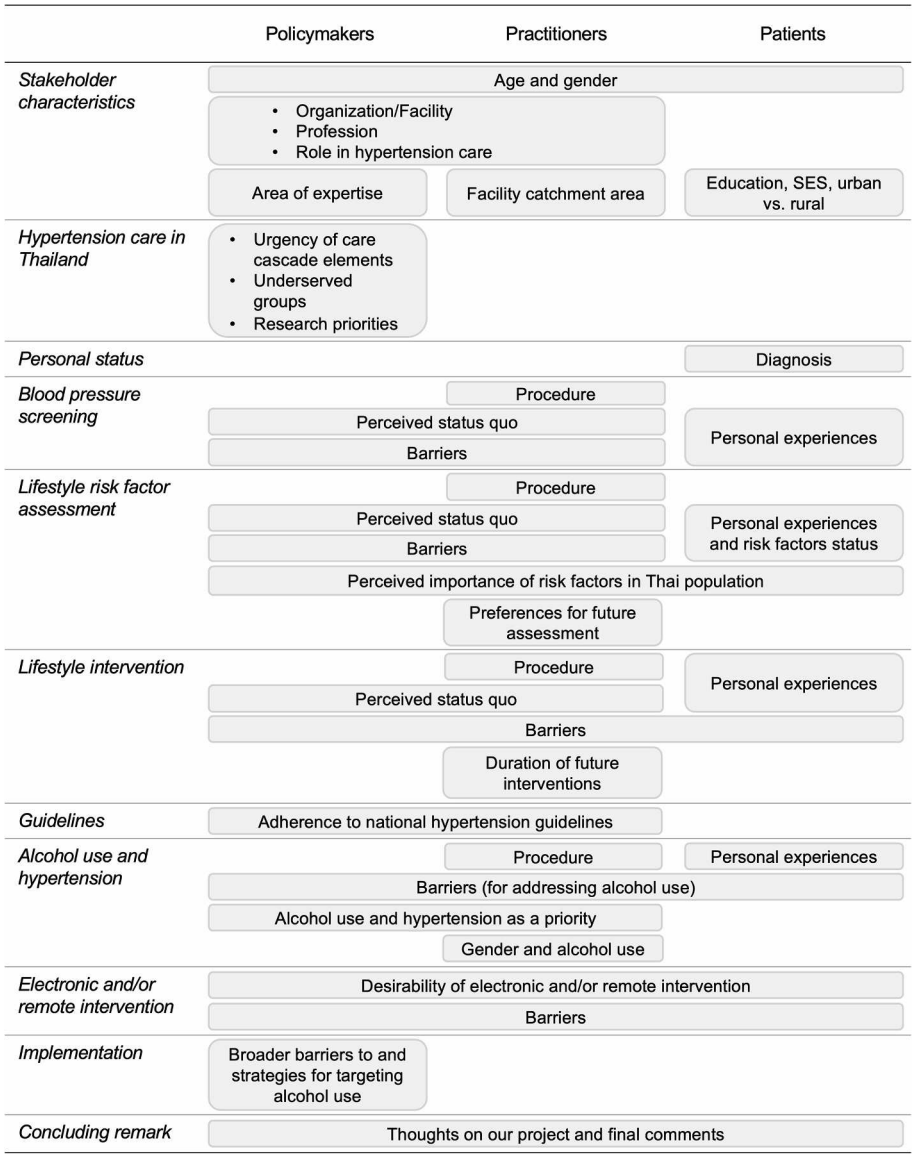

Fig. 1. Content of survey-based assessment for each stakeholder group.

scale, followed by an open-ended question or the option for additional comment by the respondent. The development of questions was loosely guided by the Consolidated Framework for Implementation Research (CFIR), a typology of constructs that have been associated with effective implementation (Damschroder et al., 2009; VanDevanter et al., 2017).

Data collection took place between December 2020 and May 2021. Policymakers were surveyed online. Practitioners responded to self-administered paper–pencil questionnaires. Patient surveys were conducted in person and responses were recorded verbatim on paper–pencil questionnaires by the interviewer. Answers to open-ended questions were translated by a professional translator using standard translation procedure.

In our analysis, we first analyzed responses and described response patterns separately within each stakeholder group before comparing results between stakeholder groups. Closed-ended questions were analyzed descriptively using R version 4.1.0 (R Core Team, 2021). For each Likert-scaled statement, we compared the share of respondents disagreeing (Completely disagree/disagree) with the share of respondents agreeing (Completely agree/agree). We show key results for each stakeholder group by illustrating selected Likert-scaled statements in a vertical bar graph anchored at the neutral response category. We further created a heat map using Excel to compare the share of respondents in each stakeholder group indicating that they "completely agree" or "agree" with the statement. Here, we only included statements that were included in the questionnaires of at least two different stakeholder groups to show varying strengths of agreement across stakeholder groups. Open-ended questions were analyzed using open coding tools from thematic content analysis. Specifically, after breaking each qualitative answer into individual response components and labeling each component, coding results were grouped by theme within the broader categories of barriers, facilitators, and implications.

2.4. Ethics

Ethics approval was obtained from the institutional ethics boards of the Centre for Addiction and Mental Health (REB# 076/2020) and Mahidol University (MUSSIRB:2020/169(B1)).

3. Results

In total, 91 stakeholders participated in our survey (Table 1). Policymakers worked at governmental policy institutions (n = 6), in

Table 1
Sample characteristics.

Variable	Policymakers	Practitioners	Patients with hypertension
N	22	24	45
Age in years, median (range)	58 (29–81)	46.5 (26–70)	52 (37–75)
Female, n (%)	14 (63.6)	19 (79.2)	6 (13.3)

governing bodies of healthcare providers (n = 3), at university or policy research institutions (n = 11), and for advocacy groups (n = 2). Detailed characteristics of policymakers are shown in Supplementary Table 1. Practitioners included 15 clinical nurses and 9 medical doctors. Detailed characteristics of practitioners are shown in Supplementary Table 2. Of 45 patients diagnosed with hypertension, 28 (62 %) consumed an alcoholic beverage at least twice a week (Supplementary Table 3).

We present key results by stakeholder group. For each group, results are divided into three sub-sections including current practices, barriers and facilitators, and areas for potential improvement. This is followed by a comparison of similarities and differences between stakeholder groups. All results were informed by responses to both closed- and open-ended questions. Exemplar verbatim quotations from stakeholders are presented in Table 2.

3.1. Policymakers

3.1.1. Current practices

There was large variation in the perceived status quo of blood pressure screening: 39 % of policymakers agreed with the statement that blood pressure screening is routinely performed in primary healthcare facilities, while 44 % disagreed, and almost half (47 %) agreed that there is no or insufficient community-based screening. Policymakers agreed that expansion of blood pressure screening should focus on places outside of clinical settings, i.e., community-, home-, or workplace-based screening. Some policymakers highlighted that screening has not been comprehensively expanded, especially in urban areas with few health volunteers, disadvantaged communities, or inaccessible areas, such as island regions. This is supported by statements that hypertension care is presently not catered to individuals with low socioeconomic status or health literacy, informal laborers, and populations whose working hours impede receiving care (Table 2). Policymakers agreed (81 %) that both lifestyle risk factor screening and lifestyle interventions among patients with hypertension are insufficiently implemented.

3.1.2. Barriers and facilitators

Smoking and alcohol were recognized as important drivers of hypertension by all policymakers. However, one respondent was critical of the importance of screening for alcohol use, arguing that there is a low prevalence of heavy drinking among hypertensive patients.

In terms of barriers, policymakers agreed (64 %) that current guidelines regarding procedures of lifestyle risk factor screening are not clear enough. Policymakers supported the statement that practitioners are insufficiently or completely unaware of the link between alcohol use and raised blood pressure (Fig. 2). A lack of appropriate screening tools for systematically assessing alcohol use in the Thai primary healthcare context was identified as another barrier (Table 2). Policymakers were split on whether there is a stigma associated with heavy drinking and whether practitioners are comfortable discussing alcohol use with patients. While there was high agreement that hypertension medication should be complemented with lifestyle intervention (95 %), insufficient resources (e.g., time, personnel, funds, or space) were seen as an important barrier to lifestyle risk factor screening and interventions (Fig. 2).

Table 2
Exemplar quotations from stakeholders and implications for potential interventions.

Area	Quotation	Rationale	Implication
Blood pressure screening			
	"Factory workers […] who are sick with hypertension often go to receive services outside their scheduled times because they fear wasting working time and having their wages deducted. There should be an accommodation for the worker care service system to better and systematically access services at their workplaces." (Professor of Public Health Nursing, female, 53 years)	At-risk populations such as informal laborers or factory workers, that are insufficiently reached through traditional routes, may profit from targeted interventions.	Identify strategies for at-risk populations.
Lifestyle risk factor screening			
	"The alcohol screening tool is complicated [and] hard to understand. There are too many questions. For example, AUDIT is not suitable for screening in the Thai social context." (Professor of Medicine, female, 56 years)"	Effective screening may improve the targeting of alcohol use as a risk factor for hypertension.	Implement standardized, easy to use assessment tools that are adapted to the Thai context.
	Using modern and easy-to-understand tools in measuring the amount of alcohol and drinking patterns, such as adopting a program that includes illustrations." (Researcher at International Health Policy Program Office, female, 40 years)		
	"There are many patients waiting and not enough time to discuss it." (Patient, male, 50 years)"	Limited resources in healthcare facilities need to be carefully divided and efficiently employed.	Identify strategies to reduce congestion at facilities and workload of practitioners.
	If there are too many patients at government facilities, it directly affects the quality of the counseling provided." – Medical doctor at District Hospital (male, 69)		
	"Asking about drinking alcohol for all males is easy and normal. Women, on the other hand, are sometimes nervous when asked." (Clinical nurse, female, 42 years, district hospital)	Create an environment where patients, in particular female patients, feel comfortable discussing their alcohol use.	Identify strategies to reduce stigmatization of (heavy) alcohol use.
	"Patients are afraid to tell the truth that they drink alcohol." (Patient, male, 37 years)		
Lifestyle interventions			
	"There should be a specific approach used as an easy-to-follow manual for personnel and a user-friendly manual for patients that they can utilize themselves […]."	Access to standardized, high-quality lifestyle support and counselling should be ensured for all patients.	Develop clear and concise guidelines for evidence-based interventions.

(*continued on next page*)

Table 2 (*continued*)

Area	Quotation	Rationale	Implication
	(Director at Department of Disease Control, female, 56 years)		
	"[Remote intervention] can be used to follow up behavior modification and to empower the patient. This will help reduce the missing of appointments." (Operation Chief of the Primary Care Services at Regional Public Health Office, male, 50 years)	Improve patient compliance and long-term lifestyle modification.	Introduce monitoring mechanisms for (changes in) lifestyle behavior and alcohol use.
	"Advantages [are] being able to get advice at anytime, anywhere with a signal, and every-one can access it, if they have electronic communication devices." (Medical doctor, male, 58 years, district hospital)	Digital tools may be used to expand equal access to lifestyle interventions.	Implement remote and electronically supported intervention elements that are compatible with the population's skillset.
	"Most of the patients with chronic diseases are the elderly. They are not skillful in using electronic devices. Some people are poor and obtaining electronic equipment is difficult." – Clinical nurse, female, 36 years, NCD clinic		
	"Advice can only be provided at the NCD clinic. Outside the clinic, there are some, but it depends on the service provider." (Clinical nurse, female, 52 years, district hospital)	Health promotion and lifestyle counselling at sub-district level may be more easily accessed by patients.	Strengthen resources and activities at sub-district level.

3.1.3. Potential improvements

Policymakers agreed that improvements in different areas of hypertension care are urgent, with 'blood pressure screening' and 'screening for and addressing lifestyle risk factors' ranking highest in urgency. Policymakers supported prioritizing lifestyle counselling in practitioners' curricula (86 %) and raised concerns about the health system's current foci:

"The medical care system that doctors learned from in medical schools still focuses on treatment with medication and spends less time promoting, preventing, and referring patients. […]" – Operation Chief of the Primary Care Services at Regional Public Health Office (male, 50).

Similarly, respondents noted that the provision of services is not sufficiently focused on *"creating systematic health literacy"* (Public Health Technical Officer, female, 60) and that *"the dimensions of health promotion are overlooked"* (Researcher at International Health Policy Program Office, female, 40). Policymakers emphasized the need for skill building among practitioners concerning health communication, effectively increasing the health literacy of patients, and screening to identify lifestyle risk factors. They agreed (90 %) that in-person lifestyle screening and interventions should be complemented by electronic tools but were divided as to whether video- or tablet-based solutions are financially sustainable (Fig. 2). Similarly, remote lifestyle interventions were viewed positively by policymakers. However, while they acknowledged the opportunity to reduce in-person time and increase the number of patients who receive a lifestyle intervention, they feared that remote e-interventions may be inaccessible to many patients due to a lack of mobile devices, internet access, or digital skills (Table 2).

3.2. Practitioners

3.2.1. Current practices

Practitioners were divided on whether blood pressure screening is routinely performed in primary healthcare facilities, with 42 % agreeing and 46 % disagreeing. However, all practitioners indicated that patients with hypertension are being screened for behavioral risk factors and receive some form of lifestyle intervention in their facilities (where applicable for patients). When instead asked what percentage of the general eligible population of hypertensive patients receive lifestyle interventions, estimates varied from 40 to 100 % with a median of 80 %. Lifestyle interventions included in-person conversation (92 %), standardized leaflet (88 %) and presentation (42 %), video (33 %), or written personalized information (33 %), and were mostly performed by doctors or nurses. For district hospitals, the estimated average maximum duration of lifestyle intervention was slightly shorter (13.2 min) compared to CHPH (16.7 min) where responses varied greatly from 0 to 60 min. All practitioners indicated that alcohol use is being discussed with hypertension patients either regularly (58 %) or sometimes (42 %). When asked about what topics are being addressed by lifestyle intervention, smoking and alcohol use ranked highest (96 % and 88 %, respectively).

3.2.2. Barriers and facilitators

Practitioners cited insufficient resources (e.g., knowledge and tools) at CHPH and patients' working hours or frequent relocation as general barriers to hypertension care. They identified migration workers and elderly patients without any caretakers as risk groups.

The majority (58 %) disagreed that practitioners know too little about blood pressure screening procedures or lifestyle risk factors for hypertension. Lifestyle risk factors were perceived as important drivers for hypertension, with smoking and salt or sodium considered slightly more important than others. Practitioners were divided on whether primary healthcare facilities have standardized tools to systematically assess lifestyle risk factors (Fig. 3). Though most practitioners perceived heavy drinking among patients as stigmatized, they disagreed with statements that their peers are insufficiently aware of the link between alcohol use and blood pressure (54 %) and that they do not feel comfortable raising the topic of alcohol use with patients (73 %) (Fig. 3).

Practitioners agreed that patients feel uncomfortable discussing their alcohol use (70 %) and several respondents worried about harming their relationship with the patient. They noted that women rarely disclose information about alcohol use, which *"makes solving the problem of alcohol drinking impossible"* (Clinical nurse, female, 45), and that female patients may feel *"more humiliated than male patients"* when asked about alcohol use (Clinical nurse, 55, female). Some practitioners asserted that women rarely drink or, congruously, that, if a patient is female, staff may not think that she drinks alcohol.

Practitioners perceived lifestyle interventions as useful. However, they overwhelmingly agreed that resources are presently lacking to perform these interventions (Fig. 3) and that congestion in district hospitals affects the quality of interventions (Table 2). Half of the practitioners agreed that there are no guidelines and procedures in place that define how and by whom lifestyle interventions should be performed (Fig. 3). While several free-text responses highlighted patient-related characteristics as barriers (e.g., noncompliance), one nurse (female, 54) acknowledged that *"[…] healthcare services are more focused on medication treatment than risk behavior management."*.

3.2.3. Potential improvements

Practitioners recognized the potential of remote or electronically supported lifestyle interventions, in particular by allowing patients to access support in any place and at any time (Table 2). This is in line with practitioners' view that many Thai people do not regularly attend primary healthcare facilities (70 %) and that patients often do not return for follow-up appointments (68 %). However, practitioners also expressed concerns about adaptability, with 75 % agreeing that a remote

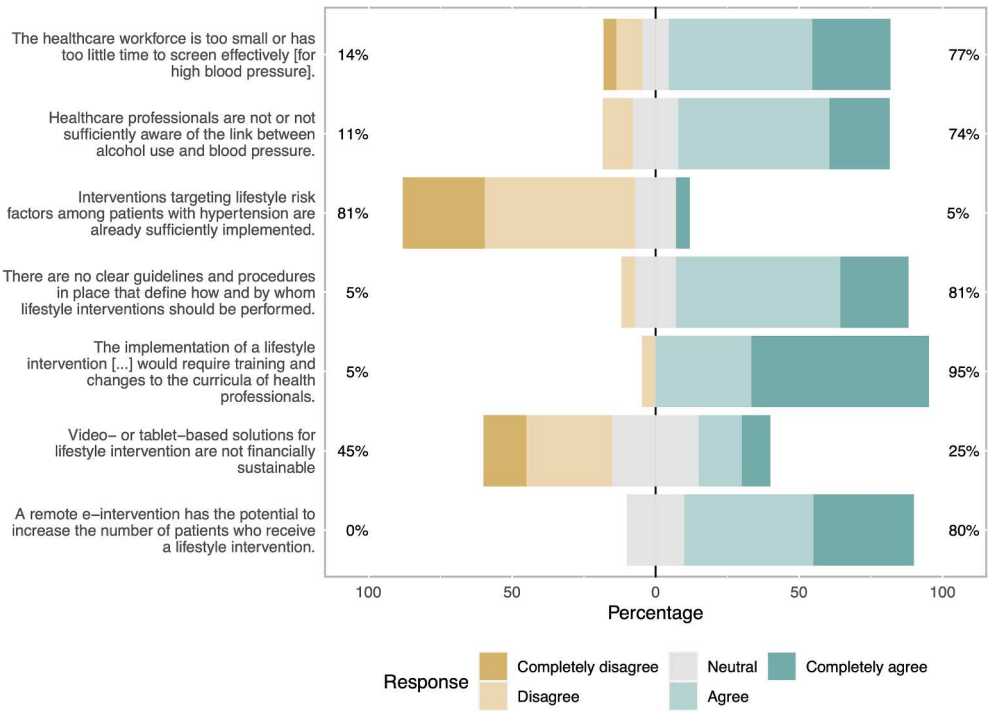

Fig. 2. Responses from policymakers (n = 22) to selected items that are relevant to implementing targeted lifestyle interventions for patients with hypertension. The percentage on the left side indicates the share of policymakers disagreeing (Completely disagree/Disagree) with the statement; the percentage on the right side indicates the share of policymakers agreeing (Completely agree/Agree) with the statement.

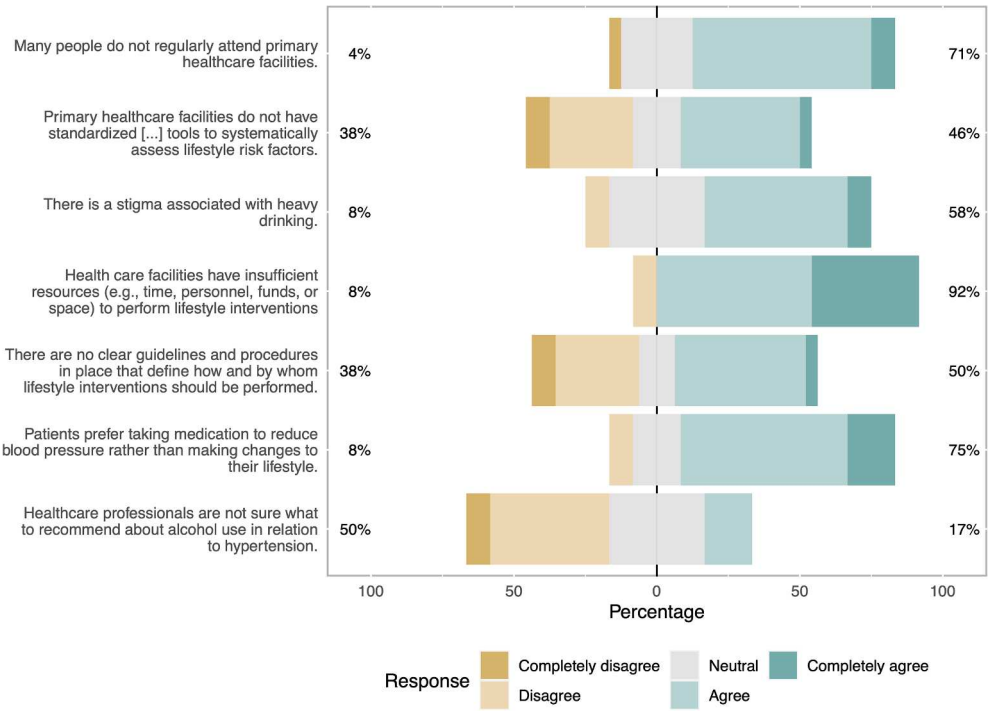

Fig. 3. Responses from practitioners (n = 24) to selected items that are relevant to implementing targeted lifestyle interventions for patients with hypertension. The percentage on the left side indicates the share of practitioners disagreeing (Completely disagree/Disagree) with the statement; the percentage on the right side indicates the share of practitioners agreeing (Completely agree/Agree) with the statement.

e-intervention will be inaccessible to many patients (Table 2).

At the same time, 79 % of practitioners agreed that it is important for patients to be able to directly consult a health care professional and they were largely undecided (50 %) as to whether patients would be willing to follow advice that is not given by an on-site health professional (e.g., by way of a remote e-intervention). Respondents noted that conversations held remotely may end up being a "one-way communication" and may impede giving feedback.

3.3. Patients diagnosed with hypertension

3.3.1. Current practices

Over two-thirds of patients (78 %) indicated that someone explained the causes of hypertension when they were first diagnosed. However, there was variation in the number of patients that reported assessment of different lifestyle risk factors, with 98 % for smoking, 96 % for alcohol use, 84 % for body weight or BMI, 73 % for diet or nutrition, and 69 % for salt or sodium intake.

