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TITLE PAGE

Title:
Type 2 diabetes and glucose intolerance in a population with intellectual disabilities: the STOP Diabetes cross-sectional screening study

Short Running Title:
Diabetes screening in intellectual disability

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ABSTRACT (284 words)

Background:

Adults with intellectual disabilities (ID) may be at increased risk of developing type 2 diabetes and cardiovascular disease, due to lifestyle factors, medications and other diagnosed conditions. Currently there is lack of evidence on prevalence and prevention in this population. The aim of this study was to conduct a diabetes screening programme to determine prevalence of previously undiagnosed type 2 diabetes and impaired glucose regulation in people with ID.

Methods:

Screening was conducted in a variety of community settings in Leicestershire, UK. Adults with ID were invited via: general practices; the Leicestershire Learning Disability Register; ID psychiatric services; and some people directly contacted the research team due to publicity about the study. Screening involved collection of anthropometric, biomedical, and questionnaire data. Type 2 diabetes and impaired glucose regulation were defined according to (venous) fasting plasma glucose or HbA1c, following current World Health Organisation criteria.

Results:

930 adults (29% of those approached) participated. Mean age was 43 years, 58% were male and 16% of South Asian ethnicity. Most participants were either overweight or obese (68%). Diabetes status was successfully assessed for 675 (73%) participants: 9 (1.3%, 95% CI 0.6 to 2.5) were found to have undiagnosed type 2 diabetes: and 35 (5.2%, 95% CI 3.6 to 7.1) had impaired glucose regulation. Key factors associated with abnormal glucose regulation included: non-white ethnicity and a first degree family history of diabetes.

Conclusions:

Results from this large multi-ethnic cohort suggest a low prevalence of screen-detected (previously undiagnosed) type 2 diabetes and impaired glucose regulation

in adults with ID. However, the high levels of overweight and obesity we found emphasise the need for targeted lifestyle prevention strategies, which are specifically tailored for the needs of people with ID.

Headline statements:
1. First large diabetes screening programme in adults with intellectual disabilities

2. Found low prevalence of screen-detected (previously undiagnosed) diabetes in adults with intellectual disabilities

3. High levels of overweight and obesity emphasise need for tailored lifestyle prevention strategies for adults with intellectual disabilities

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BACKGROUND

People with intellectual disabilities (ID) continue to experience persistent health inequalities and higher rates of mortality compared with their non-disabled peers (Heslop *et al.* 2014, Havercamp *et al.* 2004), and experience barriers in accessing healthcare. Hence, early detection of chronic conditions is important, and increasingly so for age-related conditions as life expectancy increases (Krahn and Fox 2014).

In the general background population, increasing levels of obesity and sedentary lifestyles have been associated with a continued rise in non-communicable diseases, including type 2 diabetes and cardiovascular disease (World Health Organisation 2013). For most regions, global prevalence estimates suggest around 9% of the adult population have diabetes, with type 2 diabetes accounting for the majority (~90%) of cases (International Diabetes Federation 2015, World Health Organisation 2016). However, a high proportion of people who have type 2 diabetes continue to remain undiagnosed (an estimated 39% in Europe, 47% worldwide) and are potentially at risk of developing associated health problems (International Diabetes Federation 2015). If left untreated or poorly managed, type 2 diabetes can lead to serious complications, including heart attacks, stroke, blindness, renal failure, nerve damage, amputation and associated mortality, and remains a public health priority (International Diabetes Federation 2015). Early identification of type 2 diabetes and intervention through screening has been shown to be a useful approach in the general adult population (Waugh *et al.* 2007, Gillies *et al.* 2008), given the increasing prevalence of type 2 diabetes and the conferred risk of developing cardiovascular disease. The value of screening for impaired glucose regulation (where blood

glucose does not reach the threshold for diabetes but is raised above normal levels) has also been demonstrated (Narayan and Gujral 2015).

There are a number of risk factors for type 2 diabetes that are known to be highly prevalent in people with ID, suggesting that type 2 diabetes may be more common in this group. These include: physical inactivity (Temple *et al.* 2006); obesity (Krahn and Fox 2014, Melville *et al.* 2007); antipsychotic drug use (for challenging behaviour and psychosis) associated with weight gain, hyperglycaemia and other adverse metabolic effects (American Diabetes Association *et al.* 2004); and genetic conditions associated with obesity (e.g. Prada-Willi syndrome) (Nagai and Mori 1999). However, data on the prevalence of type 2 diabetes (both known cases and undiagnosed) for people with ID are currently unclear (Emerson *et al.* 2012). Most studies have previously been unable to distinguish between type 2 diabetes and other forms of diabetes (McVilly *et al.* 2014, MacRae *et al.* 2015). Recent meta-analytic evidence, derived from a small number of studies (n=5) where type 2 diabetes has been considered separately from other types of diabetes, suggests an overall pooled prevalence of 7.6% (Dunkley 2017). However, this rate includes known cases (i.e. those that have already been diagnosed); none of the studies focused specifically on screen-detected type 2 diabetes.

People with ID have been recommended as an important group to consider for diabetes prevention strategies, given their supposed high risk of developing type 2 diabetes (NICE 2012, U.S. Department of Health and Human Services 2005). However, it is currently unknown whether screening for asymptomatic glucose

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disorders is viable in populations with ID; there is a lack of evidence on feasibility, acceptability, outcomes and benefits.

