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Supplementary information

Quasi-experimental evaluation of a nationwide diabetes prevention programme

In the format provided by the authors and unedited

Supplementary Information

Here, we provide supplementary information, including medical code algorithms, descriptive statistics, and detailed output from our regression models and robustness analyses. In **S1**, we offer details on literature on the English diabetes prevention program, our target trial protocol, description of our outcome variables, and medical code algorithms used to identify referral status for intensive lifestyle counseling and diabetes status. In **S2**, we provide all Supplementary Figures and Tables in the order of their appearance in the article. In **S3**, we provide the main results for the secondary cohort. Lastly, we provide a Supplementary Discussion for secondary results in **S4**.

This PDF file includes:

S1 Supplementary Materials

S1.1 Overview of peer-reviewed articles, abstracts and selected program statistics

Author, year	Study design	Key results	Limitation
Bakhai & Hopwood, 2020[1]	Program statistics from presentation (single-arm, pre-post design)	HbA1c reduction of 2.0 mmol/mol and weight reduction of 3.3 kg for program completers (minimum of 60% of session attended)	No causality established
Koutoukidis et al., 2022[2]	Prospective cohort study (single-arm, pre-post design)	Weight reduction of 2 kg for participants who attended at least one session	No causality established
Marsden et al., 2022[3]	Prospective cohort study (single-arm, pre-post design)	HbA1c reduction of 2.1 mmol/mol and weight reduction of 3.6 kg for program completers (final session or final measurement plus minimum of 60% of session attended)	No causality established
McManus et al., 2022[4]	Difference-in-difference event study (staggered treatment design)	Incidence rates of T2DM in program-participating practices were significantly lower than would have been expected in the absence of the DPP (difference-in-differences Incident Rate Ratio (IRR) = 0.938 (95% CI 0.905 to 0.972 and 0.927 (95% CI 0.885 to 0.972))	Some causality established, annual practice-level T2DM incidence rates as outcome only
Murray et al., 2019[5]	Pilot study of the digital version of the NHS DPP; prospective cohort study (single-arm, pre-post design)	HbA1c reduction of 1.6 mmol/mol and weight reduction of 4.0 kg at 6 months	Digital delivery only; no causality established
Poupakis et al., 2022[6]	Prospective cohort study (single-arm, pre-post design)	Every additional session attended is associated with a weight loss of 0.281 kg	No causality established
Ravindrarajah et al., 2023[7]	Matched cohort study	Probability of not converting to T2DM at 36 months since referral was 87.3% (95% CI: 86.5% to 88.2%) for referred to the program and 84.6% (95% CI: 83.9% to85.4%) for not referred to the program	No causality established, coded diagnosis as outcome only
Valabhji et al., 2020[8]	Prospective cohort study (single-arm, pre-post design)	HbA1c reduction of 1.26 and weight reduction of 2.3 for initial participants (attended at least one session); HbA1c reduction of 2.04 and weight reduction of 3.3 for completers (minimum of 8 of 13 sessions attended)	No causality established
Wise, 2018[9]	Program statistics cited (single-arm, pre-post design)	Weight reduction of 3.3 for all participants and 3.7 kg for participants excluding those with a normal BMI	No causality established

T2DM = type 2 diabetes mellitus. This table is informed by Whelan, M., & Bell, L. (2022). The English national health service diabetes prevention programme (NHS DPP): A scoping review of existing evidence. *Diabetic Medicine*, *39*(7), e14855, as well as an informal search on PubMed using the search string 'diabetes prevention programme AND England'.

S1.2 Description of outcome variables

Outcome Variable	Definition
Primary outcome	
Change in HbA1c, mmol/mol	Difference between the baseline HbA1c at the index date and final HbA1c measurement taken during follow-up. We excluded HbA1c measurements that fell outside the plausible range of 20 to 150 mmol/mol and only included HbA1c levels recorded in the IFCC standard. England has shifted from DCCT (%) to IFCC (mmol/mol) as the standard unit for HbA1c levels in 2011.
Secondary outcomes	
Change in BMI	Difference between baseline† and final BMI measurement taken during follow-up. We excluded BMI measurements that fell outside the plausible range of 10 to 80 kg/m^2. We considered both (1) BMI measurements as entered in electronic health records, and (2) manually calculated BMI measurements by dividing weight records and height records at adult age. Where both was available, we ran consistency checks and preferentially included BMI measurements as entered in electronic health records.
Change in weight, kg	Difference between baseline† and final weight measurement taken during follow-up. We excluded weight measurements that fell outside the plausible range of 35 to 250 kg.
Change in blood pressure (systolic and diastolic), mmHg	Difference between baseline and final blood pressure level taken during follow-up. Blood pressure levels were computed by averaging up to three BP measurements within a maximum of four weeks. Baseline measurements had to be taken within one month before to three days after the index date. We excluded systolic and diastolic blood pressure levels that fell outside the plausible range of 80 to 200 mm Hg, and 40 to 160 mm Hg, respectively.
Change in blood lipids (HDL [mmol/l], LDL [mmol/l], HDL-to-total cholesterol ratio, triglycerides [mmol/l])	Difference between baseline† and final serum lipid measurement taken during follow-up. We excluded lipid measurements that fell outside the following ranges: for HDL < 10 mmol/l, for LDL < 10 mmol/l, for HDL-to-total-cholesterol ratio < 15, and for triglycerides < 10 mmol/l. For secondary analysis of changes in blood lipids, we restricted the sample to patients that did not receive any hyperlipidemia diagnosis or any prescription of lipid-lowering medication before the index date.
Exploratory analyses [a]	
Incidence of T2DM, hypertension, or hyperlipidemia	We identified the first diagnosis of T2DM, hypertension, or hyperlipidemia for each patient. A recorded diagnosis of T2DM before the index date qualified as exclusion criteria for all analyses. For exploratory analyses of hypertension and hyperlipidemia incidence, we restricted the sample to patients that did not receive any hypertension or hyperlipidemia diagnosis, respectively, or any prescription of blood pressure-lowering or lipid-lowering medication, respectively, before the index date.
New prescription of diabetes, blood pressure-, or lipid-lowering medications	We identified the first prescription of diabetes, blood pressure-, or lipid-lowering medication for each patient. A prescription of diabetes medication before the index date qualified as an exclusion criteria for all analyses. For exploratory analyses of newly prescribed blood pressure- and lipid-lowering medication, we restricted the sample to patients that did not receive any prescription of blood pressure-lowering or lipid-lowering medication, respectively, before the index date.

Outcome Variable	Definition
Occurrence of any diabetes complication	The outcome indicated whether the patient had any record for a diabetes complication within the follow-up period (regardless of the number or severity of complications). We did not exclude patients that had any complication that may have been attributed to diabetes before their index date.
Emergency hospitalization for a major adverse cardiovascular (MACE) event	Emergency hospitalizations in the HES data were identified through the variable Method of admission (admimeth). We identified hopsital episodes with a major adverse cardiovascular event (MACE) by using a publicly available clinical codelist.[c] We did not exclude patients with prior MACE. The outcome indicated whether the patient had any MACE within the follow-up period (regardless of the number of distinct hospital episodes).
Mortality	Death during follow-up as recorded in electronic primary care records. [c]

The medical codes that were used to extract relevant electronic health records for each of these outcomes can be downloaded here: https://osf.io/rqz6x/?view_only=f0e0d93e52434447ab18d7d07e49480b

[†] The baseline measure constitutes the measure closest to the index date, i.e., the measure taken at the index date or within one year before the index date.

[a] For binary outcomes in the exploratory analyses, the effect estimate can be interpreted as the risk difference (RD) in absolute percentage points.

[b] Davidson J. *Clinical Codelist - HES - Major Adverse Cardiovascular Event. [Data Collection]*.; 2021. doi:10.17037/DATA.00002198

[c] There is high correctness of mortality rates calculated with CPRD data only in comparison with ONS. According to an analysis by Gallagher et al., 98.8% of deaths from ONS data were also identified in CPRD (see Gallagher AM, Dedman D, Padmanabhan S, Leufkens HGM, de Vries F. The accuracy of date of death recording in the Clinical Practice Research Datalink GOLD database in England compared with the Office for National Statistics death registrations. *Pharmacoepidemiol Drug Saf*. 2019;28(5):563-569. doi:10.1002/pds.4747).

S1.3 Target trial protocol

Protocol Component	Description	Target Trial Specification	Emulation Using Observational Cohorts and Quasi-Randomization	
			Primary cohort	**Secondary cohort**
Eligibility criteria	Who will be included in the study?	Adults (aged 18 to 80 years) who had a first HbA1c test ≥ 42 mmol/mol with no prior use of diabetes medication and no history of diabetes	Same as for target trail	Same as for target trial but excluding patients who had any HbA1c test prior to the baseline test
Treatment strategies	What interventions will eligible persons receive?	1. Referral to the program at baseline 2. No referral to the program (standard care by general practitioner)	Same as for target trail, with the referral to occur within 12 months of baseline *Required data: Date of baseline HbA1c test record, date of program referral*	
Treatment assignment	How will eligible persons be assigned to the interventions?	Eligible persons will be randomly assigned to one strategy and will be aware of which strategy they were assigned to	Eligible persons will be assigned based on threshold rule leading to quasi-randomization around the threshold	
Outcomes	What outcomes in eligible persons will be compared among intervention groups?	Primary outcome: HbA1c measurement after 3 years of baseline	Latest available HbA1c measurement within follow-up period that is recorded closest to 3 years after baseline *Required data: HbA1c test record*	
Follow-up	During which period will eligible persons be followed in the study?	From treatment assignment until HbA1c measurement, death, loss to follow-up, or administrative end of follow-up, whichever occurs first	Same as for target trail *Required data: date of loss to follow-up*	
Causal estimand	Which counterfactual contrasts will be estimated using the above data?	Intention-to-treat effect (effect of being assigned to treatment)	Local average treatment effect (effect of being assigned to treatment for the compliers)	
Statistical analysis	How will the counterfactual contrasts be estimated?	Intention-to-treat effect estimated via comparison of change in HbA1c among individuals assigned to each treatment strategy	Regression discontinuity analysis	

S1.4 Medical code algorithm to identify intensive lifestyle programme status

The aim of this algorithm is to identify referrals to the diabetes prevention programme and comparable intensive lifestyle interventions following patients' baseline HbA1c measure. We were not aiming to identify incidents of brief advice or informal lifestyle counselling. Structured diabetes education programmes are included as they may be used as a stand-in where placement in the NHS diabetes prevention programme was not possible. Medical codes are provided in table S6.

```
IF there is at least one record for intervention type == 'Diabetes
prevention' AND (program status == 'Completed' OR 'Started') AND no
succeeding record for (program status == 'Unsuitable' OR 'Declined' OR
'Did not attend or complete'), then classify as referred to intensive
lifestyle intervention

ELSE if there is at least one record for intervention type == 'Diabetes
prevention' AND (program status == 'Completed' OR 'Started') AND at least
one record for (program status == 'Unsuitable' OR 'Declined' OR 'Did not
attend or complete') after their record for 'Completed' or 'Started', then
classify as not referred to intensive lifestyle intervention

ELSE classify as not referred to intensive lifestyle intervention
```

Records that indicated invitations or offers to intensive lifestyle programmes only were not considered as referrals to intensive lifestyle intervention. We repeated the algorithm for the different intervention types (diabetes management, general, weight management, and physical activity) and determined the referral status at different times following the baseline HbA1c measure (i.e., at 3 months, 6 months, and 12 months).

S1.5 Medical code algorithm to identify diabetes status

The aim of this algorithm is to identify a patient's diabetes status based on primary care records. The identification strategy is adopted from the HDR UK Phenotype Library† but adapted for the CPRD Aurum database instead of CPRD Gold.

† https://phenotypes.healthdatagateway.org/phenotypes/PH152/version/304/detail/#home

```
IF there is at least one record for code for type 2 'Diabetes'
(diabdiag_gprd = 4) and no record for type 1 'Diabetes' (no record with
diabdiag_gprd = 3) then classify the patient as type 2 'Diabetes'

ELSE if there is at least one record for code for type I 'Diabetes'
(diabdiag_gprd = 3) and no record for type 2 'Diabetes' (no record with
diabdiag_gprd = 4) then classify the patient as type 1 'Diabetes'

ELSE if there is at least one record of type 1 'Diabetes' (diabdiag_gprd =
3) and type 2 'Diabetes' (diabdiag_gprd = 4) then classify as 'Diabetes'
other or uncertain type

ELSE if there are no diabdiag_gprd records for this patient:

If there is at least one record for Non-insulin-dependent 'Diabetes'
mellitus (NIDDM) (dm_gprd = 4) and no record for IDDM (no record with
dm_gprd = 3) then classify the patient as type 2 'Diabetes'

ELSE if there is at least one record for Insulin-dependent 'Diabetes'
mellitus (IDDM) (dm_gprd = 3) and no record for NIDDM (no record with
dm_gprd = 4) then classify the patient as type 1 'Diabetes'

ELSE if there is at least one record of 'Diabetes' (dm_gprd = 6) then
classify as 'Diabetes' other or uncertain type
ELSE classify as no 'Diabetes'
```

S2 Supplementary Figures and Tables

Table S1. Availability of primary and secondary outcomes in electronic health records (primary cohort)

Variable	Follow-up at least 6 months (N = 2 052 480) [a]		Discontinuity in outcome availability at threshold [b]		Discontinuity in time to follow-up record at threshold [b]	
	N	%	Estimate, % (95% CI)	*P* value	Estimate, months (95% CI)	*P* value
HbA1c, mmol/mol						
Baseline	2 052 480	100				
Outcome	1 043 268	50.8	8.0 (7.4, 8.6)	< 0.001	-0.38 (-0.51, -0.26)	< 0.001
BMI						
Baseline	1 285 194	62.6				
Outcome	679 542	33.1	2.7 (2.1, 3.2)	< 0.001	-0.13 (-0.28, 0.03)	0.114
Body weight, kg						
Baseline	1 399 803	68.2				
Outcome	778 500	37.9	2.7 (2.2, 3.3)	< 0.001	-0.08 (-0.22, 0.07)	0.315
Systolic BP, mmHg						
Baseline	986 677	48.1				
Outcome	700 158	34.1	0.7 (0.1, 1.2)	0.017	0.06 (-0.10, 0.21)	0.452
Diastolic BP, mmHg						
Baseline	988 154	48.1				
Outcome	701 789	34.1	0.7 (0.2, 1.3)	0.013	0.06 (-0.09, 0.22)	0.435
HDL, mmol/l						
Baseline	1 442 685	70.3				
Outcome	764 906	37.3	3.4 (2.8, 3.9)	< 0.001	-0.06 (-0.20, 0.08)	0.391
LDL, mmol/l						
Baseline	760 318	37.0				
Outcome	336 841	16.4	1.3 (0.9, 1.8)	< 0.001	-0.04 (-0.24, 0.16)	0.725
Total-to-HDL ratio						
Baseline	1 119 169	54.5				
Outcome	572 526	27.9	2.6 (2.1, 3.1)	< 0.001	-0.08 (-0.23, 0.08)	0.345
Triglycerides, mmol/l						
Baseline	1 118 366	54.5				
Outcome	528 191	25.7	2.4 (1.9, 2.9)	< 0.001	-0.08 (-0.25, 0.08)	0.321

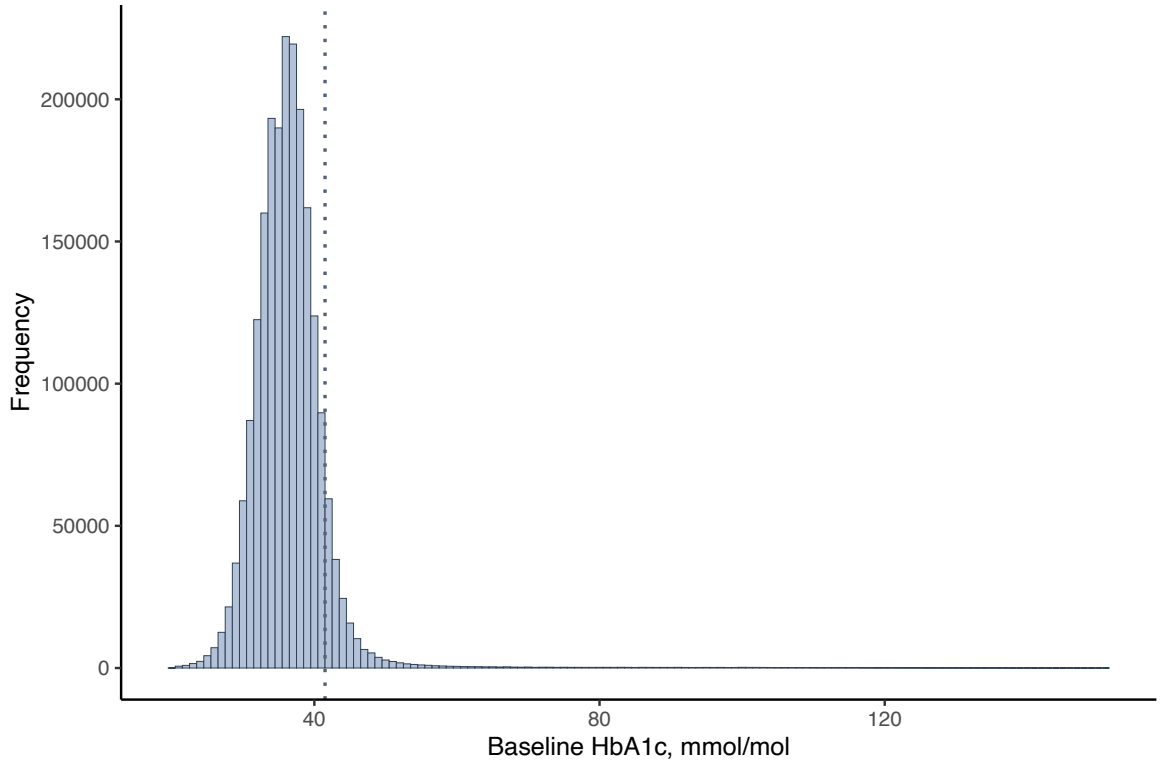


Fig. S1. Histogram of baseline HbA1c for the primary cohort.

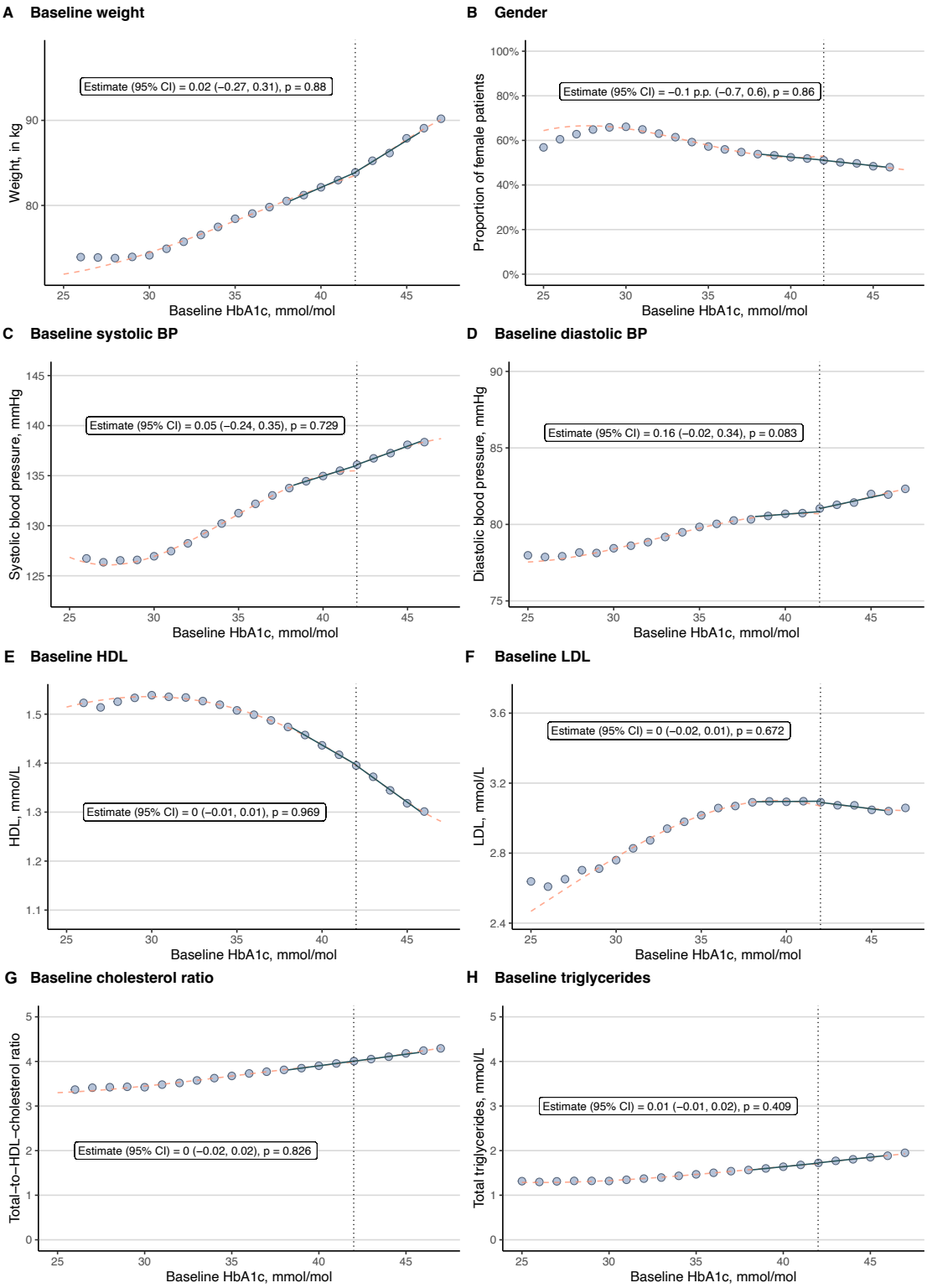


Fig. S2. Association between baseline HbA1c and baseline weight, gender, blood pressure and baseline blood serum lipids (Primary cohort). P.p. = percentage points. BP = Blood pressure. The blue lines show the local linear regression models within the bandwidth used in our primary analysis. The orange 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 quantifies the discontinuity at the HbA1c threshold, whereas discontinuities in potential confounders may jeopardize assumptions underlying regression discontinuity.