All patients except for one (98 %) indicated that they received some form of lifestyle intervention upon their initial diagnosis of hypertension. This was most often delivered or performed by a doctor (77 %), a nurse (73 %), or a pharmacist (25 %). The format and duration of advice varied within our patient group: while 16 % indicated that they have only received written information, most patients (58 %) reported that the lifestyle intervention lasted more than 5 and less than 15 min, with some reporting duration of fewer than five minutes (13 %) or of more than 15 min and up to one hour (11 %). Lifestyle interventions most often addressed diet or nutrition (86 %), alcohol use (73 %), smoking habits (73 %), body weight or BMI (61 %), or salt or sodium intake (59 %).

3.3.2. Barriers and facilitators

Patients agreed that lifestyle behaviors, including alcohol use, are relevant to the development and progression of hypertension in the Thai population. However, they were divided on whether practitioners had practicable advice for patients on how to change their lifestyle (Fig. 4).

At the same time, patients were undecided on whether the relevant patient population was motivated to change their lifestyle (50 % neutral and 47 % agreement). Patients mentioned their peers, socializing habits, and daily routines as barriers to changing their lifestyle and alcohol use. Some patients expressed the belief that medication should prevail as the first line of treatment for lowering blood pressure and that lifestyle modification alone is insufficient. Two-thirds of patients agreed with the statement that there is stigma associated with heavy drinking (60 %), noting that *"patients are afraid to tell the truth that they drink alcohol"* (Patient, male, 37; Table 2).

3.3.3. Potential improvements

Most patients agreed that it is important for them to be able to ask questions directly to a health professional (85 %). This may explain a rather skeptical view of remote and electronic interventions (Fig. 4). Many free-text answers supported the notion that not all patients have the skills to operate smart devices and/or lack access to them. While there were concerns about the reach of remote interventions, views on their efficacy were split: while 49 % agreed that remote e-interventions are a good alternative to in-person lifestyle interventions, 33 % disagreed. In free-text responses, some patients acknowledged the potential benefits of remote interventions, with reduced travel time being cited most often.

3.4. Comparison across stakeholder groups

Fig. 5 shows the strength of agreement across key areas for each stakeholder group. Both policymakers and practitioners agreed that improvements in hypertension care, especially relating to lifestyle modification, are necessary. Across groups, there was not only a general understanding that lifestyle modification is critical to hypertension care but also that alcohol is an important risk factor for hypertension (Fig. 5). However, stakeholders repeatedly mentioned that current hypertension care prioritizes medication, potentially contributing to patients' belief that lifestyle modification is secondary to lowering blood pressure.

While both practitioners and patients diagnosed with hypertension indicated that alcohol use is currently being assessed and discussed, there seems to be no standardized tools or procedures for risk assessment and lifestyle intervention that are being universally applied (Fig. 5). Lifestyle interventions that are being offered seem to vary in duration, intensity, medium, and content.

Barriers were viewed somewhat heterogeneously across stakeholder groups (Fig. 5). Policymakers and practitioners cited lacking resources

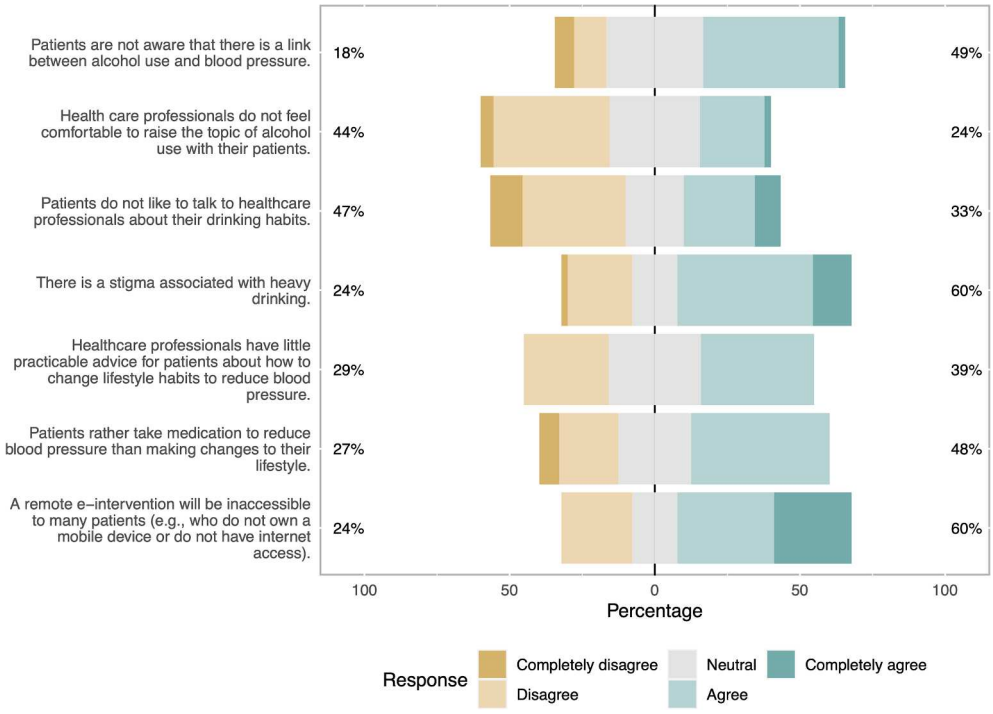

Fig. 4. Responses from patients diagnosed with hypertension (n = 45) to selected items that are relevant to implementing targeted lifestyle interventions for patients with hypertension. The percentage on the left side indicates the share of patients disagreeing (Completely disagree/Disagree) with the statement; the percentage on the right side indicates the share of patients agreeing (Completely agree/Agree) with the statement.

	Policymakers	Practitioners	Patients
1. Is alcohol use important?			
Importance of alcohol consumption for hypertension [a]	100%	92%	80%
2. What are current procedures?			
Health care facilities do not have standardized questionnaire or guides to systematically assess lifestyle risk factors [among hypertensive patients].	45%	44%	
There are no clear guidelines and procedures in place that define how and by whom lifestyle interventions should be performed [among hypertensive patients].	81%	50%	
Estimated share of hypertensive patients with whom alcohol use is being discussed [b]		88%	73%
3. What are barriers?			
Many people do not regulgarly attend primary healthcare facilities.	60%	70%	
Health care facilities have insufficient resources to perform lifestyle interventions.	86%	92%	38%
Health care professionals are not convinced of the usefulness of lifestyle interventions.	57%	4%	
Health care professionals have too little knowledge or training about how to perform lifestyle interventions.	48%	21%	
Health care professionals are not or not sufficiently aware of the link between alcohol use and blood pressure.	74%	25%	
Health care professionnals are not sure what to recommend about alcohol use in relation to hypertension.	58%	17%	
Patients prefer taking medication to reduce blood pressure rather than making changes to their lifestyle.	67%	75%	48%
Patients do not feel comfortable talking about their alcohol use.	53%	70%	31%
There is a stigma associated with heavy drinking.	42%	58%	60%
A remote e-intervention will be inaccessible to many patients (e.g., who do not own a mobile device or have internet access).	70%	75%	60%
4. What are opportunities?			
Lifestyle interventions in a health facility should be complemented by eletronic tools (e.g., informational videos).	90%	83%	
Remote e-interventions are a good alternative to in-person interventions.	75%	88%	49%
Patients are unwilling to follow advice which is not given by an on-site health professional.	35%	25%	44%
Health care professionals do not feel comfortable to raise the topic of alcohol use with their patients.	26%	17%	24%
It is important for patients to be able to ask questions directly to a health professional.	70%	79%	84%

Fig. 5. A heat map indicating the percentage of respondents in each stakeholder group indicating that they "completely agree" or "agree" with the statement. Values range from 0% (beige color) to 100% (dark turquoise color). [a] Percentage that deemed alcohol an "important" or "very important" risk factor for hypertension. [b] Percentage of respondents that reported to counsel on alcohol use or that report to have been counselled on alcohol use.

and compatibility with existing workflows as barriers. While policymakers questioned practitioners' knowledge relating to alcohol use and hypertension, and their ability to perform lifestyle interventions, surveyed practitioners recognized the link between alcohol use and hypertension and were confident addressing alcohol use and lifestyle changes with patients. Instead, practitioners cited patient-related characteristics as barriers to realizing effective lifestyle modification. Unlike policymakers, practitioners and patients perceived alcohol use as stigmatized and cited patients' reluctance in disclosing their alcohol use as a barrier.

There were competing views about remote lifestyle interventions: while stakeholders recognized the potential to reach patients that would otherwise not receive care, and to reduce congestion in hospitals, they highlighted that remote interventions may not be available to all population groups due to lacking access and skills among the elderly, poor, or less educated population segments. Patients also expressed differing opinions regarding the efficacy of remote interventions. However, policymakers and practitioners in particular, exhibited rather favorable views towards remote or electronically supported lifestyle interventions.

4. Discussion

This study assessed practices and barriers relating to screening and interventions for lifestyle risk factors among patients diagnosed with hypertension, in particular regarding alcohol use, from three different perspectives. Building on the CFIR typology (Damschroder et al., 2009), we have identified several constructs (henceforth stylized in italics) within four CFIR domains (intervention characteristics, outer and inner setting, and characteristics of individuals) that are likely relevant for the successful implementation of interventions targeting lifestyle behaviors (alcohol use) among patients diagnosed with hypertension in Thailand. In the following section, we provide a synthesis of our study results by mapping implications for implementing such interventions onto CFIR constructs.

Regarding intervention characteristics, there was a general appreciation of the *evidence strength and quality* among stakeholders that lifestyle support should play a key role when treating hypertensive patients with and without concomitant alcohol use. This is in line with previous findings that identified the efficacy of alcohol screening and brief intervention (SBI) as an enabling factor for successful implementation (Chan et al., 2021). A digital approach that provides a standardized, self-administered assessment and intervention with minimal training requirements and flexible follow-up conditional on the patient needs may further provide a *relative advantage* over existing procedures, while ensuring an inclusive approach that is *adaptable* to meet local needs (Adam et al., 2019; Wiemker et al., 2022). For example, patient groups that are both at a higher risk to engage in heavy episodic drinking and less likely to be reached through traditional primary care pathways might require targeted intervention strategies (Table 2). At the very least, improvements in standardized, context-appropriate tools and clear procedures for risk assessment and lifestyle intervention are warranted (Abidi et al., 2016).

The proposal of a (digital) SBI to reduce blood pressure has received high support by policy stakeholders which may be indicative of a positive outer setting regarding *external policy and incentives*. While effectiveness is not yet sufficiently demonstrated, smartphone applications designed to assist users to reduce hazardous alcohol consumption show potential as an inexpensive alternative to brief intervention in primary

care (Colbert et al., 2020). At the same time, wider *patient needs and resources* must be accurately known and considered: intervention strategies that rely on remote or electronic elements have to strike a balance between providing convenient care to at-risk groups and avoiding reinforcing health disparities along the digital divide that often exists between marginalized and 'connected' population segments (Levy and Janke, 2016; Khoong et al., 2021; Liu et al., 2020).

The construct *tension for change* in the inner setting domain describes the degree to which stakeholders perceive the current situation as intolerable or needing change. While stakeholders agreed that prioritization of health promotion activities is essential for improving hypertension management in Thailand, *available resources* and *access to knowledge and information* were identified as the main limiting factors. In particular concerning available resources, any potential intervention needs to carefully consider time constraints and congestion in district hospitals as well as lacking resources and coverage at the sub-district level.

With regard to *knowledge and beliefs about the intervention* (in the domain of characteristics of individuals), stakeholders mentioned concerns due to the potential stigmatization of heavy alcohol use. While the latter point underlines the importance of ensuring confidentiality and acceptance as an integral part of any intervention (preventing potential alienation of patients, in particular in relation to gender), practitioners overall showed a high self-efficacy by reporting confidence in their abilities to screen for and give advice regarding alcohol use. Self-efficacy of practitioners has been repeatedly reported to be an enabler for implementing SBI in primary care (Chan et al., 2021).

Our study results are in line with previous empirical findings on barriers to implementing SBI that generally highlight the role of adequate resources, training, and the identification of those at risk without stereotyping as main facilitators in primary care (Chan et al., 2021; Johnson et al., 2011). While there were structural barriers (e.g., the fact that practitioners have many competing tasks in the Thai primary care system), most of the identified barriers are modifiable per se and, maybe more importantly, set in a wider positive implementation climate. Thus, we argue that it may be worth focusing on hazardous alcohol use among hypertensive patients in Thai primary care, in particular given the existing evidence for positive effects of reducing alcohol intake on hypertension (Roerecke et al., 2018; Roerecke et al., 2017). Given the substantial alcohol-attributable risk in Thailand (Institute for Health Metrics and Evaluation, 2021) and that even short interventions can effectively reduce alcohol consumption (Beyer et al., 2019; O'Connor et al., 2018; Kaner et al., 2018), prioritizing hazardous alcohol use among hypertensive patients has the potential for substantial synergistic health gains and healthcare cost reductions by lowering the burden of NCDs (Rehm et al., 2017; Rehm and Roerecke, 2013; Baliunas et al., 2009; Patra et al., 2010).

4.1. Limitations

This study has several limitations. First, recruitment of respondents was conducted at only eight hospitals, all situated in Nakhon-Pathom province, and participants constitute a convenience sample. As well, relatively small sample sizes were used for each stakeholder group. Therefore, the results are not representative of all primary healthcare facilities in Thailand. However, by including three different groups with broad inclusion criteria, we ensured that diverse perspectives were assessed. Second, while we ensured that the focus on alcohol use was not obvious from the outset, respondents may have exhibited socially desirable behavior by acknowledging alcohol as an important risk factor for hypertension (Lavrakas, 2008). Third, respondents may have operated under varying assumptions of what lifestyle interventions entail as we provided a broad definition of lifestyle intervention to capture all current activities.

4.2. Conclusion

Stakeholders recognized the potential of screening and brief interventions targeting hazardous alcohol use among hypertensive patients. We identified barriers as well as potential implications that may guide the development and implementation of such interventions. Future research may establish the feasibility of such interventions, while attention should be paid to any solution that could reinforce existing inequities along social and demographic gradients.

CRediT authorship contribution statement

Julia M. Lemp: Conceptualization, Methodology, Formal analysis, Writing – original draft, Visualization. **Supa Pengpid:** Conceptualization, Investigation, Writing – review & editing, Project administration. **Doungjai Buntup:** Investigation, Writing – review & editing. **Till W. Bärnighausen:** Writing – review & editing. **Pascal Geldsetzer:** Writing – review & editing. **Karl Peltzer:** Writing – review & editing. **Jürgen Rehm:** Conceptualization, Writing – review & editing. **Bundit Sornpaisarn:** Writing – review & editing. **Charlotte Probst:** Conceptualization, Methodology, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2022.101954.

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4 PUBLICATION 3: QUASI-EXPERIMENTAL EVALUATION OF THE ENGLISH DIABETES PREVENTION PROGRAMME

Lemp, J. M., Bommer, C., Xie, M., Michalik, F., Jani, A., Davies, J. I., Bärnighausen, T., Vollmer, S., & Geldsetzer, P. (2023). Quasi-experimental evaluation of a nationwide diabetes prevention programme. *Nature*. https://doi.org/10.1038/s41586-023-06756-4

Article

Quasi-experimental evaluation of a nationwide diabetes prevention programme

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Diabetes is a leading cause of morbidity, mortality and cost of illness[1,2]. Health behaviours, particularly those related to nutrition and physical activity, play a key role in the development of type 2 diabetes mellitus[3]. Whereas behaviour change programmes (also known as lifestyle interventions or similar) have been found efficacious in controlled clinical trials[4,5], there remains controversy about whether targeting health behaviours at the individual level is an effective preventive strategy for type 2 diabetes mellitus[6] and doubt among clinicians that lifestyle advice and counselling provided in the routine health system can achieve improvements in health[7–9]. Here we show that being referred to the largest behaviour change programme for prediabetes globally (the English Diabetes Prevention Programme) is effective in improving key cardiovascular risk factors, including glycated haemoglobin (HbA1c), excess body weight and serum lipid levels. We do so by using a regression discontinuity design[10], which uses the eligibility threshold in HbA1c for referral to the behaviour change programme, in electronic health data from about one-fifth of all primary care practices in England. We confirm our main finding, the improvement of HbA1c, using two other quasi-experimental approaches: difference-in-differences analysis exploiting the phased roll-out of the programme and instrumental variable estimation exploiting regional variation in programme coverage. This analysis provides causal, rather than associational, evidence that lifestyle advice and counselling implemented at scale in a national health system can achieve important health improvements.

Diabetes prevalence and diabetes-related deaths continue to rise in most parts of the world[1,11]. By 2030, the number of adults with diabetes globally is expected to reach 578 million, representing 10% of the global adult population[11]. Consequently, there is an urgent need to implement population-based measures that prevent diabetes, enhance its early detection and address cardiovascular risk factors to prevent or delay its progression to complications.

In the seminal US Diabetes Prevention Program study (which serves as a model for many behaviour change programmes in the USA and elsewhere)[12], targeting changes in individuals' lifestyle behaviour was more successful than administering metformin in preventing or delaying diabetes. However, clinical trials such as the US Diabetes Prevention study have mainly focused on efficacy, supplying proof of principle that the intervention worked when extensive one-to-one sessions with specialists and a range of incentives are being provided[13]. Thus, although a recent meta-analysis concluded that lifestyle modification provides strong evidence for reversing prediabetes in adults[5], it remains important to establish the transferability of behaviour change programmes into real-world settings, in which resources and support are generally more limited than in the clinical research setting.

Establishing that behaviour change programmes work in routine care is essential for several reasons. First, although lifestyle counselling is the recommended first-line treatment option for people presenting with prediabetes and other cardiovascular risk factors in clinical guidelines[14], there is ample evidence from a variety of settings that clinicians often do not follow these guidelines[15–20] and instead revert to prescribing preventive medication because of limited time resources in primary care[21], insufficient knowledge and referral options for promoting healthy lifestyles[7,22] and a predominance of the biomedical model with clinicians being uncertain about the success of counselling[7,8]. In particular, doubt that behaviour change at the level required for substantial weight loss is possible to achieve for most patients is prevalent among primary care clinicians[9]. Second, participants in clinical trials for behaviour change programmes are unlikely to be representative of the broader patient population. For instance, patients enrolled in clinical cardiology trials had a lower risk profile as they tended to be

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younger, male and less likely to have a comorbid disease than individuals encountered in everyday practice[23]. A general population sample may also respond differently to behaviour change programmes because of lower health literacy and willingness to engage, higher comorbidities and greater ethnic diversity[24,25].

Using routine health data

We advance the argument that the impact of behaviour change programmes on population health must relate to real-world effectiveness and should, thus, be evaluated in an "observational, non-interventional trial in a naturalistic setting" akin to phase 4 in drug development[26,27]. However, conventional observational studies that are generally applied in health research have the disadvantage that they may fail to account for principal confounding factors such as selection biases and, thus, preclude causal interpretations[28]. In contrast, we establish causality by applying a regression discontinuity approach, one of the most credible quasi-experimental strategies for causal inference[10,29], that combines large-scale routine data from the English National Health Service (NHS) with variation in treatment probabilities generated by guidelines from the National Institute for Health and Clinical Excellence (NICE) that recommend intensive lifestyle counselling for people at high risk of progression to type 2 diabetes mellitus (T2DM)[14]. Specifically, we use the fact that the NHS Diabetes Prevention Programme (NHS DPP), a behaviour change programme with weight loss, diet and physical activity goals consisting of at least 13 group sessions over the course of 9 months and the largest DPP globally to achieve universal population coverage, is only open to patients above a prespecified threshold of HbA1c or fasting plasma glucose indicating non-diabetic hyperglycaemia[30]. By exploiting this eligibility threshold that draws a sudden distinction between the prediabetes and normal glycaemia range, we can take advantage of existing large-scale routine health data while still obtaining causal effect estimates that are not vulnerable to confounding and measurement error (Supplementary Information section 1.1 gives an overview of existing correlational evidence for the NHS DPP)[10,29].

Our study used data from the Clinical Practice Research Datalink (CPRD) Aurum and NHS England's Hospital Episode Statistics (HES). CPRD Aurum is a large primary care database of de-identified electronic health records from a network of about one-fifth of general practitioner (GP) practices across England. To ensure sufficient implementation of the NHS DPP during the study period after the start of the phased roll-out in mid-2016, our population of interest consisted of adults (aged 18 to 80 years) who received an HbA1c test between 1 January 2017 and 31 December 2018. Data were available until the end of June 2020. We identified 2,106,376 patients who had a baseline HbA1c test during the enrolment and met inclusion criteria (Methods section, 'Data source and study population'). Patient characteristics are described in Extended Data Table 1.

In all our analyses, the primary outcome was change in HbA1c. For the regression discontinuity analysis, secondary outcomes included changes in body mass index (BMI), body weight, blood pressure, serum cholesterol concentrations and serum triglyceride concentrations. We also conducted exploratory analyses investigating the effect of programme referral on the probability of diabetes, hypertension and hyperlipidaemia incidence; receipt of newly prescribed medications for these conditions; diabetes complications; all-cause mortality; and emergency hospitalization for a major adverse cardiovascular event (MACE). A detailed definition of each outcome is provided in Supplementary Information section 1.2.

Assumptions for causal effect estimation

In the first part of the analysis, we ensured that all necessary assumptions for a regression discontinuity analysis were met[31]. In particular, we assessed the continuity assumption[29], which requires that the density distribution of baseline HbA1c be continuous around the prediabetes threshold of 42 mmol mol^{-1} (6%). This assumption would be violated if patients or providers could precisely manipulate baseline HbA1c, which is virtually impossible in our scenario given that the exact blood test result is automatically uploaded into the electronic health data system. We plotted the density distribution of baseline HbA1c values around the threshold and, as expected, found no evidence of heaping or manipulation (Supplementary Fig. 1).