We conducted a programme of research among people with ID. The STOP Diabetes study (Dunkley 2017) consisted of two main components running in parallel: a population-based diabetes screening study; and the development of a lifestyle education programme. This paper focuses on the screening stage. The primary aims of this component were: 1) to develop and assess the feasibility of conducting a diabetes screening programme in adults with ID; and 2) to determine the prevalence and associated risk factors for screen-detected type 2 diabetes and impaired glucose regulation.

METHODS

A cross-sectional population-based diabetes screening study was conducted in a community setting, in Leicestershire and Rutland, UK, between December 2012 and September 2015.

Participant recruitment

Potential participants (mild to profound ID, aged 18-74 years) were invited using one of four possible approaches: 1) via general practice registers; 2) via the Leicestershire Learning Disability Register (Watson 2003, Smith *et al.* 1996); 3) via specialist ID psychiatric service clinics; or 4) people directly contacted the research team following study publicity, (see Figure 1). The initial invitation was followed up by a telephone call and/or face-to-face visit, to provide further information and conduct a preliminary assessment of a person's decision making capacity. Full study information was then provided to eligible volunteers and/or an identified consultee (personal/nominated). Exclusion criteria included: 1) a previous diagnosis of type 1 or type 2 diabetes; and 2) presence of systemic disease that may interfere with measurement and interpretation of glycated haemoglobin (HbA1c, a marker of diabetes and longer-term blood glucose).

[Figure 1 about here]

Screening process

Volunteers (and carers) were subsequently invited to attend for screening, usually conducted over two appointments (first appointment: consent and data collection; second appointment: venepuncture). A trained ID research nurse obtained informed consent from the volunteer, or signed approval from the appropriate consultee, in line with the English Mental Capacity Act (Department for Constitutional Affairs

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2007). Data collected included: anthropometric measures (weight, body mass index, waist size); blood pressure; bloods (lipids, glucose, HbA1c); and demographic, lifestyle and medical history data; For blood tests, the appropriateness of obtaining a fasting or non-fasting sample (based on possible behavioural difficulties and/or cognition) was discussed in advance with participants (and carers). The most recent WHO criteria (World Health Organisation 2011) were used to define type 2 diabetes (HbA1c ≥48 mmol/mol, 6.5%) and impaired glucose regulation (impaired fasting glucose (WHO criteria) or HbA1c 42-47 mmol/mol, 6.0-6.4%). Following screening, participants (and carers) were informed of their diabetes status; people identified as having impaired glucose regulation or type 2 diabetes were referred to their general practitioner. Further details of all study data collection procedures and assessment of outcomes are described elsewhere. (Dunkley 2017).

Sample size

Around 4,000 adults with ID were identified as potentially eligible (according to estimates provided by the local ID services). We aimed to screen 1,000 adults with ID, which would measure the overall prevalence of screen-detected type 2 diabetes and impaired glucose regulation with ~1.5% and 2% precision (95% CI) respectively, assuming similar prevalence rates of screen-detected type 2 diabetes and impaired glucose regulation in people with ID as in the general population (Webb *et al.* 2011).

Data analysis

Feasibility of screening was assessed using a flow diagram of the screening process and summarising the number of drop outs and those for which data were unobtainable at each stage. Particular outcomes of interest in terms of the feasibility

were: (i) the proportion of people invited who complete the screening programme (including the blood tests); and (ii) the proportion of people who attend the screening but do not have a blood test. We also assessed the completeness of other key data outcomes to assess the feasibility of data collection for other similar studies.

The characteristics of those screened were summarised using means (standard deviations) for continuous variables and n (%) for categorical. The overall prevalence of impaired glucose regulation, type 2 diabetes and any abnormal glucose regulation (a composite of impaired glucose regulation and type 2 diabetes) were calculated with 95% confidence intervals (CI). Logistic regression was used to assess the association between key biomedical and anthropometric characteristics and the outcome abnormal glucose regulation. Odds Ratios (OR) and 95% CIs were calculated.

Cardiovascular risk was calculated for participants aged 35-75 years with no previous history of cardiovascular disease. The Framingham risk score (Wilson *et al.* 1998, D'Agostino *et al.* 2008) was used or ETHRISK for people of South Asian origin (Brindle *et al.* 2006). The overall mean risk at 10 years, and level of risk (high, intermediate, low) based on thresholds determined by the National Cholesterol Education Program (National Cholesterol Education Program Expert Panel 2002), were calculated. All analyses were conducted using Stata version 14 (StataCorp.). Statistical significance related to $p<0.05$ and 95% CIs are presented throughout.

RESULTS

<u>Participant recruitment and screening uptake</u>

A total of 3201 adults with ID were approached to take part in the screening study (Figure 1). The majority (n=1736, 54%) were invited via their general practice (median per practice, n=19, range 3 to 116). Around 40% were approached via the Leicestershire Learning Disability Register (directly invited n=864; previous agreement for future research and contact details passed to researchers, n=418). A smaller number of people were invited via ID psychiatric clinics (n=52, 2%) or directly contacted the research team (n=131, 4%). Forty percent of people responded positively to the initial invitation. Following capacity assessment and provision of further study information, 984 (31% of those initially invited) proceeded to the screening stage (Figure 2).