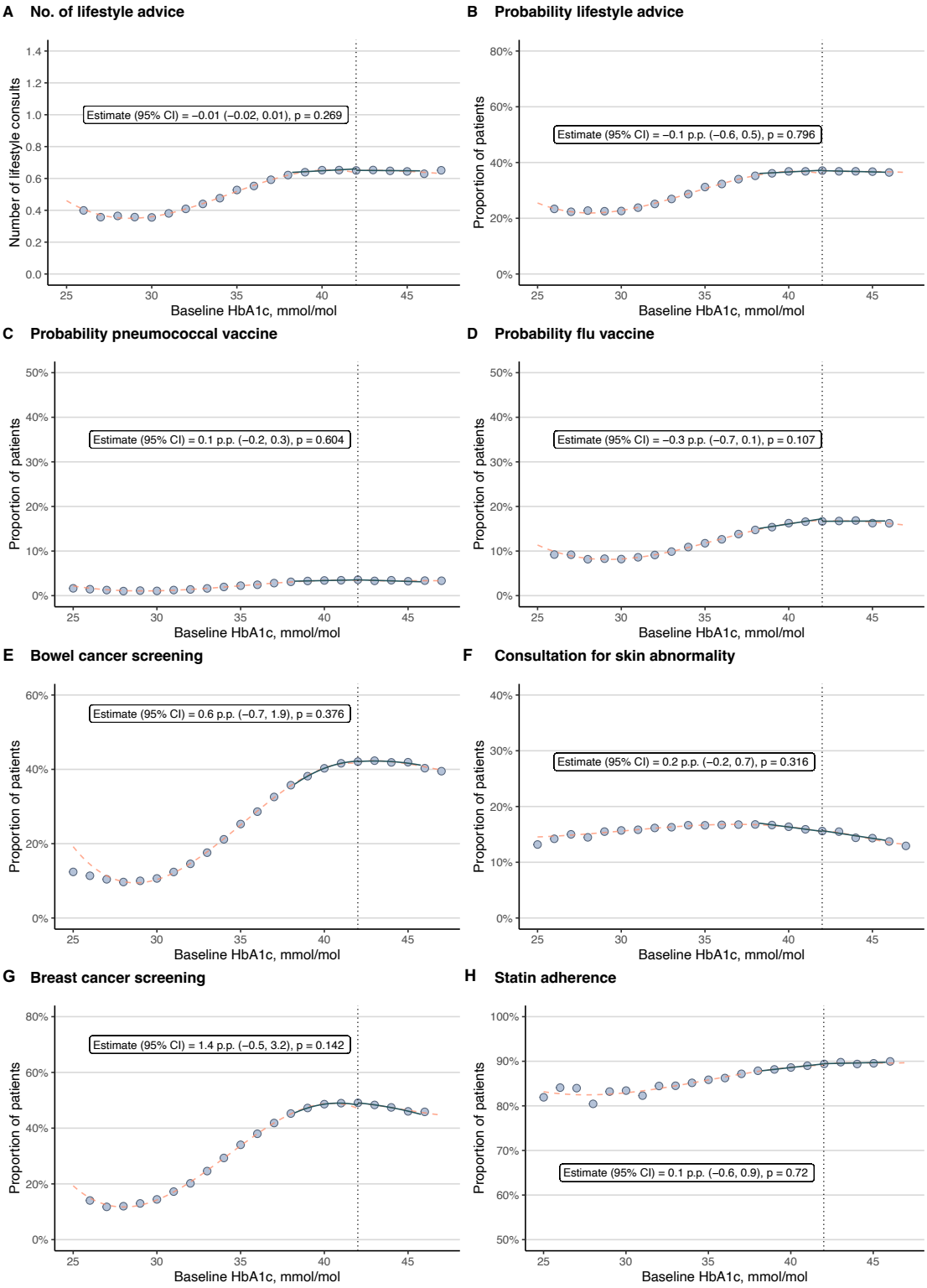


Fig. S3. Association between baseline HbA1c and previous receipt of lifestyle advice, pneumococcal vaccine, and flu vaccine, bowel cancer, skin abnormalities, breast cancer, and adherence to prior statin prescriptions (Primary cohort). P.p. = percentage points. The blue lines show the local linear regression models within the bandwidth used in our primary analysis. 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 quantifies the discontinuity at the HbA1c threshold, whereas discontinuities in potential confounders may jeopardize assumptions underlying regression discontinuity.

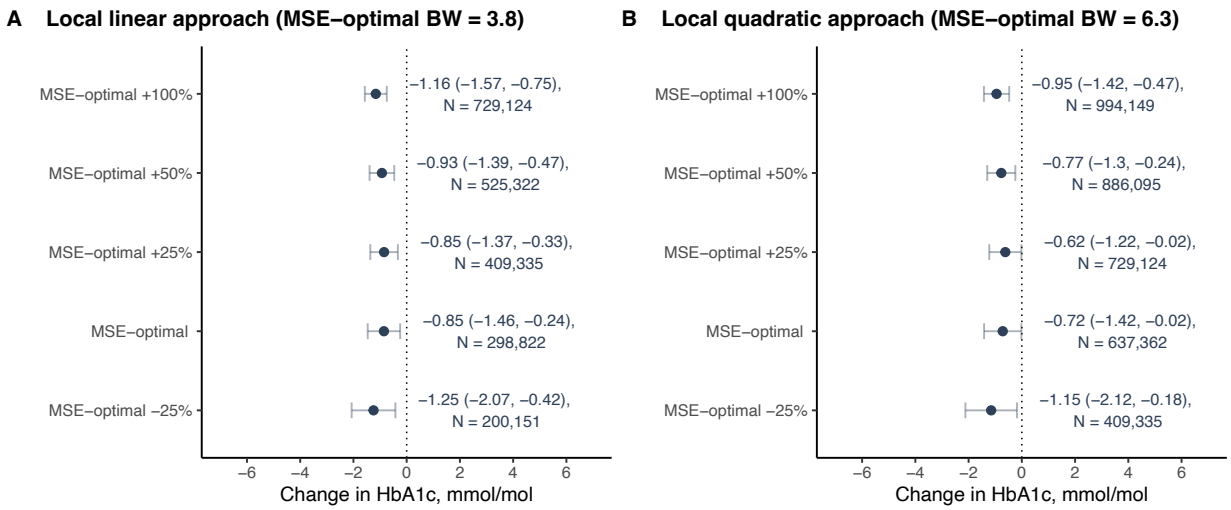


Fig. S4. Estimated effect of referral to intensive lifestyle counseling (CACE) on change in HbA1c with varying bandwidths. BW = Bandwidth. CACE = Complier average causal effect. MSE = mean-squared error. Estimated effect of referral to intensive lifestyle counseling (CACE) on endline HbA1c in A, local linear regressions and B, local quadratic regression, along varying bandwidths (i.e., 75%, 100%, 125%, 150, or 200%) of the derived mean-squared error (MSE) optimal bandwidth with robust 95% CI, fixed effects at practice-level, and triangular kernel weights. Significant effect estimates are pictured as solid, dark blue points; effects that are not significant are pictured as hollow points.

Table S2. Effect of eligibility threshold (ITT) and intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, adjusting for potential confounders and using local linear regressions (primary cohort)

		Adjusted for				
Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
HbA1c, mmol/mol						
ITT	-0.1 (-0.16, -0.03)	-0.1 (-0.17, -0.03)	-0.09 (-0.16, -0.02)	-0.11 (-0.17, -0.04)	-0.07 (-0.13, 0)	-0.08 (-0.14, -0.02)
CACE	-0.85 (-1.46, -0.24)	-0.91 (-1.51, -0.3)	-0.79 (-1.39, -0.18)	-0.94 (-1.55, -0.34)	-0.59 (-1.2, 0.02)	-0.72 (-1.27, -0.17)
BMI [b]						
ITT	-0.15 (-0.21, -0.09)	-0.16 (-0.21, -0.11)	-0.15 (-0.21, -0.09)	-	-0.15 (-0.21, -0.09)	-0.16 (-0.21, -0.11)
CACE	-1.35 (-1.88, -0.83)	-1.42 (-1.86, -0.98)	-1.35 (-1.88, -0.83)	-	-1.34 (-1.87, -0.81)	-1.41 (-1.85, -0.97)
Weight, kg [b]						
ITT	-0.33 (-0.48, -0.18)	-0.34 (-0.45, -0.23)	-0.33 (-0.48, -0.18)	-	-0.33 (-0.48, -0.18)	-0.34 (-0.45, -0.22)
CACE	-2.99 (-4.38, -1.61)	-2.98 (-3.97, -1.99)	-3.00 (-4.38, -1.61)	-	-2.99 (-4.38, -1.6)	-2.98 (-3.98, -1.98)
Diastolic BP, mmHg [b,c]						
ITT	-0.16 (-0.4, 0.07)	-0.22 (-0.46, 0.02)	-0.16 (-0.4, 0.07)	-0.19 (-0.42, 0.04)	-0.16 (-0.4, 0.08)	-0.22 (-0.45, 0.01)
CACE	-1.35 (-3.31, 0.61)	-1.84 (-3.82, 0.15)	-1.35 (-3.3, 0.61)	-1.54 (-3.44, 0.35)	-1.34 (-3.32, 0.63)	-1.82 (-3.73, 0.1)
Systolic BP, mmHg [b,c]						
ITT	-0.24 (-0.6, 0.11)	-0.32 (-0.7, 0.06)	-0.24 (-0.6, 0.11)	-0.29 (-0.63, 0.05)	-0.24 (-0.59, 0.11)	-0.32 (-0.67, 0.02)
CACE	-2.03 (-4.96, 0.91)	-2.64 (-5.78, 0.51)	-2.02 (-4.96, 0.91)	-2.41 (-5.21, 0.39)	-1.99 (-4.92, 0.94)	-2.69 (-5.58, 0.21)
HDL cholesterol, mmol/l [b,d]						
ITT	0 (0, 0.01)	0 (0, 0.01)	0 (0, 0.01)	0 (0, 0.01)	0.01 (0, 0.01)	0 (0, 0.01)
CACE	0.04 (0, 0.09)	0.04 (0, 0.09)	0.04 (0, 0.09)	0.04 (0, 0.09)	0.05 (0, 0.09)	0.05 (0, 0.09)
LDL cholesterol, mmol/l [b,d]						
ITT	0.01 (-0.01, 0.04)	0.01 (-0.02, 0.03)	0.01 (-0.01, 0.04)	0.01 (-0.01, 0.02)	0.01 (-0.01, 0.03)	0 (-0.02, 0.02)
CACE	0.11 (-0.08, 0.3)	0.05 (-0.13, 0.24)	0.11 (-0.08, 0.3)	0.04 (-0.12, 0.21)	0.10 (-0.09, 0.29)	0.03 (-0.13, 0.2)

Table S2. Effect of eligibility threshold (ITT) and intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, adjusting for potential confounders and using local linear regressions (primary cohort). (continued)

Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
Total-cholesterol-to-HDL ratio [b,d]						
ITT	0 (-0.02, 0.02)	-0.01 (-0.03, 0.01)	0 (-0.02, 0.02)	-0.01 (-0.03, 0.01)	0 (-0.02, 0.01)	-0.01 (-0.03, 0.01)
CACE	-0.03 (-0.2, 0.14)	-0.06 (-0.22, 0.11)	-0.03 (-0.2, 0.14)	-0.09 (-0.25, 0.08)	-0.04 (-0.21, 0.13)	-0.09 (-0.25, 0.07)
Triglycerides, mmol/l [b,d]						
ITT	-0.04 (-0.06, -0.01)	-0.04 (-0.06, -0.01)	-0.04 (-0.06, -0.01)	-0.04 (-0.06, -0.01)	-0.04 (-0.06, -0.01)	-0.04 (-0.06, -0.01)
CACE	-0.33 (-0.54, -0.12)	-0.33 (-0.54, -0.12)	-0.33 (-0.54, -0.12)	-0.32 (-0.52, -0.12)	-0.33 (-0.54, -0.11)	-0.33 (-0.53, -0.13)
Diabetes complication, p.p.						
ITT	0.06 (-0.07, 0.19)	0.07 (-0.06, 0.2)	0.04 (-0.1, 0.17)	0.02 (-0.11, 0.14)	-	0 (-0.12, 0.12)
CACE	0.58 (-0.62, 1.78)	0.64 (-0.58, 1.86)	0.33 (-0.89, 1.54)	0.15 (-0.98, 1.28)	-	-0.01 (-1.13, 1.11)
Mortality, p.p.						
ITT	0.05 (-0.09, 0.2)	0.05 (-0.11, 0.22)	0.01 (-0.13, 0.15)	0.07 (-0.07, 0.22)	-	0.02 (-0.14, 0.18)
CACE	0.47 (-0.81, 1.76)	0.49 (-1.02, 1.99)	0.09 (-1.2, 1.38)	0.67 (-0.62, 1.95)	-	0.17 (-1.29, 1.63)
MACE hospitalization, p.p.						
ITT	-0.05 (-0.23, 0.12)	-0.04 (-0.24, 0.16)	-0.13 (-0.3, 0.05)	-0.01 (-0.19, 0.16)	-	-0.12 (-0.32, 0.08)
CACE	-0.48 (-2.05, 1.09)	-0.37 (-2.23, 1.49)	-1.12 (-2.69, 0.44)	-0.12 (-1.68, 1.45)	-	-1.08 (-2.91, 0.74)
Diabetes medication, p.p.						
ITT	0.3 (0.18, 0.41)	0.28 (0.17, 0.4)	0.28 (0.16, 0.39)	-	-	0.25 (0.14, 0.37)
CACE	2.72 (1.66, 3.78)	2.58 (1.53, 3.63)	2.54 (1.49, 3.59)	-	-	2.31 (1.26, 3.36)
Antihypertensive medication, p.p. [b]						
ITT	0.11 (-0.38, 0.6)	0.24 (-0.25, 0.73)	-0.17 (-0.64, 0.29)	-	-	-0.08 (-0.55, 0.38)
CACE	0.93 (-3.22, 5.09)	2.02 (-2.14, 6.18)	-1.46 (-5.4, 2.47)	-	-	-0.71 (-4.64, 3.21)

Table S2. Effect of eligibility threshold (ITT) and intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, adjusting for potential confounders and using local linear regressions (primary cohort). (continued)

Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
Lipid-lowering medication, p.p.[c]						
ITT	0.29 (-0.23, 0.82)	0.42 (-0.06, 0.89)	0.14 (-0.37, 0.64)			0.27 (-0.2, 0.73)
CACE	2.61 (-2.03, 7.25)	3.66 (-0.49, 7.81)	1.21 (-3.28, 5.69)			2.35 (-1.75, 6.46)
T2DM incidence, p.p.						
ITT	0.39 (0.21, 0.57)	0.38 (0.21, 0.56)	0.36 (0.19, 0.54)	-	-	0.34 (0.17, 0.52)
CACE	3.66 (2, 5.33)	3.61 (1.94, 5.28)	3.4 (1.74, 5.06)	-	-	3.22 (1.55, 4.88)
Hypertension incidence, p.p. [c]						
ITT	-0.01 (-0.32, 0.3)	0.05 (-0.29, 0.38)	-0.08 (-0.38, 0.22)	-	-	-0.04 (-0.37, 0.28)
CACE	-0.12 (-2.71, 2.48)	0.38 (-2.43, 3.20)	-0.67 (-3.21, 1.88)	-	-	-0.37 (-3.15, 2.41)
Hyperlipidemia incidence, p.p. [d]						
ITT	-0.13 (-0.3, 0.05)	-0.12 (-0.28, 0.04)	-0.14 (-0.32, 0.04)	-	-	-0.13 (-0.29, 0.03)
CACE	-1.09 (-2.6, 0.43)	-1 (-2.37, 0.38)	-1.19 (-2.69, 0.3)	-	-	-1.1 (-2.48, 0.28)

BMI = Body mass index. BP = Blood pressure. CACE = Complier average causal effect. ITT = Intention-to-treat effect. MACE = Major adverse cardiovascular event. MSE = mean-squared error. P.p. = percentage points.

[a] The medication covariate indicates whether there was a recorded prescription of relevant medication (i.e., diabetes, lipid- or blood pressure-lowering medication) prior to the recorded endline measure.

[b] Effect estimates for BMI, weight, cholesterol levels, and BP levels represent changes between baseline and endline level to enhance precision. Regressions without adjusting for baseline levels yielded similar effect estimates but larger confidence intervals.

[c] Sample restricted to those without prior blood pressure-lowering medication prescription.

[d] Sample restricted to those without prior lipid-lowering medication prescription

Local linear regression with heteroskedasticity-robust standard errors, triangular kernel weights and MSE-optimal bandwidths.

Table S3. Effect of eligibility threshold (ITT) and intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, adjusting for potential confounders and using local quadratic regressions (primary cohort)

		Adjusted for				
Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
HbA1c, mmol/mol						
ITT	-0.08 (-0.15, 0)	-0.08 (-0.16, 0)	-0.07 (-0.15, 0)	-0.09 (-0.17, -0.01)	-0.06 (-0.13, 0.02)	-0.07 (-0.15, 0.01)
CACE	-0.72 (-1.42, -0.02)	-0.74 (-1.44, -0.04)	-0.66 (-1.36, 0.04)	-0.83 (-1.55, -0.11)	-0.52 (-1.22, 0.18)	-0.65 (-1.36, 0.07)
BMI [b]						
ITT	-0.17 (-0.23, -0.1)	-0.17 (-0.22, -0.11)	-0.17 (-0.23, -0.1)	-	-0.17 (-0.23, -0.1)	-0.16 (-0.22, -0.11)
CACE	-1.52 (-2.1, -0.93)	-1.48 (-2, -0.95)	-1.52 (-2.1, -0.93)	-	-1.51 (-2.1, -0.92)	-1.46 (-1.99, -0.94)
Weight, kg [b]						
ITT	-0.39 (-0.55, -0.22)	-0.37 (-0.51, -0.22)	-0.39 (-0.55, -0.22)	-	-0.39 (-0.55, -0.22)	-0.36 (-0.51, -0.22)
CACE	-3.58 (-5.12, -2.04)	-3.26 (-4.56, -1.97)	-3.57 (-5.11, -2.04)	-	-3.58 (-5.12, -2.03)	-3.24 (-4.53, -1.95)
Diastolic BP, mmHg [b,c]						
ITT	-0.17 (-0.52, 0.17)	-0.16 (-0.53, 0.21)	-0.17 (-0.51, 0.17)	-0.21 (-0.56, 0.15)	-0.17 (-0.52, 0.17)	-0.2 (-0.57, 0.16)
CACE	-1.47 (-4.39, 1.46)	-1.39 (-4.57, 1.79)	-1.46 (-4.39, 1.47)	-1.78 (-4.82, 1.25)	-1.46 (-4.4, 1.47)	-1.76 (-4.88, 1.36)
Systolic BP, mmHg [b,c]						
ITT	-0.23 (-0.72, 0.27)	-0.22 (-0.74, 0.3)	-0.22 (-0.72, 0.27)	-0.27 (-0.75, 0.2)	-0.22 (-0.72, 0.27)	-0.27 (-0.78, 0.23)
CACE	-1.9 (-6.04, 2.25)	-1.86 (-6.25, 2.53)	-1.89 (-6.03, 2.26)	-2.31 (-6.34, 1.73)	-1.88 (-6.04, 2.27)	-2.34 (-6.61, 1.93)
HDL cholesterol, mmol/l [b,d]						
ITT	0.01 (0, 0.02)	0.01 (0, 0.02)	0.01 (0, 0.02)	0.01 (0, 0.02)	0.01 (0, 0.02)	0.01 (0, 0.02)
CACE	0.09 (0.01, 0.17)	0.09 (0.01, 0.17)	0.09 (0.01, 0.17)	0.09 (0.01, 0.17)	0.09 (0.02, 0.17)	0.09 (0.01, 0.17)
LDL cholesterol, mmol/l [b,d]						
ITT	0.02 (-0.01, 0.06)	0.01 (-0.02, 0.05)	0.02 (-0.01, 0.06)	0.01 (-0.02, 0.04)	0.02 (-0.01, 0.06)	0.01 (-0.02, 0.04)
CACE	0.2 (-0.12, 0.52)	0.13 (-0.16, 0.41)	0.19 (-0.13, 0.52)	0.09 (-0.15, 0.33)	0.2 (-0.13, 0.52)	0.09 (-0.16, 0.33)

Table S3. Effect of eligibility threshold (ITT) and intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, adjusting for potential confounders and using local quadratic regressions (primary cohort). (continued)

Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
Total-cholesterol-to-HDL ratio [b,d]						
ITT	0 (-0.03, 0.02)	-0.01 (-0.03, 0.02)	0 (-0.03, 0.02)	0 (-0.03, 0.02)	0 (-0.03, 0.02)	0 (-0.03, 0.02)
CACE	-0.02 (-0.25, 0.2)	-0.05 (-0.25, 0.15)	-0.03 (-0.25, 0.2)	-0.04 (-0.25, 0.16)	-0.03 (-0.26, 0.19)	-0.04 (-0.24, 0.15)
Triglycerides, mmol/l [b,d]						
ITT	-0.07 (-0.11, -0.03)	-0.07 (-0.11, -0.03)	-0.07 (-0.11, -0.03)	-0.07 (-0.11, -0.03)	-0.07 (-0.11, -0.03)	-0.07 (-0.11, -0.03)
CACE	-0.7 (-1.09, -0.3)	-0.71 (-1.1, -0.31)	-0.68 (-1.07, -0.3)	-0.73 (-1.12, -0.33)	-0.69 (-1.09, -0.3)	-0.72 (-1.11, -0.33)
Diabetes complication, p.p.						
ITT	0.02 (-0.16, 0.21)	0.04 (-0.14, 0.21)	0 (-0.18, 0.19)	0.01 (-0.15, 0.17)	-	-0.01 (-0.18, 0.15)
CACE	0.24 (-1.54, 2.02)	0.35 (-1.31, 2.01)	0.04 (-1.72, 1.8)	0.14 (-1.38, 1.65)	-	-0.12 (-1.67, 1.43)
Mortality, p.p.						
ITT	0.01 (-0.17, 0.18)	-0.01 (-0.18, 0.16)	-0.04 (-0.21, 0.14)	0.01 (-0.16, 0.19)	-	-0.04 (-0.21, 0.12)
CACE	0.05 (-1.57, 1.67)	-0.1 (-1.61, 1.41)	-0.34 (-1.98, 1.3)	0.12 (-1.51, 1.74)	-	-0.4 (-1.92, 1.12)
MACE hospitalization, p.p.						
ITT	-0.12 (-0.31, 0.07)	-0.12 (-0.33, 0.08)	-0.18 (-0.37, 0)	-0.09 (-0.28, 0.1)	-	-0.18 (-0.38, 0.02)
CACE	-1.07 (-2.8, 0.66)	-1.1 (-2.96, 0.75)	-1.65 (-3.3, 0)	-0.83 (-2.56, 0.9)	-	-1.68 (-3.5, 0.15)
Diabetes medication, p.p.						
ITT	0.31 (0.18, 0.44)	0.23 (0.07, 0.39)	0.29 (0.17, 0.42)	-	-	0.21 (0.05, 0.37)
CACE	2.88 (1.7, 4.06)	2.18 (0.67, 3.7)	2.74 (1.57, 3.91)	-	-	2 (0.49, 3.51)
Antihypertensives medication, p.p.						
ITT	0.07 (-0.46, 0.59)	0.08 (-0.46, 0.63)	-0.18 (-0.68, 0.32)	-	-	-0.18 (-0.71, 0.35)
CACE	0.58 (-3.9, 5.06)	0.72 (-3.97, 5.42)	-1.54 (-5.82, 2.75)	-	-	-1.57 (-6.15, 3.02)

Table S3. Effect of eligibility threshold (ITT) and intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, adjusting for potential confounders and using local quadratic regressions (primary cohort). (continued)

Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
Lipid-lowering medication, p.p.[c]						
ITT	0.47 (-0.05, 0.99)	0.4 (-0.1, 0.9)	0.32 (-0.19, 0.83)			0.26 (-0.23, 0.76)
CACE	4.17 (-0.43, 8.77)	3.51 (-0.87, 7.89)	2.84 (-1.72, 7.4)			2.34 (-2.01, 6.69)
T2DM incidence, p.p.						
ITT	0.29 (0.08, 0.5)	0.29 (0.02, 0.55)	0.26 (0.06, 0.47)	-	-	0.26 (-0.01, 0.52)
CACE	2.79 (0.76, 4.82)	2.8 (0.20, 5.4)	2.52 (0.58, 4.47)	-	-	2.5 (-0.09, 5.09)
Hypertension incidence, p.p. [c]						
ITT	-0.05 (-0.46, 0.36)	-0.07 (-0.48, 0.34)	-0.13 (-0.54, 0.29)	-	-	-0.15 (-0.56, 0.26)
CACE	-0.43 (-4.04, 3.18)	-0.63 (-4.24, 2.98)	-1.13 (-4.77, 2.52)	-	-	-1.31 (-4.92, 2.3)
Hyperlipidemia incidence, p.p. [d]						
ITT	-0.07 (-0.28, 0.14)	-0.07 (-0.28, 0.14)	-0.08 (-0.29, 0.13)	-	-	-0.08 (-0.29, 0.13)
CACE	-0.63 (-2.47, 1.22)	-0.62 (-2.42, 1.19)	-0.71 (-2.55, 1.13)	-	-	-0.7 (-2.51, 1.11)

BMI = Body mass index. BP = Blood pressure. CACE = Complier average causal effect. ITT = Intention-to-treat effect. MACE = Major adverse cardiovascular event. MSE = mean-squared error. P.p. = percentage points.