Receipt of treatment was defined as a record of a referral to a behaviour change programme or intensive lifestyle counselling during the 12 months after the baseline HbA1c test. Treatment primarily included referrals to the NHS DPP but we also included referrals to other structured programmes and intensive lifestyle counselling as they are likely to serve as an alternative when placement in NHS DPP is not possible. We conducted analyses testing the sensitivity of results to this choice (Methods section, 'Outcome and treatment definition'). For convenience only, we henceforth refer to these treatments simply as intensive lifestyle counselling. We observed a 10.8 percentage points increase in treatment assignment at the prediabetes threshold (Fig. 1a). In relative terms, patients just above the threshold were five times more likely to be referred to intensive lifestyle counselling compared to patients just below the threshold. There is no pathophysiological phenomenon at that specific threshold value; rather, increasing HbA1c is associated with an increased risk of developing T2DM and cardiovascular disease in a more continuous fashion[32]. The somewhat arbitrary nature of the prediabetes HbA1c threshold along with the fact that HbA1c is measured with a degree of random measurement error means that patients just below and above the threshold should be close to identical in their underlying characteristics. In Fig. 1b–d, we show that, unlike for referral to intensive lifestyle counselling, there is no sudden 'jump' at the prediabetes HbA1c threshold in age, baseline BMI and frequency of GP visits, signifying that these variables cannot confound our analysis. We demonstrate this further using balance tests, empirically showing that a comprehensive set of potential confounding variables, including demographic characteristics, physiological variables and markers of healthcare use and literacy, were all continuously distributed near the threshold (Supplementary Figs. 2 and 3 and Extended Data Table 2). Taken together, our initial analyses provide strong evidence that the necessary assumptions for a valid regression discontinuity analysis were met[10], meaning that patients below and above the threshold were effectively randomized to being referred to the programme or not, as they would be in an ideal target trial (Supplementary Information section 1.3).

Establishing whether glycaemic control improves

Next, we proceed to compare patients lying closely on either side of the threshold using local linear regression. We found that patients who were referred to intensive lifestyle counselling significantly improved their HbA1c concentrations. Specifically, we evaluated the effect of referral to intensive lifestyle counselling on glycaemic control by fitting separate regression lines of the association between baseline HbA1c and change in HbA1c above and below the eligibility threshold. The difference in where these lines intersect at the threshold quantifies the discontinuity in the outcome and can be described as the effect of the threshold rule (−0.10 mmol mol^{-1}, 95% CI −0.16, −0.03). This effect merely measures the effect of being eligible for intensive lifestyle counselling as determined by the clinical guideline rather than the effect of being referred to intensive lifestyle counselling. Given that only 17.4% of eligible patients were referred to intensive lifestyle counselling, it is necessary to scale the effect of the threshold rule by the difference in the probability of treatment at the threshold to determine the effect of being referred to intensive lifestyle counselling. When doing this, we find a significant beneficial effect of referral to intensive lifestyle

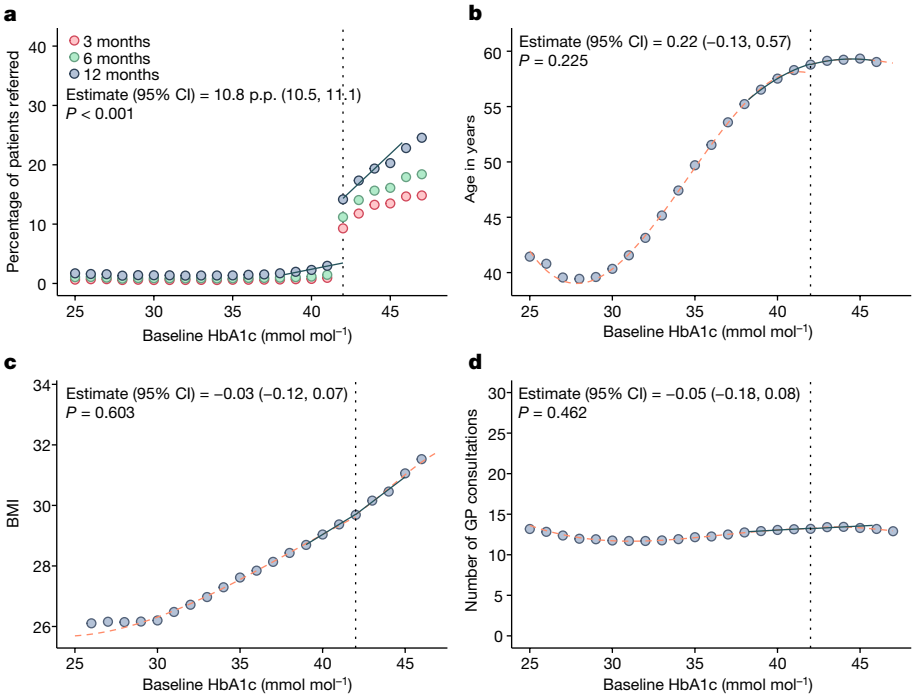

Fig. 1 | Association between baseline HbA1c and intensive lifestyle counselling and potential confounders. a, Primary exposure ('first stage'), that is, referral to intensive lifestyle counselling at 3, 6 and 12 months after baseline HbA1c. **b**–**d**, Potential confounders: age (**b**), baseline BMI (**c**) and prior GP consultations (**d**). The blue lines show the local linear regression models in the bandwidth used in our primary analysis (Methods, section 'Main analysis'). For age (**b**), we assumed a quadratic relationship with baseline HbA1c. The orange dotted lines show the global polynomial relationship. The blue circles represent the mean value for individual patients and the dotted vertical lines indicate the HbA1c cutoff. The estimate represents the discontinuity at the HbA1c threshold, whereas discontinuities in potential confounders may jeopardize assumptions underlying regression discontinuity. Significance was tested in two-sided *t*-tests ($P < 0.05$). The sample size in the bandwidth is $n = 513{,}473$ (**a**, **b** and **d**) and $n = 332{,}156$ (**c**). p.p., percentage points.

counselling on HbA1c at follow-up (−0.85 mmol mol^{-1}, 95% CI −1.46, −0.24). Details can be found in the Methods.

Although the clinical significance of a 0.85 mmol mol^{-1} reduction in HbA1c is difficult to quantify at an individual level, observational clinical data suggest a linear association between HbA1c and cardiovascular disease, even in non- or prediabetic individuals[32]. For example, as a reference point, after adjusting for principal conventional cardiovascular risk factors, individuals having HbA1c concentrations of 5.5–5.7% (which approximately translates to 37–39 mmol mol^{-1}) were almost twice as likely to be diagnosed with coronary artery disease compared to individuals with less than 5.5% (ref. 33). Thus, it is likely that a reduction of 0.85 mmol mol^{-1} is meaningful at the population level.

The effects of the threshold rule (of being eligible for a referral) and of being referred to intensive lifestyle counselling for all outcomes are shown alongside optimal bandwidth and sample size in Extended Data Table 3. To ensure that the finding of improved glycaemic control is not sensitive to our selected bandwidth or functional form (linear or quadratic), we show that effect sizes were robust to different choices (Fig. 2a, Supplementary Fig. 4 and Supplementary Tables 2 and 3). We also performed the regression discontinuity analysis using a secondary cohort, for which we only included patients whose baseline HbA1c test was their first ever recorded HbA1c test. Here, being referred to intensive lifestyle counselling led to a 1.26 mmol mol^{-1} reduction in HbA1c (95% CI −2.06, −0.46). All results for the secondary cohort can be found in Supplementary Information section 3.

Intent-to-treat versus per-protocol effect

Our estimated effects are relevant for clinicians and policy-makers who need to understand the effects of deciding to refer patients to intensive lifestyle counselling (the 'intent-to-treat' effect), regardless of whether patients then decide to attend the programme, which is largely not in the clinician's control. However, understanding programme efficacy (the 'per-protocol' effect or, in other words, the effect of the programme if everyone who is referred attends) also provides useful information. It is important to consider that programme attendance may be a function of individual characteristics such as personal motivation or available time resources. We assessed the amount of adherence by determining whether the patient started the intervention sessions of the NHS DPP according to GP records. In line with statistics from an official programme evaluation[30], among eligible patients that were referred to the NHS DPP in our primary cohort, 28.1% of patients started the intervention. By scaling up the effect of programme referral in the selected bandwidth, we approximate that patients' HbA1c concentration would be reduced by 3.0 mmol mol^{-1} if patients perfectly adhered to referrals and took up the programme. Patients who started the treatment are largely similar to patients who were referred but did not start the treatment, in particular on variables that may indicate heightened personal motivation or health literacy such as attending preventative cancer screening services or vaccine uptake (Supplementary Table 4) and our main results were robust to adjusting for variables that may serve as a proxy for personal motivation and health literacy (Supplementary Table 5).

Ruling out confounding and bias

It is important to rule out that we may falsely attribute beneficial effects to being referred to intensive lifestyle counselling whereby they were in fact induced by medication. When adjusting our results for being prescribed diabetes medication during follow-up, the estimated causal effect of referral to intensive lifestyle counselling on glycaemic control indicated a larger reduction, suggesting that improvements in

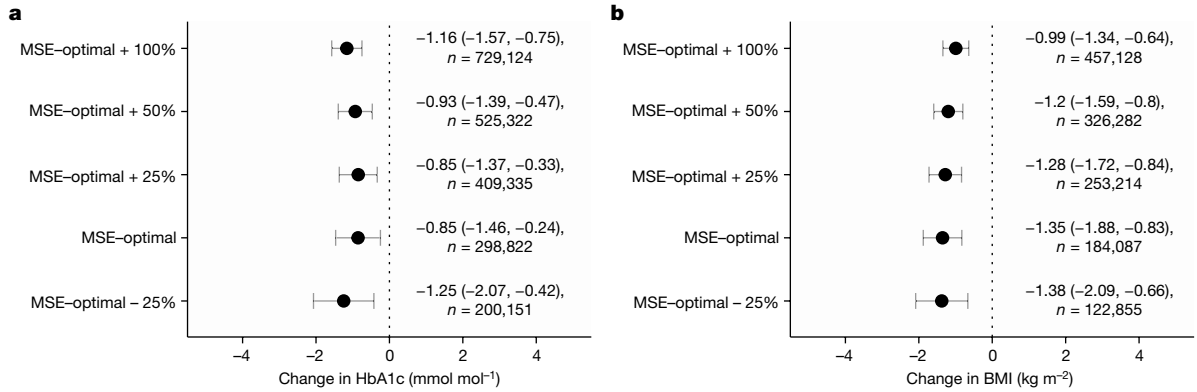

Fig. 2 | Robustness of the effects of being referred to intensive lifestyle counselling on HbA1c and BMI across bandwidth choices. The mean-squared error (MSE)-optimal bandwidth is 3.8 mmol mol^{-1} below and above the threshold. **a**,**b**, The estimated complier average causal effect of referral to intensive lifestyle counselling on change in HbA1c (**a**) and change in BMI (**b**) from local linear regressions with varying bandwidths (75%, 125%, 150% or 200%) of the MSE-optimal bandwidth with heteroskedasticity-robust 95% CI and triangular kernel weights. The sample size of patients in each bandwidth is given alongside the effect estimates. All effect estimates are statistically significant in two-sided *t*-tests ($P < 0.05$).

HbA1c were, indeed, not driven by increased use of diabetes medication (Extended Data Table 3). In general, having an HbA1c concentration above the eligibility threshold for the NHS DPP was associated with a small increase in the probability of being prescribed diabetes medication shortly after treatment assignment (risk difference in percentage points (RD) = 0.04, 95% CI 0, 0.09), which increased to 0.3 percentage points at follow-up. However, the discontinuity in the probability of being prescribed diabetes medication was not significant when using robust bias-corrected confidence intervals for inference (Extended Data Table 4). Specifically, out of 26,513 patients with a baseline HbA1c between 42 and 47 mmol mol^{-1} who were referred to intensive lifestyle counselling, only 882 (3.3%) were prescribed diabetes medication during the 12 months following treatment assignment with numbers increasing with increasing HbA1c concentrations; these numbers are unlikely to substantially impact improvements in glycaemic control. There was no discontinuity in newly prescribed lipid-lowering medication (RD = 0.29, 95% CI −0.23, 0.82) or blood pressure-lowering medication (RD = 0.11, 95% CI −0.38, 0.60).

We further performed a set of robustness checks to detect uncontrolled confounding or other sources of bias following the approach by ref. 34. First, we did a placebo analysis using an alternative patient cohort that is comparable in inclusion criteria to our primary analysis but who had baseline HbA1c measures in 2014 and 2015. During this period, patients were already identified with prediabetes on the basis of the same threshold and public health guidance. However, the key difference was that there were limited intensive lifestyle programmes in place to which GPs could refer their patients. This led to a scenario in which key potential confounders such as discontinuities in outcome availability and number of consultations could already be observed (Supplementary Fig. 5), whereas the proposed causal mechanism—the NHS DPP—was 'deactivated' (that is, a negative exposure control scenario; Supplementary Fig. 6a). We find that being eligible for the NHS DPP in these years in which the NHS DPP was not yet available did not result in an improvement in HbA1c or BMI (Supplementary Fig. 6b,c). Second, we repeated the main regression discontinuity analysis for health outcomes which we did not expect to be plausibly affected by referral to the NHS DPP (so-called negative outcome controls). Results indicate no systematic confounding in our primary cohort (Extended Data Table 5). Third, our results are robust to adjusting for the number of months between baseline and endline measurement (Supplementary Tables 2 and 3). Fourth, we restrict our sample to patients with a follow-up period of at least 12 months (and 18 months, respectively). Although some of the observed effect estimates are smaller and show greater uncertainty compared to the full sample, they still point towards health gains comparable to those in our primary analysis (Supplementary Tables 6 and 7).

Improvements in other health outcomes

In secondary analyses, we found evidence that other key cardiovascular risk factors improved. Referral to intensive lifestyle counselling significantly reduced BMI (−1.35 kg m^{-2}, 95% CI −1.88, −0.83; Fig. 2b) and weight (−2.99 kg, 95% CI −4.38, −1.61). Albeit not significant, effect estimates were also in the direction of benefit for blood pressure levels (diastolic: −1.35 mmHg, 95% CI, −3.31, 0.61; systolic: −2.03 mmHg, 95% CI −4.96, 0.91). When adjusting results for the prescription of blood pressure-lowering medication, improvements in systolic blood pressure persisted and became marginally significant ($P = 0.092$; Extended Data Table 3). Referral to intensive lifestyle counselling also significantly reduced triglyceride concentrations (−0.33 mmol l^{-1}, 95% CI −0.54, −0.12) and increased HDL concentrations (0.04 mmol l^{-1}, 95% CI 0, 0.09). There was no significant effect on other serum cholesterol concentrations (LDL and the total cholesterol-to-HDL ratio) and no effect on the probability of being prescribed lipid-lowering medication. Results were robust to adjusting for baseline observables (Supplementary Table 2) and using different bandwidths (Supplementary Figs. 7–10) or a quadratic model (Supplementary Table 3). Results for our secondary cohort yielded a very similar pattern of results but slightly larger effect sizes (Supplementary Information section 3).

Diabetes complications, emergency hospitalization for MACEs and mortality were not significantly reduced by being referred to intensive lifestyle counselling in exploratory analyses (Extended Data Table 3). The low incidence of adverse downstream events during our relatively short follow-up period, with 26,567 (1.3%) of patients dying and 36,567 (1.8% of those 2,037 384 linkable to HES data) having an emergency hospitalization for a MACE, resulted in low statistical power for detecting small, short-term changes in these outcomes. We observed a significant increase in T2DM diagnoses at the threshold (RD = 0.39, 95% CI 0.21, 0.57; Extended Data Table 3). We interpreted these results cautiously because diagnoses in electronic health records may be less reliable than biochemical measures[35] and a stronger focus on identifying and monitoring people who are at risk of T2DM is likely to initially increase the incidence of T2DM independent of health improvements. Hypertension and hyperlipidaemia incidence did not significantly change at the threshold (Supplementary Tables 2 and 3).

Men may be benefitting more than women

Results stratified by gender, age group, ethnicity, socioeconomic status (based on the Index of Multiple Deprivation (IMD) which is derived from the patient's postcode) and rural or urban practice location are presented in Supplementary Tables 8–16. Stratification led to relatively small sample sizes for practices in rural locations and patients with Asian, Black or mixed ethnicity and in the youngest age group. Being referred to an intensive lifestyle intervention led to significant improvements in HbA1c, weight, blood pressure and triglycerides in men but not women (Supplementary Tables 8, 10–12 and 16). Both men and women significantly improved their BMI although effect estimates suggest larger improvements in men compared to women (Supplementary Table 9). There was no indication that a higher socioeconomic status was consistently associated with greater benefits. We further stratified results by variables that may function as a proxy for health literacy, health services use and personal motivation (Supplementary Tables 8–16). Although the results are exploratory and limited by the absence of prespecified hypotheses and insufficient statistical power, effect estimates suggest that patients who did not receive lifestyle advice from their GP previously were more likely to benefit from being referred to intensive lifestyle counselling.

Triangulation of evidence

To further boost confidence in our findings, we triangulate the evidence from our regression discontinuity approach by (1) performing a difference-in-differences analysis, an established quasi-experimental method originating from social sciences that leverages the phased roll-out of the NHS DPP in three waves and (2) using the regional variation in programme coverage as an instrumental variable for programme referral (Methods)[31].

In the difference-in-differences analysis our estimate of interest represents how much the average outcome of the treatment group has changed in the period after the treatment, compared to what would have happened in the absence of the intervention. A key assumption is that, in the absence of treatment, the outcome trends would have been the same in the treatment group as in the comparison group[31]. We interrogated this assumption by examining whether the trends in HbA1c are visually parallel in the pre-introduction period (Extended Data Fig. 1) and by testing the interaction between wave and (pre-introduction) year in linear regressions (Wald test: wave 1, $P = 0.273$, wave 2, $P = 0.809$). The group–time average treatment effect estimates provide support for the view that implementing the NHS DPP led to an improvement in glycaemic control (Extended Data Table 6a). For each relevant comparison during the post-DPP introduction, there is a statistically significant beneficial effect on HbA1c (wave 1 versus wave 3 in 2018/2019: −0.126 mmol mol^{-1}, 95% CI −0.235, −0.018; wave 1 versus wave 3 in 2019/2020: −0.328 mmol mol^{-1}, 95% CI −0.447, −0.209; and wave 2 versus wave 3 in 2019/2020: −0.140 mmol mol^{-1}, 95% CI −0.231, −0.048; Fig. 3a). When we consider how the effect of implementing the NHS DPP changes by the length of time that the programme has been in place, these parameters paint largely the same picture as the group–time average treatment effects (Fig. 3b). The effect of implementing the NHS DPP on HbA1c is negative and increasing in magnitude the longer practices have implemented the NHS DPP. By applying a conditional parallel trends assumption in a secondary analysis, we ensured that the results were not confounded by the extension of routine HbA1c testing during programme roll-out (Methods section, 'Difference-in-differences analysis'; Extended Data Table 6b and Supplementary Fig. 11).

As the NHS DPP was not rolled out in parallel across regions in England (Extended Data Fig. 2), we were able to leverage the time-variant regional differences in NHS DPP coverage as an instrument for actual referral to the programme. Specifically, we estimated the effect of NHS DPP referral on glycaemic control from comparing those who changed from not being referred to being referred because of a change in programme coverage in their region. Although this instrumental variable analysis is relatively imprecise because it relies on time-by-region variation instead of patient-level variation, we continue to find a significant beneficial effect of programme referral on endline HbA1c (result from two-stage least squares (2SLS) regression with practice- and year-fixed effects: −3.77 mmol mol^{-1}, 95% CI −7.52, −0.01).

Finally, we also provide correlational evidence from propensity score matching, multivariate regression and panel regression with individual- and year-fixed effects (Methods section, 'Multivariate regression analyses, propensity score matching and panel regression'). The results of these analyses were consistent with those from our regression discontinuity approach (Supplementary Table 17). We provide an overview of all effect estimates measuring the change in HbA1c in Extended Data Table 7.

Discussion

Although clinical trials have shown that intensive lifestyle counselling is efficacious in improving cardiovascular risk factors in controlled research settings[4,5,36–38], we present evidence that these health benefits can be successfully translated to and scaled up in routine care. In our study using electronic health records from more than 2 million patients, we found causal evidence that referral to the largest behaviour change programme for prediabetes globally led to improved glycaemic control and reductions in BMI, weight, HDL and triglycerides. Systematic reviews and meta-analyses of controlled clinical trials studying effects of lifestyle interventions (including diabetes prevention programmes in US settings) on weight loss and blood pressure in adults with prediabetes found effect sizes comparable to those in our study[36,38–40]. Although evidence on improvements in glycaemic control from controlled trials seems more mixed[38–40], our study substantiates indications from earlier correlational studies that suggest beneficial effects of NHS DPP participation on HbA1c and weight (Supplementary Information section 1.1). We discuss results from secondary and stratified analyses in the Supplementary Discussion.

We demonstrated the use of a regression discontinuity approach for evaluating a population-wide health service intervention by leveraging a threshold in treatment assignment induced by clinical guidelines. Thresholds are ubiquitous in clinical medicine and, thus, represent a rich opportunity to generate causal, rather than associational, evidence of treatment effectiveness. In conjunction with increasing access to routine electronic health records and detailed health information, regression discontinuity analyses have the potential to advance evidence-based healthcare and implementation science. For example, many conceivable research questions that are of interest to clinical medicine and health systems research cannot be studied in conventional or pragmatic randomized trials, either for feasibility (such as very long follow-up periods to establish the effectiveness of anti-aging agents) or ethical reasons (such as withholding treatments that have become the standard of care). Regression discontinuity designs may also be used to investigate aspects of health equity, for example, heterogenous treatment effects between patient groups linked to sociodemographic characteristics and comorbidities, for which randomized controlled trials usually have too small a sample size or an insufficiently diverse study population.