[Figure 2 about here]

Subsequently, at consent, a total of 930 people were recruited into the study, see Figure 2; 350 participants (38%) were able to consent for themselves and a consultee (personal 23%, nominated 39%) was required for other participants. Key screening outcomes were successfully measured for most participants, including blood pressure for around 89% and anthropometric measures for around 86%, see Table 1. The main documented reasons for not obtaining measurements were participant refusal (for blood pressure) and physical or behavioural difficulties (for anthropometric measures).

[Table 1 about here]

Most participants (n=825) agreed to attend an appointment for a blood test. Subsequently, bloods were successfully obtained for 653 (70% of those recruited). For five participants, HbA1c results were classed as possibly unreliable and not

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included in the assessment of diabetes status (due to possible Hb variant, n=1; poor kidney function, n=4). For 27 participants where the blood test was refused or unsuccessful, an HbA1c test had been taken during the study period as part of their routine healthcare (primary/secondary) and this result was obtained from their medical records, see Figure 2 and Table 1. Therefore, diabetes status was successfully assessed for a total of 675 participants.

Demographic and biomedical characteristics

The key characteristics of participants are summarised in Table 1. Overall, 58% were male, mean age was 43 years (SD 14.2) and 80% were of white ethnicity. Similar proportions of participants were classified as having mild, moderate or severe ID (~30% each), 4% as profound and for 6% severity of ID was not known. Most participants (~70%) had no identified cause of their ID; where known, the most common cause was Down's syndrome (14%). A high proportion of participants required 24 hour support (71%) and only 7% reported being independent; most lived either with family (36%) or in a residential/nursing home (38%), with 6% living alone.

The majority of participants were classed as either overweight (31%) or obese (37%), with mean body mass index (SD 7.1). Mean HbA1c was 35.0 (SD 5.1) mmol/mol (5.3%; SD 1.5), fasting plasma glucose 4.7 mmol/l (SD 0.7) and non-fasting 5.3 mmol/l (SD 1.5). Data reported directly by participants and/or carers indicated that only 30% of participants were eating the recommended five or more daily portions of fruit, vegetables or salad; most people did at least "some" walking on a typical day but only 25% achieved "a lot" of walking; around half reported spending "a lot" or "most/all" of the day sitting.

The overall prevalence of existing cardiovascular disease was 2% (stroke 1.3%, coronary heart disease 0.6%, and one person had both). A history of high cholesterol and/or use of lipid lowering medication was reported for 8%, hypertension (previously diagnosed and/or currently prescribed an anti-hypertensive) for 9%, and 4% were prescribed an anti-thrombotic. A minority of participants were either current smokers (8%) or ex-smokers (4%).

Prevalence of type 2 diabetes and impaired glucose regulation

Of the 675 participants with outcome data to establish prevalence of screen-detected impaired glucose regulation/ type 2 diabetes, nine participants (1.3%, 95% CI 0.6 to 2.5) had previously undiagnosed type 2 diabetes, see Table 2. Thirty-five participants (5.2%, 95% CI 3.6 to 7.1) had impaired glucose regulation. Prevalence of abnormal glycaemia (combined type 2 diabetes and impaired glucose regulation) was 6.5% (95% CI 4.7, 8.4).

[Table 2 about here]

Factors associated with abnormal glucose regulation

Table 3 shows the association of anthropometric and biomedical characteristics with having screen-detected abnormal glycaemia. Participants of non-white ethnicity were almost four times more likely to have abnormal glucose levels compared with white European participants (OR 3.93; 95% 2.10 to 7.33); those with a first degree family history of diabetes were over three times more likely (OR 3.35; 95% 1.64 to 6.86). In addition, abnormal glucose levels were associated with increasing weight, BMI, waist circumference, hip circumference, diastolic blood pressure and triglycerides, and decreasing high density lipoprotein cholesterol.

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[Table 3 about here]

Cardiovascular risk

Cardiovascular risk, was able to be assessed for 376 (40.4%) participants, based on Framingham (Wilson et al. 1998, D'Agostino et al. 2008) or ETHRISK (Brindle et al. 2006). The mean predicted 10-year risk for coronary heart disease was 5.9% (SD 4.9%) and for cardiovascular disease was 7.3% (SD 6.2%). The majority of participants were classed as low (<10%) future risk for coronary heart disease (83.5%) and for cardiovascular disease (75.3%). However, 16% of participants were classed as high or intermediate risk of developing coronary heart disease in the next 10 years, and 25% of developing cardiovascular disease.

DISCUSSION

Summary of main findings

To our knowledge, this is the first large diabetes screening programme conducted in adults with ID (who are often classed as a 'hard-to-reach' or 'seldom-heard' group). In total, 930 adults with ID (29% of those approached) participated in the screening programme. Most participants were either overweight or obese; 2% had a history of existing cardiovascular disease. A high proportion agreed to a blood test and subsequently, diabetes status was assessed for 675 participants (73%). The overall prevalence of screen-detected (previously undiagnosed) type 2 diabetes was 1.3% and impaired glucose regulation 5.2%. Participants of non-white ethnicity (OR 3.93) or with a first degree family history of diabetes (OR 3.35) were more likely to have abnormal glucose levels.