[a] The medication covariate indicates whether there was a recorded prescription of relevant medication (i.e., diabetes, lipid- or blood pressure-lowering medication) prior to the recorded endline measure.

[b] Effect estimates for BMI, weight, cholesterol levels, and BP levels represent changes between baseline and endline level to enhance precision. Regressions without adjusting for baseline levels yielded similar effect estimates but larger confidence intervals.

[c] Sample restricted to those without prior blood pressure-lowering medication prescription.

[d] Sample restricted to those without prior lipid-lowering medication prescription

Local quadratic regression with heteroskedasticity-robust standard errors, triangular kernel weights and MSE-optimal bandwidths.

Table S4. Comparison between those who referred to the NHS DPP and those who were referred and started the NHS DPP according to their GP records (primary cohort)

Variable at baseline[a]	Referred to NHS DPP (n = 15 077)	Started NHS DPP (n = 5 886)	*P* value	SMD
Age in years	57.95 (12.92)	58.91 (12.60)	< 0.001	0.075
Female [a]	0.50 (0.50)	0.53 (0.50)	< 0.001	0.057
Baseline BMI	30.66 (6.44)	30.67 (6.36)	0.965	0.001
Baseline weight, kg	86.91 (20.60)	86.15 (20.14)	0.035	0.037
Average yearly number of GP consultations	12.44 (10.77)	13.72 (11.75)	< 0.001	0.114
Baseline blood pressure, mmHg				
Systolic	136.72 (17.97)	136.48 (17.65)	0.527	0.013
Diastolic	81.76 (11.01)	81.57 (10.91)	0.404	0.017
Baseline lipids				
HDL, mmol/l	1.36 (0.40)	1.37 (0.38)	0.137	0.026
LDL, mmol/l	3.06 (1.00)	3.06 (1.00)	0.868	0.004
Total-cholesterol-to-HDL ratio	4.10 (1.33)	4.02 (1.27)	0.002	0.060
Triglycerides, mmol/l	1.81 (1.11)	1.74 (0.99)	0.002	0.061
Flu vaccination [a]	0.17 (0.38)	0.19 (0.40)	0.001	0.051
Pneumococcal vaccincation [a]	0.03 (0.18)	0.05 (0.22)	< 0.001	0.071
Lifestyle advice [a]	0.37 (0.48)	0.38 (0.49)	0.056	0.029
Weight loss counseling [a]	0.05 (0.22)	0.05 (0.23)	0.310	0.015
Routine screening [a]				
Colorectal	0.43 (0.49)	0.45 (0.50)	0.001	0.052
Skin	0.16 (0.37)	0.17 (0.37)	0.317	0.015
Breast	0.53 (0.50)	0.55 (0.50)	0.036	0.045
Statin adherence [a]	0.96 (0.20)	0.96 (0.20)	0.887	0.004
IMD	2.99 (1.43)	3.01 (1.47)	0.398	0.013
Urban practice location [a]	0.90 (0.31)	0.87 (0.34)	< 0.001	0.088

BMI = body mass index. GP = General practitioner. SMD = Standardized Mean Difference (Cohen's d). 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. All SMD are below 0.2 which is usually considered to be a small effect. All SMD except for the average yearly number of GP consultations are below 0.1.

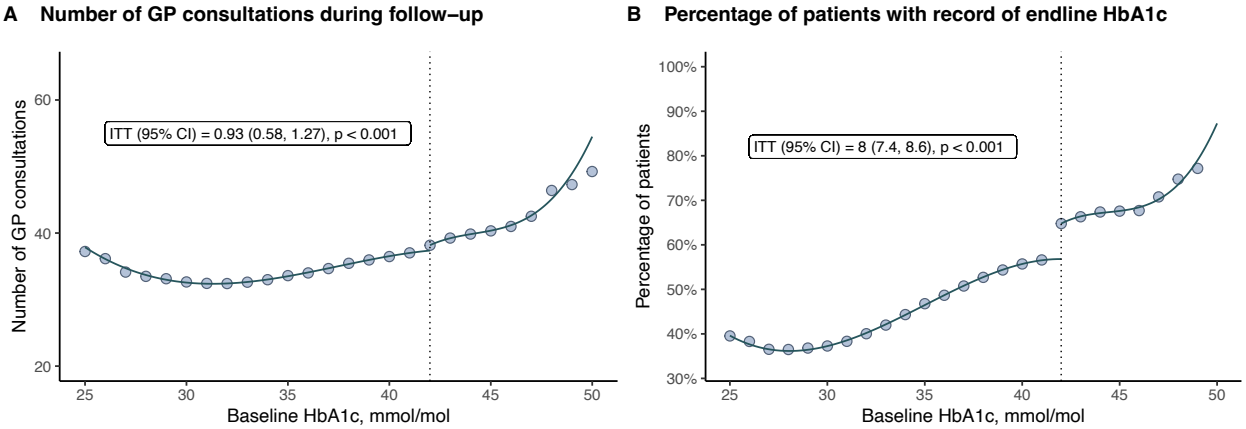
[a] Proportion of patients.

Table S5. Effect of referral to intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, adjusting for health promotion behavior variables, using local linear regressions (primary cohort)

Outcome	Unadjusted	Adjusted for				
		Flu vaccination	General lifestyle advice	Weight loss counseling	Screening for skin abnormalities	Screening for colorectal cancer
HbA1c, mmol/mol	-0.85 (-1.46, -0.24)	-0.87 (-1.48, -0.26)	-0.85 (-1.46, -0.24)	-0.85 (-1.46, -0.24)	-0.85 (-1.46, -0.24)	-0.89 (-1.5, -0.28)
BMI [a]	-1.35 (-1.88, -0.83)	-1.37 (-1.9, -0.85)	-1.36 (-1.89, -0.84)	-1.35 (-1.88, -0.83)	-1.35 (-1.88, -0.83)	-1.38 (-1.87, -0.89)
Weight, kg [a]	-2.99 (-4.38, -1.61)	-3.05 (-4.42, -1.67)	-3.02 (-4.4, -1.65)	-2.99 (-4.38, -1.61)	-2.98 (-4.37, -1.6)	-3.17 (-4.5, -1.83)
Diastolic BP, mmHg [a,b]	-1.35 (-3.31, 0.61)	-1.35 (-3.31, 0.61)	-1.34 (-3.31, 0.62)	-1.35 (-3.31, 0.61)	-1.35 (-3.31, 0.62)	-1.64 (-3.57, 0.29)
Systolic BP, mmHg [a,b]	-2.03 (-4.96, 0.91)	-2.02 (-4.96, 0.91)	-2.01 (-4.92, 0.91)	-2.02 (-4.96, 0.91)	-2.02 (-4.95, 0.9)	-2.45 (-5.51, 0.61)
HDL cholesterol, mmol/l [a,b]	0.04 (0, 0.09)	0.05 (0, 0.09)	0.04 (0, 0.09)	0.05 (0, 0.09)	0.04 (0, 0.09)	0.04 (0, 0.09)
LDL cholesterol, mmol/l [a,c]	0.11 (-0.08, 0.3)	0.10 (-0.08, 0.29)	0.11 (-0.08, 0.3)	0.11 (-0.08, 0.3)	0.11 (-0.08, 0.3)	0.07 (-0.12, 0.26)
Total-cholesterol-to-HDL ratio [a,c]	-0.03 (-0.20, 0.14)	-0.03 (-0.21, 0.14)	-0.03 (-0.2, 0.14)	-0.03 (-0.2, 0.14)	-0.03 (-0.2, 0.14)	-0.05 (-0.22, 0.12)
Triglycerides, mmol/l [a,c]	-0.33 (-0.54, -0.12)	-0.33 (-0.54, -0.12)	-0.33 (-0.54, -0.12)	-0.33 (-0.54, -0.12)	-0.33 (-0.53, -0.12)	-0.33 (-0.54, -0.12)
Diabetes complication, p.p.	0.58 (-0.62, 1.78)	0.6 (-0.62, 1.81)	0.57 (-0.65, 1.79)	0.57 (-0.63, 1.78)	0.58 (-0.64, 1.79)	0.6 (-0.62, 1.82)
Mortality, p.p.	0.47 (-0.81, 1.76)	0.54 (-0.75, 1.83)	0.47 (-0.82, 1.76)	0.46 (-0.82, 1.74)	0.47 (-0.81, 1.76)	0.53 (-0.81, 1.87)
MACE hospitalization, p.p.	-0.48 (-2.05, 1.09)	-0.38 (-1.95, 1.18)	-0.47 (-2.04, 1.11)	-0.48 (-2.05, 1.08)	-0.48 (-2.05, 1.09)	-0.32 (-1.93, 1.28)
Diabetes medication, p.p.	2.72 (1.66, 3.78)	2.71 (1.66, 3.77)	2.72 (1.67, 3.78)	2.71 (1.66, 3.77)	2.72 (1.67, 3.78)	2.64 (1.58, 3.69)
Antihypertensive medication, p.p,[b]	0.93 (-3.22, 5.09)	1.03 (-3.11, 5.18)	0.9 (-3.24, 5.03)	0.91 (-3.24, 5.06)	0.93 (-3.22, 5.09)	1.37 (-2.72, 5.47)
Lipid-lowering medication, p.p.[c]	2.61 (-2.03, 7.25)	2.78 (-1.83, 7.39)	2.46 (-2.03, 6.96)	2.61 (-2.03, 7.25)	2.58 (-2.05, 7.21)	3.29 (-0.99, 7.58)

BMI = Body mass index, BP = Blood pressure, CACE = Complier average causal effect, MACE = Major adverse cardiovascular event, MSE = mean-squared error, P.p, = percentage points. [a] Effect estimates for BMI, weight, cholesterol levels, and BP levels represent changes between baseline and endline level to enhance precision. Regressions without adjusting for baseline levels yielded similar effect estimates but larger confidence intervals. [b] Sample restricted to those without prior blood pressure-lowering medication prescription. [c] Sample restricted to those without prior lipid-lowering medication prescription.
Local linear regression with heteroskedasticity-robust standard errors, triangular kernel weights and MSE-optimal bandwidths.

Main analysis



Placebo analysis

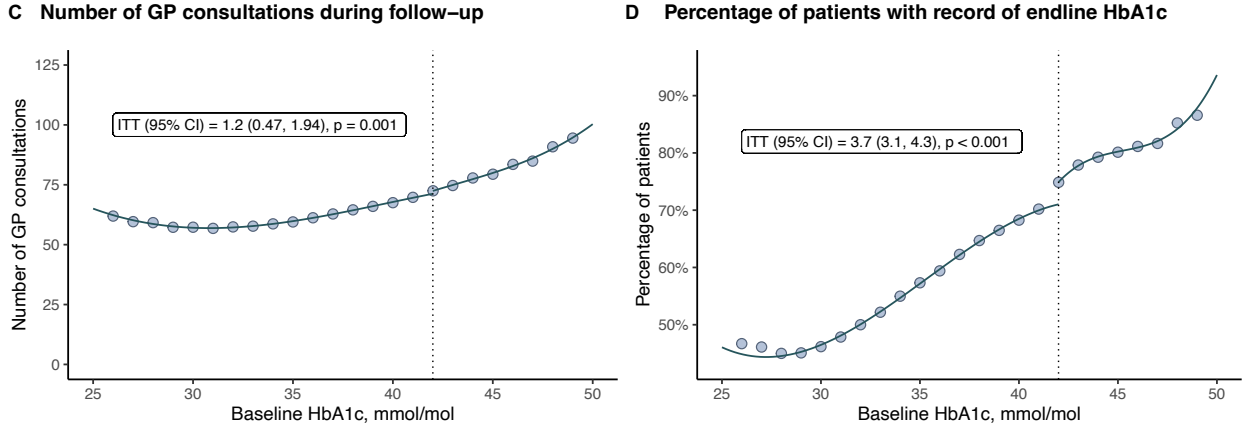


Fig. S5. Potential confounders in main and placebo analysis. Here are shown the associations between baseline HbA1c and (A and C) number of GP consultations during follow-up and (B and D) availability of endline HbA1c in the main and in the placebo analysis. The blue lines show the global polynomial relationship between baseline HbA1c and the outcome. The blue circles represent the mean value for individual patients and the dotted vertical lines indicate the HbA1c cutoff. In the placebo analysis, we applied the same inclusion criteria as for the primary cohort in the main analysis but for patients who had a baseline HbA1c measure in 2014 and 2015 (as opposed to 2017 and 2018).

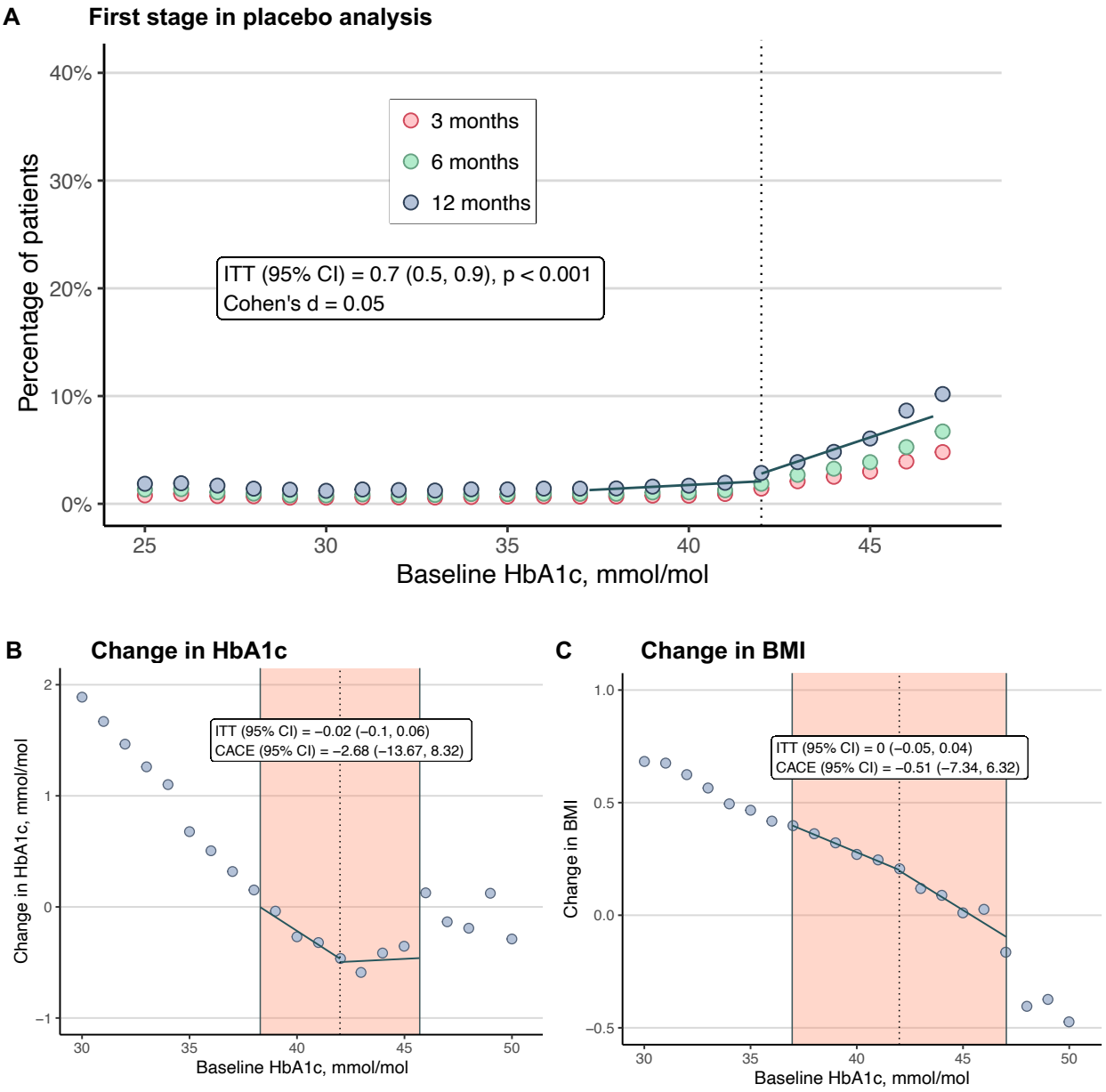


Fig. S6. Regression discontnuity results in placebo analysis. Here are shown the associations between (A) baseline HbA1c and referral to intensive lifestyle counseling ('First stage'), (B) baseline and change in HbA1c, and (C) baseline and change in BMI in years 2014-15 (prior to roll-out of the NHS DPP). The blue circles represent the mean value for individual patients and the dotted lines indicate the eligibility threshold. The associations are modelled using a local linear approach. The shaded area shows the mean-squared error (MSE) optimal local linear regression bandwidth. Results demonstrate that prior to roll-out of the NHS DPP, there was no discontinuity in lifestyle intervention referrals, change in HbA1c or change in BMI at the eligibility threshold.

Table S6. Effect of eligibility threshold (ITT) and intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, restricted to patients with a minimum follow-up time of 12 months (primary cohort)

	Unadjusted				Adjusted for medication[a]			
	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 [b]
Primary outcome								
HbA1c, mmol/mol	-0.08 (-0.15, 0)	0.057	-0.71 (-1.44, 0.02)	0.057	-0.79 (-1.47, -0.1)	0.024	4.0	334,467
Secondary outcomes								
BMI, kg/m^2	-0.13 (-0.2, -0.07)	< 0.001	-1.29 (-1.92, -0.66)	< 0.001	-	-	3.8	148,581
Weight, kg	-0.26 (-0.43, -0.1)	0.002	-2.56 (-4.21, -0.92)	0.002	-	-	3.6	164,322
Diastolic BP, mmHg [c]	-0.16 (-0.45, 0.12)	0.264	-1.45 (-4, 1.09)	0.264	-1.71 (-4.19, 0.77)	0.176	6.8	136,547
Systolic BP, mmHg [c]	-0.28 (-0.73, 0.16)	0.205	-2.52 (-6.42, 1.38)	0.206	-2.93 (-6.7, 0.83)	0.127	6.7	136,386
HDL cholesterol, mmol/l [d]	0.01 (0, 0.01)	0.028	0.06 (0.01, 0.1)	0.029	0.09 (-0.13, 0.3)	0.440	6.5	235,070
LDL cholesterol, mmol/l [d]	0.01 (-0.01, 0.04)	0.254	0.13 (-0.09, 0.36)	0.255	0.04 (-0.12, 0.21)	0.596	5.7	85,191
Total-cholesterol-to-HDL ratio [d]	0 (-0.02, 0.02)	0.715	-0.03 (-0.21, 0.14)	0.715	-0.1 (-0.26, 0.07)	0.251	5.8	160,078
Triglycerides, mmol/l [d]	-0.03 (-0.06, -0.01)	0.008	-0.34 (-0.59, -0.09)	0.008	-0.32 (-0.56, -0.09)	0.008	4.3	100,225
Exploratory outcomes								
Diabetes medication, RD	0.30 (0.18, 0.42)	< 0.001	2.76 (1.68, 3.85)	< 0.001	-	-	3.4	486,179
Antihypertensive medication, RD [c]	0.09 (-0.41, 0.59)	0.7362	0.72 (-3.49, 4.93)	0.7362	-	-	4.5	378,199
Lipid-lowering medication, RD [d]	0.29 (-0.25, 0.83)	0.291	2.57 (-2.2, 7.34)	0.291	-	-	3.1	333,605
Diabetes complication, RD	0.06 (-0.07, 0.18)	0.398	0.50 (-0.66, 1.67)	0.398	0.07 (-1.08, 1.22)	0.907	3.7	478,601
Mortality, RD	0.04 (-0.09, 0.16)	0.554	0.33 (-0.76, 1.42)	0.554	0.50 (-0.58, 1.59)	0.364	5.1	896,401
Emergency MACE hospitalization, RD	-0.07 (-0.25, 0.1)	0.416	-0.65 (-2.22, 0.92)	0.416	-0.31 (-1.88, 1.25)	0.695	4.9	677,565

[a] 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).
[b] Sample size within MSE-optimal bandwidth.
[c] Sample restricted to those without prior lipid-lowering medication prescription.
[d] Sample restricted to those without prior blood pressure-lowering medication prescription.

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 those from the primary cohort with a minimum of at least 12 months follow-up time, 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').