Inherent to any regression discontinuity analysis is the limitation that we can only estimate the causal effect for those who initiate the treatment because they crossed the eligibility threshold. This effect may differ from the (unobserved) treatment effects for patients who would have been referred to intensive lifestyle counselling regardless of baseline HbA1c concentrations (the 'always takers'), for example, because of clinical symptoms or patients who would not have participated in any programme or counselling even if eligible (the 'never

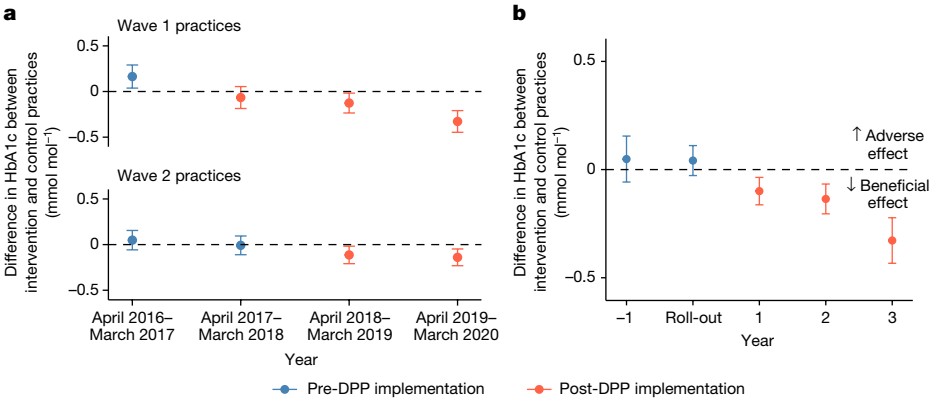

Fig. 3 | Difference-in-differences effect estimates of NHS DPP implementation. a, Group–time average treatment effects for patients from wave 1 and wave 2 compared with patients from wave 3 practices. **b**, Partially aggregated average effect by length of exposure, that is, programme implementation, in years. Roll-out for wave 1 practices started in June 2016 and roll-out for wave 2 practices started in April 2017. Effect estimates are presented with 95% CI on the basis of standard errors clustered at the practice level using multiplier bootstrap procedures (Methods section, 'Difference-in-differences analysis').

takers'). Also, effects may not be generalizable to those further away from the HbA1c threshold that defines prediabetes. This is, however, not a concern in this study given that the NHS DPP specifically targets people with prediabetes, which in turn is defined by a fairly narrow HbA1c range. In our analysis, we mainly relied on the complier average causal effect (CACE), estimating the effect for those who were actually referred to an intervention. Given that there was a large percentage of individuals presenting above the HbA1c threshold who were not referred to any lifestyle counselling, it is important to not mistake the observed CACE effects for the population health effect of the NHS DPP. Although the NHS DPP is operating at a large scale, with 100,000 referrals being offered in 2021 (ref. 41), there remains a substantial proportion of adults in England with impaired glycaemic control who are presently not taking part in intensive lifestyle counselling, whether it is because of system-level (for example, placements in the NHS DPP are not available) or physician- and patient-level reasons (for example, GPs are not compliant with the guidelines). Especially given low uptake and high attrition rates among socio-economically disadvantaged and diverse ethnic groups[42], our study lends support to calls for further investment in behavioural interventions and targeted prevention strategies for individuals at risk for diabetes that are at present not reached through care pathways. It should be further investigated whether some groups may benefit from combining programmes such as the NHS DPP with continuing, long-term support through social prescribing and community engagement initiatives that increases attention to patients' wider social context and health choice architecture[43].

This study has several other limitations. First and foremost, we observed considerable missingness in outcomes such as HbA1c or BMI, which were also measured more frequently by GPs in the follow-up period if patients had crossed the prediabetes threshold. This differential missingness in our outcome variables will be a source of bias if individuals with missing outcome data have systematically different outcome values compared with those who do not. Having said that, we show that crossing the prediabetes threshold and subsequent closer monitoring of biomarkers by GPs was not associated with improvements in our outcome variables before NHS DPP roll-out. Closer monitoring of patients, however, may be the reason for which we find that referral to intensive lifestyle counselling increased the probability of being diagnosed with T2DM independently of improvements in biomarkers.

Another potential limitation is violation of the exclusion restriction, whereby treatments or exposures other than intensive lifestyle counselling are affected by crossing the cutoff. Although we could not precisely control for the relationship between drug dosage and secondary outcomes, we are confident that the observed health effects were not attributable to increased medication following treatment assignment as effect estimates were robust to adjusting for drug prescriptions. In addition, testing a diverse set of negative outcome controls suggests no systematic confounding. We further conditioned our results on variables that may function as a proxy for health literacy, health services use and personal motivation, which did not substantially change our results and performed a robustness analysis restricting our sample to patients with regular GP visits before their treatment assignment.

Finally, because of the use of electronic health records we had no detailed information about adherence or persistence to behaviour change programmes and lifestyle counselling over time. Early evidence suggests that the number of attended sessions in the NHS DPP acts as a mediator for successful weight loss at follow-up[44]. However, our primary interest was in whether the benefits of the NHS DPP are seen in real-world circumstances, outside the controlled conditions of a randomized controlled trial. Non-adherence to the programme, for example because patients feel that the visits are too frequent or lengthy, are part and parcel of such a real-world effectiveness assessment. We discuss limitations of our two other quasi-experimental approaches; difference-in-differences analysis and instrumental variable estimation in the Supplementary Discussion.

Taken together, our findings demonstrate that referral for intensive lifestyle counselling in routine care, in the form of a population-wide diabetes prevention programme, is effective in improving glycaemic control and reducing body weight. Scepticism about the effectiveness of lifestyle counselling for successful behaviour change may stem from clinicians' experience that brief lifestyle counselling—that is often the only feasible approach in time-constrained GP consultations—may be of no or very limited benefit. Investments in structured, intensive behaviour change programmes, on the other hand, may help to promote primary and secondary prevention of T2DM and reduce the risk of complications from diabetes and cardiovascular events. Their positive effects may also extend to other non-communicable diseases such as cancer, which is increasingly thought to be connected to unhealthy lifestyle habits and environments[45] or communicable diseases such as influenza or COVID-19, which more gravely affect people with known cardiovascular risk factors such as diabetes[46]. Thus, our study not only demonstrates the potential of intensive lifestyle counselling for improving the health of patients with prediabetes in routine care but potentially also suggests a promising route for improving population health more broadly.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41586-023-06756-4.

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Methods

Description of the NHS Diabetes Prevention Programme

UK NICE public health guideline 38 recommends that people who have non-diabetic hyperglycaemia (HbA1c concentration of 42–47 mmol mol^{-1} (6.0–6.4%) or fasting plasma glucose of 5.5–6.9 mmol l^{-1}) and are thus at high risk of progression to type 2 diabetes (T2DM) are referred to a "local, evidence-based, quality-assured intensive lifestyle change programme" to prevent or delay the onset of T2DM[14]. The NHS DPP began phased roll-out in 2016. The provider contracts require the intervention to be delivered face-to-face to groups of 15–20 adults over at least 13 sessions (totalling 16 h) with a minimum of 9 months' duration, with the aim of supporting behaviour change to result in improved diet, increased physical activity and weight loss. Activities include a mixture of education, group support, knowledge testing, visual activities and activities led by patients[47,48]. Eligible individuals (a recorded HbA1c measure of 42–47 mmol mol^{-1} in the past 12 months or a history of gestational diabetes) are generally identified by their GP for inclusion in the programme. HbA1c concentrations may be measured as part of routine clinical practice or an NHS Health Check (a health check-up offered by GPs for adults in England aged 40 to 74 years to detect early signs of stroke, kidney disease, heart disease, type 2 diabetes or dementia)[30]. An option to self-refer based on the Diabetes UK 'Know your Risk' tool had been added temporarily as a referral route during the Covid-19 pandemic (after our study period)[49]. According to guidelines, people below the HbA1c eligibility threshold for the programme should be offered brief advice or intervention and receive information about services that could help them change their lifestyle, bearing in mind their risk profile. Our analysis studies the original framework of the NHS DPP before changes such as more commercial providers or the provision of a digital option were introduced in 2020 (ref. 50).

Initial projections by Public Health England and NHS England expected that GP identification would generate demand for around 100,000 participants a year once the programme was rolled out nationally by 2020. Official reported statistics from the National Diabetes Audit confirm that referral numbers (offers that were made and not declined) increased steadily from 2017 to 2020, with reporting periods covering January to March of the next year exceeding modelled targets as early as 2018 (2017, 103,295; 2018, 241,255; 2019, 386,025; and 2020, 559,770)[51]. In a recent analysis from the DIPLOMA research programme (Diabetes Prevention—Long Term Multimethod Assessment), it was reported that by April 2020, providers had received a total of 513,312 referrals, of which 271,208 (52.8% of total referrals) had attended an initial assessment and 101,175 (19.7% of total referrals) had attended at least 60% of the programme's sessions[50]. Publications report on uptake rate and progression through the programme in different ways. According to a scoping review published in early 2022, uptake of the initial assessment following a referral varied from 40% to 78% (ref. 42). Others report on attendance at the first intervention session with rates varying from 36% to 94% (ref. 42). Similarly, numbers on how many participants reached the mid- or end-point of the programme vary considerably. According to an early service evaluation, as of the end of December 2018, 36% attended at least one intervention session and 19% attended at least 60% of the sessions[30]. In this early service evaluation, younger age, Asian and mixed ethnicity (compared to white ethnicity), a lower socioeconomic status and baseline obesity were associated with lower rates of completion.

Data source and study population

The study used data from the CPRD Aurum[52] and the NHS England Hospital Episode Statistics Admitted Patient Care (HES APC) database[53]. CPRD Aurum is a large primary care database of de-identified electronic health records from a network of about one-fifth of GP practices across the United Kingdom. The data are representative of the broader English population in terms of geographical coverage, socioeconomic deprivation, age and gender[52]. In July 2020, anonymized longitudinal data from 35.9 million patients and 1,296 at present contributing English GP practices were available. HES APC is a secondary care database in England and records patient data related to presentations in NHS hospitals or private healthcare institutions for which the NHS provides partial funding. It covers all NHS hospitals in the country. The study protocol was approved by the Independent Scientific Advisory Committee (ISAC) for MHRA research (protocol no. 20_000052). Ethics approval for observational research using the CPRD and linked anonymized NHS healthcare data with approval from ISAC was granted by a National Research Ethics Service committee (Multiple Research Ethics Committee ref. 05/MRE04/87).

In contrast to CPRD Aurum data, which do not contain lifetime follow-up of patients because patients are entering the database when they register with a contributing GP practice and exiting the database when they leave that practice, patients in HES APC maintain the same ID throughout their time in the database[54]. As this information was only available for patients linkable to HES APC, we kept all patients in the analysis regardless of whether they seemed under several CPRD IDs. Results were insensitive to dropping all patients with several CPRD IDs for a single HES ID from the study population.

We followed a target trial approach to mimic a randomized controlled trial that would be ideally conducted to estimate the causal programme impact as closely as possible (Supplementary Information section 1.3)[55,56]. The population of interest consists of adults (aged 18 to 80 years) who received an HbA1c test between 1 January 2017 and 31 December 2018. Data were available until end of June 2020. Exclusion criteria were all patients who (1) exceeded the HbA1c threshold for diabetes or prediabetes before their index date (that is, date of their baseline HbA1c record) or (2) received any diabetes medication before their index date (all codes available in our Open Science Framework (OSF) repository). In a set of further analyses, we also excluded patients who had any HbA1c test before their index date to avoid any repeated HbA1c testing before treatment assignment. All results for this secondary cohort can be found in Supplementary Information section 3. Although specified in the NICE guideline as an alternative entry requirement, we did not use fasting plasma glucose as treatment assignment variable because routine testing of fasting plasma glucose to determine non-diabetic hyperglycaemia is rare compared to HbA1c testing[57].

Outcome and treatment definition

The primary outcome was glycaemic control measured as change in HbA1c between baseline and the final HbA1c taken during follow-up. Secondary outcomes included change in BMI, body weight, systolic and diastolic blood pressure, serum cholesterol concentrations (HDL cholesterol, LDL cholesterol and ratio between total and HDL cholesterol) and serum triglycerides concentration. We conducted exploratory analyses investigating the effect of programme entry onto probability of newly prescribed diabetes medications, blood pressure-lowering and/or lipid-lowering medication (evaluated separately), probability of any diabetes complication (ophthalmic, neurological or renal), all-cause mortality and emergency hospitalization for a MACE[58] during follow-up. The follow-up started at 6 months after the date of the baseline HbA1c record and continued until the date of an outcome or censoring event (such as death or transfer-out of the patient). Details on how each outcome was defined are shown in Supplementary Information section 1.1.

Receipt of treatment was captured as the record of a referral to a behaviour change programme or intensive lifestyle counselling during the 12 months after the baseline HbA1c test. Treatment primarily included referrals to the NHS DPP but we also included referrals to other structured programmes and intensive lifestyle counselling as they are likely to serve as an alternative when placement in NHS DPP is

not possible. A total of 26,970 patients with a baseline HbA1c between 42 and 47 mmol mol^{-1} were referred to a behaviour change programme or intensive lifestyle counselling, of which 20,963 (77.7%) were referred to the NHS DPP. A total of 4,800 patients declined NHS DPP referrals offered by their GP. All records considered as treatments are listed in Supplementary Table 18. The NHS DPP guidelines stipulate that patients without a test indicating non-diabetic hyperglycaemia in their general practice records are not accepted into the programme (unless they have a history of gestational diabetes). However, patients may have been referred to an intensive lifestyle intervention that we considered to be comparable to the NHS DPP (for example, a structured weight loss programme) at the discretion of their GP (for example, due to other risk factors such as excess weight) or based on a second HbA1c test that exceeded the threshold within the referral window of 12 months. Thus, we performed a robustness analysis in which we restrict the referral window to 3 months after the baseline HbA1c measurement and only consider referrals to the NHS DPP as the treatment variable. This led to substantially fewer patients below the eligibility threshold being referred (n = 620). We observed similar treatment effects, with a comparable but slightly larger reduction in HbA1c compared to the primary analysis (Supplementary Table 19).

Main analysis

We used a regression discontinuity approach to estimate the effect of referral to intensive lifestyle counselling on our outcomes. The analysis consisted of two steps. First, we estimated the association between individual's baseline HbA1c and being referred to intensive lifestyle counselling ('first stage'). Second, we estimated the association between baseline HbA1c and each outcome by fitting separate regression lines above and below the HbA1c eligibility threshold. The difference in where these lines intersect the threshold quantifies the discontinuity in the outcome, our effect of interest.

Specifically, our analysis represents a fuzzy regression discontinuity (FRD) design, for which the treatment is not assigned deterministically but probabilistically. In the FRD design, we can estimate the effect of the patient presenting just above the eligibility threshold, that is, the effect of treatment eligibility as determined by the threshold rule or guideline itself. To obtain the effect of referral to intensive lifestyle counselling itself on those induced to accept a referral because of the threshold rule (so-called compliers), it is necessary to scale the effect of the threshold rule by the difference in the probability of treatment at the threshold. This results in a so-called CACE (or local average treatment effect), which is analogous to the intention-to-treat effect in a target trial (Supplementary Information section 1.3).

We used a local linear approach, which minimizes bias by limiting the study sample to a defined bandwidth around the threshold in which a linear regression can be estimated[59]. The size of the bandwidth was automatically selected using a data-driven method that seeks to optimally balance the bias-variance trade-off[59]. In addition, a triangular kernel was applied, such that individuals closer to the threshold were more heavily weighted than those further away. For computing confidence intervals, we used heteroskedasticity-robust standard errors. All tests for statistical significance in our regression discontinuity analyses are two-sided t-tests. Further analyses were performed to assess the robustness of results to bandwidth size, using a quadratic form and using a robust bias-corrected variance estimator for inferences[60].

We plotted the relationship between baseline HbA1c and referral to intensive lifestyle counselling to show the discontinuity in treatment assignment. We also present visual evidence in support of key identifying assumptions that can be tested in the data. The first is that the density of the data should be continuous around the threshold. This would be violated if patients (or GPs) could precisely manipulate the baseline HbA1c value. The second is that baseline covariates should be balanced (that is, continuous) at the threshold. As in randomized controlled clinical trials, evidence of balance on baseline observables provides confidence that patients assigned to treatment and control conditions are exchangeable. We tested balance of baseline observables in a series of placebo tests in which we calculated local linear as well as global polynomial regressions over the entire support of the data to detect potential violations of this assumption.

Robustness checks

Our regression discontinuity approach achieves causal effect estimation through quasi-randomization rather than active adjustment for variables that may confound the association between treatment and outcome. Nevertheless, in robustness checks, we adjusted for variables that may be associated with outcomes to show robustness and improve precision of effect estimates[61]. These were age, gender, number of GP consultations during follow-up, time to follow-up record (that is, months between baseline and endline measurement) and prescription of relevant medications. For HbA1c, we adjusted results for diabetes medication prescription; for blood pressure, we adjusted for blood pressure-lowering medication prescription; and for cholesterol and triglycerides concentrations, we adjusted for lipid-lowering medication prescription, in particular statins, before the endline measure. Estimates for mortality and MACE hospitalization were adjusted for whether patients received any of these three types of medications before their death or first MACE hospitalization. We did further analyses to show that results are robust when restricting our sample to patients for whom we observe at least 12 and 18 months between baseline and endline measurement (Supplementary Tables 6 and 7).

All analyses were complete-case analyses and we assessed whether this could give rise to bias by evaluating if missingness in outcomes or time to follow-up changed discontinuously at the eligibility threshold (Supplementary Table 1). Following this, we performed a set of extra robustness checks following the approach by others to further investigate if there are any other inherent sources of bias or confounding[34]. The core idea is "to repeat the experiment under conditions in which it is expected to produce a null result and verify that it does indeed produce a null result"[34]. First, we tested a set of negative outcome control variables, that is, health outcomes for which we assumed that any causal effect through intensive lifestyle counselling (our proposed mechanism) would be impossible. Those variables are the probability of recording flu vaccination, pneumococcal vaccination, fracture, accidental injuries, routine cancer screenings (bowel, breast and cervical), consultation for skin abnormalities, asthma attacks, allergic reactions, hay fever, use of oral contraceptives, use of an intra-uterine device and onset of cancer or dementia. Second, we created a negative exposure control scenario, that is, we mimicked an analysis as closely as possible to our primary study design without the 'essential ingredient'—the NHS DPP programme. To do so, we leveraged the fact that NICE guidelines recommending monitoring and intensive lifestyle counselling for patients with an HbA1c of 42 mmol mol^{-1} or higher had already been in place since late 2012, whereas the NHS DPP was only rolled out starting 2016. We performed a placebo analysis using an alternative patient cohort that is comparable in inclusion criteria to our primary analysis but who had baseline HbA1c measures in 2014 and 2015. During this period, individuals were already identified with prediabetes on the basis of the same threshold and public health guidance. However, the key difference was that there were limited intensive lifestyle programmes in place to which GPs could refer their patients. This led to a scenario in which potential confounders (for example, the effects of a diagnosis of prediabetes on patient and GP behaviours) could already be observed, whereas the proposed causal mechanism was 'deactivated'. We suggest that in this scenario, patients did not exhibit any significant health improvements.

All analyses were performed using RStudio and R statistical software (v.4.2.1)[62]. Mean-squared error (MSE) optimal bandwidths were automatically selected by the rdbwselect command of the rdrobust package[63]. The two-sided significance level was set at 0.05. Blinding

and randomization of research participants is not actively performed in quasi-experimental study designs. We did not use statistical methods to predetermine sample size.

Difference-in-differences analysis

As further evidence, we present a difference-in-differences analysis leveraging the phased national roll-out of the NHS DPP programme in three waves (first wave start date, 1 June 2016; second wave start state, 1 April 2017; and third wave start date, 1 April 2018). Our approach is similar to the study design used by others who estimate the impact of the NHS DPP on type 2 diabetes incidence rates based on National Diabetes Audit data[50]. Thanks to the differential timing of the NHS DPP for each wave, it is possible to compare patients from practices belonging to waves 1 and 2 with patients from practices belonging to wave 3 as the control group. To determine to which wave each CPRD practice belonged, we computed the share of eligible patients (patients scoring between 42 and 47 mmol mol^{-1}) who were referred in each roll-out phase for each practice. We considered practices to be participating in the NHS DPP in a given wave if they referred at least 3% of their eligible patients to the NHS DPP during that wave. Data were drawn from 1,383 practices (20.1% of all practices in England) covering more than 11 million registered patients. Of these practices, 188 were first wave, 433 second wave and 475 third wave practices based on the timing of their first recorded NHS DPP referral. We excluded 13 practices that already referred patients during a pilot phase before June 2016 and 274 practices that did not refer any patients at any time or closed before March 2020.

In our analysis, we treated April 2015 to May 2016 for the comparison of wave 1 to wave 3 practices and April 2015 to April 2017 for the comparison of wave 2 to wave 3 practices, as the pre-intervention period, capturing the trends before the implementation of the NHS DPP. We considered an implementation period to be 12 months because there is a lag between a practice enroling in the NHS DPP, patients participating in the programme and notable effects of the 9 months' long programme on patients' health. Thus, the impact of the NHS DPP will be tested during the post-DPP introduction period. This post-period is April 2017 to March 2020 for the comparison of wave 1 to wave 3 practices and April 2018 to March 2020 for the comparison of wave 2 to wave 3 practices. We present group–time average treatment effects (with a 'group' being patients from GP practices in a given wave) for each relevant comparison as well as aggregated treatment effects that average effects in waves and across different lengths of exposure to the treatment (that is, implementation of the NHS DPP).

Specifically, we applied the framework by ref. 64 and used their accompanying R package did[65] for the case with repeated cross-sections data to account for variation in treatment timing and aggregate the several observed timepoints. We first estimated the group–time average treatment effect among the treated, ATT(g,t), in each post-period, t, for wave 1 and wave 2, g, using wave 3 as control. The group–time ATT were estimated by regressing the individual-level HbA1c measure (latest available record in each period) on a treatment indicator (that is, whether the NHS DPP has already been implemented at the practice level), a time indicator for the current period and an interaction between those two indicators using ordinary least squares regression. The treatment effect was measured by the interaction term between the treatment indicator and the time indicator.

Next, we used different aggregation methods to summarize these group–time average treatment effects: a simple effects aggregation that reports the weighted average (by group size) of all available group–time average treatment effects, a group-specific effects aggregation that summarizes average treatment effects by the timing of the NHS DPP implementation and an event study aggregation. Event study aggregation uses a weighted average of the estimates grouped by length of time since NHS DPP implementation. We obtained standard errors clustered at the practice level and corresponding confidence intervals for our estimates using the multiplier bootstrap procedures as described in ref. 64.