Comparison with previous evidence

Data to enable comparison of rates for both screen-detected type 2 diabetes and impaired glucose regulation in ID populations are currently limited. We are aware of two previous studies (de Winter *et al.* 2015, Wee *et al.* 2014) where screening for diabetes has been part of the study aim. However, no studies have previously included screening for impaired glucose regulation. The Healthy Ageing and Intellectual Disability (HA-ID) study (de Winter et al. 2015), which assessed diabetes status for a sample of 702 older adults with ID from the Netherlands, found an overall prevalence of 12.5% for type 2 diabetes. However, identification of diabetes was based on venepuncture (fasting serum glucose level >6.1 mmol/l) and/or current medication (use of glucose lowering drugs), and the authors estimate that only around half of those identified with diabetes were previously undiagnosed. This is

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substantially higher than the prevalence (1.3%) that we identified, but may reflect the relatively older age of the HA-ID cohort (age ≥50 years, mean 61) in comparison to our study (≥18 years, mean 43). A smaller study (n=227) conducted in Singapore (Wee et al. 2014) which explored health screening for people with ID and cardiovascular risks factors, found an overall prevalence of type 2 diabetes of 10.6% but only 3.1% for new screen-detected cases (based on fasting blood glucose). Similarly, the population was older than for our study (age ≥40 years, median 46).

Despite finding a lower rate of type 2 diabetes, the high levels of overweight and obesity we found (a combined 68%) were broadly the same as those reported by the HA-ID study (~64%) and Wee et al (~65%), (de Winter *et al.* 2012, Wee et al. 2014). The proportion of participants who were immobile and/or wheelchair bound across all three studies was also very similar (10%, our study; 9% (Wee et al. 2014); 11% (de Winter et al. 2015)).

In addition, the low prevalence of abnormal glucose regulation (impaired glucose regulation or type 2 diabetes) we found was substantially less than for previous diabetes screening studies conducted in non-ID populations, in the same multi-ethnic locality. The Let's Prevent Diabetes and the Walking Away from Diabetes studies both identified around 30% of people as having undiagnosed type 2 diabetes or impaired glucose regulation (Gray *et al.* 2012). Although, for these studies, only high risk individuals were invited to be screened.

Strengths and limitations

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The integration of a multi-disciplinary team, consisting of experienced researchers and ID healthcare professionals, enabled the successful development and conduct of the STOP Diabetes screening programme. This multi-disciplinary approach allowed for sharing of knowledge and best practice, and was complemented by service user involvement, particularly in the early stages of developing and trialling study procedures/processes (Tyrer *et al.* 2016).

The screening programme developed utilised robust methods. All data were collected by staff who had undertaken study specific training and following standard operating procedures. Minimal exclusion criteria were applied for including people in the study, and 'reasonable adjustments' to facilitate inclusion, such as easy-read documents, flexible appointments, and carer involvement, maximised participation. This ensured that people with all levels of ID (mild to severe/profound) had the opportunity to take part and were not arbitrally excluded. Additionally, we applied a staged approach to invitation and made efforts to contact/follow-up all people where possible.

It is acknowledged that we were unable to establish any contact with approximately 30% of people, who were non-responders. We therefore do not know if they are different in any way to people included in the screening programme; evidence suggests that people with mild ID may be at increased risk due to unhealthier lifestyles but less likely to access services (Hatton *et al.* 2014). However, similarities in the demographic characteristics of participants in this study (58% male, 20% non-white ethnicity, 66% aged <50 years), when compared with adults with ID on the Leicestershire Learning Disability Register (57% male, 17% non-white ethnicity, 68%

<50 years, from data supplied by local ID services), suggests that the STOP Diabetes cohort is a representative sample of the ID population known to services within the Leicester, Leicestershire and Rutland area.

We recognise that the recruitment approach utilised for the screening study may not be transferable to other areas. Recruitment was facilitated by the Leicestershire Learning Disability Register, only one of three adult ID case registers in England (Watson 2003), and accounted for 40% of people invited (~39% of participants). However, we only approached people via this route for general practices that declined to take part in the study and we feel that approaches such as direct invitation and invitation via ID psychiatric service clinics could possibly be replicated in other areas.

A potential limitation of this study is that we were unable to provide an overall prevalence rate for type 2 diabetes. Our study specifically aimed to screen adults with ID for undiagnosed type 2 diabetes and impaired glucose regulation, using similar methodology to previous large studies conducted in the general population (Gray *et al.* 2012). Based on current data for both screen-detected and previously diagnosed diabetes supplied at the end of the study by 40 (55%) of the participating general practices, the prevalence of diagnosed diabetes (type not specified) locally is 9.5% (n=148 of 1553 adults 18-74 years with ID), thus inferring a prevalence of around 8.5% for type 2 diabetes (based on 85-90% of all diabetes being type 2 (Hex *et al.* 2012)). These rates, alongside the higher recorded uptake of health checks conducted annually for people with ID by local general practices (57-66% (Public Health England 2014a)) compared with the national average (44%) (Public Health

England 2014b), suggest that our findings may simply reflect a successful local annual health checks programme. However, it is acknowledged that the proportion of adults with ID who currently have bloods checked, including for diabetes, as part of their annual health check is unclear.