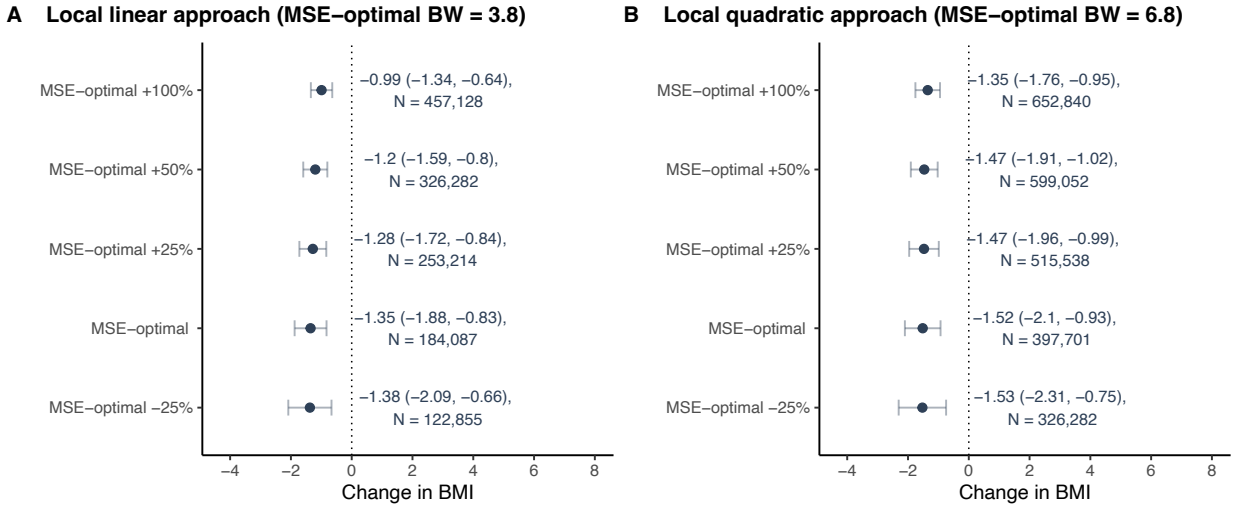
Table S7. Effect of eligibility threshold (ITT) and intensive lifestyle counseling (CACE) on Primary, Secondary, and Exploratory Outcomes, restricted to patients with a minimum follow-up time of 18 months (primary cohort)

	Unadjusted				Adjusted for medication[a]			
	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 [b]
Primary outcome								
HbA1c, mmol/mol	-0.11 (-0.22, 0)	0.046	-1.01 (-2.01, -0.02)	0.046	-1.12 (-2.1, -0.15)	0.024	4.3	152,425
Secondary outcomes								
BMI, kg/m^2	-0.13 (-0.22, -0.05)	0.002	-1.23 (-2.02, -0.45)	0.002	-	-	4.3	93,244
Weight, kg	-0.26 (-0.47, -0.05)	0.014	-2.43 (-4.38, -0.48)	0.014	-	-	4.5	103,463
Diastolic BP, mmHg [c]	-0.27 (-0.64, 0.09)	0.144	-2.6 (-6.1, 0.89)	0.145	-3.07 (-6.48, 0.34)	0.078	6.9	79,793
Systolic BP, mmHg [c]	-0.35 (-0.9, 0.21)	0.224	-3.3 (-8.64, 2.03)	0.225	-3.89 (-8.71, 0.92)	0.113	7.0	93,565
HDL cholesterol, mmol/l [d]	0 (0, 0.01)	0.250	0.04 (-0.03, 0.11)	0.250	0.04 (-0.03, 0.11)	0.262	6.1	111,599
LDL cholesterol, mmol/l [d]	0.05 (0.01, 0.09)	0.014	0.41 (0.08, 0.74)	0.015	0.22 (-0.08, 0.51)	0.149	5.3	40,749
Total-cholesterol-to-HDL ratio [d]	0.01 (-0.02, 0.04)	0.581	0.07 (-0.19, 0.34)	0.581	-0.07 (-0.3, 0.16)	0.578	5.2	71,780
Triglycerides, mmol/l [d]	-0.05 (-0.09, -0.01)	0.007	-0.48 (-0.84, -0.13)	0.008	-0.51 (-0.84, -0.17)	0.003	4.1	50,513
Exploratory outcomes								
Diabetes medication, RD	0.34 (0.19, 0.5)	< 0.001	3.06 (1.68, 4.44)	< 0.001	-	-	3.4	268,558
Antihypertensive medication, RD [c]	0.39 (-0.24, 1.02)	0.229	3.25 (-2.05, 8.55)	0.229	-	-	4.3	237,896
Lipid-lowering medication, RD [d]	-0.08 (-0.71, 0.54)	0.794	-0.71 (-6.07, 4.65)	0.794	-	-	3.7	203,939
Diabetes complication, RD	0.08 (-0.08, 0.25)	0.308	0.75 (-0.69, 2.19)	0.307	0.23 (-1.14, 1.6)	0.739	3.8	265,389
Mortality, RD	-0.12 (-0.29, 0.05)	0.168	-1.03 (-2.49, 0.43)	0.168	-0.96 (-2.43, 0.5)	0.196	4.4	370,742
Emergency MACE hospitalization, RD	-0.11 (-0.34, 0.12)	0.367	-0.93 (-2.94, 1.09)	0.367	-0.79 (-2.8, 1.22)	0.440	4.3	367,883

[a] 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).
[b] Sample size within MSE-optimal bandwidth.
[c] Sample restricted to those without prior lipid-lowering medication prescription.
[d] Sample restricted to those without prior blood pressure-lowering medication prescription.

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 those from the primary cohort with a minimum of at least 18 months follow-up time, 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').

BMI



Weight

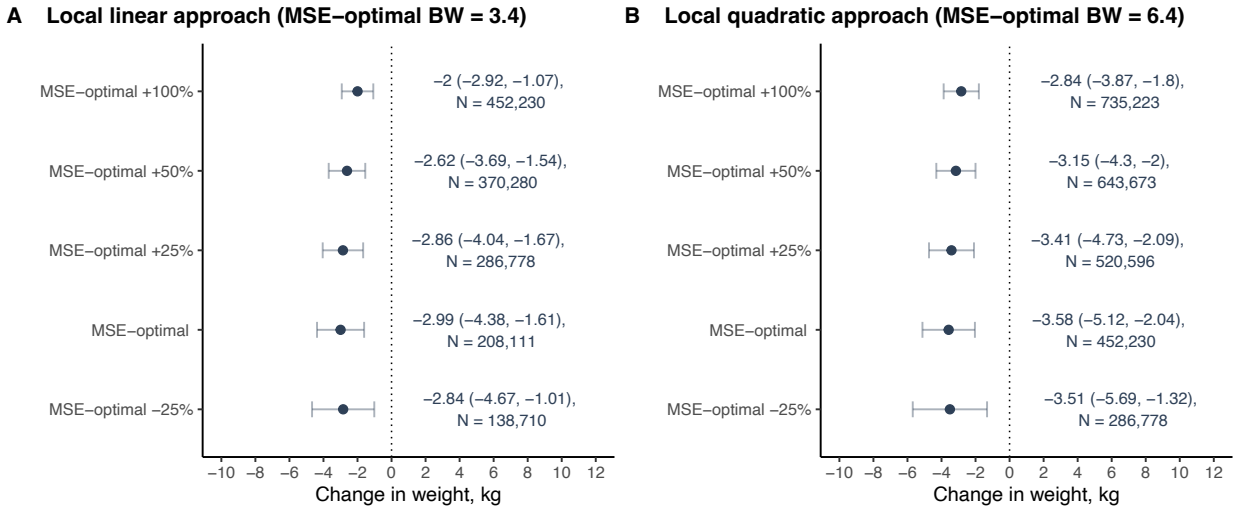


Fig. S7. Estimated effect of referral to intensive lifestyle counseling (CACE) on change in BMI and weight with varying bandwidths (primary cohort). BW = Bandwidth. CACE = Complier average causal effect. MSE = mean-squared error. Estimated effect of referral to intensive lifestyle counseling (CACE) on endline BMI and endline weight in A, local linear regressions and B, local quadratic regression, along varying bandwidths (i.e., 75%, 100%, 125%, 150, or 200%) of the derived mean-squared error (MSE) optimal bandwidth with heteroskedasticity-robust 95% CI and triangular kernel weights. Significant effect estimates are pictured as solid, dark blue points; effects that are not significant are pictured as hollow points.

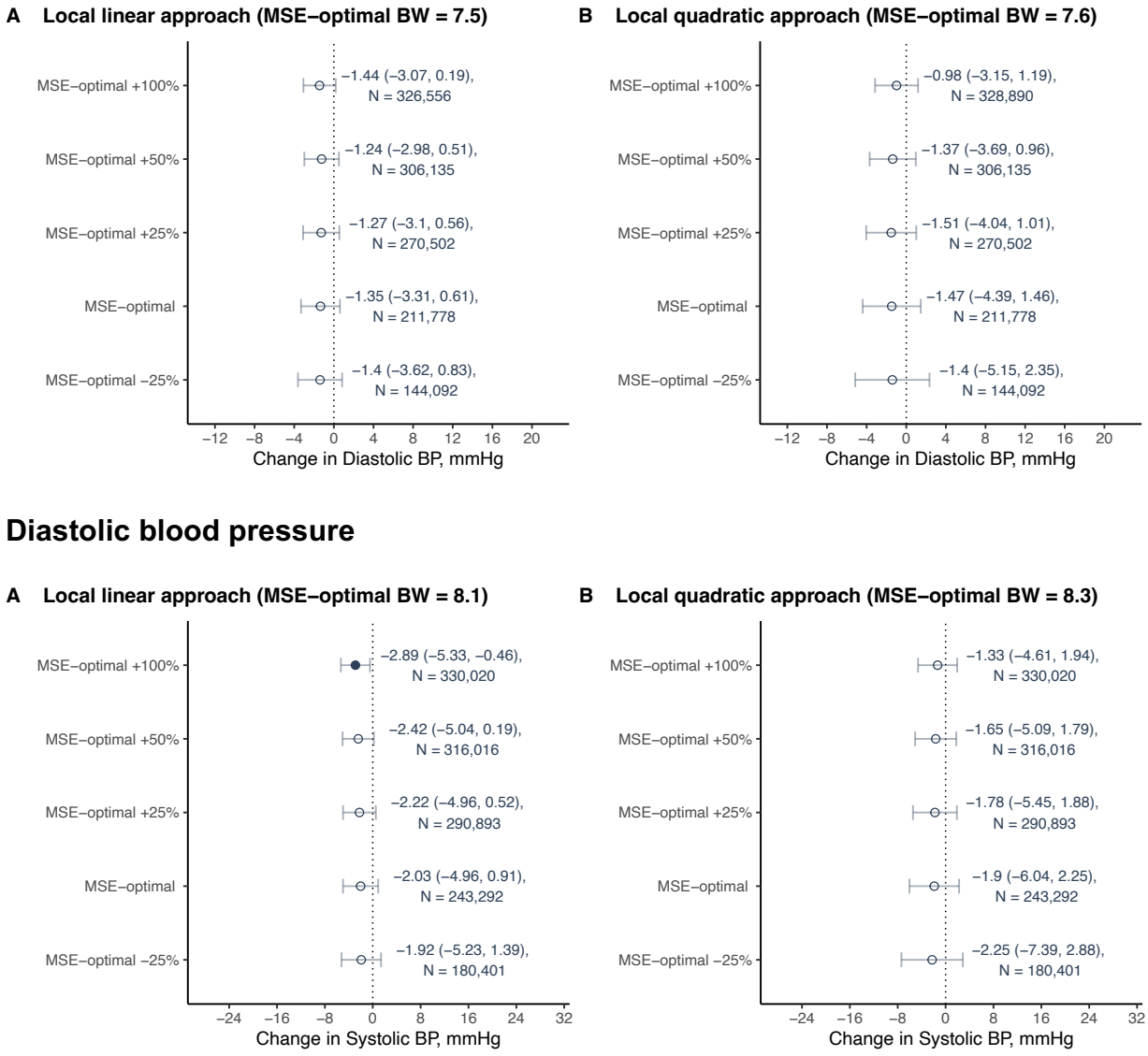
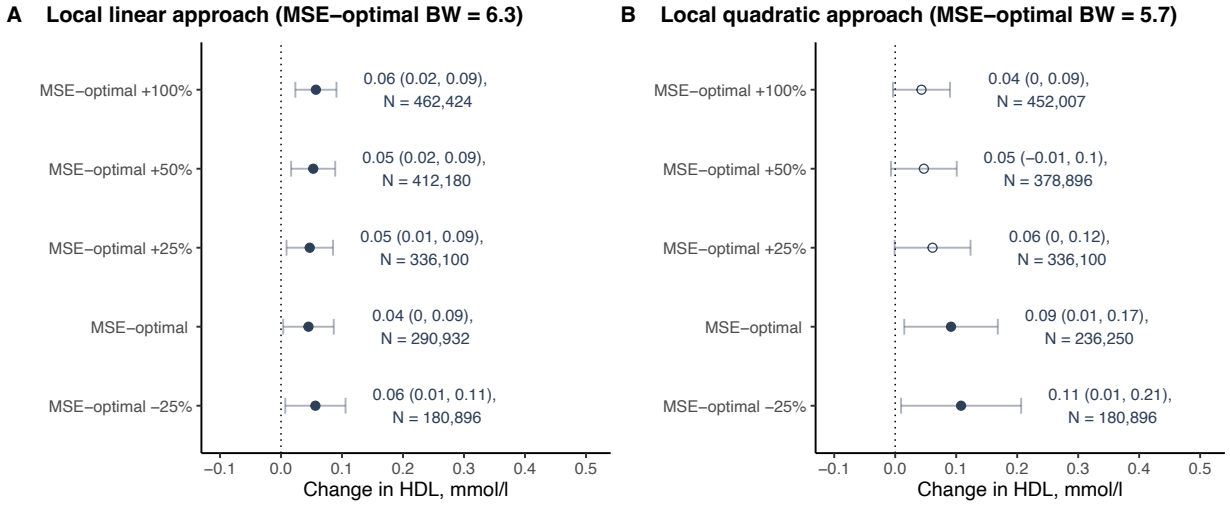


Fig. S8. Estimated effect of referral to intensive lifestyle counseling (CACE) on change in blood pressure with varying bandwidths (primary cohort). BW = Bandwidth. CACE = Complier average causal effect. MSE = mean-squared error. Estimated effect of referral to intensive lifestyle counseling (CACE) on endline (systolic and diastolic) blood pressure in A, local linear regressions and B, local quadratic regression, along varying bandwidths (i.e., 75%, 100%, 125%, 150, or 200%) of the derived mean-squared error (MSE) optimal bandwidth with heteroskedasticity-robust 95% CI and triangular kernel weights. Significant effect estimates are pictured as solid, dark blue points; effects that are not significant are pictured as hollow points.

HDL



Total-cholesterol-to-HDL

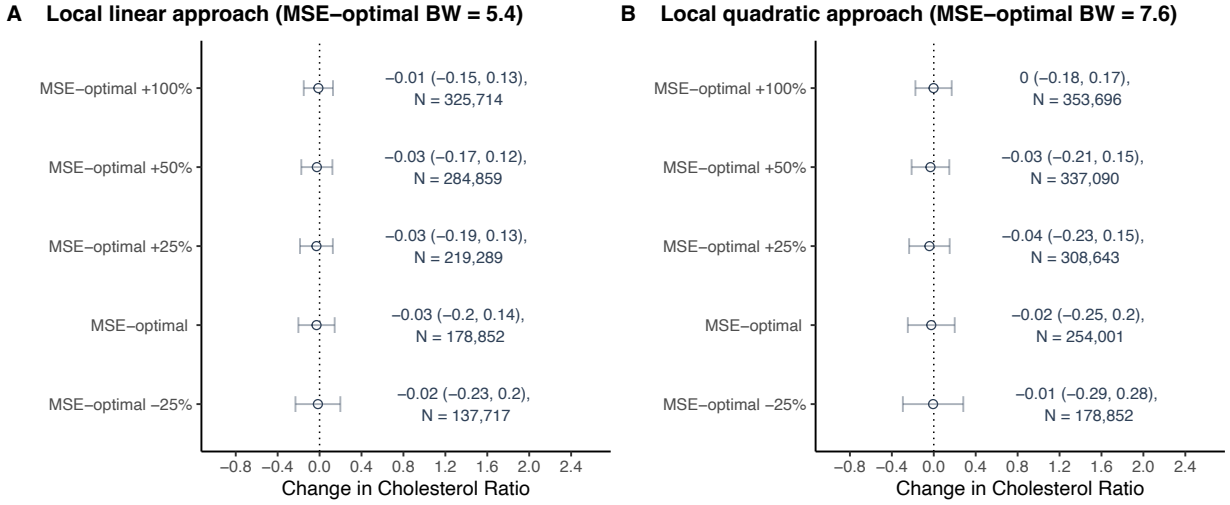
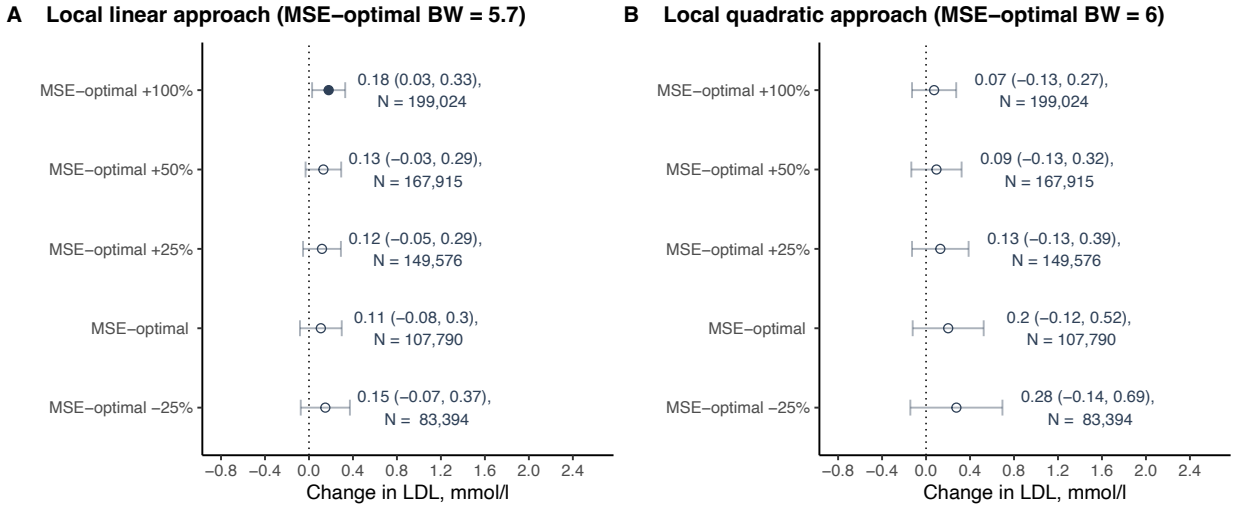


Fig. S9. Estimated effect of referral to intensive lifestyle counseling (CACE) on change in HDL and total-cholesterol-to-HDL with varying bandwidths (primary cohort). BW = Bandwidth. CACE = Complier average causal effect. MSE = mean-squared error. Estimated effect of referral to intensive lifestyle counseling (CACE) on change in HDL and total-cholesterol-to-HDL in A, local linear regressions and B, local quadratic regression, along varying bandwidths (i.e., 75%, 100%, 125%, 150, or 200%) of the derived mean-squared error (MSE) optimal bandwidth with r heteroskedasticity-robust 95% CI and triangular kernel weights. Significant effect estimates are pictured as solid, dark blue points; effects that are not significant are pictured as hollow points.

LDL



Triglycerides

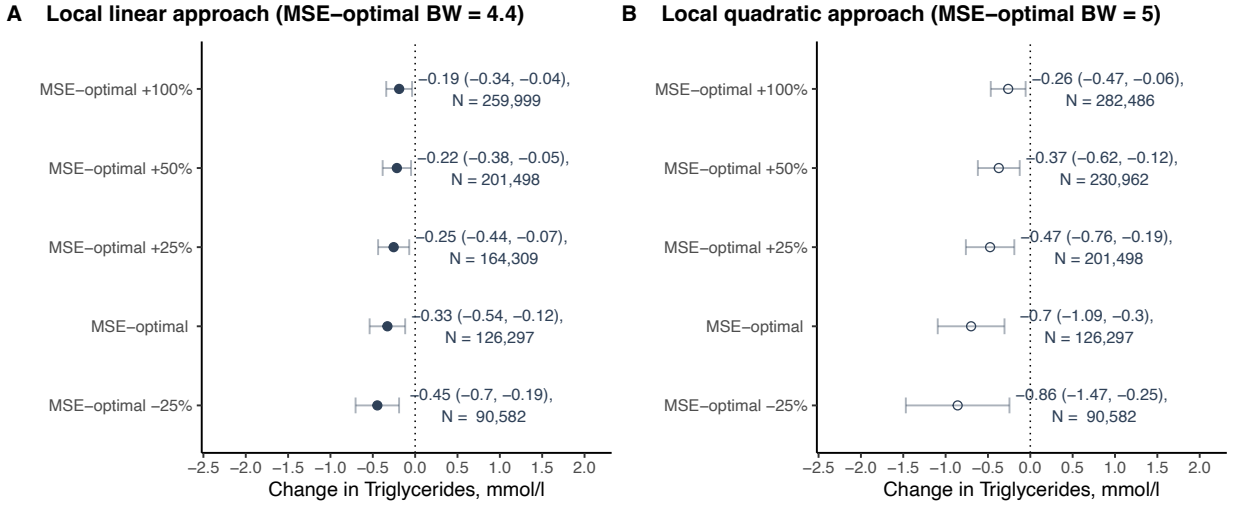


Fig. S10. Estimated effect of referral to intensive lifestyle counseling (CACE) on change in LDL and triglycerides with varying bandwidths (primary cohort). BW = Bandwidth. CACE = Complier average causal effect. MSE = mean-squared error. Estimated effect of referral to intensive lifestyle counseling (CACE) on change in systolic blood pressure in A, local linear regressions and B, local quadratic regression, along varying bandwidths (i.e., 75%, 100%, 125%, 150, or 200%) of the derived mean-squared error (MSE) optimal bandwidth with heteroskedasticity-robust 95% CI and triangular kernel weights. Significant effect estimates are pictured as solid, dark blue points; effects that are not significant are pictured as hollow points.

