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Incidental Findings of Elevated Random Plasma Glucose in the ED as a Prompt for Outpatient Diabetes Screening: A Retrospective Study

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Contributorship: SMF was senior responsible author, designed the trial and implemented the plan. BB and JV performed chart review and telephone interview. SF and BB analyzed the data. SF, BB, and JV drafted the manuscript. SF revised the draft paper.

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Abstract

Objective: To determine if Random Plasma Glucose (RPG) collected in ED patients without known impaired glucose metabolism (IGM) is a useful screen for diabetes or pre-diabetes.

Design: Retrospective cohort study

Setting: Emergency Department (ED) of a Canadian teaching hospital over one month.

Participants: Adult ED patients with RPG over 7.0 mmol/l were recruited for participation. Exclusion criteria included known diabetes, hospital admission, and inability to consent. Subjects were contacted by mail, encouraged to follow-up with their FP for further testing, and subsequently interviewed.

Outcome Measures: The primary outcome measure was the proportion of ED patients with RPG over 7.0 mmol/l) and no previous diagnosis of IGM who were diagnosed with diabetes or pre-diabetes as defined by secondary testing by FP with OGTT or FPG. Secondary outcomes included patient characteristics (age, gender, BMI, language) and (2) compliance with advice to seek appropriate follow-up care.

Results: Random plasma glucose (RPG) was drawn on approximately one third (33%, n=1149) of the 3470 ED patients in March 2010. RPG over 7.0 mmol/l was detected in 24% (n=278) and after first telephone follow-up, 32% (n=88/278) met inclusion criteria and were advised to seek confirmatory testing. 41.0% (n=114/278) were excluded for known diabetes. 73% of patients contacted (n=64/88) followed up with their FP. 12.5% (n=11/88) had abnormal fasting plasma glucose, and of these 11% (n=10/88) were encouraged to initiate lifestyle modifications, and 1% (n=1/88) was started on an oral hypoglycemic agent. For 7% (n=6/88) of the patients, FP's declined to do follow-up fasting bloodwork.

Conclusion: Elevated RPG in the ED is useful for identification of patients at risk for IGM and in need of further diabetic screening. Emergency physicians should advise patients with elevated RPG to consider screening for diabetes. For ED screening to be successful, patient education and collaboration with family physicians is essential.

Keywords: Diabetes Mellitus, Type 2, Emergency Medicine, Screening, Blood Glucose

Article Summary

Article Focus

- An estimated 15.3% of the Canadian population does not have a family physician (FP) and these patients as well as those who do not visit their FP routinely are being missed by diabetes current screening practices

- We followed up on patients in the emergency department who were noted to have a random (nonfasting) plasma glucose > 7.0 mmol/l

- We hypothesized that a proportion of these patients would have previously undetected diabetes or impaired glucose metabolism.

Key Messages

- Approximately 1 in 8 people without previously diagnosed diabetes who completed follow-up were found to have IGM.

- When using an appropriate cut-off, RPG (random plasma glucose) can reliably detect a significant portion of undiagnosed diabetes with acceptable specificity

- This pilot study suggests that the ED has good potential to screen for T2DM, and supports the use of RPG as an opportunistic screening tool

Strengths and Limitations of the Study

- A small sample size may have precluded determination of significant differences between subgroups.

- Logistics of the study and health privacy concerns precluded collection of follow-up test results (i.e. HbA1c, FPG and OGTT) directly from the FPs as opposed to the participants of the study.

- As the study was performed at a single site, generalization to the Canadian urban ED population should be viewed cautiously.

Introduction

Approximately 300 million adults are affected with diabetes worldwide, and this number is expected to rise to 439 million over the next 2 decades <1>. In Canada, an estimated 2.8 million people have been diagnosed with diabetes <2> and approximately 6% of the population may be living with undiagnosed diabetes and pre-diabetes <3>. Diabetes is a cause of significant morbidity and mortality; it is a major contributor to cardiovascular and cerebrovascular disease, and is the leading cause of blindness, end-stage renal failure and non-traumatic amputations in Canadians <4>. In 2010, the estimated cost of diabetes to the Canadian economy was $6.3 billion annually, and this is expected to nearly triple over the next decade <5>.