In line with changes in NICE guidelines[14], the share of patients who have a recorded HbA1c test in each practice increased from 2015 to 2020. The increasing trends were similar across waves, except for wave 2 practices in 2019/2020 which were lower compared to wave 3 practices (Supplementary Fig. 11). Hence, as a robustness analysis, we applied a conditional parallel trends assumption; that is, we assume only that practices with the same share of patients having taken a HbA1c test would follow the same trend in HbA1c in the absence of treatment. This resulted in similar effect estimates (Extended Data Table 6b).

Instrumental variable estimation

To further triangulate evidence on the effect of the NHS DPP on glycaemic control, we present an analysis in which we use the regional variation in NHS DPP coverage as an instrumental variable for the actual receipt of programme referral.

Instrumental variable (IV) estimation is a statistical technique used to address endogeneity in regression analysis, for which the independent variable (in our case, being referred to the NHS DPP) is correlated with the error term, for example, due to selection bias in treatment assignment. The IV estimation requires several assumptions to be valid. First, the IV used in the analysis, that is, the regional variation in NHS DPP coverage, must be correlated with the endogenous variable of interest, that is, the patient-level probability of being referred to the NHS DPP. Second, the IV must be independent of the error term in the regression equation, meaning that it cannot be correlated with any other factors that affect the outcome variable. This assumption requires that the instrumental variable is not affected by any unmeasured confounding variables that are also affecting the outcome variable. Third, the IV must affect the outcome variable only through their effect on the endogenous variable and not through any other pathways. This assumption requires that the IV does not have any direct effect on the outcome variable. Last, the IV must have a monotonic effect on the endogenous variable.

We computed the regional NHS DPP coverage by dividing the number of patients registered with practices eligible for the DPP (which varies by programme wave) by the total number of patients registered in each region (Extended Data Fig. 2). The regional variable in CPRD refers to nine Strategic Health Authorities (SHAs), namely East Midlands, East of England, London, North East, North West, South Central, South East Coast, South West, West Midlands and Yorkshire and the Humber, which were part of the structure of the NHS in England between 2002 and 2013. We were able to match information that we received from the National Diabetes Audit on NHS DPP practice eligibility in each wave (practices listed by clinical commissioning groups, CCGs) to the SHAs through publicly available information on primary care trusts (PCTs)[66]. In cases in which we found no match through PCTs, we matched the CCGs through output area, available from the Office for National Statistics[67,68]. We constructed a panel dataset, consisting of yearly observations for all patients eligible for the NHS DPP from April 2016 to March 2020. Specifically, patients entered the panel in the year in which they first had an HbA1c test scoring between 42 and 47 mmol mol^{-1} and were retained for each year during which HbA1c test results were available in their GP records. We applied the same inclusion criteria (aged 18 to 80 years, no previous use of diabetes medication and no history of diabetes) as for the regression discontinuity analysis.

We computed a cumulative treatment status for each year t; that is, a patient was considered treated if receiving a referral by the end of year t and remained treated thereafter. We verified the first assumption of IV estimation by regressing the cumulative treatment status on the NHS DPP coverage in each region in the previous year $t-1$ (first stage). We found that the regional NHS DPP coverage was significantly associated with the probability of being referred by the end of the following year (0.038, 95% CI 0.014, 0.063, $P < 0.001$).

We then used a 2SLS regression to estimate the effect of lagged treatment status on current HbA1c, with the lagged regional NHS DPP coverage serving as the instrumental variable for the lagged treatment status. We accounted for cases in which several HbA1c measurements were recorded for a patient within a year by averaging the measurements. We controlled for practice- and year-level fixed effects and clustered standard errors at the practice level. The resulting effect estimate represents the local average treatment effect, the causal effect of the endogenous treatment variable among those who would comply with the treatment if assigned to receive it. In other words, it measures the average effect of being referred to the NHS DPP for patients whose referral status changes only because of the variation in regional NHS DPP coverage, rather than because of their own characteristics or preferences. In addition, we report the intention-to-treat effect, which was estimated by regressing the lagged NHS DPP coverage directly onto current HbA1c. Overall, this approach allowed us to address potential endogeneity issues from conventional OLS regression and provide more reliable estimates of the treatment effect on HbA1c concentrations. We used the R package lfe[69] for this analysis.

Multivariate regression analyses, propensity score matching and panel regression

We also performed a set of extra regression-based analyses for our primary outcome HbA1c. On the basis of our target trial approach, these analyses included all patients eligible for the NHS DPP in our study period, that is, adults (aged 18 to 80 years) who had a HbA1c test greater than or equal to 42 mmol mol^{-1} and less than 47 mmol mol^{-1} between January 2017 and December 2018 with no previous use of diabetes medication and no history of diabetes.

First, we report unadjusted and adjusted associations between referral to the NHS DPP and endline HbA1c from linear regressions with robust standard errors clustered at the practice level and practice-fixed effects. In multivariate regression, we successively added (1) baseline variables that were available for the full sample, that is, baseline HbA1c measure, gender, age at baseline, average yearly number of GP consultations in 3 years before baseline, IMD, receipt of flu vaccination in previous 5 years, receipt of pneumococcal vaccination in previous 5 years, previous receipt of lifestyle advice, previous receipt of weight loss counselling, previous consultation for skin abnormalities and previous participation in bowel cancer screening, (2) baseline BMI and (3) post-baseline diabetes medication and time between baseline and endline HbA1c measurement (in months), as covariates.

Second, we used propensity score matching to estimate the average marginal effect of the NHS DPP referral on HbA1c accounting for confounding by the included covariates. We estimated propensity scores by performing a logistic regression of programme referral on the covariates and using a 1-to-1 nearest-neighbour propensity score matching without replacement (using the R package MatchIt[70]). The covariates that we successively added to the matching procedure were (1) baseline HbA1c, age and gender, (2) number of average yearly GP consultations (in previous 3 years), (3) IMD and region, (4) receipt of previous lifestyle advice, (5) time between baseline and endline HbA1c measurement (in months) and (6) post-baseline diabetes medication. After matching, all standardized mean differences for the covariates were below 0.1 and all standardized mean differences for squares and two-way interactions between covariates were below 0.15, indicating adequate balance. We used *g*-estimation to estimate average treatment effects[71,72]. Briefly, the first step is to specify a model for the outcome based on the treatment and covariates and potential outcomes are then estimated for each unit by computing predicted values for both treatment and control groups. The mean of estimated potential outcomes is computed for each group and the difference or ratio of these averages is used to estimate the treatment effect. Combining propensity score matching and *g*-computation has been shown to effectively minimize confounding bias[73]. We used the R package marginaleffects[74] to implement *g*-computation with a linear model, treatment–covariate interactions, covariates and cluster-robust standard errors and estimated the average marginal effect of NHS DPP referral on HbA1c.

Third, using the same panel dataset as for the IV estimation described above, we estimated the one-year lagged treatment effect of programme referral on HbA1c from a regression with individual-fixed effects to account for time-invariant unobserved patient characteristics and year-fixed effects to control for the secular variation. As in the IV estimation, we accounted for cases in which several HbA1c measurements were recorded for a patient within a year by averaging the measurements. We used the R package lfe[69] to specify the linear model with several fixed effects and standard errors clustered at the practice level.

Heterogenous treatment effects

We present stratified regression discontinuity analyses for primary and secondary outcomes, using local linear regressions with automatically selected optimal bandwidths for each subgroup, in Supplementary Tables 8–16. Prespecified stratifying variables used in this analysis were gender (male versus female), age group (18–39, 40–59, 60–80 years), ethnicity (Asian, Black, mixed or other, white; based on the HES APC dataset), socioeconomic status and practice residency (rural versus urban). Socioeconomic status was based on the 2015 English IMD composite score, resulting in five quintiles ranging from 1 (least deprived) to 5 (most deprived) and mapped through postcode of residence for patients in English practices that have consented to participate in the linkage scheme. We further stratified our analyses for the following exploratory comparisons: having previously received general lifestyle advice versus not; having previously received counselling on weight loss versus not; having previously received a consultation for skin abnormalities versus not (that is, record, photography, excision, biopsy or removal skin lesion or mole); having previously participated in a bowel cancer screening activity versus not (that is, record of faecal occult blood testing or participation in NHS bowel cancer screening programme); having previously received a flu vaccination versus not; and having previously adhered to a statin prescription versus not. For the last, we defined a patient as non-compliant if the interval of prescriptions since their first prescription within 5 years before the baseline test exceeded 3 months. Statin prescriptions must generally be renewed every 2 months. All medical codes are available in our OSF repository.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

This study used data from the CPRD Aurum and NHS England HES APC database. The data are available from CPRD (https://cprd.com) but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. Owing to CPRD license restrictions, we are unable to share data.

Code availability

All medical codes and algorithms to define variables and R analysis code are available in the Supplementary Information or at the OSF repository (https://osf.io/rqz6x/?view_only=abc4c7a3abcb457596cec9fe2664f542).

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Additional information

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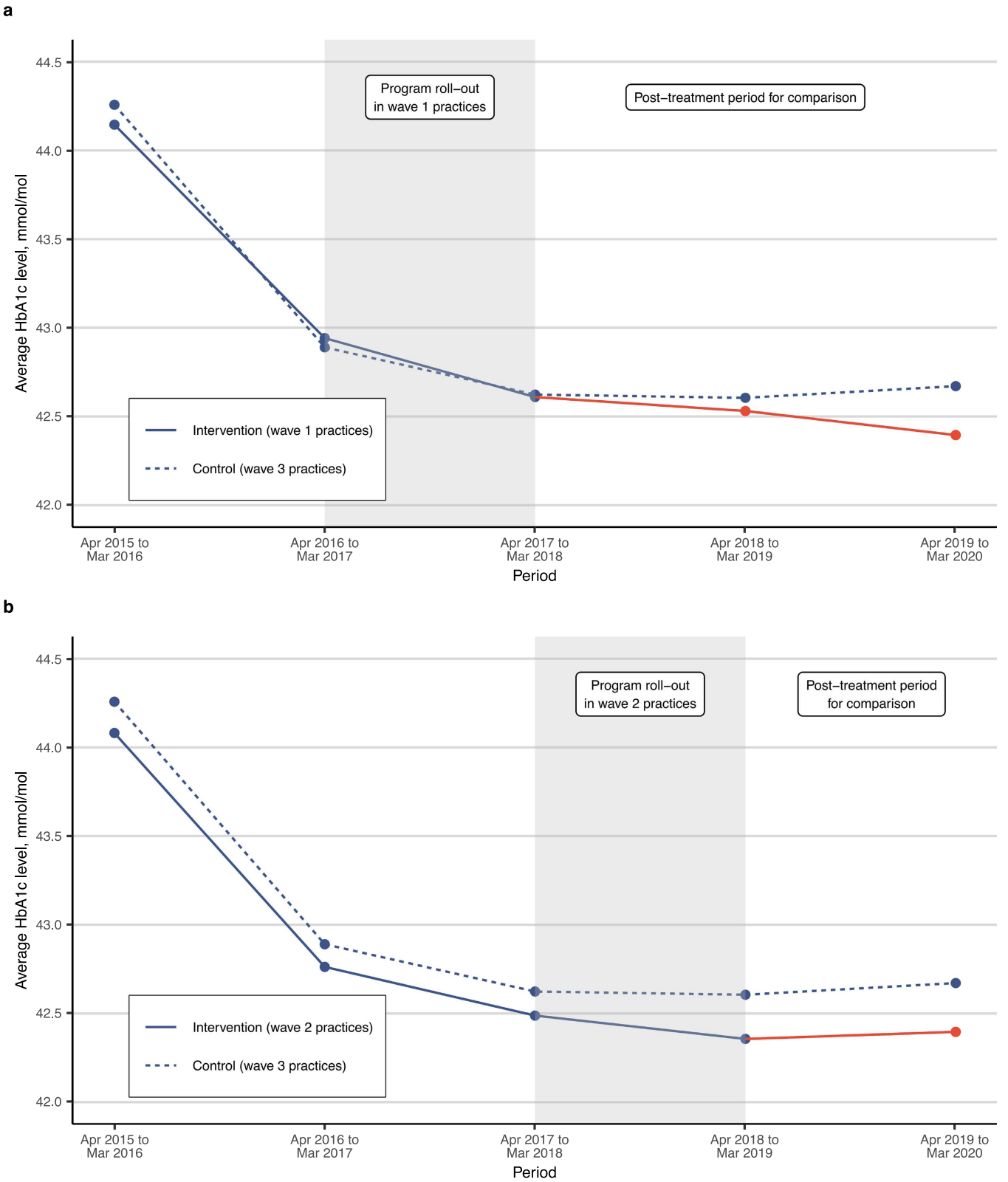
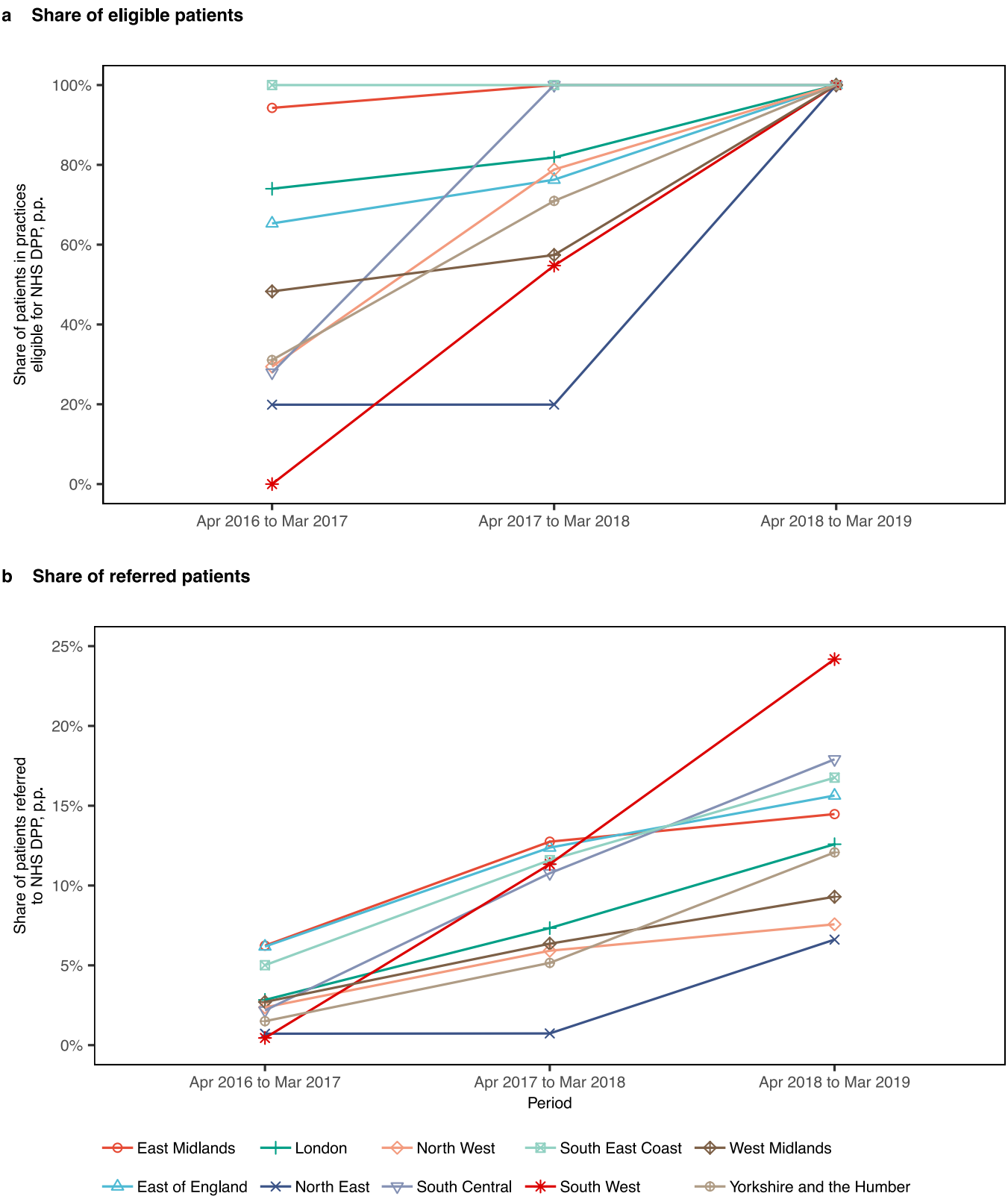


Extended Data Fig. 1 | Trends in glycated haemoglobin (HbA1c) before, during and after programme roll-out. Weighted average HbA1c in one-year intervals from April 2015 to March 2020, for (**a**) wave 1 and (**b**) wave 2 practices (intervention) compared to wave 3 practices (control). The y-axis does not start from 0, weighting by number of individuals for each practice, by year. The roll-out of the NHS DPP started in June 2016 for wave 1, in April 2017 for wave 2 and in April 2018 for wave 3.



Extended Data Fig. 2 | Regional and temporal variation in NHS DPP programme implementation. (**a**) Share of patients eligible for NHS DPP derived via official practice eligibility by roll-out wave and (**b**) share of patients referred to NHS DPP in each of the nine Strategic Health Authorities.

Extended Data Table 1 | Sample characteristics

Variable	%	N
Age in years, mean (SD)	51 (16)	
18 to 29	11.6	243 793
30 to 39	14	295 282
40 to 49	19.5	411 201
50 to 59	21.9	461 006
60 to 69	17.9	377 073
70 to 80	15.1	318 021
Gender		
Female	56.5	915 717
Male	43.5	1 190 659
BMI, mean (SD)	28.1 (6.1)	
< 25	33.1	436 041
25 to 29.9	35.2	464 217
30 to 34.9	19.6	258 266
35 to 39.9	7.7	101 321
≥ 40	4.4	58 444
Hypertension stage based on systolic and diastolic blood pressure		
Normal (< 120 and 80)	19.3	188 906
Prehypertension (120-139 or 80-89)	59.6	583 428
Stage 1 Hypertension (140-159 or 90-99)	18.6	182 074
Stage 2 Hypertension (≥160 or ≥ 100)	2.5	24 222
	Mean	SD
Baseline blood pressure		
Diastolic, mmHg	80	11
Systolic, mmHg	132	18
Baseline lipids		
HDL, mmol/l	1.47	0.45
LDL, mmol/l	3.02	0.96
Total-cholesterol-to-HDL ratio	3.77	1.25
Triglycerides, mmol/l	1.55	0.97
Number of yearly GP consultations	12.4	10.8
Number of prior emergency hospitalization	1.13	5.37

Description of the primary cohort including information on age, gender, body mass index (BMI), hypertension stage, blood pressure, serum lipids, number of yearly general practitioner (GP) consultations and number of previous emergency hospitalization at baseline. Age, gender and number of yearly GP consultations was available for the full sample. The primary cohort consists of 2,106,376 patients. 2 052 480 of these (97.4%) had been registered with their GP for at least 6 months following the index date. The primary outcome of endline HbA1c was available for 1 043 268 patients (50.8% of 2 052 480, table S1) and the median time to endline HbA1c during follow-up was 20.5 months (interquartile range, 13.5-26.8). Of the 2 052 480 patients who had a follow-up time of at least 6 months, 2 037 384 (99.3%) were linkable to HES hospitalization data. Missingness in baseline and endline BMI, blood pressure and lipids are shown in table S1. Exchangeability of patients below and above the threshold are demonstrated in placebo tests with baseline characteristics (balance tests) in Extended Data Table 2. The secondary cohort is described in the Supplementary Information S4.1.

Extended Data Table 2 | Placebo tests with baseline characteristics (Balance tests)

Variable at baseline*	Primary cohort		Secondary cohort	
	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value
Age in years‡	0.22 (-0.13, 0.57)	0.225	0.255 (-0.085, 0.595)	0.141
Female, p.p.	-0.1 (-0.7, 0.6)	0.860	0.1 (-0.7, 0.8)	0.866
Baseline BMI	-0.03 (-0.12, 0.07)	0.603	-0.03 (-0.14, 0.08)	0.566
Baseline weight, kg	0.02 (-0.27, 0.31)	0.880	-0.05 (-0.39, 0.30)	0.794
Average yearly number of GP consultations†	-0.05 (-0.18, 0.08)	0.462	0.07 (-0.08, 0.21)	0.371
Baseline blood pressure, mmHg				
Diastolic	0.053 (-0.25, 0.35)	0.729	-0.13 (-0.49, 0.24)	0.486
Systolic	0.16 (-0.02, 0.34)	0.083	0.05 (-0.17, 0.27)	0.655
Baseline lipids				
HDL, mmol/l	0 (-0.006, 0.006)	0.969	0.009 (0.002, 0.016)	0.008
LDL, mmol/l	-0.004 (-0.022, 0.014)	0.672	-0.023 (-0.045, 0)	0.045
Total-cholesterol-to-HDL ratio	-0.002 (-0.022, 0.017)	0.826	-0.031 (-0.055, -0.007)	0.010
Triglycerides, mmol/l	0.006 (-0.009, 0.022)	0.409	0 (-0.018, 0.019)	0.961
Number of flu vaccinations†	-0.01 (-0.03, 0)	0.054	-0.01 (-0.02, 0.01)	0.314
Flu vaccination†, p.p.	-0.3 (-0.7, 0.1)	0.107	-0.1 (-0.5, 0.4)	0.787
Pneumococcal vaccincation†, p.p.	0.1 (-0.2, 0.3)	0.604	0 (-0.3, 0.2)	0.899
Number of lifestyle advice†	-0.01 (-0.02, 0.01)	0.269	-0.01 (-0.02, 0.01)	0.424
Lifestyle advice†, p.p.	-0.1 (-0.6, 0.5)	0.796	0.1 (-0.5, 0.7)	0.771
Weight loss counseling†, p.p.	0.1 (-0.2, 0.3)	0.436	0 (-0.3, 0.2)	0.887
Routine screening†, p.p.				
Colorectal‡	0.6 (-0.7, 1.9)	0.376	0.3 (-0.9, 1.5)	0.642
Skin	0.2 (-0.2, 0.7)	0.316	0.2 (-0.3, 0.7)	0.517
Breast‡	1.4 (-0.5, 3.2)	0.142	1.7 (0, 3.4)	0.050
Statin adherence†, p.p.	0.1 (-0.6, 0.9)	0.720	0.2 (-0.8, 1.2)	0.713

*Missingness in baseline variables is shown in Supplementary Table S2.