Table S8. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in HbA1c (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	-0.15 (-0.24, -0.05)	0.002	-1.34 (-2.2, -0.48)	0.002	4.7	189,817
Women	-0.05 (-0.13, 0.04)	0.264	-0.42 (-1.16, 0.32)	0.265	3.5	159,116
Age group						
18 to 39 years	-0.27 (-0.59, 0.05)	0.103	-2.36 (-5.24, 0.51)	0.107	4.4	32,364
40 to 59 years	-0.06 (-0.18, 0.06)	0.311	-0.51 (-1.5, 0.48)	0.312	4.2	155,825
60 to 80 years	-0.08 (-0.15, -0.02)	0.013	-0.76 (-1.36, -0.16)	0.013	2.9	111,734
IMD						
1, least deprived	-0.1 (-0.22, 0.01)	0.086	-0.76 (-1.62, 0.11)	0.086	5.0	106,615
2	-0.2 (-0.33, -0.07)	0.002	-1.69 (-2.77, -0.62)	0.002	4.6	82,219
3	0 (-0.15, 0.14)	0.954	-0.04 (-1.38, 1.3)	0.954	4.1	78,868
4	-0.12 (-0.25, 0)	0.056	-1.22 (-2.49, 0.04)	0.058	5.1	104,611
5, most deprived	-0.06 (-0.2, 0.08)	0.375	-0.57 (-1.84, 0.7)	0.375	5.1	102,852
Practice location						
Urban	-0.11 (-0.19, -0.04)	0.002	-1.03 (-1.69, -0.37)	0.002	3.9	257,392
Rural	-0.02 (-0.17, 0.12)	0.755	-0.21 (-1.54, 1.12)	0.755	5.2	69,896
Ethnicity						
Asian	-0.04 (-0.21, 0.13)	0.683	-0.3 (-1.76, 1.15)	0.683	7.5	49,637
Black	0.13 (-0.2, 0.47)	0.429	0.93 (-1.38, 3.24)	0.429	5.5	19,589
Mixed or other	-0.43 (-0.75, -0.1)	0.011	-3.67 (-6.61, -0.74)	0.014	5.6	14,097
White	-0.11 (-0.19, -0.03)	0.010	-1.01 (-1.78, -0.24)	0.010	3.8	204,392
Prior receipt of flu vaccination						
No	-0.09 (-0.17, -0.01)	0.020	-0.83 (-1.53, -0.13)	0.021	3.8	241,717
Yes	-0.13 (-0.26, -0.01)	0.034	-1.07 (-2.06, -0.07)	0.035	4.8	77,156
Prior counselling on weight loss						
No	-0.1 (-0.17, -0.03)	0.005	-0.9 (-1.52, -0.27)	0.005	3.7	284,289
Yes	-0.02 (-0.29, 0.24)	0.875	-0.16 (-2.13, 1.81)	0.875	6.8	30,757
Prior receipt of general lifestyle advice						
No	-0.13 (-0.21, -0.04)	0.005	-1.13 (-1.94, -0.33)	0.006	4.0	237,695
Yes	-0.05 (-0.14, 0.04)	0.279	-0.45 (-1.26, 0.37)	0.280	4.1	171,640
Prior attendance of bowel cancer screening						
No	-0.09 (-0.19, 0.01)	0.072	-0.81 (-1.7, 0.07)	0.072	4.1	217,284
Yes	-0.08 (-0.16, 0.01)	0.087	-0.68 (-1.46, 0.1)	0.088	2.8	96,501
Prior consultation for skin abnormalities						
No	-0.09 (-0.17, -0.01)	0.019	-0.82 (-1.51, -0.13)	0.020	3.9	246,820
Yes	-0.13 (-0.25, 0)	0.049	-1.05 (-2.11, 0)	0.050	4.3	72,052
Adherence to prior statin prescriptions [b]						
No	-0.08 (-0.32, 0.17)	0.544	-0.7 (-2.97, 1.57)	0.544	6.0	10,276
Yes	-0.04 (-0.14, 0.05)	0.367	-0.4 (-1.29, 0.48)	0.368	4.3	131,175

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.
[a] Sample size within MSE-optimal bandwidth.
[b] Sample restricted to those with prior lipid-lowering medication prescription.
Local linear regression with robust standard errors and triangular kernel weights.

Table S9. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in BMI (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	-0.19 (-0.25, -0.12)	< 0.001	-1.73 (-2.36, -1.09)	< 0.001	4.8	117,074
Women	-0.11 (-0.18, -0.03)	0.006	-0.92 (-1.57, -0.26)	0.006	4.2	136,140
Age group						
18 to 39 years	-0.2 (-0.39, -0.01)	0.042	-1.57 (-3.1, -0.03)	0.045	6.4	45,623
40 to 59 years	-0.17 (-0.26, -0.09)	< 0.001	-1.4 (-2.11, -0.69)	< 0.001	4.3	95,414
60 to 80 years	-0.15 (-0.2, -0.09)	< 0.001	-1.37 (-1.91, -0.83)	< 0.001	5.8	169,247
IMD						
1, least deprived	-0.15 (-0.25, -0.05)	0.005	-1.18 (-1.99, -0.36)	0.005	5.3	59,730
2	-0.08 (-0.18, 0.02)	0.103	-0.66 (-1.47, 0.14)	0.104	5.5	63,194
3	-0.18 (-0.29, -0.07)	0.002	-1.65 (-2.68, -0.61)	0.002	5.1	62,297
4	-0.18 (-0.3, -0.06)	0.002	-1.81 (-3, -0.62)	0.003	4.3	52,832
5, most deprived	-0.19 (-0.32, -0.06)	0.004	-1.74 (-2.95, -0.54)	0.005	3.8	41,301
Practice location						
Urban	-0.15 (-0.21, -0.09)	< 0.001	-1.37 (-1.93, -0.81)	< 0.001	4.0	221,386
Rural	-0.14 (-0.27, -0.01)	0.032	-1.29 (-2.47, -0.1)	0.033	5.8	39,150
Ethnicity						
Asian	0.02 (-0.15, 0.18)	0.849	0.13 (-1.19, 1.44)	0.849	5.2	19,863
Black	-0.1 (-0.32, 0.12)	0.370	-0.66 (-2.11, 0.79)	0.371	5.8	12,221
Mixed or other	-0.09 (-0.38, 0.19)	0.519	-0.74 (-2.98, 1.51)	0.522	5.7	8,283
White	-0.17 (-0.25, -0.1)	< 0.001	-1.64 (-2.32, -0.96)	< 0.001	3.8	129,241
Prior receipt of flu vaccination						
No	-0.16 (-0.22, -0.09)	< 0.001	-1.45 (-2.07, -0.84)	< 0.001	3.8	145,93
Yes	-0.13 (-0.23, -0.04)	0.008	-1.06 (-1.85, -0.28)	0.008	5.5	65,887
Prior counselling on weight loss						
No	-0.15 (-0.2, -0.09)	< 0.001	-1.32 (-1.86, -0.79)	< 0.001	3.8	172,378
Yes	-0.18 (-0.41, 0.04)	0.108	-1.52 (-3.39, 0.35)	0.111	5.9	20,501
Prior receipt of general lifestyle advice						
No	-0.13 (-0.2, -0.06)	0.001	-1.15 (-1.8, -0.49)	0.001	4.3	128,239
Yes	-0.16 (-0.24, -0.09)	< 0.001	-1.45 (-2.09, -0.82)	< 0.001	4.6	124,975
Prior attendance of bowel cancer screening						
No	-0.16 (-0.23, -0.09)	< 0.001	-1.39 (-2.03, -0.74)	< 0.001	4.2	135,539
Yes	-0.16 (-0.22, -0.1)	< 0.001	-1.39 (-1.95, -0.84)	< 0.001	5.5	147,651
Prior consultation for skin abnormalities						
No	-0.16 (-0.23, -0.1)	< 0.001	-1.49 (-2.08, -0.9)	< 0.001	3.7	152,789
Yes	-0.1 (-0.2, 0)	0.060	-0.79 (-1.61, 0.04)	0.061	6.3	69,136
Adherence to prior statin prescriptions [b]						
No	-0.1 (-0.3, 0.1)	0.314	-0.97 (-2.86, 0.92)	0.315	6.0	6,352
Yes	-0.12 (-0.19, -0.04)	0.004	-1.14 (-1.92, -0.36)	0.004	5.3	102,397

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.

[a] Sample size within MSE-optimal bandwidth.

[b] Sample restricted to those with prior lipid-lowering medication prescription. Local linear regression with robust standard errors and triangular kernel weights.

Table S10. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in weight (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	-0.56 (-0.78, -0.35)	< 0.001	-5.28 (-7.33, -3.24)	< 0.001	3.9	96,798
Women	-0.14 (-0.32, 0.05)	0.140	-1.21 (-2.82, 0.4)	0.140	4.2	155,042
Age group						
18 to 39 years	-0.33 (-0.86, 0.2)	0.220	-2.79 (-7.27, 1.69)	0.223	5.6	39,038
40 to 59 years	-0.35 (-0.56, -0.13)	0.002	-2.79 (-4.54, -1.03)	0.002	4.6	107,868
60 to 80 years	-0.33 (-0.47, -0.2)	< 0.001	-3.12 (-4.38, -1.86)	< 0.001	6.5	224,299
IMD						
1, least deprived	-0.44 (-0.7, -0.17)	0.001	-3.49 (-5.62, -1.36)	0.001	5.3	67,700
2	-0.53 (-0.81, -0.24)	< 0.001	-4.28 (-6.61, -1.96)	< 0.001	4.5	55,076
3	-0.29 (-0.55, -0.02)	0.032	-2.66 (-5.1, -0.22)	0.033	5.4	71,159
4	-0.24 (-0.54, 0.06)	0.122	-2.49 (-5.65, 0.68)	0.124	4.2	59,457
5, most deprived	-0.27 (-0.6, 0.06)	0.107	-2.54 (-5.63, 0.56)	0.108	3.7	46,530
Practice location						
Urban	-0.35 (-0.52, -0.19)	< 0.001	-3.24 (-4.71, -1.76)	< 0.001	3.5	181,558
Rural	-0.2 (-0.52, 0.12)	0.216	-1.89 (-4.9, 1.11)	0.217	5.9	45,394
Ethnicity						
Asian	0.08 (-0.32, 0.49)	0.683	0.69 (-2.6, 3.98)	0.683	5.2	23,562
Black	-0.39 (-1, 0.21)	0.205	-2.52 (-6.43, 1.4)	0.207	4.8	11,286
Mixed or other	0.33 (-0.4, 1.06)	0.380	2.74 (-3.39, 8.87)	0.382	5.0	7,492
White	-0.38 (-0.56, -0.2)	< 0.001	-3.61 (-5.36, -1.86)	< 0.001	3.5	146,065
Prior receipt of flu vaccination						
No	-0.32 (-0.49, -0.16)	< 0.001	-3.02 (-4.58, -1.46)	< 0.001	3.7	165,729
Yes	-0.43 (-0.69, -0.16)	0.002	-3.47 (-5.66, -1.28)	0.002	5.0	73,367
Prior counselling on weight loss						
No	-0.33 (-0.49, -0.18)	< 0.001	-3.08 (-4.52, -1.63)	< 0.001	3.3	195,218
Yes	-0.3 (-0.86, 0.26)	0.294	-2.39 (-6.87, 2.09)	0.296	6.3	27,673
Prior receipt of general lifestyle advice						
No	-0.33 (-0.53, -0.13)	0.001	-3.05 (-4.92, -1.18)	0.001	3.7	108,544
Yes	-0.32 (-0.5, -0.13)	0.001	-2.76 (-4.39, -1.13)	0.001	4.8	136,810
Prior attendance of bowel cancer screening						
No	-0.35 (-0.56, -0.13)	0.002	-3.14 (-5.08, -1.19)	0.002	3.7	110,292
Yes	-0.35 (-0.5, -0.2)	< 0.001	-3.06 (-4.38, -1.74)	< 0.001	6.1	195,553
Prior consultation for skin abnormalities						
No	-0.32 (-0.49, -0.15)	< 0.001	-2.98 (-4.55, -1.42)	< 0.001	3.3	172,533
Yes	-0.37 (-0.64, -0.09)	0.009	-2.98 (-5.22, -0.73)	0.009	5.5	64,235
Adherence to prior statin prescriptions [b]						
No	-0.52 (-0.99, -0.05)	0.031	-5.01 (-9.67, -0.36)	0.035	7.3	7,907
Yes	-0.33 (-0.52, -0.14)	0.001	-3.14 (-4.98, -1.31)	0.001	5.8	113,988

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.
[a] Sample size within MSE-optimal bandwidth.
[b] Sample restricted to those with prior lipid-lowering medication prescription.
Local linear regression with robust standard errors and triangular kernel weights.

Table S11. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in diastolic blood pressure (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	-0.38 (-0.76, 0)	0.052	-3.29 (-6.61, 0.04)	0.053	5.9	67,146
Women	0.04 (-0.28, 0.37)	0.796	0.34 (-2.24, 2.93)	0.796	7.7	116,502
Age group						
18 to 39 years	-0.21 (-0.86, 0.43)	0.517	-1.79 (-7.2, 3.62)	0.517	9.9	59,341
40 to 59 years	-0.32 (-0.66, 0.03)	0.077	-2.51 (-5.3, 0.27)	0.077	7.2	101,927
60 to 80 years	-0.07 (-0.47, 0.32)	0.715	-0.63 (-3.99, 2.74)	0.715	6.4	63,615
IMD						
1, least deprived	-0.62 (-1.23, -0.02)	0.045	-4.79 (-9.5, -0.09)	0.046	6.4	33,403
2	0.17 (-0.38, 0.72)	0.542	1.57 (-3.48, 6.63)	0.542	8.2	46,431
3	-0.23 (-0.82, 0.37)	0.449	-2.06 (-7.41, 3.29)	0.449	6.3	34,827
4	-0.42 (-0.9, 0.06)	0.090	-4.02 (-8.68, 0.63)	0.090	8.3	51,008
5, most deprived	0.16 (-0.34, 0.67)	0.530	1.13 (-2.41, 4.67)	0.531	6.7	38,833
Practice location						
Urban	-0.28 (-0.54, -0.01)	0.039	-2.29 (-4.46, -0.12)	0.039	6.9	156,226
Rural	0.65 (-0.09, 1.38)	0.083	5.93 (-0.86, 12.72)	0.087	6.4	23,049
Ethnicity						
Asian	-0.45 (-1.31, 0.41)	0.306	-3.18 (-9.28, 2.93)	0.307	5.9	11,425
Black	-0.06 (-1.16, 1.03)	0.912	-0.37 (-6.92, 6.18)	0.911	6.1	7,985
Mixed or other	0.13 (-1.07, 1.32)	0.837	0.98 (-8.38, 10.34)	0.837	7.5	7,168
White	-0.02 (-0.36, 0.31)	0.895	-0.2 (-3.18, 2.78)	0.895	6.3	111,364
Prior receipt of flu vaccination						
No	-0.18 (-0.45, 0.08)	0.180	-1.54 (-3.8, 0.71)	0.180	6.8	157,933
Yes	-0.06 (-0.73, 0.62)	0.870	-0.4 (-5.13, 4.34)	0.869	6.6	22,676
Prior counselling on weight loss						
No	-0.16 (-0.42, 0.1)	0.219	-1.32 (-3.42, 0.78)	0.219	6.6	173,388
Yes	-0.11 (-1.45, 1.23)	0.871	-0.95 (-12.38, 10.48)	0.871	5.2	5,771
Prior receipt of general lifestyle advice						
No	-0.24 (-0.54, 0.05)	0.110	-2.1 (-4.68, 0.48)	0.110	7.2	143,67
Yes	-0.01 (-0.43, 0.4)	0.953	-0.09 (-3.26, 3.07)	0.953	7.1	68,108
Prior attendance of bowel cancer screening						
No	-0.27 (-0.55, 0.01)	0.057	-2.28 (-4.62, 0.07)	0.057	7.8	148,535
Yes	-0.03 (-0.47, 0.4)	0.886	-0.26 (-3.74, 3.23)	0.885	5.7	47,110
Prior consultation for skin abnormalities						
No	-0.21 (-0.48, 0.06)	0.127	-1.78 (-4.07, 0.51)	0.127	6.6	153,093
Yes	0.08 (-0.53, 0.7)	0.788	0.61 (-3.84, 5.07)	0.788	7.5	32,443
Adherence to prior statin prescriptions [b]						
No	-0.33 (-1.74, 1.08)	0.650	-2.67 (-14.29, 8.95)	0.653	5.3	1,432
Yes	0.09 (-0.61, 0.79)	0.805	0.73 (-5.07, 6.53)	0.806	5.9	16,494

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.
[a] Sample size within MSE-optimal bandwidth.
[b] Sample restricted to those with prior lipid-lowering medication prescription.
Local linear regression with robust standard errors and triangular kernel weights.

Table S12. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in systolic blood pressure (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	-0.52 (-1.06, 0.02)	0.059	-4.51 (-9.19, 0.17)	0.059	5.9	82,546
Women	0.06 (-0.46, 0.58)	0.830	0.45 (-3.63, 4.52)	0.830	7.7	116,385
Age group						
18 to 39 years	-0.3 (-1.19, 0.58)	0.504	-2.64 (-10.39, 5.11)	0.504	9.9	38,633
40 to 59 years	-0.52 (-1.06, 0.02)	0.061	-4.12 (-8.45, 0.2)	0.062	7.2	86,973
60 to 80 years	-0.04 (-0.7, 0.62)	0.911	-0.32 (-5.92, 5.28)	0.911	6.4	63,485
IMD						
1, least deprived	-0.51 (-1.43, 0.42)	0.282	-3.94 (-11.14, 3.25)	0.283	6.4	39,404
2	-0.36 (-1.17, 0.44)	0.379	-3.3 (-10.68, 4.07)	0.380	8.2	51,658
3	-0.05 (-0.91, 0.8)	0.907	-0.46 (-8.14, 7.22)	0.907	6.3	40,927
4	-0.33 (-1.11, 0.45)	0.403	-3.16 (-10.58, 4.25)	0.403	8.3	44,367
5, most deprived	-0.04 (-0.75, 0.66)	0.903	-0.31 (-5.27, 4.65)	0.903	6.7	45,065
Practice location						
Urban	-0.36 (-0.76, 0.03)	0.068	-2.99 (-6.2, 0.23)	0.068	6.9	183,180
Rural	0.91 (-0.32, 2.13)	0.146	8.48 (-3.04, 20.01)	0.149	6.4	18,223
Ethnicity						
Asian	-0.38 (-1.5, 0.75)	0.512	-2.69 (-10.7, 5.33)	0.512	5.9	15,940
Black	-0.41 (-1.87, 1.06)	0.586	-2.43 (-11.17, 6.32)	0.587	6.1	7,975
Mixed or other	-0.66 (-2.44, 1.12)	0.469	-5.17 (-19.3, 8.95)	0.473	7.5	6,100
White	-0.06 (-0.57, 0.46)	0.823	-0.52 (-5.1, 4.05)	0.823	6.3	111,253
Prior receipt of flu vaccination						
No	-0.31 (-0.69, 0.07)	0.111	-2.63 (-5.87, 0.61)	0.112	7.9	185,517
Yes	0.18 (-0.9, 1.25)	0.745	1.25 (-6.31, 8.82)	0.745	6.8	22,660
Prior counselling on weight loss						
No	-0.23 (-0.6, 0.14)	0.216	-1.91 (-4.95, 1.12)	0.216	7.7	203,154
Yes	0.28 (-1.72, 2.28)	0.783	2.37 (-14.56, 19.3)	0.784	5.0	5,771
Prior receipt of general lifestyle advice						
No	-0.44 (-0.92, 0.04)	0.073	-3.78 (-7.92, 0.36)	0.074	6.3	121,654
Yes	0.2 (-0.49, 0.88)	0.578	1.5 (-3.78, 6.78)	0.578	5.8	47,412
Prior attendance of bowel cancer screening						
No	-0.42 (-0.84, 0)	0.048	-3.57 (-7.11, -0.03)	0.048	6.8	124,151
Yes	-0.06 (-0.76, 0.64)	0.866	-0.48 (-6.1, 5.14)	0.866	6.2	56,250
Prior consultation for skin abnormalities						
No	-0.35 (-0.76, 0.05)	0.086	-2.98 (-6.38, 0.42)	0.086	7.0	179,126
Yes	0.45 (-0.56, 1.45)	0.384	3.25 (-4.07, 10.58)	0.384	6.9	27,492
Adherence to prior statin prescriptions [b]						
No	-2.53 (-5.02, -0.03)	0.047	-19.22 (-39.87, 1.43)	0.068	5.6	1,432
Yes	0.07 (-1.04, 1.18)	0.902	0.57 (-8.6, 9.75)	0.902	6.7	19,333

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.
[a] Sample size within MSE-optimal bandwidth.
[b] Sample restricted to those with prior lipid-lowering medication prescription. Local linear regression with robust standard errors and triangular kernel weights.

Table S13. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in HDL (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	0 (0, 0.01)	0.320	0.03 (-0.03, 0.09)	0.320	6.1	129,639
Women	0.01 (0, 0.01)	0.054	0.05 (0, 0.11)	0.054	7.4	186,492
Age group						
18 to 39 years	0.01 (-0.01, 0.02)	0.335	0.06 (-0.06, 0.18)	0.336	6.4	24,611
40 to 59 years	0 (-0.01, 0.01)	0.942	0 (-0.07, 0.06)	0.942	5.1	119,146
60 to 80 years	0.01 (0, 0.02)	0.004	0.1 (0.03, 0.17)	0.004	6.6	118,319
IMD						
1, least deprived	0.01 (0, 0.02)	0.130	0.06 (-0.02, 0.15)	0.131	6.1	57,458
2	0.01 (0, 0.02)	0.026	0.11 (0.01, 0.21)	0.027	6.5	58,359
3	0 (-0.01, 0.01)	0.762	0.02 (-0.09, 0.13)	0.762	5.6	45,716
4	0 (-0.01, 0.01)	0.522	0.03 (-0.07, 0.14)	0.522	6.0	48,516
5, most deprived	0 (-0.01, 0.01)	0.979	0 (-0.08, 0.08)	0.979	6.8	56,978
Practice location						
Urban	0 (0, 0.01)	0.107	0.04 (-0.01, 0.08)	0.107	6.2	253,205
Rural	0.01 (0, 0.03)	0.078	0.13 (-0.01, 0.27)	0.079	6.9	35,536
Ethnicity						
Asian	0 (-0.01, 0.02)	0.572	0.03 (-0.08, 0.14)	0.572	6.4	23,311
Black	0 (-0.02, 0.02)	0.735	-0.03 (-0.17, 0.12)	0.735	5.7	11,389
Mixed or other	-0.02 (-0.05, 0)	0.099	-0.22 (-0.5, 0.05)	0.111	5.6	7,573
White	0.01 (0, 0.01)	0.015	0.07 (0.01, 0.12)	0.015	7.7	211,241
Prior receipt of flu vaccination						
No	0.01 (0, 0.01)	0.028	0.05 (0.01, 0.1)	0.028	6.0	252,953
Yes	0 (-0.01, 0.01)	0.955	0 (-0.1, 0.1)	0.955	6.4	37,979
Prior counselling on weight loss						
No	0.01 (0, 0.01)	0.021	0.05 (0.01, 0.1)	0.021	6.0	277,265
Yes	-0.01 (-0.03, 0.01)	0.345	-0.1 (-0.3, 0.1)	0.346	5.8	11,182
Prior receipt of general lifestyle advice						
No	0.01 (0, 0.01)	0.039	0.07 (0, 0.13)	0.039	4.9	107,366
Yes	0 (0, 0.01)	0.424	0.03 (-0.04, 0.1)	0.424	5.3	96,155
Prior attendance of bowel cancer screening						
No	0 (0, 0.01)	0.601	0.01 (-0.04, 0.07)	0.601	5.7	148,196
Yes	0.01 (0, 0.02)	0.011	0.09 (0.02, 0.16)	0.011	6.8	106,033
Prior consultation for skin abnormalities						
No	0 (0, 0.01)	0.110	0.04 (-0.01, 0.08)	0.110	6.9	242,809
Yes	0.01 (0, 0.02)	0.122	0.08 (-0.02, 0.18)	0.123	5.7	38,574
Adherence to prior statin prescriptions [b]						
No	-	-	-	-	-	-
Yes	-	-	-	-	-	-

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.
[a] Sample size within MSE-optimal bandwidth.
[b] Sample restricted to those with prior lipid-lowering medication prescription. Local linear regression with robust standard errors and triangular kernel weights.