Implications for clinical practice and future research

Obesity and sedentary behaviour are both major modifiable risk factors for type 2 diabetes and cardiovascular disease, and continue to be the focus of diabetes prevention initiatives (International Diabetes Federation 2015, World Health Organisation 2013). In our study we found high levels of overweight/obesity (68%) and sedentary behaviour (around half of participants in our study reported spending "a lot" or "most/all" of the day sitting). These findings are in keeping with previously reported evidence in the ID population (Hsieh *et al.* 2014, Stancliffe *et al.* 2011, Melville *et al.* 2017) and emphasise the need for targeted lifestyle prevention strategies which are specifically tailored for the needs of people with ID.

The screening uptake of 29% of those approached was relatively favourable when compared with two previous screening/prevention studies conducted locally in the general population, where 22% and 19% of those invited took part (Gray et al. 2012). Due to the heterogeneity of the ID population and the involvement of carers who often act as gate keepers, it may be helpful for future research to explore possible reasons for non-participation. Bloods to enable diabetes screening were successfully obtained for a high proportion of participants. However, future research may wish to consider allowing for separate consent for blood tests so as to not deter people at the initial recruitment stage. Very few people directly expressed "the blood test" as a

reason for refusal to participate in the screening study; but anecdotal evidence suggests this may have deterred some. Alternatively, a staged approach to screening, involving risk stratification as recommended by the National Institute for Health and Care Excellence in the UK (NICE 2012). This could involve integrating a diabetes risk score at practice level to identify high risk people to screen and/or development of an accessible risk score for use by carers.

Although the cost effectiveness of screening programmes for impaired glucose regulation and diabetes in the general population has been evaluated, we were unable to conduct similar work in the ID population owing to the low prevalence of screen-detected type 2 diabetes and lack of referral pathways in clinical care.

Conclusion

In conclusion, results from this large multi-ethnic cohort suggest a low prevalence of screen-detected (previously undiagnosed) type 2 diabetes and impaired glucose regulation in adults with ID. Studies conducted in the same locality in a non-ID population identified 30% with undiagnosed type 2 diabetes or impaired glucose regulation. However, the high levels of overweight and obesity we found emphasise the need for targeted lifestyle prevention strategies, which are specifically tailored for the needs of people with ID.

ACKNOWLEDGEMENTS

Author contributions:
AJD was the lead researcher/project manager for the programme and was responsible for its design and conduct, and drafted and revised the manuscript. FT led on recruitment from the Leicestershire Learning Disability Register and drafted and revised the manuscript. LJG designed the statistical analysis plan, analysed the quantitative results and oversaw their reporting and interpretation, and contributed to drafting and revising the manuscript. SB was the Principal Investigator from Leicestershire Partnership NHS Trust, and had input into the design and conduct of

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the study and reviewed the final manuscript. RS contributed to all components of the research and reviewed the final manuscript. YC analysed the quantitative results and led on their reporting and interpretation (under the supervision of LG), and reviewed the final manuscript. S-AC was involved with the design and conduct of the study and reviewed the final manuscript. SKG had input into the design and conduct of the study and reviewed the final manuscript. MJD contributed methodological and practical advice to the research programme and reviewed the final manuscript. KK was the Chief Investigator for the study and conceived the idea for the study, contributed methodological and practical advice to all components of the research programme, and commented on drafts of the manuscript and approved the final version.

Conflicts of interest:
SB has been a member of the NIHR Health Services and Delivery Research (researcher-led) panel for the last three years. S-AC has received grants from the NIHR during the conduct of the study, and grants from the NIHR and from the Scottish Government outside of the submitted work. MJD and KK (Chair) are members of the National Institute for Health and Clinical Excellence (NICE) public health guidance on preventing type 2 diabetes and both are advisers to the UK Department of Health for the NHS Health Checks Programme. MJD has acted as consultant, advisory board member and speaker for Novo Nordisk, Sanofi-Aventis, Lilly, Merck Sharp & Dohme, Boehringer Ingelheim, AstraZeneca and Janssen and as a speaker for Mitsubishi Tanabe Pharma Corporation. She has received grants in support of investigator and investigator-initiated trials from Novo Nordisk, Sanofi-Aventis and Lilly. She has received grants and support from the NIHR during the

conduct of this study. KK has acted as a consultant, served on advisory boards for and speaker for Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Janssen, Boehringer Ingelheim and Merck Sharp & Dohme. He has received grants in support of investigator and investigator-initiated trials from Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Roche, Boehringer Ingelheim and Merck Sharp & Dohme. He has also received grants and support from the NIHR during the conduct of this study. For all other authors, no potential conflicts of interest relevant to this article were reported.

Ethical approval

The study was conducted in accordance with the approvals granted by the East of England - Cambridge Central Research Ethics Committee (reference: 12/EE/0340), Leicestershire Partnership NHS Trust, Leicester City Clinical Commissioning Group (CCG), East Leicestershire & Rutland CCG, West Leicestershire CCG, and University Hospitals of Leicester NHS Trust.

The study is registered with ClinicalTrials.gov, number NCT02513277

Supplementary information and data are available on request from the authors.