†The pre-period refers to five years prior to the baseline HbA1c test.

‡For age, colorectal screening and breast cancer screening, we assumed a quadratic relationship with baseline HbA1c.

BMI = body mass index. GP = General practitioner. P.p. = percentage points. This table shows placebo tests that demonstrate exchangeability of patients above and below the eligibility threshold. We used local linear regression with heteroskedasticity-robust standard errors and triangular kernel weights, within the bandwidth used in our primary analysis. For gender, vaccinations, lifestyle advice, weight loss counselling and statin adherence, effect estimates can be interpreted as the difference in percentage points at the threshold. The results for routine breast screening are restricted to women only. The results for statin adherence are restricted to patients with a record of statin prescription in the pre-period.

Extended Data Table 3 | Regression discontinuity results of being eligible for and of being referred to, intensive lifestyle counselling

	Unadjusted				Adjusted for medication*			
	Effect of being eligible		Effect of referral		Effect of referral			
Outcome	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value	MSE-optimal BW	Sample size†
Primary outcome								
HbA1c, mmol/mol	-0.10 (-0.16, -0.03)	0.006	-0.85 (-1.46, -0.24)	0.006	-0.94 (-1.55, -0.34)	0.002	3.8	298 822
Secondary outcomes								
BMI, kg/m^2	-0.15 (-0.21, -0.09)	< 0.001	-1.35 (-1.88, -0.83)	< 0.001	-	-	3.8	184 087
Weight, kg	-0.33 (-0.48, -0.18)	< 0.001	-2.99 (-4.38, -1.61)	< 0.001	-	-	3.4	208 111
Diastolic BP, mmHg‡	-0.16 (-0.4, 0.07)	0.178	-1.35 (-3.31, 0.61)	0.178	-1.54 (-3.44, 0.35)	0.111	7.5	211 778
Systolic BP, mmHg‡	-0.24 (-0.6, 0.11)	0.175	-2.03 (-4.96, 0.91)	0.176	-2.41 (-5.21, 0.39)	0.092	5.6	243 292
HDL cholesterol, mmol/l§	0 (0, 0.01)	0.033	0.04 (0, 0.09)	0.033	0.04 (0, 0.09)	0.034	6.3	290 932
LDL cholesterol, mmol/l§	0.01 (-0.01, 0.04)	0.265	0.11 (-0.08, 0.3)	0.265	0.04 (-0.12, 0.21)	0.596	5.7	107 790
Total-cholesterol-to-HDL ratio§	0 (-0.02, 0.02)	0.741	-0.03 (-0.20, 0.14)	0.741	-0.09 (-0.25, 0.08)	0.286	5.4	178 852
Triglycerides, mmol/l§	-0.04 (-0.06, -0.01)	0.002	-0.33 (-0.54, -0.12)	0.002	-0.32 (-0.52, -0.12)	0.002	4.4	126 297
Exploratory outcomes								
Diabetes diagnosis, RD	0.39 (0.21, 0.57)	< 0.001	3.66 (2.00, 5.33)	< 0.001	-	-	3.1	327 756
Diabetes medication, RD	0.30 (0.18, 0.41)	< 0.001	2.72 (1.66, 3.78)	< 0.001	-	-	3.5	501 241
Antihypertensive medication, RD‡	0.11 (-0.38, 0.6)	0.660	0.93 (-3.22, 5.09)	0.659	-	-	4.5	390 878
Lipid-lowering medication, RD§	0.29 (-0.23, 0.82)	0.271	2.61 (-2.03, 7.25)	0.271	-	-	3.2	344 522
Diabetes complication, RD	0.06 (-0.07, 0.19)	0.344	0.58 (-0.62, 1.78)	0.344	0.15 (-0.98, 1.28)	0.797	3.3	493 431
Mortality, RD	0.05 (-0.09, 0.20)	0.471	0.47 (-0.81, 1.76)	0.471	0.67 (-0.62, 1.95)	0.307	4.9	698 224
Emergency MACE hospitalization, RD	-0.05 (-0.23, 0.12)	0.550	-0.48 (-2.05, 1.09)	0.550	-0.12 (-1.68, 1.45)	0.883	7.5	211 778

*Effects for HbA1c and diabetes complication were adjusted for diabetes medication prescription; effects for lipid levels were adjusted for lipid-lowering medication prescription; effects for diastolic and systolic blood pressure were adjusted for blood pressure-lowering medication; and effects for mortality and MACE hospitalization were adjusted for all three medication groups. All relevant medications are listed in our Open Science Framework project (see code availability statement).

†Sample size within MSE-optimal bandwidth.

‡Sample restricted to those without prior lipid-lowering medication prescription. At baseline, 411 288 (20.0%) people had already received at least one prescription for a lipid-lowering medication.

§Sample restricted to those without prior blood pressure-lowering medication prescription. At baseline, 749 884 (36.5%) people had already received at least one prescription for a blood pressure-lowering medication.

BMI = Body mass index. BP = Blood pressure. MACE = Major adverse cardiovascular event. RD = Risk difference (i.e., difference in the probability of the outcome in percentage points). This table shows the main regression discontinuity results for the primary cohort including effect size estimate, 95% confidence intervals (95% CI), *P* values, mean-squared error (MSE) optimal bandwidth (BW) and sample size. The effects were estimated in local linear regressions with heteroskedasticity-robust standard errors and triangular kernel weight and evaluated using two-sided *t*-tests ($p < 0.05$). The definition of all outcomes is detailed in the Supplementary Information 1.2. Additional details are available in Methods ('Main Analysis'). We compared statistical significance to results using robust bias-corrected confidence intervals, which yielded the same statistical inferences except for diabetes medication, which was no longer significant (Extended Data Table 4). Results for the secondary cohort are available in the Supplementary Information S4.

Extended Data Table 4 | Regression discontinuity results with robust bias-corrected confidence intervals of being eligible for and of being referred to, intensive lifestyle counselling

	Unadjusted				Adjusted for medication*			
	Effect of being eligible		Effect of referral		Effect of referral			
Outcome	Estimate (Rob. 95% CI)	*P* value	Estimate (Rob. 95% CI)	*P* value	Estimate (Rob. 95% CI)	*P* value	MSE-optimal BW	Sample size†
Primary outcome								
HbA1c, mmol/mol	-0.10 (-0.35, -0.07)	0.004	-0.85 (-3.26, -0.69)	0.003	-0.94 (-3.3, -0.76)	0.002	3.8	298 822
Secondary outcomes								
BMI, kg/m^2	-0.15 (-0.28, -0.02)	0.029	-1.35 (-2.59, -0.23)	0.019	-	-	3.8	184 087
Weight, kg	-0.33 (-0.58, 0.08)	0.133	-2.99 (-5.59, 0.46)	0.097	-	-	3.4	208 111
Diastolic BP, mmHg‡	-0.16 (-0.52, 0.17)	0.328	-1.35 (-4.31, 1.38)	0.314	-1.54 (-4.47, 1.02)	0.219	7.5	211 778
Systolic BP, mmHg‡	-0.24 (-0.74, 0.28)	0.371	-2.03 (-6.17, 2.24)	0.360	-2.41 (-6.24, 1.66)	0.255	5.6	243 292
HDL cholesterol, mmol/l§	0 (0, 0.01)	0.031	0.04 (0.01, 0.14)	0.024	0.04 (0.01, 0.14)	0.025	6.3	290 932
LDL cholesterol, mmol/l§	0.01 (-0.01, 0.06)	0.209	0.11 (-0.1, 0.51)	0.195	0.04 (-0.15, 0.37)	0.414	5.7	107 790
Total-cholesterol-to-HDL ratio§	0 (-0.03, 0.03)	0.970	-0.03 (-0.29, 0.27)	0.961	-0.09 (-0.34, 0.21)	0.658	5.4	178 852
Triglycerides, mmol/l§	-0.04 (-0.11, -0.03)	0.001	-0.33 (-1.06, -0.32)	< 0.001	-0.32 (-1.05, -0.34)	< 0.001	4.4	126 297
Exploratory outcomes								
Diabetes diagnosis, RD	0.39 (-0.46, 0)	0.046	3.66 (-3.67, 0.6)	0.160	-	-	3.1	327 756
Diabetes medication, RD	0.30 (-0.06, 0.37)	0.152	2.72 (-0.35, 3.58)	0.107	-	-	3.5	501 241
Antihypertensive medication, RD‡	0.11 (-0.69, 1.01)	0.718	0.93 (-5.84, 8.61)	0.706	-	-	4.5	390 878
Lipid-lowering medication, RD§	0.29 (-0.63, 1.47)	0.434	2.61 (-5.45, 13.14)	0.417	-	-	3.2	344 522
Diabetes complication, RD	0.06 (-0.09, 0.19)	0.677	0.58 (-2.89, 1.94)	0.698	0.15 (-3.11, 1.66)	0.550	3.3	493 431
Mortality, RD	0.05 (-0.3, 0.19)	0.664	0.47 (-2.69, 1.76)	0.683	0.67 (-2.66, 1.8)	0.705	4.9	698 224
Emergency MACE hospitalization, RD	-0.05 (-0.42, 0.19)	0.460	-0.48 (-3.82, 1.68)	0.446	-0.12 (-3.76, 1.73)	0.468	7.5	211 778

*Effects for HbA1c and diabetes complication were adjusted for diabetes medication prescription; effects for lipid levels were adjusted for lipid-lowering medication prescription; effects for diastolic and systolic blood pressure were adjusted for blood pressure-lowering medication; and effects for mortality and MACE hospitalization were adjusted for all three medication groups. All relevant medications are listed in our Open Science Framework project (see code availability statement).

†Sample size within MSE-optimal bandwidth.

‡Sample restricted to those without prior lipid-lowering medication prescription. At baseline, 411 288 (20.0%) people had already received at least one prescription for a lipid-lowering medication.

§Sample restricted to those without prior blood pressure-lowering medication prescription. At baseline, 749 884 (36.5%) people had already received at least one prescription for a blood pressure-lowering medication.

BMI = Body mass index. BP = Blood pressure. MACE = Major adverse cardiovascular event. RD = Risk difference (i.e., difference in the probability of the outcome in percentage points). Rob. = Robust. This table shows the main regression discontinuity results for the primary cohort including effect size estimate, robust bias-corrected 95% confidence intervals (95% CI), *P* values, mean-squared error (MSE) optimal bandwidth (BW) and sample size. The effects were estimated in local linear regressions with triangular kernel weight and evaluated using two-sided *t*-tests ($p < 0.05$). The definition of all outcomes is detailed in the Supplementary Information 1.2. Additional details are available in Methods ('Main Analysis').

Extended Data Table 5 | Negative outcome controls

Outcome	Bandwidth	Estimate (95% CI)	*P* value	Sample size
Flu vaccination	3.1	0.10 (-0.43, 0.63)	0.714	513 473
Number of flu vaccinations*	3.1	0.22 (-0.85, 1.28)	0.689	480 703
Pneumococcal vaccincation	4.2	-0.11 (-0.27, 0.05)	0.184	720 264
Fracture	5.2	-0.05 (-0.2, 0.11)	0.537	946 230
Accidental injuries	5.9	0.05 (-0.11, 0.21)	0.545	946 230
Number of accidental injuries*	6.1	0.18 (-0.12, 0.48)	0.241	117 3602
Routine screenings				
Colorectal	2.3	-0.41 (-1.2, 0.37)	0.303	513 473
Breast	2.8	-0.79 (-1.84, 0.26)	0.141	173 177
Cervical	2.8	0.15 (-0.81, 1.11)	0.759	173 177
Skin abnomality	4.6	-0.48 (-0.79, -0.16)	0.003	720 264
Allergic reaction	5.8	-0.01 (-0.17, 0.16)	0.950	946 230
Contraceptive use				
IUD	3.8	0.04 (-0.15, 0.24)	0.662	267 133
Oral	2.1	-0.24 (-0.89, 0.4)	0.459	173 177
Short-term onset of†				
Cancer	5.5	0.14 (-0.02, 0.31)	0.077	889 887
Dementia	6.5	-0.02 (-0.09, 0.05)	0.547	1 166 480

*Effect estimate can be interpreted as the difference in number of events during the follow-up period at the threshold.
†Sample restricted to those without any previous diagnosis of cancer or dementia, respectively. While healthy lifestyle behaviours are assumed to be protective factors for cancer and dementia onset, the median follow-up time (29 months) is sufficiently short to assume that any plausible effects are negligible.
IUD = Intra-uterine device. Regression coefficients from local linear regression with MSE-optimal bandwidth, 95% confidence intervals (95% CI), *P* values and sample size. This table shows the main regression discontinuity analysis (primary cohort) for health outcomes which we did not expect to be plausibly affected by referral to the NHS DPP ('negative outcome controls'). Effect estimates can be interpreted as the difference in percentage points at the threshold. The results for routine breast and cervical cancer screening as well as contraceptive use are restricted to women only.

Extended Data Table 6 | Aggregated treatment effect estimates of NHS DPP implementation on HbA1c from difference-in-differences analysis

	Partially aggregated (95% CI), mmol/mol			Single parameters (95% CI), mmol/mol
*(**a**) Unadjusted*				
Simple weighted average				
				-0.144
				(-0.188, -0.100)
Group-specific effects	Wave 1	Wave 2		
	-0.173	-0.126		-0.140
	(-0.253, -0.094)	(-0.196, -0.057)		(-0.186, -0.094)
Event study	Year 1	Year 2	Year 3	
	-0.099	-0.136	-0.328	-0.188
	(-0.163, -0.036)	(-0.205, -0.067)	(-0.433, -0.223)	(-0.235, -0.141)
*(**b**) Adjusted for share of patients with a recorded HbA1c test*				
Simple weighted average				
				-0.155
				(-0.196, -0.113)
Group-specific effects	Wave 1	Wave 2		
	-0.103	-0.187		-0.162
	(-0.185, -0.021)	(-0.251, -0.122)		(-0.210, -0.115)
Event study	Year 1	Year 2	Year 3	
	-0.119	-0.165	-0.245	-0.176
	(-0.183, -0.055)	(-0.229, -0.100)	(-0.354, -0.136)	(-0.227, -0.126)

This table reports aggregated treatment effect parameters under (**a**) the unconditional parallel trend assumption and the (**b**) conditional parallel trend assumption, adjusted for the practice-level share of patients with a recorded HbA1c test in each year. The row 'Simple weighted average' reports the weighted average (by group size) of all available group–time average treatment effects. The row 'Group-specific effects' summarizes average treatment effects by the timing of the NHS DPP implementation. The row 'Event study' reports average treatment effects by the length of exposure to the NHS DPP implementation. The column 'Single parameters' represents a further aggregation of each type of parameter as discussed in Callaway and Sant'Anna (2021).

Extended Data Table 7 | Overview of estimated effects of intensive lifestyle counselling on glycemic control

Analysis	Name of estimand	Interpretation	Sample	Change in HbA1c, mmol/mol		Location of details
				Estimate (95% CI)	*P* value	
Regression discontinuity	Effect of being eligible	Causal effect for those who are eligible for intensive lifestyle counseling as determined by the clinical guideline (irrespective of actual referral or adherence)	Primary cohort*	-0.10 (-0.16, -0.03)	0.006	Methods 'Main Analysis'; Extended Data Tables 3-4; Supplementary Tables S2-3
				Robust bias-corrected CI: (-0.35, -0.07)	Robust bias-corrected: 0.004	
			Secondary cohort†	-0.15 (-0.24, -0.05)	0.002	Supplementary Information 4
	Effect of referral (Complier average causal effect)	Causal effect for those who are referred to intensive lifestyle counseling because they crossed the eligibility threshold (i.e., may be conceptualized as the "intent-to-treat" effect in a target trial, irrespective of adherence)	Primary cohort*	-0.85 (-1.46, -0.24)	0.006	Methods 'Main Analysis'; Extended Data Tables 3-4; Supplementary Tables S2-3
				Robust bias-corrected CI (-3.26, -0.69):	Robust bias-corrected: 0.003	
			Secondary cohort†	-1.26 (-2.06, -0.46)	0.002	Supplementary Information 4
Difference-in-differences	Simple weighted average	Weighted average of all available group-time treatment effects, grouped by group size	Eligible patients‡ in roll-out practices	-0.14 (-0.19, -0.10)	< 0.001	Methods 'Difference-in-differences analysis'; Extended Data Table 6; Extended Data Figure 1
	Event-aggregated average	Weighted average of all available group-time treatment effects, grouped by length of time since DPP implementation		-0.19 (-0.24, -0.14)	< 0.001	
	Event-specific effect at 3-year post-DPP introduction	Effect of comparing wave 1 practices to control practices during the last available observation period from April 2019 to March 2020		-0.33 (-0.44, -0.22)	< 0.001	
Instrumental variable	Effect of being eligible (Intent-to-treat effect in a 2SLS regression)	Effect of being eligible due to a change in program coverage in their region (irrespective of actual referral or adherence)	Eligible patients‡ from 2016 to 2020	-0.14 (-0.29, -0.001)	0.048	Methods 'Instrumental variable estimation'; Supplementary Table S17; Extended Data Figure 1
	Effect of referral (Complier average causal effect in 2SLS regression)	Effect for those who changed from not being referred to being referred due to a change in program coverage in their region		-3.77 (-7.52, -0.01)	0.049	
Individual fixed-effect regression	Treatment coefficient	One-year lagged effect of DPP referral from a regression with individual-fixed effects to account for time-invariant unobserved patient characteristics, and year-fixed effects to control for the secular variation	Eligible patients‡ in 2017 and 2018	-0.62 (-0.74, -0.51)	< 0.001	Methods 'Multivariate regression analyses, propensity score matching, and panel regression'; Supplementary Table S17
Propensity score matching	Fully adjusted average marginal effect (treatment coefficient via *g* computation)	Average marginal effect of DPP referral, matched based on and adjusted for baseline and post-baseline variables		-0.32 (-0.47, -0.16)	< 0.001	
Multivariable regression	Fully adjusted treatment coefficient	Association between DPP referral and endline HbA1c, adjusted for baseline and post-baseline variables		-0.33 (-0.46, -0.20)	< 0.001	

*The primary cohort consists of adult patients (aged 18 to 80 years) who had a recorded HbA1c measure between January 1st, 2017 and December 31st, 2018. We excluded all patients who exceeded the HbA1c threshold for diabetes or prediabetes (42 mmol/mol) prior to their index date (i.e., date of their baseline HbA1c record), or received any diabetes medication prior to their index date. The endline HbA1c measure must have been recorded at least six months after the baseline test.

†As for the secondary cohort, we additionally excluded patients who had any HbA1c measure (whether it exceeded the prediabetes threshold or not) prior to their index date

‡Eligible patients are all adult patients who had a HbA1c measure between 42 and 47 mmol/mol in the specified period.

This table shows the estimated effect of intensive lifestyle counselling (i.e., eligibility for, referral to, or implementation of the NHS DPP) on glycemic control (change in HbA1c in mmol/mmol) from all analyses presented in this article. Details for each methodology can be found in the Methods (see column 'Location of Details').

5 DISCUSSION

In the three presented publications, I investigated key aspects in the assessment, development, implementation, and evaluation of lifestyle interventions for cardiometabolic diseases. In the following, I will first discuss lessons for each phase in the Public Health Action Cycle (Fig. 1) before highlighting cross-cutting implications and conclusions that have emerged.

5.1 Lessons learned: Assessment phase

Results from Publication 1 and 2 have informed the assessment phase of the Public Health Action Cycle. The shared key finding is that despite national public health guidance recommending lifestyle interventions, patients with conditions that predispose them to cardiometabolic diseases do not seem to have adequate access to such interventions in either England's or Thailand's primary healthcare settings. I will now briefly summarize results from each publication before jointly presenting the lessons learned.

In Publication 1, I determined that substantial proportions of individuals initially diagnosed with hypertension, hyperlipidaemia, or obesity in English GP practices do not receive support in making changes to their lifestyle. I also observed significant variation in the recorded use of lifestyle interventions across conditions. For example, approximately 45.8% of individuals with an initial diagnosis of hypertension had some form of lifestyle intervention documented (increasing to 55.6% when signposting is considered). This percentage decreased to about 35.4% (or 45.2% with signposting) for those with an initial hyperlipidaemia diagnosis. Notably, a substantial proportion of individuals had no recorded support (medication, lifestyle intervention, or signposting) within 12 months of diagnosis, ranging from 12% for hypertension to 44% for obesity. Furthermore, only a small fraction of patients had a recorded lifestyle intervention before receiving medication for hypertension, hyperlipidaemia, or obesity, raising questions about why more individuals are not offered lifestyle interventions as a primary approach.

In Publication 2, I identified current practices in hypertension and provision of lifestyle interventions to patients with hypertension in Thai primary health care settings in a mixed-methods survey among three stakeholder groups (policy- and

decisionmakers, healthcare practitioners, and patients diagnosed with hypertension). While representative figures from Thailand are missing, surveyed stakeholders agreed that improvements in access to hypertension treatment, in particular in the areas of lifestyle risk factor screening and lifestyle interventions, are needed. Results suggests that lifestyle interventions that are being offered vary substantially in duration, intensity, medium, and content. Special attention may be warranted to ensure access for individuals with low socioeconomic status or health literacy, informal laborers, and populations whose working hours impede receiving care.

5.1.1 Reasons for inadequate access

While the proportion of Thai adults who are aware of their hypertension and have their blood pressure under control has increased from 2009 to 2014 from 50% to 55% and from 21% to 30% respectively (Buranakitjaroen et al., 2020; Roubsanthisuk et al., 2018), my findings corroborate large differences between the care outlined by the Thai Hypertension Society in their newest guidelines and the reality on the ground (Lemp, Pengpid, et al., 2022; Thai Hypertension Society, 2019). In Publication 2, reasons given by Thai stakeholders why healthcare professionals currently offer limited advice about lifestyle modification included the fear that doing so will take too much time, the impression that behavior change required for substantial improvement is a fruitless endeavor, and the dominance of a biomedical model of health where preference is given to medical treatment options. Similar reasons have also been expressed by healthcare professionals elsewhere (Dewhurst et al., 2017; Hébert et al., 2012; Keyworth et al., 2019; Rubio-Valera et al., 2014). For instance, in an interview study with patient-facing healthcare professionals working in the NHS across the UK, participants reported both that they were under considerable time pressure to see their allocation of patients and that they did not give sufficient priority to providing opportunistic lifestyle interventions to patients, but instead focused on ensuring that the correct medication was prescribed (Keyworth et al., 2019). Similar to Thai healthcare professionals, while participants acknowledged the importance of lifestyle factors for disease progression, they were skeptical about their capabilities to facilitate behavior change with patients (Keyworth et al., 2019).