Table S14. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in LDL (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	0 (-0.03, 0.04)	0.828	0.03 (-0.26, 0.32)	0.828	6.3	58,031
Women	0.02 (-0.01, 0.05)	0.132	0.18 (-0.06, 0.42)	0.133	5.9	60,154
Age group						
18 to 39 years	-0.02 (-0.09, 0.05)	0.510	-0.18 (-0.73, 0.36)	0.513	5.5	9,058
40 to 59 years	0.03 (0, 0.06)	0.044	0.23 (0.01, 0.46)	0.045	7.2	78,833
60 to 80 years	-0.02 (-0.05, 0.02)	0.415	-0.13 (-0.45, 0.19)	0.415	6.0	50,743
IMD						
1, least deprived	0.04 (-0.01, 0.09)	0.133	0.28 (-0.09, 0.65)	0.135	6.9	22,628
2	0.05 (-0.01, 0.12)	0.080	0.42 (-0.06, 0.9)	0.084	4.6	15,646
3	-0.01 (-0.06, 0.04)	0.713	-0.1 (-0.64, 0.44)	0.713	5.9	19,612
4	0.03 (-0.01, 0.07)	0.198	0.25 (-0.13, 0.63)	0.201	8.0	38,135
5, most deprived	-0.03 (-0.07, 0.02)	0.281	-0.2 (-0.58, 0.17)	0.283	5.5	24,010
Practice location						
Urban	0.01 (-0.01, 0.04)	0.359	0.09 (-0.11, 0.29)	0.360	5.6	95,994
Rural	0.02 (-0.06, 0.1)	0.609	0.18 (-0.52, 0.88)	0.610	6.1	13,668
Ethnicity						
Asian	0.01 (-0.05, 0.07)	0.658	0.12 (-0.41, 0.64)	0.657	7.5	11,868
Black	-0.01 (-0.08, 0.05)	0.650	-0.1 (-0.52, 0.33)	0.651	5.7	7,161
Mixed or other	-0.01 (-0.11, 0.09)	0.819	-0.1 (-0.98, 0.78)	0.819	7.7	5,847
White	0.01 (-0.02, 0.04)	0.408	0.1 (-0.14, 0.35)	0.408	7.1	89,695
Prior receipt of flu vaccination						
No	0.01 (-0.02, 0.03)	0.629	0.05 (-0.16, 0.26)	0.629	5.6	93,112
Yes	0.05 (-0.01, 0.12)	0.095	0.37 (-0.07, 0.8)	0.099	5.6	14,678
Prior counselling on weight loss						
No	0.01 (-0.01, 0.04)	0.270	0.11 (-0.08, 0.3)	0.270	5.7	102,854
Yes	0.01 (-0.08, 0.1)	0.815	0.12 (-0.9, 1.15)	0.816	7.6	6,819
Prior receipt of general lifestyle advice						
No	0 (-0.03, 0.03)	0.869	-0.02 (-0.28, 0.24)	0.869	5.5	64,467
Yes	0.04 (0, 0.07)	0.051	0.29 (0, 0.58)	0.052	5.3	43,323
Prior attendance of bowel cancer screening						
No	0.02 (-0.01, 0.05)	0.137	0.17 (-0.06, 0.4)	0.138	5.9	69,271
Yes	-0.01 (-0.05, 0.03)	0.531	-0.1 (-0.43, 0.22)	0.531	5.8	38,519
Prior consultation for skin abnormalities						
No	0.01 (-0.01, 0.04)	0.392	0.09 (-0.12, 0.3)	0.392	5.7	90,385
Yes	0.03 (-0.02, 0.09)	0.238	0.24 (-0.16, 0.65)	0.241	6.8	21,567
Adherence to prior statin prescriptions [b]						
No	-	-	-	-	-	-
Yes	-	-	-	-	-	-

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.
[a] Sample size within MSE-optimal bandwidth.
[b] Sample restricted to those with prior lipid-lowering medication prescription. Local linear regression with robust standard errors and triangular kernel weights.

Table S15. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in Total-cholesterol-to-HDL ratio (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	-0.01 (-0.04, 0.01)	0.317	-0.14 (-0.41, 0.13)	0.317	6.8	97,774
Women	0.01 (-0.01, 0.04)	0.284	0.11 (-0.09, 0.31)	0.284	5.4	98,895
Age group						
18 to 39 years	-0.03 (-0.1, 0.04)	0.387	-0.3 (-0.98, 0.38)	0.387	7.1	22,840
40 to 59 years	0.01 (-0.02, 0.04)	0.606	0.06 (-0.18, 0.31)	0.606	5.8	89,525
60 to 80 years	-0.01 (-0.04, 0.02)	0.455	-0.09 (-0.33, 0.15)	0.455	5.9	75,149
IMD						
1, least deprived	-0.02 (-0.06, 0.02)	0.301	-0.15 (-0.42, 0.13)	0.301	7.1	49,456
2	0 (-0.04, 0.03)	0.894	-0.02 (-0.38, 0.33)	0.894	7.9	51,967
3	-0.01 (-0.05, 0.03)	0.601	-0.13 (-0.6, 0.35)	0.601	5.4	35,737
4	0.03 (-0.02, 0.07)	0.238	0.26 (-0.17, 0.7)	0.238	5.3	37,303
5, most deprived	-0.02 (-0.07, 0.03)	0.416	-0.18 (-0.61, 0.25)	0.416	4.7	26,200
Practice location						
Urban	0 (-0.02, 0.02)	0.757	0.03 (-0.16, 0.22)	0.757	5.4	156,259
Rural	-0.03 (-0.09, 0.02)	0.242	-0.32 (-0.86, 0.22)	0.242	5.4	21,269
Ethnicity						
Asian	0.01 (-0.06, 0.08)	0.832	0.08 (-0.65, 0.81)	0.832	4.7	11,981
Black	0.07 (0, 0.13)	0.061	0.48 (-0.02, 0.98)	0.061	4.6	6,989
Mixed or other	0.06 (-0.04, 0.16)	0.231	0.67 (-0.43, 1.76)	0.231	6.3	7,149
White	0 (-0.03, 0.02)	0.729	-0.04 (-0.26, 0.18)	0.729	6.4	136,622
Prior receipt of flu vaccination						
No	0 (-0.02, 0.02)	0.944	-0.01 (-0.2, 0.19)	0.944	5.3	155,088
Yes	0 (-0.05, 0.05)	0.995	0 (-0.38, 0.38)	0.997	6.8	28,597
Prior counselling on weight loss						
No	0 (-0.02, 0.02)	0.877	-0.01 (-0.2, 0.17)	0.877	5.4	171,209
Yes	0.06 (-0.03, 0.15)	0.203	0.5 (-0.27, 1.28)	0.219	5.9	7,643
Prior receipt of general lifestyle advice						
No	-0.02 (-0.04, 0.01)	0.233	-0.15 (-0.39, 0.09)	0.233	5.7	107,579
Yes	0.02 (0, 0.05)	0.107	0.19 (-0.04, 0.42)	0.108	6.5	87,012
Prior attendance of bowel cancer screening						
No	0 (-0.02, 0.03)	0.810	0.03 (-0.2, 0.26)	0.810	5.8	112,235
Yes	-0.01 (-0.04, 0.02)	0.405	-0.1 (-0.33, 0.14)	0.407	6.5	79,883
Prior consultation for skin abnormalities						
No	0 (-0.02, 0.02)	0.873	-0.02 (-0.21, 0.18)	0.873	5.4	149,746
Yes	0.01 (-0.03, 0.05)	0.710	0.06 (-0.27, 0.4)	0.711	7.1	42,170
Adherence to prior statin prescriptions [b]						
No	-	-	-	-	-	-
Yes	-	-	-	-	-	-

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.
[a] Sample size within MSE-optimal bandwidth.
[b] Sample restricted to those with prior lipid-lowering medication prescription. Local linear regression with robust standard errors and triangular kernel weights.

Table S16. Stratified effects of eligibility threshold (ITT) and referral to intensive lifestyle intervention (CACE) on change in triglycerides (primary cohort)

Stratifiying variable	Effect (95% CI)				MSE-optimal BW	Sample size [a]
	Eligibility threshold	*P* value	Lifestyle intervention	*P* value		
Sex						
Men	-0.08 (-0.12, -0.03)	0.001	-0.71 (-1.13, -0.29)	0.001	3.9	41,006
Women	-0.02 (-0.04, 0)	0.108	-0.15 (-0.34, 0.03)	0.109	6.8	111,619
Age group						
18 to 39 years	-0.13 (-0.23, -0.02)	0.015	-1 (-1.83, -0.17)	0.018	4.8	10,124
40 to 59 years	-0.03 (-0.06, 0)	0.072	-0.24 (-0.51, 0.02)	0.072	5.9	84,124
60 to 80 years	-0.02 (-0.04, 0.01)	0.261	-0.15 (-0.4, 0.11)	0.261	5.4	66,229
IMD						
1, least deprived	-0.05 (-0.11, 0)	0.069	-0.41 (-0.86, 0.04)	0.071	4.1	22,859
2	-0.05 (-0.1, -0.01)	0.018	-0.49 (-0.91, -0.08)	0.020	6.3	40,263
3	-0.03 (-0.08, 0.02)	0.231	-0.31 (-0.83, 0.2)	0.233	5.7	30,142
4	-0.03 (-0.07, 0.02)	0.215	-0.25 (-0.65, 0.15)	0.216	6.2	42,331
5, most deprived	0 (-0.04, 0.04)	0.921	-0.02 (-0.35, 0.31)	0.921	6.9	42,889
Practice location						
Urban	-0.02 (-0.04, 0)	0.059	-0.2 (-0.4, 0.01)	0.059	5.2	146,470
Rural	-0.15 (-0.23, -0.07)	< 0.001	-1.38 (-2.15, -0.62)	< 0.001	4.0	12,495
Ethnicity						
Asian	-0.05 (-0.11, 0.02)	0.155	-0.38 (-0.92, 0.15)	0.156	6.8	16,635
Black	0.03 (-0.03, 0.08)	0.355	0.18 (-0.2, 0.55)	0.356	6.8	10,310
Mixed or other	0.04 (-0.07, 0.15)	0.513	0.36 (-0.72, 1.43)	0.514	6.2	6,985
White	-0.03 (-0.06, 0)	0.023	-0.32 (-0.6, -0.04)	0.024	4.9	75,272
Prior receipt of flu vaccination						
No	-0.04 (-0.06, -0.01)	0.003	-0.34 (-0.57, -0.12)	0.003	4.8	110,144
Yes	0 (-0.05, 0.05)	0.987	0 (-0.38, 0.38)	0.987	5.9	20,880
Prior counselling on weight loss						
No	-0.04 (-0.06, -0.01)	0.002	-0.33 (-0.55, -0.12)	0.002	4.5	120,072
Yes	0.03 (-0.05, 0.11)	0.488	0.29 (-0.54, 1.12)	0.489	6.6	9,803
Prior receipt of general lifestyle advice						
No	-0.03 (-0.06, 0)	0.033	-0.28 (-0.53, -0.02)	0.033	5.4	98,007
Yes	-0.03 (-0.06, 0)	0.068	-0.26 (-0.54, 0.02)	0.069	5.1	66,302
Prior attendance of bowel cancer screening						
No	-0.03 (-0.06, 0)	0.022	-0.3 (-0.56, -0.04)	0.023	4.9	79,973
Yes	-0.03 (-0.05, 0)	0.074	-0.23 (-0.48, 0.02)	0.075	5.9	59,355
Prior consultation for skin abnormalities						
No	-0.03 (-0.06, -0.01)	0.013	-0.28 (-0.51, -0.06)	0.013	4.8	106,001
Yes	-0.04 (-0.09, 0.01)	0.103	-0.36 (-0.79, 0.07)	0.105	5.4	26,762
Adherence to prior statin prescriptions [b]						
No	-	-	-	-	-	-
Yes	-	-	-	-	-	-

CACE = Complier average causal effect. ITT = Intention-to-treat effect. MSE = mean-squared error.
[a] Sample size within MSE-optimal bandwidth.
[b] Sample restricted to those with prior lipid-lowering medication prescription. Local linear regression with robust standard errors and triangular kernel weights.

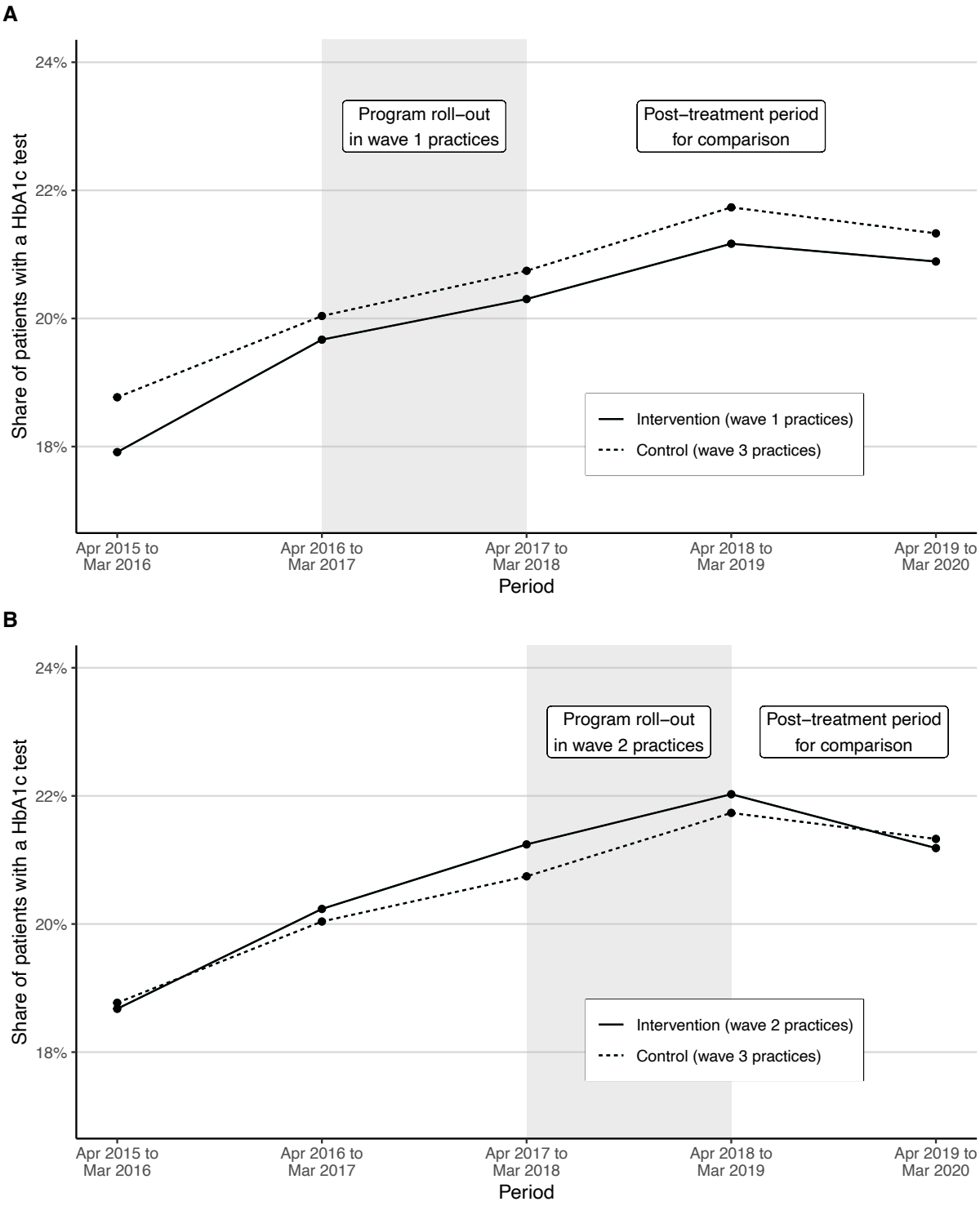


Fig. S11. Trends in HbA1c testing. Weighted average share of patients with a recorded HbA1c test compared to the total number of patients within each practice from April 2015 to March 2020, for (A) wave 1 and (B) wave 2 practices (intervention) compared to wave 3 practices (control). The y-axis does not start from 0, weighting by number of individuals for each practice, by year.

Table S17. Treatment effect estimates of NHS DPP referral on HbA1c (mmol/mol)

	N	Parameter	95% CI	*P* value
Sample as specified in target trial protocol[a]				
Unadjusted regression	102 681	-0.15	-0.28, -0.02	0.021
Adjusted regression				
Baseline variables[b]	101 937	-0.35	-0.46, -0.23	< 0.001
+ baseline BMI	71 779	-0.42	-0.55, -0.29	< 0.001
+ post-baseline variables[c]	71 779	-0.33	-0.46, -0.20	< 0.001
Propensity score matching				
Baseline HbA1c, age, and gender	29 738[e]	-0.49	-0.70, -0.28	< 0.001
+ previous GP consults	29 738[e]	-0.39	-0.55, -0.22	< 0.001
+ IMD and region	29 476[e]	-0.52	-0.69, -0.36	< 0.001
+ previous lifestyle advice	29 476[e]	-0.37	-0.53, -0.21	< 0.001
+ post-baseline time to endline	29 476[e]	-0.21	-0.37, -0.06	0.007
+ post-baseline diabetes medication	29 476[e]	-0.32	-0.47, -0.16	< 0.001
Extended sample[d]				
Individual fixed-effect regression	308 817	-0.623	-0.74, -0.51	< 0.001
Instrumental variable estimation				
First stage	308 817	0.038	0.014, 0.063	< 0.001
ITT		-0.143	-0.286, -0.001	0.0484
LATE		-3.767	-7.522, -0.012	0.0495

IMD = Index of Multiple Deprivation. The table reports treatment effect parameters from a set of regression-based analyses. All standard errors were clustered at practice-level. The rows 'Unadjusted regression' and 'Adjusted regression' reports treatment coefficients from linear regression with practice-level fixed effects. The rows 'Propensity score matching' reports average treatment effects (ATE) using propensity score matching and g-computation to estimate the average marginal effect of NHS DPP referral on HbA1c accounting for confounding by the included covariates. We used 1:1 nearest neighbor propensity score matching without replacement with a propensity score estimated using logistic regression of the treatment on the covariates. The outcome for 'Unadjusted regression', 'Adjusted regression', and 'Propensity score matching' was the final HbA1c measurement taken during follow-up. The row 'Individual fixed-effect regression' reports the one-year lagged treatment effect of program referral on HbA1c from a regression with individual-fixed effects to account for time-invariant differences between patients and year-fixed effects to control for the secular variation. For this, we used a panel dataset of patients with HbA1c records in the years 2016 to 2020. When multiple HbA1c measurements were recorded for a patient within a year, we averaged measurements. The column 'Instrumental variable estimation' reports the first stage, intention-to-treat (ITT) and local average treatment effects (LATE) from a 2SLS regression using the time-variant regional NHS DPP coverage as instrument for program referral and for the same panel of patients as for the individual fixed-effect regression.

[a] Adults (aged 18 to 80 years) who had a first HbA1c test ≥ 42 mmol/mol and < 47 mmol/mol with no prior use of diabetes medication and no history of diabetes.

[b] Baseline variables are baseline HbA1c measure, gender, age at baseline, average yearly number of GP consultations prior to baseline, IMD, receipt of flu vaccination in previous five years, receipt of pneumococcal vaccination in previous five years, prior receipt lifestyle advice, prior receipt of weight loss counselling, prior consultation for skin abnormalities, and prior participation in bowel cancer screening.

[c] Post-baseline variables are receipt of diabetes medication during follow-up and time (in months) to endline HbA1c.

[d] Inclusion criteria remain the same but the cohort was extended to patients with a first HbA1c test ≥ 42 mmol/mol and < 47 mmol/mol between January 2016 and March 2020.

[e] Matched observations with endline HbA1c.

Table S18. Medical codes for intensive lifestyle counseling

Medical code	Term	Intervention type	Program status
1979341000006116	Attended NHS diabetes prevention programme	Diabetes prevention	Completed
1979321000006111	Did not attend NHS diabetes prevention programme	Diabetes prevention	Did not attend or complete
1979331000006114	Did not complete NHS diabetes prevention programme	Diabetes prevention	Did not attend or complete
2587521000000117	NHS Diabetes Prevention Programme	Diabetes prevention	Started
1979231000006118	NHS diabetes prevention programme (NHS DPP) administration	Diabetes prevention	Unclear
2588201000000110	NHS Diabetes Prevention Programme completed	Diabetes prevention	Completed
1979241000006111	NHS diabetes prevention programme invitation	Diabetes prevention	Invited or offered only
1979251000006113	NHS diabetes prevention programme invitation first letter	Diabetes prevention	Invited or offered only
1979261000006110	NHS diabetes prevention programme invitation second letter	Diabetes prevention	Invited or offered only
1979301000006118	NHS diabetes prevention programme invitation SMS text message	Diabetes prevention	Invited or offered only
1979271000006115	NHS diabetes prevention programme invitation third letter	Diabetes prevention	Invited or offered only
2588121000000110	NHS Diabetes Prevention Programme not completed	Diabetes prevention	Did not attend or complete
2588241000000113	NHS Diabetes Prevention Programme started	Diabetes prevention	Started
1979281000006117	NHS diabetes prevention programme telephone invitation	Diabetes prevention	Invited or offered only
1979291000006119	NHS diabetes prevention programme verbal invitation	Diabetes prevention	Invited or offered only
1920591000006111	Pre-diabetes structured education programme declined	Diabetes prevention	Declined
1979311000006115	Referral to NHS diabetes prevention programme	Diabetes prevention	Started
2588351000000115	Referral to NHS Diabetes Prevention Programme	Diabetes prevention	Started
2588311000000119	Referral to NHS Diabetes Prevention Programme declined	Diabetes prevention	Declined
1920581000006113	Referral to pre-diabetes structured education programme	Diabetes prevention	Started
1990701000006118	Unsuitable for NHS Diabetes Prevention Programme	Diabetes prevention	Unsuitable
8124991000006119	DNA (did not attend) cardiovascular disease primary prevention programme	CVD prevention	Did not attend or complete
1705111000006117	DNA cardiovascular disease primary prevention programme	CVD prevention	Did not attend or complete
8098281000006117	Attended DAFNE (dose adjustment for normal eating) diabetes structured education programme	Diabetes management	Completed
8082941000006118	Attended DESMOND (diabetes education and self management for ongoing and newly diagnosed) structured programme	Diabetes management	Completed
546071000000117	Attended DAFNE diabetes structured education programme	Diabetes management	Completed
8082951000006116	Attended diabetes education and self management for ongoing and newly diagnosed structured programme	Diabetes management	Completed
6843971000006117	Attended diabetes structured education program	Diabetes management	Completed
2533102013	Attended diabetes structured education programme	Diabetes management	Completed
8098261000006110	Attended dose adjustment for normal eating diabetes structured education programme	Diabetes management	Completed
8098221000006116	Attended expert patient education versus routine treatment diabetes structured education programme	Diabetes management	Completed