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Figure Legends

Figure 1: Recruitment pathway: invitation to screening

Figure 2: Flow chart of recruitment

Table 1: Key characteristics of participants

Characteristics		Total no with measure	Mean (± SD) or n (%)
Demographic			
Age (years)		930	43.3 (± 14.2)
Sex, Male, n (%)		930	537 (57.7)
Ethnicity, n (%)		930	
White			748 (80.4)
Asian			147 (15.8)
Black			14 (1.5)
Mixed			13 (1.4)
Other			8 (0.9)
Severity of ID		865	
Not known			49 (5.7)
Known			816 (84.3)
Mild			260 (30.1)
Moderate			244 (28.2)
Severe			279 (32.3)
Profound			33 (3.8)
Anthropometric Measurements			
Waist circumference (cm)		796	100.4 (± 16.5)
Weight (kg)		799	76.4 (± 20.7)
BMI (kg/m2)		782	28.7 (± 7.1)
BMI Categories, n (%)	Underweight		30 (3.8)
	Normal		223 (28.5)
	Overweight		241 (30.8)
	Obese		288 (36.8)
Blood Pressure Measurements		826	
Systolic (mmHg)			121.4 (± 16.9)
Diastolic (mmHg)			78.2 (± 11.1)
Bloods			
Glycated haemoglobin		675 (27)	
HbA1c (mmol/mol)			35.0 (± 5.1)
Derived HbA1c (%)			5.4 (± 0.5)
Plasma glucose			
Fasting (mmol/l)		425 (8)	4.7 (± 0.7)
Non-fasting (mmol/l)		239 (16)	5.3 (± 1.5)
Lipids			
Total cholesterol (mmol/l)		653	4.9 (± 1.0)
HDL Cholesterol (mmol/l)		644	1.3 (± 0.4)
LDL Cholesterol (mmol/l)		631	2.9 (± 0.9)
Triglycerides (mmol/l) [a]		407	1.4 (± 0.9)
Medical history			
Physical Health		929	
Stroke			13 (1.4)
Coronary heart disease			7 (0.8)
Congenital heart disease			19 (2.1)
Other heart problems			15 (1.6)
High blood pressure			63 (6.8)

High cholesterol		62 (6.7)
Hypothyroidism		93 (10.0)
Chronic breathing problems		88 (9.5)
Epilepsy		262 (28.2)
Mental Health	929	
Dementia		18 (1.9)
Schizophrenia, schizotypal, delusional		35 (3.8)
Mood (affective) disorders		152 (16.4)
Neurotic, stress-related, somatoform		143 (15.4)
Personality disorders		13 (1.4)
Attention Deficit Hyperactivity Disorder		8 (0.9)
Autistic spectrum disorders		165 (17.8)
Behavioural problems		128 (13.8)
Current medication	928	
Anti-psychotic		240 (25.9)
Depression / Anxiety/ OCD or related		258 (27.8)
For ADHD4 (0.4)		
Anti-epileptic		311 (33.5)
Anti-thrombotic		36 (3.9)
Lipid lowering		74 (8.0)
Anti-hypertensive		85 (9.2)
Thyroid medication		93 (10.0)
Steroids		80 (8.6)
Smoking status	929	
Current		76 (8.2)
Ex		38 (4.1)
Never		815 (87.7)
Family history of diabetes	592	180 (30.4)
<u>Mobility</u>		
Able to walk	927	
Yes (with or without walking stick, aid)		787 (84.9)
Yes, with assistance from person(s)		83 (9.0)
No		57 (6.2)
Amount of walking per day	927	
None		74 (8.0)
A short distance		259 (27.9)
Some		359 (38.7)
Lots		235 (25.4)
<u>Nutrition and diet</u>		
Problems relating to eating and drinking		
Difficulties with chewing or swallowing	929	227 (24.4)
Needs help or assistance to feed self	926	118 (12.7)
Daily portions of fruit and vegetables	920	
5 or more		271 (29.5)

[a] only if fasted.
Data given as mean (±SD) for continuous outcomes and n (%) for categorical.
ADHD, Attention deficit hyperactivity disorder; BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high density lipoprotein; ID, intellectual disability; LDL, low density lipoprotein; OCD, Obsessive compulsive disorder.