Correspondingly, while a higher proportion of the English population is aware of and is managing their hypertension and other conditions predisposing to cardiometabolic diseases compared to the Thai population (Buranakitjaroen et al.,

2020; Campbell et al., 2023; Roubsanthisuk et al., 2018), Publication 1 suggests that there is likewise a stark discrepancy between what guidelines recommend and what is implemented in practice in terms of lifestyle interventions as a first-line treatment for hypertension, hyperlipidemia, and obesity. While it is possible that lifestyle intervention rates have been underestimated through a lack of formal recording in medical records and, as a starting point, improvements in formal recording of lifestyle interventions in routine medical records are needed, this cannot solely explain the observed discrepancy. Low intervention rates among at-risk individuals are especially worrying given the fact that the reduction in cardiovascular mortality in high-income countries has slowed down, and some suspect that the observed population-level increases in body mass index may reverse this trend altogether, as obesity is causally linked to many cardiovascular diseases (Larsson, Bäck, et al., 2020; Sattar et al., 2020). The options for preventive measures are diverse and, at least in principle, there is a wide range of services available from which English GPs can choose to support individuals with known risk factors in realizing a healthy and sustainable lifestyle. Therefore, while unpicking the factors that contribute to the results presented in Publication 1 will take additional study, one possible explanation for the disparities between guidelines and real-world practice could be the absence of streamlined and effective mechanisms within primary care to identify and refer at-risk individuals to relevant services, including structured lifestyle interventions (Lemp, Nuthanapati, et al., 2022).

5.1.2 Starting points to increase access

While programs with structured pathways have been proven to be successful in improving cardiovascular risk factors, there are other conceivable starting points to increase access to interventions and improve overall care for at-risk patients. For instance, the pay-for-performance scheme that was introduced in the UK in the form of the Quality and Outcomes Framework (QOF) in 2004 has been credited for reducing geographical variation in general practice quality, leading to almost universal adoption of electronic health records and promoting multidisciplinary team-working for long-term conditions (Bramwell et al., 2022). However, the framework fell short to promote patient-centered care and achieve any meaningful improvements in overall mortality, to which its narrow focus on processes for single diseases with static standards may have contributed (Forbes et al., 2017; Ryan et al., 2016). Since 2019 a novel approach led and articulated by the Royal College of General Practitioners (RCGP) that

incentivizes quality improvement rather than achievement of quality indicators has been pursued (Bramwell et al., 2022). While GP staff reported broadly favorable views of incentivized quality improvement in an early qualitative evaluation, several questioned the choices of topic to focus on, recognizing greater need and potential for improving quality of care in other clinical areas.

As a means to achieve more holistic, inclusive and patient-centered care, social prescribing may also hold promise (Jani et al., 2020): Social prescribing usually involves linking patients in primary care with services provided by the voluntary and community sector to help improve their health and well-being (Bickerdike et al., 2017; Drinkwater et al., 2019). Specifically, social prescriptions encompass activities like sports, leisure, or arts, to promote both mental and physical well-being (Polley et al., 2017). Additionally, they can tackle social factors by emphasizing activities related to housing, food, education, or skills development. A mixed-methods study investigating the potential of social prescribing for T2DM prevention concluded that lack of disease (or diabetes)-specific eligibility criteria simplified the referral of patients to social prescriptions during routine GP consultations, which resulted in increased access of at-risk individuals to health promotion and wellbeing activities (compared to the NHS DPP) (Calderón-Larrañaga et al., 2023). While an inclusive approach to T2DM prevention seems especially relevant given the overall benefits of a healthier diet and regular exercise, a systematic review on social prescribing determined that existing evidence remains insufficient to judge its success or cost-effectiveness (Bickerdike et al., 2017). If social prescribing is to realize its potential, future evaluations should carefully consider various factors, including the timing of the interventions, the target population, the effectiveness of the interventions, and the associated costs, which can help to bring social prescriptions on par with pharmaceutical prescriptions (Bickerdike et al., 2017; Jani et al., 2019).

5.1.3 Synthesis

In summary, the reasons behind inadequate access to lifestyle interventions in both England and Thailand primary healthcare are multilayered and involve time and resource constraints, skepticism about behavior change, and a dominant biomedical model of health. These challenges mirror experiences reported by healthcare professionals in other settings and countries, emphasizing the need for a holistic approach to improve patient care and lifestyle interventions as a first-line treatment.

Moving forward, there are promising starting points to enhance access to lifestyle interventions for at-risk patients. For example, structured referral pathways or pay-for-performance schemes have shown success in reducing variations in quality of care. However, it is crucial to consider a broader focus on patient-centered care, which initiatives like social prescribing aim to achieve. Overall, findings in the assessment phase emphasize the need for a more streamlined and effective approach within primary care to bridge the gap between guidelines and actual routine practice, providing individuals at risk of cardiometabolic diseases with better access to lifestyle interventions. These lessons lay the groundwork for the subsequent phases of the Public Health Action Cycle.

5.2 Lessons learned: Development and implementation phase

Results from Publication 2 have also informed the development and implementation phase of the Public Health Action Cycle. I will now briefly summarize barriers and challenges for implementing a screening and brief intervention approach in Thai primary healthcare settings, with a focus on high-risk patients with both hypertension and hazardous or harmful alcohol use, followed by discussing three key aspects and the lessons derived from them.

Publication 2 revealed important implications for preventive measures in Thai primary healthcare and beyond. Specifically, stakeholder survey and interview results indicated the need for standardized assessment, clear guidelines for brief interventions, improved alcohol use monitoring, and a reduction in the stigma associated with heavy alcohol use. Results also underscored the importance of lifestyle interventions being adaptable to the existing conditions in the Thai healthcare system, which has limited resources and requires culturally sensitive screening and lifestyle interventions. While Thai stakeholders acknowledged repeatedly that expanding access to lifestyle interventions at a national scale demands significant effort, they also identified key steps to be taken. Some of these steps, such as the development of guidelines linking alcohol use and hypertension for healthcare professionals to provide specific, actionable, and evidence-based advice, or a seamless integration of lifestyle interventions into existing procedures, are not unique to the Thai context.

Considering Thailand’s alcohol consumption patterns and the evident causal link between alcohol use and hypertension, a primary motivator for prioritizing hazardous

and harmful alcohol use among hypertensive patients is the potential for considerable synergistic health gains and healthcare cost reductions by lowering the burden of non-communicable diseases, particularly cardiovascular diseases (Baliunas et al., 2009; Patra et al., 2010; Rehm et al., 2017b; Rehm & Roerecke, 2013). Despite stakeholders recognizing the potential of addressing hazardous alcohol use as means to lessen the hypertension burden in Thai primary healthcare, several barriers emerged that need considerable attention for screening and alcohol brief interventions to realize their potential. In the following sections, I will discuss three emerging aspects: identification of at-risk individuals, equitable health services, and integration of local health centers.

5.2.1 Identification of at-risk individuals

There is evidence indicating that selective prevention, that is, preventive measures specifically targeting only those at higher than average risk, may represent the most effective approach for mitigating rising cardiometabolic disease rates (Král et al., 2019). Nonetheless, public health experts have repeatedly determined that the identification and management of those at increased risk of developing cardiovascular disease, diabetes, or other cardiometabolic diseases remains fragmented, and is not linked to meaningful lifestyle advice (L.-S. Chang et al., 2019; Reiter-Brennan et al., 2021; Sattar et al., 2020). The implementation of selective cardiometabolic disease prevention continues to be a topic of debate, with ongoing discussions about the optimal setting, preferred strategies, and logistical approaches for identification (Král et al., 2019). For example, a key challenge is how to efficiently identify individuals at increased risk in the general population to initiate necessary prevention activities, including lifestyle counselling, with open questions remaining particularly about the effectiveness of systematic versus opportunistic screening (Crossan et al., 2017; Feldman et al., 2017; Krogsbøll et al., 2019).

In my work in Thailand, identifying those with elevated blood pressure and/or relevant alcohol consumption was one of the first important barriers to targeting patients with concomitant hypertension and alcohol use and implementing lifestyle interventions. In Thailand, newly diagnosed hypertension cases may be identified through both organized community-based or opportunistic screening during regular services. However, according to interviewed stakeholders blood pressure screening is inadequate: For instance, 44 percent of policymakers and 46 percent of practitioners disagreed with the statement that blood pressure screening is routinely performed in

primary healthcare facilities, and almost half (47 percent) of policymakers agreed that there is no or insufficient community-based screening. Some policymakers highlighted that screening has not been comprehensively expanded, especially in urban areas with few health volunteers, disadvantaged communities, or inaccessible areas, such as island regions. At the same time, the identification of those with lifestyle risk factors, and with hazardous or harmful alcohol use specifically, may be hampered by a lack of standardized procedures or appropriate screening tools that are being universally applied. Thus, expanding the reach of blood pressure screening as well as ensuring comprehensive and reliable risk factor assessment must be a prerequisite for successfully scaling up alcohol brief intervention as a means to reduce the hypertension burden in Thailand.

5.2.2 Equitable health services

Considering health equity aspects when developing and implementing preventative services for cardiometabolic diseases is of utmost importance. For instance, when looking at representative data from the UK, fewer people from socioeconomically deprived or black and minority ethnic communities participate in check-ups as part of the NHS Health Check, a national cardiovascular risk assessment program in England, which already had a relatively low coverage of 21.4 percent between 2019 and 2013, with large variations between practices (0 to 72.7 percent) and regions (9.4 to 30.7 percent) (K. C.-M. Chang et al., 2015; Sattar et al., 2020). Similarly, early service evaluations of the NHS DPP revealed low uptake and high attrition rates among socio-economically disadvantaged and diverse ethnic groups (Whelan & Bell, 2022).

In my work in Thailand, the fact that blood pressure screening has not been comprehensively expanded, especially in urban areas with few health volunteers, disadvantaged communities, or inaccessible areas, such as island regions, is already the first hint that there may be unequal provision of services between socioeconomic strata. In their statements, stakeholders emphasized that hypertension care is presently not catered to individuals with low socioeconomic status or health literacy, informal laborers, and populations whose working hours impede receiving care. In the UK, propositions to foster equitable access have included widening access to health checks in pharmacies and other local places (e.g., community centers or places of worship) as well as targeting public health communication to those that are

insufficiently reached through traditional routes (Sattar et al., 2020). Remarkably similar to this, Thai stakeholders identified the need to accommodate workers' schedules in healthcare services and to enable them to access services directly at their workplaces. At-risk populations such as informal laborers or factory workers may profit from tailored interventions such as the expansion of blood pressure screening in places outside of clinical settings, that is, community-, home-, or workplace-based screening.

Relevant to my proposed intervention strategy is also the inclusion of digital or mobile tools with the potential to expand access to health promotion activities broadly, and lifestyle interventions specifically (Khoong et al., 2021; McCool et al., 2022; World Health Organization, 2019). While access to the internet is rapidly increasing in Thailand, and the government is actively pursuing an e-health strategy (Ministry of Public Health Thailand, 2017), several aspects must be considered to unlock the potential of digital health promotion more broadly and to ensure health equity in the process. In alignment with the systematic review by Ferretti and colleagues (2023), researchers must first and foremost pay careful attention to the digital divide and structural injustice in data-related practices (Ferretti et al., 2023; Khoong et al., 2021). Additionally, the target population (including practitioners and patients) must be closely engaged in a stakeholder-informed process to address their specific needs, considering their economic, cultural, and social contexts, and ensuring the interventions' compatibility with the population's skillset (Liu et al., 2020). Lastly, monitoring the quality and impact of digital health promotion over time is indispensable to ensure its effectiveness, equity, and sustainable implementation (Ferretti et al., 2023).

5.2.3 Integration of local health centers

The integration of local health centers and task-shifting (that is, transferring a task normally performed by a physician to a health professional with a different or lower levels of training) has been at the forefront of the global health agenda for a while now (Singh & Sachs, 2013). While task-shifting has historically been used for chronic conditions such as HIV, given the changing demographics of cardiovascular disease, large underserved population segments, and physician shortages in low- and middle-income countries, there has been a renewed focus on extending task-shifting to cardiovascular health. A systematic review has identified task-shifting from physicians

to non-physician health workers as a potentially effective and affordable strategy for improving access to healthcare for non-communicable diseases (Joshi et al., 2014). Furthermore, a meta-analysis of RCTs determined that task-shifting interventions are effective in improving blood pressure control among adults in low- and middle-income countries (Anand et al., 2019).

In my work in Thailand, stakeholders welcomed the idea of increasingly shifting care to more local and community-based settings, possible involving family physicians. While the vision for a Thai family physician system is not new, the healthcare system has historically focused on specialized care units, training a limited number of family physicians, in particular in rural settings (Wiwanitkit, 2016). This is in contrast to other South East Asian countries, such as the Philippines, where family physicians are central to serving the population's health (Laude & Sana, 2016). Currently, limited access to hypertension care in community-based settings and local health centers contributes to the large influx of patients to district hospitals and hypertension clinics, which, in turn, lack the resources to provide "less essential" services such as lifestyle counseling (Lemp, Pengpid, et al., 2022).

It is important to understand roles and tasks that are appropriate for different cadres of healthcare workers and to identify the skills required to deliver interventions to the community (Tsolekile et al., 2015). In hypertension care, risk factor screening, medication adherence support, and preventive interventions, such as lifestyle counseling, are examples of tasks that can be shifted "down" to provide relief for physicians and clinical nurses who are currently primarily responsible for hypertension management in secondary and tertiary settings (Thai Hypertension Society, 2019). While highly skilled healthcare personnel are often tasked with educating and counseling patients on diet, physical activity, and alcohol use, such tasks could be shifted to local health workers to allow continuous care as well as support at the community level (Tsolekile et al., 2015). Additionally, this might enable targeted training in effective counseling techniques to help patients realize the required lifestyle changes.

5.2.4 Synthesis

In summary, the challenges identified for implementing a screening and brief intervention approach in Thai primary healthcare settings are complex, ranging from a lack of standardized assessment tools and intervention guidelines to inadequate

alcohol use monitoring and existing stigma associated with heavy alcohol use. Specifically, I have highlighted three key lessons: First, to successfully scale up alcohol brief intervention and reduce the hypertension burden, comprehensive and reliable risk factor assessment, coupled with the expansion of blood pressure screening, is essential. Second, disparities in access to healthcare services based on socio-economic status and ethnicity are evident in Thailand. The unequal provision of services highlights the urgent need for targeted and tailored interventions. Lastly, stakeholders are appreciating the potential of shifting care to community-based settings and local health centers, potentially involving family physicians where possible and appropriate. This shift could ease the burden on district hospitals and hypertension clinics, enabling local health workers to play a more active role in risk factor screening and lifestyle counseling and, thus, ensuring continued care and support at the local level. Overall, findings from my work in Thailand offers valuable insights into the development and implementation of lifestyle interventions, not only in the Thai context but also with implications for addressing cardiometabolic diseases and preventive healthcare more broadly. These lessons can contribute to the overarching goal of building effective intervention strategies that improve risk factor screening, promote health equity, and ensure accessible and high-quality healthcare for all.

5.3 Lessons learned: Evaluation phase

Results from Publication 3 have informed the evaluation phase of the Public Health Action Cycle. I will now give a brief overview of the rationale behind the utilization of quasi-experimental study designs and summarize the main results when employing them to evaluate of a nationwide behavior change program. Subsequently, I will highlight three essential conditions that must be met to maximize the effectiveness of these methods in advancing evidence-based healthcare and implementation science with a focus on regression discontinuity designs.

The primary motivation to employ quasi-experimental methods for evaluating the NHS DPP was to estimate a causal treatment effect under real-life conditions that is not vulnerable to confounding as are conventional observational study designs, e.g., from selection biases. My work illustrates that all three quasi-experimental study designs methods can be used to establish causality in situations where randomization is not feasible. Specifically, in Publication 3, I successfully employed quasi-

experimental methods to demonstrate the effectiveness of the nationwide behavior change program in improving cardiovascular risk factors among individuals with non-diabetic hyperglycemia (commonly referred to as prediabetes). In this study, which used electronic health records from over two million patients, referral to the largest behavior change program for prediabetes globally resulted in improved glycemic control as well as reductions in body mass index, weight, high-density lipoprotein cholesterol, and triglycerides. This extends causal evidence for health benefits, which were previously largely limited to RCTs, into a real-world setting, serving as a testament to the scalability of intensive lifestyle interventions for behavior change in routine care. In particular, the regression discontinuity approach can be effectively applied to evaluate population-wide health service interventions by leveraging thresholds in treatment assignment induced by clinical guidelines. As briefly discussed in Publication 3, thresholds are pervasive in clinical medicine and, as such, present a rich opportunity to generate causal, rather than associational, evidence of treatment effectiveness. In the following sections, I will discuss three important conditions to fully realize the potential of regression discontinuity and other quasi-experimental study designs in advancing evidence-based health care and implementation science.

5.3.1 Digitizing health information

It is crucial to accelerate access to routine electronic health records and comprehensive health information. While several European countries, in addition to England, are at the forefront of healthcare digitization by establishing routine monitoring systems and supporting research through electronic health records (e.g., Wales or Denmark), others, including Germany, have been hesitant or slow to establish ethically sound processes to collect and for researchers to access (anonymized) health records (Oliveira Gonçalves et al., 2018; Pohlmann et al., 2020). This is unfortunate given that many conceivable research questions of interest to clinical medicine and health systems research cannot be studied through conventional or pragmatic randomized trials due to feasibility constraints (such as very long follow-up periods to establish the effectiveness of anti-aging agents) or ethical considerations (such as potential harmful side effects of medical treatments) (Goulden et al., 2021; Soukas et al., 2019). While it remains paramount to maintain ethical standards in data collection and research access (e.g., full transparency of health data sharing processes for patients and the possibility to opt-out) and to ensure responsible use of

health data (e.g., ethical oversight through institutional review boards), countries – particularly those lagging behind in digitization – should accelerate their efforts in establishing routine health monitoring systems and supporting research access in line with existing best practices.

5.3.2 Improving policy evaluation

Since quasi-experimental evaluation using routine data is much less cost- and time-intensive compared to randomized controlled trials, it has the potential to expedite the Public Health Action Cycle and to reconcile diverging interests between key stakeholders. For example, in a study evaluating the impact of performance-based financing in Burkina Faso, researchers were able to respond to policymaker's evaluation needs by deciding on a quasi-experimental study design with a nested experimental component (De Allegri et al., 2019). Specifically, in this scenario, the World Bank was interested in evaluating the added benefit of moving from the standard performance-based financing to one that combined performance-based financing with specific equity measures, while the Ministry of Health wanted to assess the overall impact of introducing performance-based financing for future health financing decisions. Initially, a random allocation of health facilities was considered, but this was deemed unfeasible by policymakers due to the decentralized healthcare system, potential spill-over effects, and the complex nature of the intervention. Instead, within each of the six targeted regions, control districts were identified that were comparable in terms of health indicators and health system structures. While the twelve control districts received no performance-based financing intervention at all, within the intervention districts, the facilities were allocated across the different performance-based financing models in 'randomization ceremonies', attended by health facility representatives, district health managers, and other important district and regional stakeholders to maximize transparency (De Allegri et al., 2019).

This study design addressed the policymakers' concerns about the complexity of implementation while retaining the ability to answer all relevant research questions. As this example illustrates, it is crucial to educate implementation researchers and policymakers about such methodological possibilities and encourage them to incorporate quasi-experimental methods into their toolkit when designing the implementation and evaluation of new policies and health service interventions.

5.3.3 Fostering health equity research

Quasi-experimental study design methods, and regression discontinuity designs in particular, may also be used to investigate aspects of health equity, for example, heterogenous treatment effects between patient groups due to sociodemographic characteristics and comorbidities, for which randomized controlled trials usually have too small of a sample size or an insufficiently diverse study population. However, while several countries have established access to digitized health information, the records itself often remain fragmented and crucial information to disentangle causal pathways for heterogenous treatment effects (e.g., environmental, commercial, or behavioral risk factors, but also causes of death) are missing or not well-documented (Gallagher et al., 2019; Langner et al., 2020). Healthcare practitioners may consider information of risk factors secondary to their provision of medical services, severely limiting the type of research questions that can be answered based on electronic health record data alone. One way to overcome this limitation of routine data is the linkage to data sources containing the missing information, which is in principle feasible if the data are pseudonymized (Langner et al., 2020). Thus, establishing a dataflow that incorporates the person identifiers required for linkage (while ensuring that the identity of the individuals is not disclosed to the data users at any point) is crucial to be able to link routine data to other data sources and to answer research questions of health equity reliably.

5.3.4 Synthesis

In summary, the increased use of quasi-experimental study designs is desirable to improve the estimation of causal treatment effects in real-world conditions. Through the successful application in evaluating a nationwide diabetes prevention program, I demonstrated the scalability of intensive lifestyle interventions for behavior change and provide an excellent use-case for similar evaluations in the future. Furthermore, I have highlighted three crucial conditions to maximize the potential of quasi-experimental study design: the need for digitizing health information, including ethical processes for routine data collection and research access to ensure the necessary data supply; the need for incorporating quasi-experimental methods into policy design and evaluation to improve policy evaluation and meet the needs of all stakeholders; and the need of linking routine data with other sources to effectively address research

questions related to health equity. Overall, these insights inform evidence-based healthcare by promoting rigorous evaluation and equitable healthcare services.