Medical code	Term	Intervention type	Program status
8098241000006111	Attended XPERT (expert patient education versus routine treatment) diabetes structured education programme	Diabetes management	Completed
546001000000113	Attended XPERT diabetes structured education programme	Diabetes management	Completed
8098311000006115	DAFNE (dose adjustment for normal eating) diabetes structured education programme completed	Diabetes management	Completed
546151000000110	DAFNE diabetes structured education programme completed	Diabetes management	Completed
8098341000006116	DESMOND (diabetes education and self management for ongoing and newly diagnosed) structured programme completed	Diabetes management	Completed
546221000000114	DESMOND diabetes structured education programme completed	Diabetes management	Completed
8098321000006111	Diabetes education and self management for ongoing and newly diagnosed structured programme completed	Diabetes management	Completed
532331000000119	Diabetes structured education programme completed	Diabetes management	Completed
546471000000114	Diabetes structured education programme declined	Diabetes management	Declined
8099301000006111	Did not attend DAFNE (dose adjustment for normal eating) diabetes structured education programme	Diabetes management	Did not attend or complete
548121000000116	Did not attend DAFNE diabetes structured education programme	Diabetes management	Did not attend or complete
8099331000006115	Did not attend DESMOND (diabetes education and self management for ongoing and newly diagnosed) structured programme	Diabetes management	Did not attend or complete
1628621000006112	Did not attend DESMOND diabetes structured education program	Diabetes management	Did not attend or complete
8099311000006114	Did not attend diabetes education and self management for ongoing and newly diagnosed structured programme	Diabetes management	Did not attend or complete
8099341000006113	Did not attend expert patient education versus routine treatment diabetes structured education programme	Diabetes management	Did not attend or complete
547191000000117	Did not attend diabetes structured education programme	Diabetes management	Did not attend or complete
8099361000006112	Did not attend XPERT (expert patient education versus routine treatment) diabetes structured education programme	Diabetes management	Did not attend or complete
548131000000119	Did not attend XPERT diabetes structured education programme	Diabetes management	Did not attend or complete
8099151000006112	Did not complete DAFNE (dose adjustment for normal eating) diabetes structured education programme	Diabetes management	Did not attend or complete
547441000000118	Did not complete DAFNE diabetes structured education program	Diabetes management	Did not attend or complete
8099181000006116	Did not complete DESMOND (diabetes education and self management for ongoing and newly diagnosed) structured programme	Diabetes management	Did not attend or complete
1627291000006113	Did not complete DESMOND diabetes structured educat program	Diabetes management	Did not attend or complete
8099161000006114	Did not complete diabetes education and self management for ongoing and newly diagnosed structured programme	Diabetes management	Did not attend or complete
547331000000115	Did not complete diabetes structured education programme	Diabetes management	Did not attend or complete
8099131000006117	Did not complete dose adjustment for normal eating diabetes structured education programme	Diabetes management	Did not attend or complete

Medical code	Term	Intervention type	Program status
1628311000006111	Did not complete XPERT diabetes structured education program	Diabetes management	Did not attend or complete
7804621000006115	Not suitable for DESMOND (Diabetes Education and Self Management for Ongoing and Newly Diagnosed) program	Diabetes management	Unsuitable
7804601000006113	Not suitable for Diabetes Education and Self Management for Ongoing and Newly Diagnosed program	Diabetes management	Unsuitable
1966441000006113	Recommendation self-refer for diabetes structured education	Diabetes management	Started
8098881000006116	Referral to DAFNE (dose adjustment for normal eating) diabetes structured education programme	Diabetes management	Started
8297051000006113	Referral to DAFNE (dose adjustment for normal eating) diabetes structured education programme declined	Diabetes management	Started
546871000000112	Referral to DAFNE diabetes structured education programme	Diabetes management	Started
8098951000006115	Referral to DESMOND (diabetes education and self management for ongoing and newly diagnosed) diabetes structured programme	Diabetes management	Started
8243411000006117	Referral to DESMOND (diabetes education and self management for ongoing and newly diagnosed) structured programme declined	Diabetes management	Declined
8098931000006110	Referral to diabetes education and self management for ongoing and newly diagnosed diabetes structured programme	Diabetes management	Started
546961000000111	Referral to DESMOND diabetes structured education programme	Diabetes management	Started
6872991000006113	Referral to diabetes structured education program	Diabetes management	Started
2533110014	Referral to diabetes structured education programme	Diabetes management	Started
8098861000006114	Referral to dose adjustment for normal eating diabetes structured education programme	Diabetes management	Started
8098961000006118	Referral to expert patient education versus routine treatment diabetes structured education programme	Diabetes management	Started
8098981000006111	Referral to XPERT (expert patient education versus routine treatment) diabetes structured education programme	Diabetes management	Started
547061000000110	Referral to XPERT diabetes structured education programme	Diabetes management	Started
8413691000006118	X-PERT (expert patient education versus routine treatment) First Steps diabetes self-management programme completed	Diabetes management	Completed
1987971000006114	X-PERT First Steps diabetes self-management programme complt	Diabetes management	Completed
8098371000006112	XPERT (expert patient education versus routine treatment) diabetes structured education programme completed	Diabetes management	Completed
546291000000112	XPERT diabetes structured education programme completed	Diabetes management	Completed
449270018	Referral to public health physician	General	Started
1775551000006118	Referred to Public Health and Lifestyle Service	General	Started
301331000000117	Declined referral to physical exercise programme	Physical activity	Declined
454407012	Exercise on prescription	Physical activity	Started
6649531000006117	Group exercise program	Physical activity	Started
1773561018	Group exercise programme	Physical activity	Started
4989031000006114	Home exercise program	Physical activity	Started
343410018	Home exercise programme	Physical activity	Started
Medical code	Term	Intervention type	Program status

1138611000000114	Referral for exercise on prescription declined	Physical activity	Declined
1138611000000114	Referral for exercise on prescription declined	Physical activity	Declined
1709601000000118	Referral for physical activity service offered	Physical activity	Invited or offered only
1174481000000114	Referral to exercise on referral programme	Physical activity	Started
6516041000006114	Referral to physical activity program	Physical activity	Started
1476247014	Referral to physical activity programme	Physical activity	Started
6900171000006111	Referred for exercise program	Physical activity	Started
2549517012	Referred for exercise programme	Physical activity	Started
1986761000006119	Attending slimming club	Weight management	Started
264760012	Attends slimming clinic	Weight management	Started
1574721000006116	Community Dietician Referral	Weight management	Started
567001000000116	Counterweight programme	Weight management	Started
628891000000118	Counterweight weight management programme	Weight management	Started
4636861000006111	Has seen dietitian - obesity	Weight management	Started
247867015	Dietician	Weight management	Started
4518171000006113	Dietitian	Weight management	Started
449720017	Discharge from dietetics service	Weight management	Completed
264756014	Has seen dietician – obesity	Weight management	Started
743171000000110	Healthy lifestyle programme commenced	Weight management	Started
743351000000116	Healthy lifestyle programme completed	Weight management	Completed
743411000000112	Healthy lifestyle programme declined	Weight management	Declined
743291000000116	Healthy lifestyle programme not completed	Weight management	Did not attend or complete
1897591000006111	Healthy lifestyle programme offered	Weight management	Invited or offered only
2364711000000112	Healthy lifestyle programme offered	Weight management	Invited or offered only
2364711000000112	Healthy lifestyle programme offered	Weight management	Invited or offered only
12716081000006120	Healthy lifestyle programme status	Weight management	-
1705001000006119	Healthy lifestyle programme status	Weight management	-
404661000000111	In-house dietetics discharge appointment	Weight management	Completed
404641000000110	In-house dietetics first appointment	Weight management	Started
404681000000119	In-house dietetics follow-up appointment	Weight management	Started
2326311000000114	Intensive weight management programme commenced	Weight management	Started
2326491000000114	Intensive weight management programme declined	Weight management	Declined
2326451000000118	Intensive weight management programme ended	Weight management	Completed
2235141000000110	Nutritional therapy	Weight management	Started
4095601000006118	Patient referral to dietitian	Weight management	Started
1776861000006112	Reason for referral: Nutrition and Dietetics	Weight management	Started
1219016011	Refer to dietician	Weight management	Started
4095621000006111	Refer to dietitian	Weight management	Started
1787271000006110	Refer to slimming club	Weight management	Started
6759901000006112	Refer to weight management program	Weight management	Started
2154209017	Refer to weight management programme	Weight management	Started
2214201000000110	Referral to community dietician	Weight management	Started
5955121000006113	Referral to community dietitian	Weight management	Started
5955111000006117	Referral to community-based dietitian	Weight management	Started
216191012	Referral to dietician declined	Weight management	Started
1880041000006111	Referral to healthy lifestyle programme	Weight management	Started
2297611000000117	Referral to healthy lifestyle programme	Weight management	Started
2297611000000117	Referral to healthy lifestyle programme	Weight management	Started
1863491000006117	Referral to hospital dietitian	Weight management	Started
5955141000006118	Referral to hospital-based dietitian	Weight management	Started

Medical code	Term	Intervention type	Program status

1721501000000113	Referral to local authority weight management programme	Weight management	Started
2303211000000117	Referral to multidisciplinary obesity clinic	Weight management	Started
2173321000000116	Referral to residential weight management programme	Weight management	Started
2134641000000119	Referral to slimming club	Weight management	Started
8278851000006114	Referral to weight management GPwSI (general practitioner with special interest)	Weight management	Started
1709681000000111	Referral to weight management service offered	Weight management	Invited or offered only
1775491000006113	Referred to Nutrition and Dietetics Service	Weight management	Started
1844501000006115	Referral to weight management special interest GP	Weight management	Started
1124961000000110	Referral to weight management service declined	Weight management	Declined
285287012	Seen by dietician	Weight management	Started
4734201000006114	Seen by dietitian	Weight management	Started
285155016	Seen in dietician clinic	Weight management	Started
297861000000115	Weight management plan completed	Weight management	Completed
297841000000116	Weight management plan started	Weight management	Started
297811000000117	Weight management programme offered	Weight management	Invited or offered only
857681000006117	Weight reduction clinic	Weight management	Started

Table S19. Effect of eligibility threshold (ITT) and NHS DPP referral within 3 months (CACE) on Primary, Secondary, and Exploratory Outcomes (primary cohort)

	Unadjusted				Adjusted for medication[a]			
	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 [b]
Primary outcome								
HbA1c, mmol/mol	-0.10 (-0.16, -0.03)	0.006	-1.17 (-2.00, -0.34)	0.006	-1.29 (-2.11, -0.47)	0.002	3.5	298,822
Secondary outcomes								
BMI, kg/m^2	-0.15 (-0.21, -0.09)	< 0.001	-1.94 (-2.69, -1.19)	< 0.001	-	-	3.6	184,087
Weight, kg	-0.33 (-0.48, -0.18)	< 0.001	-4.22 (-6.17, -2.27)	< 0.001	-	-	3.3	208,111
Diastolic BP, mmHg [c]	-0.16 (-0.4, 0.07)	0.178	-1.81 (-4.44, 0.82)	0.178	-2.05 (-4.57, 0.47)	0.111	6.7	211,778
Systolic BP, mmHg [c]	-0.24 (-0.6, 0.11)	0.175	-2.67 (-6.55, 1.2)	0.176	-3.15 (-6.82, 0.51)	0.092	8.2	243,292
HDL cholesterol, mmol/l [d]	0 (0, 0.01)	0.033	0.06 (0.01, 0.12)	0.033	0.06 (0, 0.12)	0.034	6.0	290,932
LDL cholesterol, mmol/l [d]	0.01 (-0.01, 0.04)	0.265	0.15 (-0.11, 0.4)	0.265	0.06 (-0.16, 0.28)	0.596	5.7	107,790
Total-cholesterol-to-HDL ratio [d]	0 (-0.02, 0.02)	0.741	-0.04 (-0.28, 0.2)	0.741	-0.12 (-0.35, 0.1)	0.286	5.4	178,852
Triglycerides, mmol/l [d]	-0.04 (-0.06, -0.01)	0.002	-0.46 (-0.76, -0.17)	0.002	-0.45 (-0.74, -0.17)	0.002	4.2	126,297
Exploratory outcomes								
Diabetes medication, RD	0.29 (0.18, 0.41)	< 0.001	3.77 (2.32, 5.22)	< 0.001	-	-	3.5	513,473
Antihypertensive medication, RD [c]	0.11 (-0.38, 0.6)	0.659	1.3 (-4.48, 7.08)	0.659	-	-	4.5	390,878
Lipid-lowering medication, RD [d]	0.29 (-0.23, 0.82)	0.271	3.54 (-2.76, 9.85)	0.271	-	-	3.2	344,522
Diabetes complication, RD	0.06 (-0.07, 0.19)	0.344	0.81 (-0.86, 2.48)	0.344	0.21 (-1.36, 1.78)	0.797	3.3	493,431
Mortality, RD	0.05 (-0.09, 0.20)	0.471	0.66 (-1.14, 2.47)	0.471	0.94 (-0.86, 2.74)	0.307	4.6	703,310
Emergency MACE hospitalization, RD	-0.05 (-0.23, 0.12)	0.550	-0.67 (-2.88, 1.53)	0.550	-0.16 (-2.36, 2.03)	0.883	4.9	698,224

[a] 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).
[b] Sample size within MSE-optimal bandwidth.
[c] Sample restricted to those without prior lipid-lowering medication prescription.
[d] Sample restricted to those without prior blood pressure-lowering medication prescription.

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 with a different exposure definition (i.e., patients are considered to be treated if they have received a referral to the NHS DPP program within three months after the index HbA1c measure), 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 ('Outcome and treatment definition' and 'Main Analysis').

S3 Results for secondary cohort

This Supplementary Information **S3** provides the **main results for our secondary cohort**. Parallel to the primary cohort, our secondary 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. In addition, for the secondary cohort, we additionally excluded patients who had any HbA1c measure (whether or not it exceeded the prediabetes threshold or not) prior to their index date.

We happily provide results for the secondary cohort from additional robustness analyses upon request.

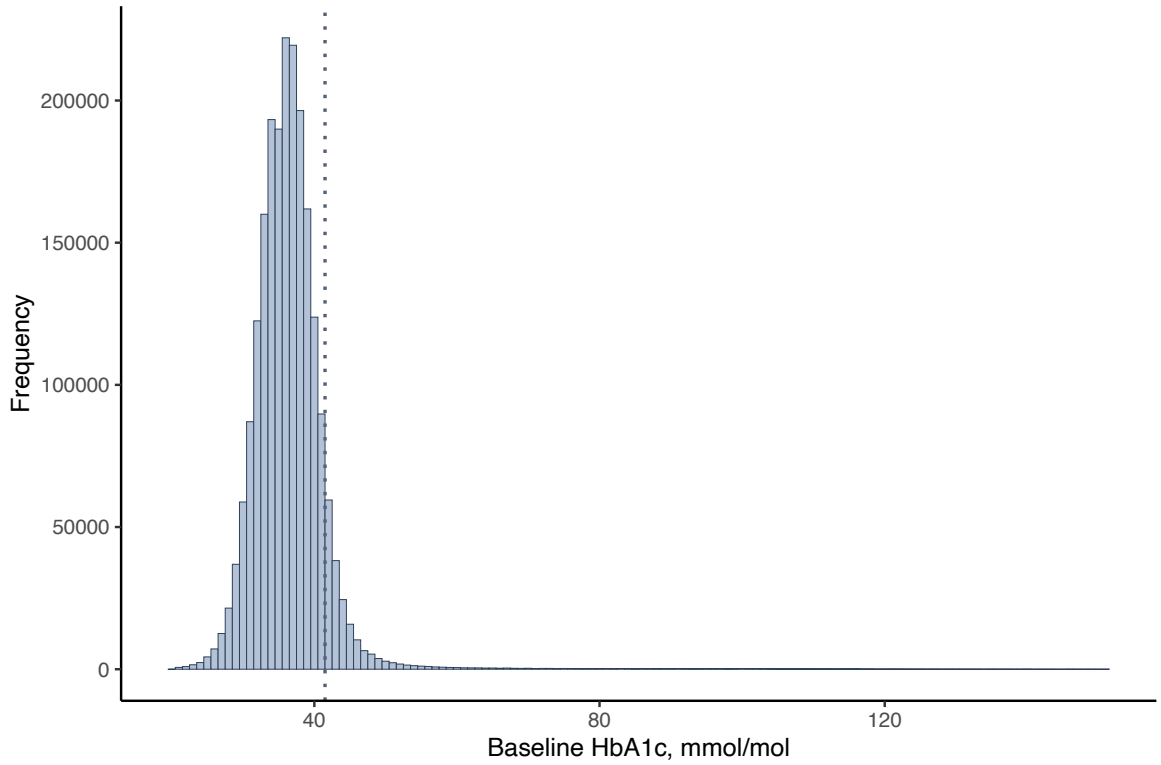
S3.1. Sample characteristics (secondary cohort)

Variable	%	N
Age in years, mean (SD)	48 (16)	
18 to 29	15.7	190 394
30 to 39	17	204 999
40 to 49	20.5	247 886
50 to 59	20.4	246 243
60 to 69	15	181 528
70 to 80	11.4	137 856
Gender		
Female	44.0	532 079
Male	56.0	676 827
BMI, mean (SD)	27.6 (6.1)	
< 25	36.3	265 410
25 to 29.9	34.6	252 864
30 to 34.9	18.2	133 287
35 to 39.9	7	50 941
≥ 40	3.9	28 675
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	1.46	0.44
LDL, mmol/l	3.04	0.96
Total-cholesterol-to-HDL ratio	3.82	1.27
Triglycerides, mmol/l	1.55	0.99
Number of yearly GP consultations	10.0	9.5
Number of prior emergency hospitalization	1.0	4.3

N = 1 208 906. BMI = body mass index. GP = General Practitioner. Age, gender, and number of consultation was available for the full sample. Missingness in baseline BMI, blood pressure and lipids are shown in Supplementary Table S3.2. Exchangeability of patients below and above the threshold are demonstrated in placebo tests with baseline characteristics (balance tests) in Extended Data Table 2.

S3.2. Availability of primary and secondary outcomes in electronic health records (secondary cohort)

Variable	Follow-up at least 6 months (N = 1 174 784) [a]		Discontinuity in outcome availability at threshold [b]		Discontinuity in time to follow-up record at threshold [b]	
	N	%	Estimate, % (95% CI)	*P* value	Estimate, months (95% CI)	*P* value
HbA1c, mmol/mol						
Baseline	1 174 784	100				
Outcome	487 963	41.5	8.8 (8.0, 9.6)	< 0.001	-0.51 (-0.69, -0.34)	< 0.001
BMI						
Baseline	710 662	60.4				
Outcome	332 891	28.3	2.5 (1.8, 3.2)	< 0.001	-0.07 (-0.30, 0.15)	0.520
Body weight, kg						
Baseline	775 926	66.0				
Outcome	383 672	32.7	2.6 (1.9, 3.3)	< 0.001	0 (-0.21, 0.21)	0.994
Systolic BP, mmHg						
Baseline	558 796	47.6				
Outcome	356 101	30.2	0 (-0.7, 0.7)	0.977	-0.02 (-0.24, 0.19)	0.830
Diastolic BP, mmHg						
Baseline	559 866	47.7				
Outcome	357 173	30.4	0 (-0.7, 0.7)	0.975	-0.02 (-0.23, 0.20)	0.866
HDL, mmol/l						
Baseline	757 185	64.4				
Outcome	335 631	28.6	3.2 (2.5, 3.9)	< 0.001	-0.05 (-0.25, 0.15)	0.641
LDL, mmol/l						
Baseline	395 164	33.6				
Outcome	147 193	12.5	1.5 (0.9, 2)	< 0.001	0.03 (-0.27, 0.32)	0.852
Total-to-HDL ratio						
Baseline	587 552	50.0				
Outcome	249 387	21.2	2.3 (1.6, 2.9)	< 0.001	0 (-0.23, 0.23)	0.990
Triglycerides, mmol/l						
Baseline	588 730	50.1				
Outcome	237 042	20.2	2.5 (1.9, 3.1)	< 0.001	0.01 (-0.23, 0.24)	0.963



S3.3. Histogram of baseline HbA1c for the secondary cohort.

S3.4 Regression discontinuity results of being eligible for (ITT), and of being referred to (CACE), intensive lifestyle counseling, unadjusted and adjusted for potential confounders and using local linear regressions (secondary cohort)

		Adjusted for				
Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
HbA1c, mmol/mol						
ITT	-0.15 (-0.24, -0.05)	-0.15 (-0.25, -0.06)	-0.14 (-0.23, -0.05)	-0.16 (-0.25, -0.07)	-0.11 (-0.21, -0.02)	-0.13 (-0.23, -0.04)
CACE	-1.26 (-2.06, -0.46)	-1.33 (-2.16, -0.5)	-1.18 (-1.97, -0.39)	-1.37 (-2.16, -0.58)	-0.98 (-1.78, -0.17)	-1.16 (-1.99, -0.32)
BMI [b]						
ITT	-0.13 (-0.2, -0.05)	-0.14 (-0.21, -0.07)	-0.13 (-0.2, -0.05)	-	-0.12 (-0.2, -0.05)	-0.14 (-0.21, -0.07)
CACE	-1.08 (-1.69, -0.46)	-1.2 (-1.78, -0.62)	-1.08 (-1.7, -0.46)	-	-1.07 (-1.69, -0.45)	-1.2 (-1.78, -0.62)
Weight, kg [b]						
ITT	-0.31 (-0.49, -0.12)	-0.34 (-0.5, -0.18)	-0.3 (-0.49, -0.12)	-	-0.31 (-0.49, -0.12)	-0.34 (-0.5, -0.18)
CACE	-2.68 (-4.29, -1.08)	-2.98 (-4.39, -1.57)	-2.68 (-4.28, -1.07)	-	-2.68 (-4.29, -1.08)	-3 (-4.42, -1.58)
Diastolic BP, mmHg [b,c]						
ITT	-0.3 (-0.64, 0.04)	-0.32 (-0.64, 0)	-0.3 (-0.64, 0.04)	-0.31 (-0.61, 0)	-0.3 (-0.64, 0.04)	-0.33 (-0.63, -0.02)
CACE	-2.61 (-5.54, 0.33)	-2.76 (-5.5, -0.02)	-2.58 (-5.51, 0.35)	-2.64 (-5.3, 0.02)	-2.62 (-5.56, 0.32)	-2.83 (-5.46, -0.2)
Systolic BP, mmHg [b,c]						
ITT	-0.27 (-0.79, 0.24)	-0.35 (-0.84, 0.14)	-0.26 (-0.78, 0.25)	-0.33 (-0.79, 0.12)	-0.27 (-0.79, 0.24)	-0.38 (-0.83, 0.07)
CACE	-2.33 (-6.78, 2.11)	-3.01 (-7.24, 1.21)	-2.28 (-6.7, 2.14)	-2.89 (-6.82, 1.05)	-2.34 (-6.79, 2.12)	-3.31 (-7.23, 0.62)
HDL cholesterol, mmol/l [b,d]						
ITT	0 (0, 0.01)	0 (0, 0.01)	0 (0, 0.01)	0 (0, 0.01)	0 (0, 0.01)	0 (0, 0.01)
CACE	0.03 (-0.03, 0.09)	0.03 (-0.03, 0.09)	0.03 (-0.03, 0.09)	0.03 (-0.03, 0.08)	0.03 (-0.03, 0.09)	0.03 (-0.03, 0.09)
LDL cholesterol, mmol/l [b,d]						
ITT	0.03 (0, 0.06)	0.03 (-0.01, 0.06)	0.03 (0, 0.06)	0.01 (-0.01, 0.04)	0.03 (0, 0.06)	0.03 (0, 0.06)
CACE	0.24 (-0.04, 0.52)	0.21 (-0.06, 0.47)	0.24 (-0.03, 0.52)	0.12 (-0.1, 0.34)	0.25 (-0.03, 0.53)	0.25 (-0.02, 0.51)