Table 2: Prevalence of previously undiagnosed type 2 diabetes and impaired glucose regulation
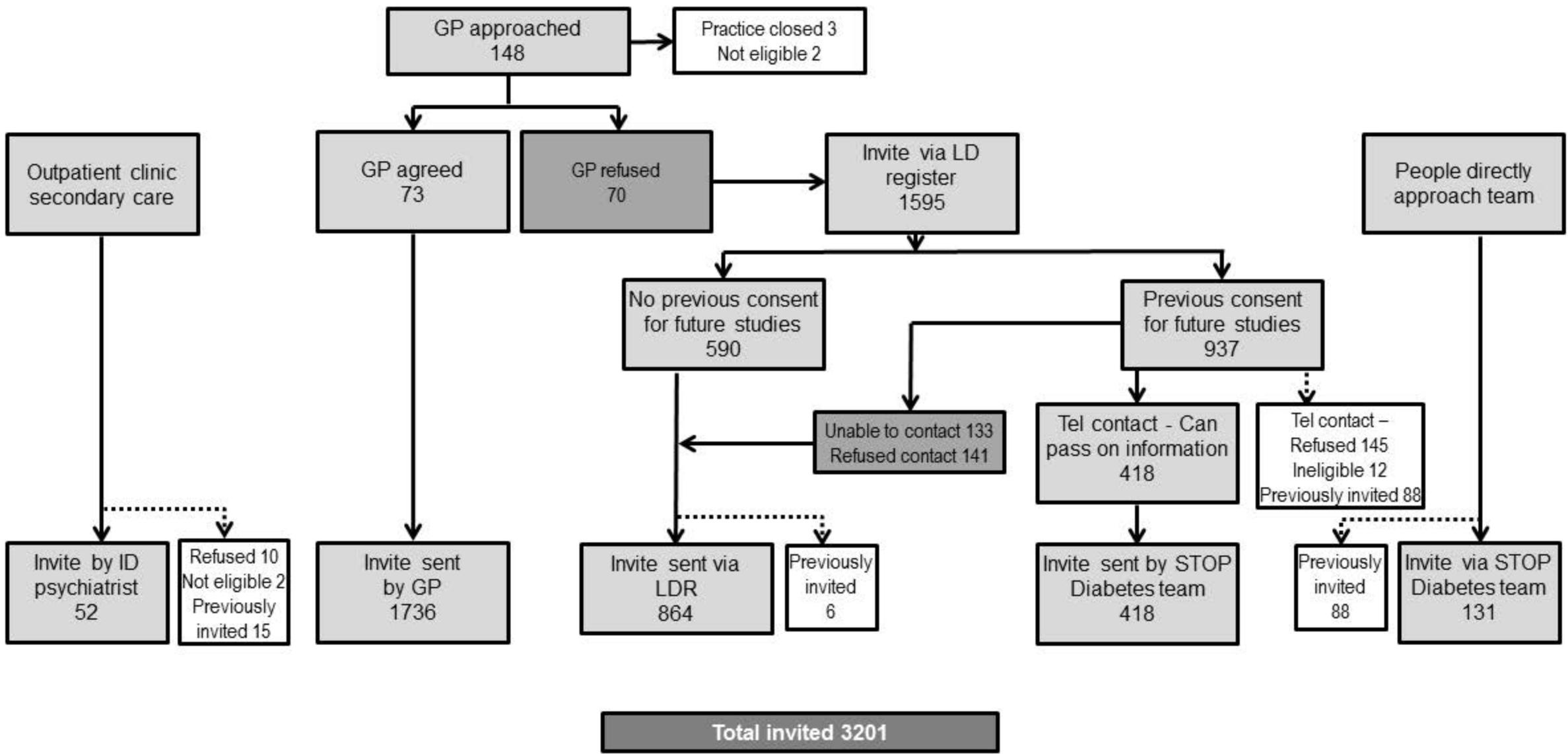
	N (%)	95% CI
Outcome:		
Normal glucose	631 (93.5)	(91.3, 95.2)
Impaired glucose regulation	35 (5.2)	(3.6, 7.1)
Type 2 diabetes	9 (1.3)	(0.6, 2.5)
Abnormal glucose	44 (6.5)	(4.7, 8.4)

Table 3: Comparison of anthropometric and biomedical characteristics of those with normal and abnormal glucose regulation
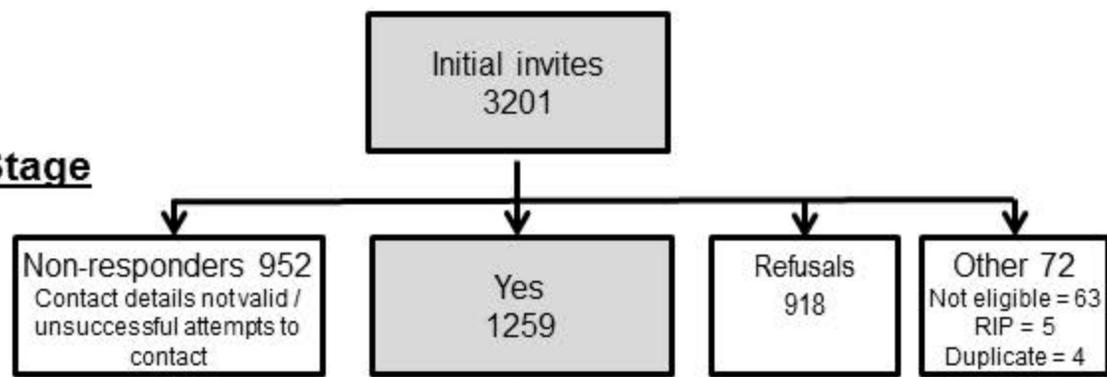
	Normal Glucose (n = 631)	Abnormal Glucose (n=44)	OR (95% CI)	P value
Age, years	43.0 (±14.3)	45.4 (±13.5)	1.01 (0.99, 1.03)	0.27
Male	377 (59.8)	28 (63.6)	1.18 (0.63, 2.22)	0.61
Non-white ethnicity	119 (18.9)	21 (47.7)	3.93 (2.10, 7.33)	<0.0001
Weight, kg	76.6 (±20.2)	91.7 (±27.3)	1.03 (1.01, 1.04)	<0.0001
Waist circumference, cm	100.1 (±16.2)	114.0 (±19.0)	1.04 (1.03, 1.07)	<0.0001
Hip circumference, cm	107.4 (±13.5)	115.6 (±19.1)	1.03 (1.01, 1.06)	0.001
Body mass index, kg/m^2	28.6 (±6.9)	34.1 (±10.2)	1.08 (1.04, 1.13)	<0.0001
Current smoker	56 (8.9)	6 (13.6)	1.62 (0.66, 4.00)	0.30
FH of diabetes	132 (29.9)	20 (58.8)	3.35 (1.64, 6.86)	0.001
Systolic BP, mmHg	121.8 (±17.3)	126.5 (±14.4)	1.01 (1.00, 1.03)	0.09
Diastolic BP, mmHg	78.0 (±11.2)	83.7 (±10.0)	1.04 (1.02, 1.07)	0.002
Total cholesterol, mmol/l	4.9 (±1.0)	4.7 (±0.9)	0.78 (0.56, 1.10)	0.15
HDL cholesterol, mmol/l	1.4 (±0.4)	1.2 (±0.3)	0.14 (0.05, 0.43)	0.001
LDL cholesterol, mmol/l	2.9 (±0.9)	2.7 ±(0.8)	0.71 (0.48, 1.07)	0.10
Triglycerides, mmol/l	**1**.4 (±0.9)	1.9 (±1.0)	1.53 (1.11, 2.11)	0.01