5.4 General implications

Determining access to, successfully implementing, and rigorously evaluating lifestyle interventions in real-word practice is arguably a more intricate endeavor than conducting drug trials. As a result, clinical guidelines for cardiometabolic diseases often place less emphasis on lifestyle and behavioral changes compared to medication regimes. However, if we could effect truly sustainable improvements in lifestyle, the potential impact might be transformative for preventive healthcare (Sattar et al., 2020). To achieve this ambitious goal, comprehensive research conducted at every phase of the Public Health Action Cycle becomes imperative. My dissertation showcases that to do so, we require a diverse array of methodologies and perspectives. While quasi-experimental study designs can be a great supplement to our methodological toolbox to demonstrate the impact (or lack thereof) of health service interventions at the population level, primary mixed-methods research is needed to uncover the reasons why certain groups may benefit more or less from a given intervention and to identify intervention needs within the target population.

5.4.1 Synergies in cardiometabolic disease prevention and beyond

Intensive lifestyle counseling can be beneficial to a myriad of health conditions. This has been substantiated once again in my third publication, which showed that prediabetic individuals referred to a diabetes prevention program not only lowered their glycated hemoglobin, but the benefits of lifestyle changes also extended to improving body weight and serum lipid levels. Similarly, a recent narrative review identifying knowledge gaps in behavioral science relating to T2DM discussed that it is thus far unclear to what extent disease-specific advice is critical to the effectiveness of diabetes prevention programs and determined that there is currently little evidence to support disease-specific diet or physical activity recommendations for T2DM (French et al., 2023). This display of synergies bear the question whether going forward, there is merit in screening simultaneously for cardiovascular risk factors and diabetes risk, potentially creating a harmonized referral scheme for cardiometabolic diseases where similar programs do not compete but complement each other (Sattar et al., 2020).

Taking this thought even further, there was no consensus over the statement that “selective cardiometabolic prevention should be a separate prevention program not combined with other programs (e.g., cancer prevention)”, as discussed in a consensus-based expert panel to develop a universal concept of selective cardiometabolic disease prevention that can guide implementation within European primary care (Král et al., 2019). This discussion is driven by the fact that cardiometabolic disease and various cancers have a number of risk factors in common, e.g., alcohol use is not only causally linked to hypertension but also to cancers of the upper aerodigestive tract (oral cavity, pharynx, larynx, and esophagus) and cancers of the colon, rectum, liver, and female breast (Rumgay et al., 2021). Some conditions also increase the risk of others; e.g., T2DM is associated with the risk of colorectal cancer (Peeters et al., 2015), opening the possibility of sizeable synergistic health gains in cancer outcomes stemming from effective lifestyle interventions.

Lastly, further positive spill-over effects of lifestyle interventions on other conditions are likely, as epidemiological studies show that a healthy lifestyle is, for example, associated with a substantially lower risk of Alzheimer’s dementia (Dhana et al., 2020). Fittingly, during the writing of this synopsis, the German Health Minister, Dr. Karl Lauterbach, presented plans to create a new federal agency that will open its doors in 2025, dedicated to preventative healthcare and with a focus on the primary prevention of cancer, dementia, and cardiovascular diseases (Bundesministerium für Gesundheit [Federal Ministry for Health], 2023). While disease control and prevention of communicable diseases, such as influenza, remain within the scope of action of the Robert Koch-Institute, cross-links between cardiometabolic diseases and communicable diseases became evident during the recent coronavirus disease pandemic: People with known cardiovascular risk factors, such as diabetes, were more gravely affected by the virus (Silverio et al., 2021). Overall, the benefits of lifestyle interventions are relevant in addressing a range of health conditions. Further research should critically consider potential synergies between prevention programs for cardiometabolic diseases and other conditions, potentially setting the stage for more comprehensive and integrated preventive healthcare strategies in the future.

5.4.2 Digital health

A cross-cutting aspect that cannot be left unmentioned is digital health, which is highly relevant in all Public Health Action Cycle phases and across all of the presented studies.

First, digitization of health records is a prerequisite for leveraging routine data to monitor real-world access to lifestyle interventions and for applying quasi-experimental study designs to measure intervention effectiveness. Monitoring evidence-based processes of care and outcomes is the first step in improving the quality of care and must be continuously strengthened (L. W. Green et al., 2012).

Second, the development of a digital tool that offers standardized screening with minimal training requirements, facilitates self-assessment, and generates tailored advice based on a patient's alcohol use and associated health risks has been identified as a potential feasible and low-cost approach to improving the assessment of alcohol consumption and delivery of alcohol brief intervention in Thai primary healthcare settings. Whether or not implementing such a strategy could ultimately mitigate a share of the alcohol-attributable hypertension burden must be evaluated. However, my findings demonstrate a positive implementation climate for digital solutions to support Thai health practitioners in delivering alcohol screening and brief intervention.

Third, it is important to highlight that my quasi-experimental evaluation studies the original framework of the NHS DPP before changes such as additional commercial providers or the provision of a digital option were introduced in 2020 (McManus et al., 2022). In-person and group-based program structures may not be suitable for everyone due to barriers such as work and caregiving responsibilities or transportation issues (Johnson & Melton, 2016; Shawley-Brzoska & Misra, 2018). Such barriers may explain some of the observed low uptake and high attrition rates in the NHS DPP, especially among socio-economically disadvantaged and diverse ethnic groups (Whelan & Bell, 2022). While the provision of a digital option may expand access to the program beyond its current reach (also because presently not enough physical NHS DPP placements are available), it remains to be seen whether the observed effects translate to the digital sphere and whether uptake and high attrition rates improve across sub-groups.

5.5 Conclusion

When combatting the rising number of people with cardiometabolic diseases, it is important to remember that an individual's lifestyle is shaped by environmental and social factors that may render healthy lifestyle choices more or less easy (Martin-Moreno et al., 2021). In particular, given the size of the diabetes epidemic and the number of at-risk individuals, approaches aimed solely on changing individual behavior are unlikely to be sufficient for effectively controlling diabetes at the population-level (L. W. Green et al., 2012). However, while lifestyle interventions can always be just one tool in the "prevention toolbox", my dissertation clearly shows that there are tangible and achievable improvements in assessment, development, implementation, and evaluation of lifestyle interventions for mitigating cardiometabolic disease risk. In particular, my quasi-experimental evaluation of the NHS DPP demonstrates that selective prevention in T2DM by prioritizing behavioral change among at-risk individuals can be an effective strategy to achieve meaningful improvements in glycemic control and other cardiovascular risk factors. Thus, to truly enable individuals to take health back into their hands, political investments are needed, e.g., in the form of accessible programs and strategic policies such as changes in reimbursement for preventive services. Cardiometabolic disease prevention requires urgent and coordinated attention by policymakers accompanied by infrastructural and environmental changes, sustainable funding, and an experimental attitude to allow public health researchers to develop, implement, and evaluate the ingredients of successful lifestyle interventions.

6 SUMMARIES

6.1 English summary

Cardiometabolic diseases, including cardiovascular diseases, diabetes mellitus, and chronic kidney disease, are the leading cause of premature disability and death globally. Lifestyle interventions can be instrumental in improving relevant behavioral risk factors in individuals and, thus, in preventing the development and progression of cardiometabolic diseases. Yet, lifestyle interventions often remain underutilized in primary healthcare settings, their design and implementation can pose challenges, and evaluating their causal impact on health outcomes may not always be straightforward. In my dissertation, I tackle these three aspects across two different contexts, namely English and Thai primary healthcare.

The first objective (Publication 1) was to quantify the extent to which patients with cardiovascular risk factors were offered lifestyle interventions in English general practices in line with clinical guidelines. In my retrospective cohort study using electronic health data from approximately one-fifth of all general practices in England, results indicated limited lifestyle advice for adult patients who received a new diagnosis of hypertension, hyperlipidaemia, or obesity between 2010 and 2019. The proportion of individuals who had any recorded lifestyle intervention in the 12 months before to 12 months after their diagnosis varied across conditions, ranging from 55.6% for hypertension to 45.2% for hyperlipidemia and 43.9% for obesity.

The second objective (Publication 2) was to identify current practices for lifestyle interventions for patients diagnosed with hypertension in Thai primary healthcare settings. In my cross-sectional, mixed-method study among stakeholders with relevant knowledge about hypertension care in Thailand (including policy- and decisionmakers, healthcare practitioners, and patients diagnosed with hypertension), respondents agreed that improvements in access to hypertension treatment, in particular in the areas of lifestyle risk factor screening and lifestyle interventions, are needed. Results suggested that lifestyle interventions that are being offered vary substantially in duration, intensity, medium, and content. Special attention may be warranted to ensure access for individuals with low socioeconomic status or health literacy, informal laborers, and populations whose working hours impede receiving care.

Closely related to my findings about current practices in Thai hypertension care, the third objective (Publication 2) was to determine barriers and facilitators for a screening and brief intervention approach targeting lifestyle behaviors among Thai primary health care patients diagnosed with concomitant hypertension and alcohol use. Stakeholder survey results indicated the need for standardized alcohol use assessment, clear guidelines for brief interventions, improved alcohol use monitoring, and a reduction in the stigma associated with heavy alcohol use. Results also underscored the importance of lifestyle interventions being adaptable to the existing conditions in the Thai healthcare system, as well as the importance equitable health services, particularly when considering the inclusion of digital or mobile tools for expanding access to lifestyle interventions.

Lastly, the fourth objective (Publication 3) was to establish the transferability of behavior change programs to real-world settings by determining if routine referral to the English Diabetes Prevention Programme leads to improvements in key health outcomes. To this end, I employed several quasi-experimental study designs that allow for a causal interpretation of the treatment effect in electronic health data, using the same data source as for my first objective. In my primary analytical approach, the regression discontinuity design, program referral led to significant improvements in patients' glycated hemoglobin, body mass index, body weight, serum high-density lipoprotein cholesterol and serum triglycerides levels. Blood pressure and other exploratory health outcomes such as hospitalization for a major adverse cardiovascular event did not significantly improve during the median follow-up period of approximately two years. I confirmed my main finding, the improvement of glycated hemoglobin, with the difference-in-differences design (exploiting the phased roll-out of the program) and with the instrumental variable design (exploiting regional variation in program coverage). This study provides causal, rather than associational, evidence that lifestyle interventions implemented at scale in a national health system can achieve important health improvements and that quasi-experimental study designs are extremely valuable for health policy evaluation.

In conclusion, while individuals' lifestyle activities are markedly shaped by environmental and social factors, my dissertation clearly shows that there are tangible and achievable advancements in the access, development, implementation, and evaluation of lifestyle interventions aimed at mitigating cardiometabolic disease risk.

6.2 German summary [Zusammenfassung in deutscher Sprache]

Kardiometabolische Erkrankungen, wie Herz-Kreislauf-Erkrankungen, Diabetes und chronische Nierenerkrankungen, sind weltweit die Hauptursachen für einen frühzeitigen Tod und körperliche Einschränkungen. Lebensstilinterventionen können dazu beitragen, individuelle Verhaltensweisen, die das Risiko von kardiometabolischen Erkrankungen erhöhen, zu verändern und so der Entstehung und dem Fortschreiten der Erkrankungen entgegenzuwirken. Dennoch werden solche Lebensstilinterventionen in der medizinischen Primärversorgung oft nicht ausreichend angeboten, ihre Gestaltung und Umsetzung bringt Herausforderungen mit sich, und die Beurteilung ihres kausalen Effekts auf gesundheitliche Folgen ist nicht immer eindeutig. In meiner Dissertation untersuche ich diese drei Aspekte am Beispiel der englischen und thailändischen Primärversorgung.

Das erste Ziel meiner Dissertation war es, zu bestimmen, inwieweit Patient*innen in englischen Allgemeinarztpraxen, die aufgrund kardiovaskulärer Risikofaktoren gemäß den klinischen Leitlinien Anspruch auf Lebensstilinterventionen hatten, diese tatsächlich angeboten bekamen. Meine retrospektive Kohortenstudie, die elektronische Gesundheitsdaten von etwa einem Fünftel aller Allgemeinarztpraxen in England nutzte, ergab, dass Erwachsene, bei denen zwischen 2010 und 2019 Bluthochdruck, Hyperlipidämie oder Adipositas diagnostiziert wurde, nur begrenzt darin unterstützt wurden ihren Lebensstil umzustellen. Der Anteil der Personen, denen im Zeitraum von 12 Monaten vor bis 12 Monaten nach der Diagnose nachweislich eine Lebensstilintervention angeboten wurde, variierte je nach Erkrankung und war 55,6 % bei Bluthochdruck, 45,2 % bei Hyperlipidämie und 43,9 % bei Adipositas.

Das zweite Ziel bestand darin, die derzeit gängige Praxis für Lebensstilinterventionen für Personen mit Bluthochdruck in thailändischen Einrichtungen der Primärversorgung zu ermitteln. In meiner Befragung unter Akteur*innen mit Wissen über die Behandlung von Bluthochdruck in Thailand (einschließlich Entscheidungsträger*innen, Gesundheitspersonal und Personen mit Bluthochdruck) stimmten die Befragten darin überein, dass der Zugang zu Behandlungsoptionen, insbesondere in den Bereichen Screening und Lebensstilberatung, verbessert werden muss. Die Ergebnisse deuten darauf hin, dass sich die angebotenen Lebensstilinterventionen hinsichtlich Dauer, Intensität, Methode und Inhalt stark unterscheiden. Besonderes Augenmerk sollte daraufgelegt werden,

die Versorgung für Personen mit niedrigem sozioökonomischem Status, geringer Gesundheitskompetenz oder informeller Beschäftigung sicherzustellen.

Das dritte Ziel bestand darin, sowohl begünstigende als auch hinderliche Faktoren zu ermitteln, die bei der Umsetzung eines Behandlungsansatzes zur Umstellung des Lebensstils von thailändischen Patient*innen, bei denen sowohl Bluthochdruck als auch riskanter Alkoholkonsum vorliegt, relevant sind. Akteur*innen gaben an, dass eine standardisierte Erfassung des Konsums, klare Richtlinien für Beratungsinhalte sowie eine Entstigmatisierung von übermäßigem Konsum erforderlich sei. Die Ergebnisse bekräftigen die Bedeutung einer Anpassung von Lebensstilinterventionen an die bestehenden Gegebenheiten im thailändischen Gesundheitssystem sowie einer sozial gerechten Gestaltung der Angebote, insbesondere im Hinblick auf die Nutzung digitaler oder mobiler Hilfsmittel.

Das vierte Ziel bestand darin, zu untersuchen, ob eine routinemäßige Überweisung an das englische Diabetes-Präventionsprogramm zu Verbesserungen bei wichtigen Gesundheitsparametern führt. Die Kombination quasi-experimenteller Studiendesigns mit elektronischen Gesundheitsdaten ermöglichte eine kausale Interpretation des Behandlungseffekts. Mithilfe meiner primären Analysestrategie, dem Regressions-Diskontinuitäts-Ansatz, konnte ich zeigen, dass eine Überweisung an das Programm bei Patient*innen zu einer signifikanten Verbesserung des glykierten Hämoglobins, des Body-Mass-Index, des Körpergewichts, des High-Density-Lipoprotein-Cholesterins und der Triglyceride führte. Explorativ zeigte sich, dass sich Blutdruck und andere abhängige Variablen wie Krankenhausaufenthalte in der mittleren Nachbeobachtungszeit von zwei Jahren nicht signifikant verbesserten. Die Reduktion des glykierten Hämoglobins wurde mittels eines Differenz-in-Differenzen-Ansatzes sowie eines Instrumentalvariablen-Ansatzes repliziert. Die Ergebnisse sind kausale Evidenz dafür, dass groß angelegte Implementierungen von Lebensstilinterventionen signifikante gesundheitliche Verbesserungen bewirken können. Sie verdeutlichen auf diese Weise auch den hohen Stellenwert von quasi-experimenteller Methodik bei der Beurteilung von Gesundheitsmaßnahmen.

Zusammenfassend lässt sich festhalten, dass der Lebensstil des Einzelnen zwar stark von Umwelt- und sozialen Faktoren geprägt ist, konkrete Verbesserungen in Bezug auf den Zugang, die Entwicklung, Umsetzung und Bewertung von Lebensstilinterventionen zur Verringerung des Risikos kardiometabolische Erkrankungen jedoch möglich und umsetzbar sind.

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8 PERSONAL CONTRIBUTIONS

This is a cumulative thesis consisting of the following three peer-reviewed articles:

1. **Lemp, J. M.**, Nuthanapati, M. P., Bärnighausen, T. W., Vollmer, S., Geldsetzer, P., & Jani, A. (2022). Use of lifestyle interventions in primary care for individuals with newly diagnosed hypertension, hyperlipidaemia or obesity: A retrospective cohort study. *Journal of the Royal Society of Medicine*, *115*(8), 289–299. https://doi.org/10.1177/01410768221077381

2. **Lemp, J. M.**, Pengpid, S., Buntup, D., Bärnighausen, T. W., Geldsetzer, P., Peltzer, K., Rehm, J., Sornpaisarn, B., & Probst, C. (2022). Addressing alcohol use among blood pressure patients in Thai primary care: Lessons from a survey-based stakeholder consultation. *Preventive Medicine Reports*, *29*, 101954. https://doi.org/10.1016/j.pmedr.2022.101954

3. **Lemp, J. M.**, Bommer, C., Xie, M., Michalik, F., Jani, A., Davies, J. I., Bärnighausen, T., Vollmer, S., & Geldsetzer, P. (2023). Quasi-experimental evaluation of a nationwide diabetes prevention programme. *Nature*. https://doi.org/10.1038/s41586-023-06756-4

As the first author on all three articles, I played a substantial role in conceiving the studies, conducting literature research, developing the analysis plan and independently leading all statistical analyses, under the supervision of more senior co-authors. I wrote all three original manuscripts and incorporated revisions based on input from co-authors and the reviewers.

For **Publication** 1, the initiative was primarily driven by Dr. Anant Jani and me. I had substantial involvement in all study aspects (including conception, literature research, study design, statistical analyses, interpretation, manuscript writing and revision). In particular, I took lead in study design, statistical analysis, initial manuscript drafting, and addressing reviewers' comments. Dr. Jani contributed primarily to the study's conception, ethics approval and providing contextual insights into English primary healthcare. All co-authors provided critical input in shaping the original manuscript and approved the final version.

Publication 2 was conducted as part of the project *Improving Primary Care for Hypertension and Alcohol Problems in Thailand,* led by Dr. Charlotte Probst. Upon the project's logistical overhaul due to the Covid-19 pandemic, my contributions primarily focused on developing the study design, particularly the theory-driven design of the questionnaires, as well as analyzing, visualizing, and interpreting of qualitative and quantitative response data. I coordinated data collection with our valued partners, Prof. Dr. Supa Pengpid and Dr. Doungjai Buntup, who administered online surveys

and in-person interviews in Thailand and provided essential insights into the healthcare context. Prof. Dr. Supa Pengpid, Prof. Dr. Karl Peltzer and Dr. Bundit Sornpaisarn contributed to the questionnaires' content. Prof. Dr. Jürgen Rehm provided critical input for shaping the manuscript's clarity and direction. I drafted the manuscript under Dr. Probst's supervision and led extensive revisions in response to reviewer comments. All co-authors provided critical input to refine the original manuscript and approved the final version.

Publication 3 was initiated as part of a broader research agenda by Dr. Pascal Geldsetzer, aiming to apply quasi-experimental methods to electronic health records for generating evidence in routine healthcare settings. Starting in 2019, I was heavily involved in coordinating data access, conceptualizing the study, and obaining ethical approval. Throughout my doctoral studies, I led the study design, data preparation, and statistical analysis under the guidance of Dr. Christian Bommer and Dr. Pascal Geldsetzer. Dr. Min Xie and Prof. Dr. Sebastian Vollmer provided valuable advice for statistical analyses and Dr. Min Xie contributed to secondary analyses as proposed by reviewers during the revision process. Prof. Dr. Justine Davies and Dr. Anant Jani provided essential context for English primary healthcare, supporting the interpretation of the results. I independently drafted and revised the manuscript under Dr. Geldsetzer's supervision, with critical input from Dr. Sebastian Vollmer and Dr. Dr. Till Bärnighausen. All co-authors contributed to refining the original manuscript draft and approved the final version.

Further publications:

4. **Lemp, J. M.**, Kilian, C., & Probst, C. (in press). Here to stay? Policy changes in alcohol home delivery and "to-go" sales during and after COVID-19 in the United States. *Drug and Alcohol Review*.
5. Llamosas-Falcón, L., Rehm, J., Bright, S., Buckley, C., Carr, T., Kilian, C., Lasserre, A. M., **Lemp, J. M.**, Zhu, Y., & Probst, C. (2023). The Relationship Between Alcohol Consumption, BMI, and Type 2 Diabetes: A Systematic Review and Dose-Response Meta-analysis. *Diabetes Care*, *46*(11), 2076–2083. https://doi.org/10.2337/dc23-1015
6. Kilian, C., **Lemp, J. M.**, & Probst, C. (2023). Who benefits from alcohol screening and brief intervention? A mini-review on socioeconomic inequalities with a focus on evidence from the United States. *Addictive Behaviors*, *145*, 107765. https://doi.org/10.1016/j.addbeh.2023.107765
7. Kilian, C., **Lemp, J. M.**, Llamosas-Falcón, L., Carr, T., Ye, Y., Kerr, W. C., Mulia, N., Puka, K., Lasserre, A. M., Bright, S., Rehm, J., & Probst, C. (2023). Reducing alcohol use through alcohol control policies in the general population and population subgroups: A systematic review and meta-analysis. *eClinicalMedicine*, *59*, 101996. https://doi.org/10.1016/j.eclinm.2023.101996

8. Theilmann, M., **Lemp, J. M.**, Winkler, V., Manne-Goehler, J., Marcus, M. E., Probst, C., Lopez-Arboleda, W. A., Ebert, C., Bommer, C., Mathur, M., Andall-Brereton, G., Bahendeka, S. K., Bovet, P., Farzadfar, F., Ghasemi, E., Mayige, M. T., Saeedi Moghaddam, S., Mwangi, K. J., Naderimagham, S., … Geldsetzer, P. (2022). Patterns of tobacco use in low and middle income countries by tobacco product and sociodemographic characteristics: Nationally representative survey data from 82 countries. *BMJ*, e067582. https://doi.org/10.1136/bmj-2021-067582
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