S3.4 Regression discontinuity results of being eligible for (ITT), and of being referred to (CACE), intensive lifestyle counseling, unadjusted and adjusted for potential confounders and using local linear regressions (secondary cohort). (continued)

Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
Total-cholesterol-to-HDL ratio [b,d]						
ITT	0.01 (-0.02, 0.04)	0.01 (-0.02, 0.04)	0.01 (-0.02, 0.04)	0 (-0.03, 0.02)	0.01 (-0.02, 0.04)	0.01 (-0.01, 0.04)
CACE	0.12 (-0.13, 0.37)	0.1 (-0.15, 0.34)	0.12 (-0.13, 0.37)	-0.02 (-0.25, 0.21)	0.12 (-0.13, 0.36)	0.13 (-0.13, 0.38)
Triglycerides, mmol/l [b,d]						
ITT	-0.04 (-0.07, -0.01)	-0.04 (-0.07, -0.01)	-0.04 (-0.07, -0.01)	-0.04 (-0.07, -0.01)	-0.04 (-0.07, -0.01)	-0.04 (-0.07, -0.01)
CACE	-0.35 (-0.64, -0.07)	-0.35 (-0.64, -0.07)	-0.36 (-0.65, -0.07)	-0.39 (-0.67, -0.11)	-0.36 (-0.65, -0.07)	-0.34 (-0.62, -0.06)
Diabetes complication, p.p.						
ITT	0.09 (-0.07, 0.25)	0.1 (-0.07, 0.26)	0.05 (-0.12, 0.21)	0.04 (-0.12, 0.19)	-	0.01 (-0.15, 0.16)
CACE	0.8 (-0.63, 2.23)	0.86 (-0.62, 2.34)	0.44 (-1.05, 1.92)	0.35 (-1.03, 1.74)	-	0.05 (-1.31, 1.41)
Mortality, p.p.						
ITT	-0.13 (-0.32, 0.06)	-0.11 (-0.32, 0.1)	-0.19 (-0.38, -0.01)	-0.12 (-0.31, 0.07)	-	-0.17 (-0.38, 0.04)
CACE	-1.12 (-2.79, 0.54)	-0.98 (-2.83, 0.87)	-1.69 (-3.33, -0.06)	-1.03 (-2.7, 0.64)	-	-1.52 (-3.36, 0.32)
MACE hospitalization, p.p.						
ITT	-0.11 (-0.34, 0.12)	-0.08 (-0.33, 0.18)	-0.21 (-0.44, 0.01)	-0.09 (-0.32, 0.14)	-	-0.18 (-0.43, 0.07)
CACE	-0.94 (-2.97, 1.08)	-0.68 (-2.95, 1.59)	-1.88 (-3.88, 0.11)	-0.79 (-2.81, 1.22)	-	-1.61 (-3.85, 0.62)
Diabetes medication, p.p.						
ITT	0.34 (0.19, 0.49)	0.32 (0.17, 0.48)	0.3 (0.15, 0.45)	-	-	0.28 (0.13, 0.43)
CACE	3.01 (1.66, 4.36)	2.9 (1.56, 4.25)	2.72 (1.37, 4.07)	-	-	2.52 (1.17, 3.86)
Antihypertensive medication, p.p. [b]						
ITT	0.39 (-0.23, 1)	0.41 (-0.18, 1)	-0.07 (-0.65, 0.51)	-	-	-0.03 (-0.56, 0.5)
CACE	3.29 (-1.93, 8.5)	3.45 (-1.5, 8.41)	-0.6 (-5.52, 4.31)	-	-	-0.26 (-4.75, 4.23)

S3.4 Regression discontinuity results of being eligible for (ITT), and of being referred to (CACE), intensive lifestyle counseling, unadjusted and adjusted for potential confounders and using local linear regressions (secondary cohort). (continued)

Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
Lipid-lowering medication, p.p.[c]						
ITT	-0.07 (-0.68, 0.54)	0.11 (-0.44, 0.65)	-0.3 (-0.9, 0.3)			-0.12 (-0.67, 0.43)
CACE	-0.62 (-5.89, 4.66)	0.91 (-3.77, 5.6)	-2.62 (-7.83, 2.58)			-1.04 (-5.74, 3.66)
T2DM incidence, p.p.						
ITT	0.53 (0.31, 0.74)	0.52 (0.29, 0.74)	0.46 (0.27, 0.65)	-	-	0.46 (0.25, 0.66)
CACE	4.78 (2.85, 6.71)	4.71 (2.64, 6.79)	4.16 (2.44, 5.88)	-	-	4.15 (2.27, 6.02)
Hypertension incidence, p.p. [c]						
ITT	0.05 (-0.3, 0.39)	0.08 (-0.3, 0.46)	-0.06 (-0.4, 0.28)	-	-	-0.02 (-0.39, 0.34)
CACE	0.39 (-2.44, 3.21)	0.69 (-2.46, 3.85)	-0.51 (-3.34, 2.31)	-	-	-0.2 (-3.28, 2.88)
Hyperlipidemia incidence, p.p. [d]						
ITT	-0.19 (-0.4, 0.02)	-0.18 (-0.38, 0.03)	-0.2 (-0.42, 0.01)	-	-	-0.19 (-0.4, 0.01)
CACE	-1.58 (-3.36, 0.21)	-1.49 (-3.2, 0.22)	-1.71 (-3.51, 0.08)	-	-	-1.63 (-3.35, 0.1)

BMI = Body mass index. BP = Blood pressure. CACE = Complier average causal effect. ITT = Intention-to-treat effect. MACE = Major adverse cardiovascular event. MSE = mean-squared error. P.p. = percentage points.

[a] The medication covariate indicates whether there was a recorded prescription of relevant medication (i.e., diabetes, lipid- or blood pressure-lowering medication) prior to the recorded endline measure.

[b] Effect estimates for BMI, weight, cholesterol levels, and BP levels represent changes between baseline and endline level to enhance precision. Regressions without adjusting for baseline levels yielded similar effect estimates but larger confidence intervals.

[c] Sample restricted to those without prior blood pressure-lowering medication prescription.

[d] Sample restricted to those without prior lipid-lowering medication prescription

Local linear regression with heteroskedasticity-robust standard errors, triangular kernel weights and MSE-optimal bandwidths.

S3.5 Regression discontinuity results of being eligible for (ITT), and of being referred to (CACE), intensive lifestyle counseling, unadjusted and adjusted for potential confounders and using local quadratic regressions (secondary cohort)

		Adjusted for				
Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
HbA1c, mmol/mol						
ITT	-0.17 (-0.29, -0.06)	-0.17 (-0.29, -0.06)	-0.16 (-0.28, -0.05)	-0.19 (-0.31, -0.07)	-0.14 (-0.26, -0.03)	-0.16 (-0.28, -0.04)
CACE	-1.5 (-2.53, -0.48)	-1.52 (-2.53, -0.51)	-1.43 (-2.45, -0.41)	-1.68 (-2.74, -0.61)	-1.25 (-2.28, -0.23)	-1.43 (-2.5, -0.37)
BMI [b]						
ITT	-0.13 (-0.22, -0.04)	-0.13 (-0.22, -0.04)	-0.13 (-0.22, -0.04)	-	-0.13 (-0.22, -0.04)	-0.13 (-0.22, -0.04)
CACE	-1.12 (-1.92, -0.31)	-1.11 (-1.86, -0.36)	-1.12 (-1.92, -0.31)	-	-1.11 (-1.92, -0.3)	-1.09 (-1.85, -0.33)
Weight, kg [b]						
ITT	-0.34 (-0.57, -0.11)	-0.34 (-0.55, -0.13)	-0.34 (-0.57, -0.11)	-	-0.34 (-0.57, -0.11)	-0.34 (-0.55, -0.13)
CACE	-3 (-5.06, -0.93)	-2.93 (-4.74, -1.11)	-2.99 (-5.06, -0.93)	-	-3 (-5.06, -0.93)	-2.93 (-4.75, -1.11)
Diastolic BP, mmHg [b,c]						
ITT	-0.37 (-0.82, 0.08)	-0.36 (-0.83, 0.12)	-0.36 (-0.81, 0.08)	-0.38 (-0.81, 0.06)	-0.37 (-0.82, 0.08)	-0.37 (-0.81, 0.07)
CACE	-3.25 (-7.2, 0.71)	-3.17 (-7.38, 1.03)	-3.22 (-7.16, 0.73)	-3.3 (-7.1, 0.5)	-3.25 (-7.21, 0.7)	-3.27 (-7.14, 0.6)
Systolic BP, mmHg [b,c]						
ITT	-0.31 (-0.9, 0.28)	-0.31 (-0.94, 0.32)	-0.3 (-0.89, 0.28)	-0.35 (-0.92, 0.22)	-0.31 (-0.9, 0.28)	-0.34 (-0.9, 0.22)
CACE	-2.67 (-7.75, 2.41)	-2.68 (-8.12, 2.75)	-2.62 (-7.63, 2.39)	-2.99 (-7.92, 1.93)	-2.67 (-7.76, 2.42)	-2.92 (-7.77, 1.93)
HDL cholesterol, mmol/l [b,d]						
ITT	0.01 (0, 0.02)	0.01 (0, 0.02)	0.01 (0, 0.02)	0.01 (0, 0.02)	0.01 (0, 0.02)	0.01 (0, 0.02)
CACE	0.08 (-0.02, 0.19)	0.09 (-0.02, 0.19)	0.08 (-0.02, 0.19)	0.08 (-0.02, 0.19)	0.09 (-0.02, 0.19)	0.08 (-0.02, 0.19)
LDL cholesterol, mmol/l [b,d]						
ITT	0.06 (0, 0.11)	0.06 (0, 0.11)	0.06 (0, 0.11)	0.02 (-0.02, 0.06)	0.06 (0, 0.11)	0.04 (-0.01, 0.09)
CACE	0.51 (0.03, 0.98)	0.49 (0.03, 0.96)	0.5 (0.03, 0.97)	0.19 (-0.15, 0.52)	0.5 (0.03, 0.97)	0.35 (-0.05, 0.75)

S3.5 Regression discontinuity results of being eligible for (ITT), and of being referred to (CACE), intensive lifestyle counseling, unadjusted and adjusted for potential confounders and using local quadratic regressions (secondary cohort). (continued)

Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
Total-cholesterol-to-HDL ratio [b,d]						
ITT	0.02 (-0.02, 0.06)	0.02 (-0.02, 0.05)	0.02 (-0.02, 0.06)	0.01 (-0.03, 0.04)	0.02 (-0.02, 0.06)	0.02 (-0.02, 0.06)
CACE	0.2 (-0.14, 0.55)	0.15 (-0.16, 0.47)	0.2 (-0.15, 0.55)	0.05 (-0.25, 0.34)	0.2 (-0.15, 0.55)	0.16 (-0.16, 0.48)
Triglycerides, mmol/l [b,d]						
ITT	-0.09 (-0.15, -0.04)	-0.09 (-0.15, -0.04)	-0.09 (-0.15, -0.04)	-0.1 (-0.15, -0.04)	-0.09 (-0.15, -0.04)	-0.09 (-0.15, -0.04)
CACE	-0.89 (-1.44, -0.34)	-0.9 (-1.46, -0.35)	-0.88 (-1.43, -0.33)	-0.95 (-1.5, -0.4)	-0.89 (-1.44, -0.34)	-0.91 (-1.47, -0.36)
Diabetes complication, p.p.						
ITT	0.1 (-0.11, 0.32)	0.1 (-0.13, 0.33)	0.07 (-0.13, 0.27)	0.06 (-0.13, 0.25)	-	0.03 (-0.17, 0.22)
CACE	0.96 (-1, 2.92)	0.93 (-1.17, 3.03)	0.61 (-1.24, 2.45)	0.55 (-1.21, 2.31)	-	0.25 (-1.52, 2.02)
Mortality, p.p.						
ITT	-0.19 (-0.41, 0.03)	-0.19 (-0.41, 0.02)	-0.25 (-0.47, -0.03)	-0.17 (-0.39, 0.05)	-	-0.24 (-0.46, -0.03)
CACE	-1.72 (-3.68, 0.25)	-1.71 (-3.59, 0.17)	-2.22 (-4.21, -0.23)	-1.56 (-3.53, 0.41)	-	-2.16 (-4.09, -0.24)
MACE hospitalization, p.p.						
ITT	-0.21 (-0.44, 0.02)	-0.19 (-0.44, 0.06)	-0.28 (-0.51, -0.06)	-0.18 (-0.41, 0.05)	-	-0.27 (-0.52, -0.02)
CACE	-1.84 (-3.83, 0.15)	-1.68 (-3.91, 0.55)	-2.47 (-4.46, -0.49)	-1.54 (-3.53, 0.45)	-	-2.36 (-4.56, -0.15)
Diabetes medication, p.p.						
ITT	0.36 (0.19, 0.52)	0.3 (0.12, 0.49)	0.31 (0.14, 0.48)	-	-	0.27 (0.08, 0.45)
CACE	3.23 (1.72, 4.74)	2.79 (1.09, 4.48)	2.82 (1.26, 4.38)	-	-	2.47 (0.75, 4.18)
Antihypertensive medication, p.p. [b]						
ITT	0.41 (-0.34, 1.15)	0.34 (-0.4, 1.09)	-0.03 (-0.7, 0.64)	-	-	-0.06 (-0.74, 0.63)
CACE	3.5 (-2.9, 9.9)	2.96 (-3.47, 9.38)	-0.28 (-6.01, 5.45)	-	-	-0.5 (-6.41, 5.41)

S3.5 Regression discontinuity results of being eligible for (ITT), and of being referred to (CACE), intensive lifestyle counseling, unadjusted and adjusted for potential confounders and using local quadratic regressions (secondary cohort). (continued)

Outcome	Unadjusted	Age, sex	No. GP visits	Medication [a]	Time to endline record	Fully adjusted
Lipid-lowering medication, p.p.[c]						
ITT	0.03 (-0.57, 0.63)	-0.12 (-0.77, 0.53)	-0.15 (-0.74, 0.44)			-0.3 (-0.94, 0.34)
CACE	0.23 (-4.89, 5.34)	-1.05 (-6.69, 4.58)	-1.28 (-6.34, 3.77)			-2.65 (-8.23, 2.94)
T2DM incidence, p.p.						
ITT	0.47 (0.13, 0.81)	0.47 (0.13, 0.81)	0.43 (0.15, 0.71)	-	-	0.42 (0.08, 0.76)
CACE	4.4 (1.19, 7.62)	4.42 (1.2, 7.63)	4.02 (1.43, 6.62)	-	-	3.97 (0.75, 7.18)
Hypertension incidence, p.p. [c]						
ITT	-0.01 (-0.49, 0.47)	-0.04 (-0.51, 0.43)	-0.1 (-0.59, 0.39)	-	-	-0.13 (-0.6, 0.33)
CACE	-0.1 (-4.18, 3.97)	-0.35 (-4.37, 3.66)	-0.87 (-5.12, 3.39)	-	-	-1.16 (-5.17, 2.86)
Hyperlipidemia incidence, p.p. [d]						
ITT	-0.1 (-0.39, 0.19)	-0.1 (-0.39, 0.18)	-0.12 (-0.4, 0.17)	-	-	-0.12 (-0.4, 0.17)
CACE	-0.88 (-3.37, 1.62)	-0.9 (-3.4, 1.6)	-1.02 (-3.52, 1.48)	-	-	-1.03 (-3.54, 1.47)

BMI = Body mass index. BP = Blood pressure. CACE = Complier average causal effect. ITT = Intention-to-treat effect. MACE = Major adverse cardiovascular event. MSE = mean-squared error. P.p. = percentage points.

[a] The medication covariate indicates whether there was a recorded prescription of relevant medication (i.e., diabetes, lipid- or blood pressure-lowering medication) prior to the recorded endline measure.

[b] Effect estimates for BMI, weight, cholesterol levels, and BP levels represent changes between baseline and endline level to enhance precision. Regressions without adjusting for baseline levels yielded similar effect estimates but larger confidence intervals.

[c] Sample restricted to those without prior blood pressure-lowering medication prescription.

[d] Sample restricted to those without prior lipid-lowering medication prescription

Local quadratic regression with heteroskedasticity-robust standard errors, triangular kernel weights and MSE-optimal bandwidths.

S3.6 Negative outcome controls (secondary cohort)

Outcome	Bandwidth	Estimate (95% CI)	*P* value	Sample size
Flu vaccination	4.3	-0.43 (-0.94, 0.08)	0.099	393 145
Number of flu vaccinations[a]	4.3	-0.63 (-1.63, 0.36)	0.214	371 433
Pneumococcal vaccincation	4.4	-0.03 (-0.23, 0.17)	0.787	393 145
Fracture	6.3	-0.08 (-0.27, 0.1)	0.361	637 295
Accidental injuries	5.5	0.05 (-0.16, 0.25)	0.659	512 712
Number of accidental injuries [a]	5.9	0.2 (-0.18, 0.59)	0.301	512 712
Routine screenings				
Colorectal	2.6	-0.53 (-1.33, 0.26)	0.190	284 818
Breast	3.0	-0.31 (-1.67, 1.05)	0.656	144 578
Cervical	4.6	0.70 (-0.15, 1.54)	0.106	201 194
Skin abnomality	7.7	-0.51 (-0.82, -0.21)	0.001	747 319
Allergic reaction	5.5	0.05 (-0.15, 0.26)	0.614	512 712
Contraceptive use				
IUD	4.8	0.04 (-0.19, 0.27)	0.726	201 194
Oral	2.2	-0.68 (-1.59, 0.23)	0.142	95 939
Short-term onset of [b]				
Cancer	6.0	0.09 (-0.11, 0.29)	0.364	605 526
Dementia	7.9	0 (-0.08, 0.08)	0.994	744 256

[a] Effect estimate can be interpreted as the difference in number of events during the follow-up period at the threshold.
[b] Sample restricted to those without any previous diagnosis of cancer or dementia, respectively. While healthy lifestyle behaviors are assumed to be protective factors for cancer and dementia on-set, the median follow-up time (29 months) is sufficiently short to assume that any plausible effects are negligible.

IUD = Intrauterine 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 (secondary 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.

S4 Supplementary Discussion

Secondary results

Our results from secondary outcomes suggest a beneficial effect on HDL and triglycerides but not LDL. This is congruent with some evidence from clinical trials suggesting that lifestyle changes are more likely to consistently improve HDL and triglycerides levels while LDL is less likely to be affected[10]. However, this evidence is not conclusive[11].

Our results stratified by gender suggest that men, but not women, achieved significant improvement in HbA1c, and while BMI and weight reductions were significant for both men and women, effect sizes suggest greater improvements for men. This is consistent with studies showing that while women are more likely to report attempting to lose weight and join weight loss programs, men are often more successful in losing weight conditional on participating in interventions[12–14]. Our results further suggest that patients whose glycemic control has not been previously tested and who have not already received prior lifestyle counseling from their GP at baseline may benefit more from being referred to an intensive lifestyle counseling program compared to their counterparts. Lastly, while we found no meaningful differences between patients who have been referred and did not start the NHS DPP compared to patients who started based on their GP records, it is probable that health literacy, personal motivation and personal preferences play a role in who ultimately benefits from being referred.

Limitations for difference-in-differences analysis and instrumental variable estimation

We were able to replicate our main finding, the improvement of glycemic control, in two other quasi-experimental approaches; difference-in-differences analysis and instrumental variable estimation. There are several limitations that are important to the interpretation of these results. First, for the difference-in-differences analysis, we were not able to match practice-level program roll-out from official sources to CPRD practices but had to derive to which wave each practice belonged by estimating the share of eligible patients being referred. By contrast, in the instrumental variable estimation, we were able to compute the regional variation in NHS DPP implementation based on official program information. Second, while the key assumption of parallel pre-trends for the difference-in-differences analysis was met, there were differences in average HbA1c between groups, which may indicate that assignment of the practices to waves was not random. Third, the instrumental variable estimation relied on time-by-region instead of patient-level variation which led to more imprecise estimates. However, because all three methods estimate the causal effect for somewhat different patient groups (e.g., among all patients rather than close to the program threshold) and make different assumptions, the finding that all three approaches

demonstrate a beneficial effect of referral to or implementation of the NHS DPP on glycemic control strengthens the confidence in our findings.

References

1. Bakhai, C. & Hopwood, B. Optimising Engagement with the NHS Diabetes Prevention Programme. (2020).
2. Koutoukidis, D. A. *et al.* Association between the month of starting a weight management program and weight change in people at high risk of type 2 diabetes: A prospective cohort study. *Obesity* **31**, 1707–1716 (2023).
3. Marsden, A. M. *et al.* 'Finishing the race' – a cohort study of weight and blood glucose change among the first 36,000 patients in a large-scale diabetes prevention programme. *Int. J. Behav. Nutr. Phys. Act.* **19**, 7 (2022).
4. McManus, E., Meacock, R., Parkinson, B. & Sutton, M. Population level impact of the NHS Diabetes Prevention Programme on incidence of type 2 diabetes in England: An observational study. *Lancet Reg. Health - Eur.* **19**, 100420 (2022).
5. Murray, E. *et al.* A National Digital Diabetes Prevention Programme: Feasible, acceptable and effective? *Eur. J. Public Health* **29**, ckz185.149 (2019).
6. Poupakis, S., Kolotourou, M., MacMillan, H. J. & Chadwick, P. M. Attendance, Weight Loss, and Participation in a Behavioural Diabetes Prevention Programme. *Int. J. Behav. Med.* (2023) doi:10.1007/s12529-022-10146-x.
7. Ravindrarajah, R. *et al.* Referral to the NHS Diabetes Prevention Programme and conversion from nondiabetic hyperglycaemia to type 2 diabetes mellitus in England: A matched cohort analysis. *PLOS Med.* **20**, e1004177 (2023).
8. Valabhji, J. *et al.* Early Outcomes From the English National Health Service Diabetes Prevention Programme. *Diabetes Care* **43**, 152–160 (2020).
9. Wise, J. NHS diabetes prevention programme helps weight loss, analysis shows. *BMJ* k1196 (2018) doi:10.1136/bmj.k1196.
10. Jonas, D. E. *et al.* Screening for Prediabetes and Type 2 Diabetes. *JAMA* **326**, 744 (2021).
11. Aucott, L., Gray, D., Rothnie, H., Thapa, M. & Waweru, C. Effects of lifestyle interventions and long-term weight loss on lipid outcomes - a systematic review. *Obes. Rev.* **12**, e412–e425 (2011).
12. Williams, R. L., Wood, L. G., Collins, C. E. & Callister, R. Effectiveness of weight loss interventions – is there a difference between men and women: a systematic review. *Obes. Rev.* **16**, 171–186 (2015).
13. Santos, I., Sniehotta, F. F., Marques, M. M., Carraça, E. V. & Teixeira, P. J. Prevalence of personal weight control attempts in adults: a systematic review and meta-analysis: Weight control attempts in adults. *Obes. Rev.* **18**, 32–50 (2017).
14. Robertson, C. *et al.* Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. *Health Technol. Assess.* **18**, (2014).