Data given as mean (±SD) for continuous outcomes and n (%) for categorical.
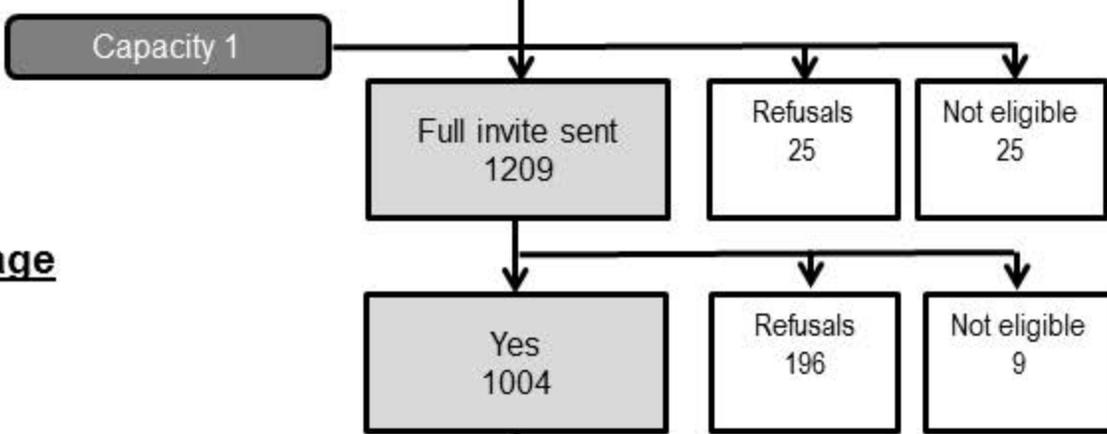
BP, blood pressure; FH, family history; HDL, high density lipoprotein; LDL, low density lipoprotein.
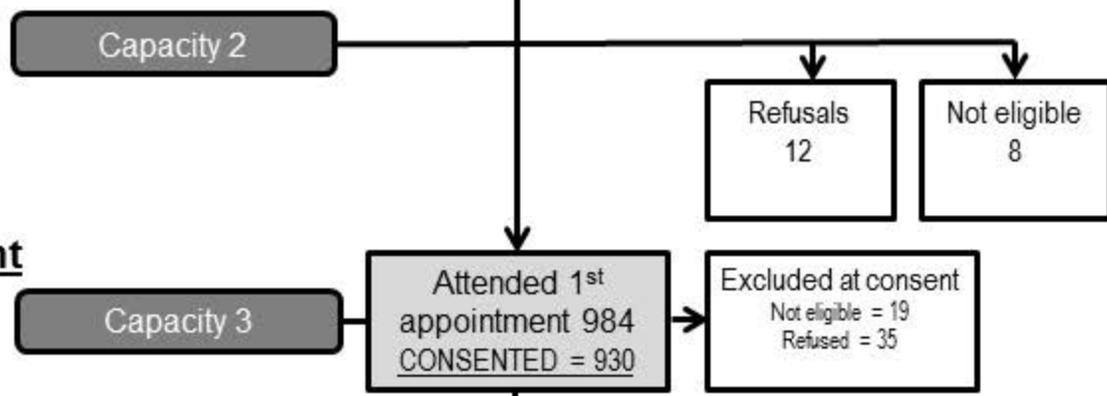
Initial Stage

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                        Initial invites
                           3201
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Initial Stage

Non-responders 952	Yes	Refusals	Other 72
Contact details not valid / unsuccessful attempts to contact	1259	918	Not eligible = 63 RIP = 5 Duplicate = 4

Capacity 1

Full invite sent 1209	Refusals 25	Not eligible 25

Full Stage

Yes 1004	Refusals 196	Not eligible 9

Capacity 2

Refusals 12	Not eligible 8

Consent

Capacity 3

Attended 1st appointment 984 CONSENTED = 930	Excluded at consent Not eligible = 19 Refused = 35

Arranged blood appointment 825	Refusals 105 Withdrew (ill health) = 2 Refused = 103

Bloods

Blood results possibly unreliable = 5	Attended blood appointment 825	Not assessed 172 Refused bloods = 125 Unable to obtain bloods = 47	If available Blood results (HbA1c) obtained from medical records = 27

NORMAL 631	IGR 35	T2DM 9