Approximately 90% of diabetes in the population is type II diabetes (T2DM) <6>, which has a prolonged asymptomatic period of 5-12 years <7>. During this time hyperglycemia develops insidiously and causes significant functional changes to various target tissues. <7,8> At time of diagnosis, about 20% to 30% have developed diabetes related complications <8>. Screening tests for diabetes allow diagnosis during the asymptomatic diabetic and pre-diabetic stages, and can contribute to reduced morbidity and mortality. The implementation of lifestyle and pharmacological interventions during the pre-diabetic stage can prolong and even prevent the onset of diabetes <9,10>, and control of hyperglycemia during the early diabetic stage has long-term benefits in delaying the progression of complications and reducing the risk of premature death. <11>

The diagnosis of diabetes is typically made on the basis of a Fasting Plasma Glucose (FPG) > 7.0 mmol/l, or random plasma glucose (RPG) > 11.1 mmol/l with symptoms of diabetes, or a 2 hour plasma glucose >=11.1 mmol/l in a 75 G OGTT. The term “prediabetes” is a term for impaired fasting glucose or impaired glucose tolerance, which are conditions that place the patient at high risk of developing diabetes. Prediabetes is diagnosed on the basis of a fasting plasma glucose between 6.1mmol/l and 6.9 mmol/l, and warrants further confirmatory testing. <4>

Screening initiatives for diabetes have generally focused on the primary care setting and the use of fasting plasma glucose and oral glucose tolerance tests (OGTT). <12> More recently, glycated hemoglobin (HbA1C) has been accepted as an alternative diagnostic test for T2DM. The Canadian Task Force on Preventive Health Care advises HbA1C testing every 3-5 years for routine screening of adults at high risk of diabetes. <13> However, an estimated 15.3% of the Canadian population does not have a family physician (FP) and these patients as well as those who do not visit their FP routinely are being missed by the current screening practices <14>.

Several studies have characterized the emergency department (ED) as a promising venue for diabetes screening, particularly of benefit for those individuals who do not have access to routine primary care. It is estimated that half of all ED patients have a random plasma glucose (RPG) drawn and there is emerging support of RPG as an opportunistic screening tool in the ED. RPG

has a moderate correlation with HbA1c, and has been used to identify a significant portion of patients in EDs with undiagnosed impaired glucose metabolism (IGM) <15,16,17,18,19>.

There have been no studies that have looked at RPG screening for diabetes in Canadian EDs. The primary objective of this study was to determine if RPG collected in a Canadian ED is a useful way to screen for patients at risk for IGM who may otherwise not be identified. There are currently no guidelines for using RPG as a screening tool. In this study, a screening threshold of RPG > 7.0 mmol/l was selected to minimize false positives yet provide adequate sensitivity to prompt further confirmatory testing for prediabetes and diabetes. This selection was based on studies including that by Ziemer et al. which explored the sensitivity and specificity of various RPG cut-offs and found that a cut-off of 7.0 mmol/l was provided 93% specificity and 40% sensitivity for identifying diabetes.<19>

Methods:

Study Design: Retrospective cohort study

Setting: ED in Toronto Western Hospital (TWH), an urban teaching hospital in downtown Toronto that sees more than 40,000 emergency visits annually.

Participants:

Using electronic chart review, we retrospectively identified patients visiting the ED over a one month period who had a random plasma glucose drawn in the ED. Patients 18 years of age and older with RPG >7.0 mmol/l, with access to telephone services, and who were able to provide verbal consent and were willing to complete follow-up testing (see below) were included in the study. Patients were excluded from the study if they: (1) had known IGM or a prior history of diabetes, (3) were on diabetic medication, (4) were admitted to hospital, (5) were deceased, or (6) were unable to provide informed consent as they were non-English speaking or confused.

Methods:

The hospital electronic patient record data was searched retrospectively for ED visits during a one month period in cases where RPG was sampled and was >7.0 mmol/l. Flagged charts were reviewed by the researchers (BB) to identify inclusion/exclusion criteria and for recording of additional demographic information (i.e. age, gender, language). A letter of introduction to the study (with opt-out option) was mailed to patients meeting inclusion criteria. The letter also included the level of the patient's elevated RPG, with instructions to follow-up with their family doctor for further diabetic screening. Within two to four weeks of posting the letter these patients were contacted by telephone by one of the researchers (JVP, BB, AS). If the patient provided verbal consent, a brief standardized telephone interview was conducted, and the patient was advised to seek confirmatory testing with a primary care providor. A second post-intervention phone follow-up was made to determine if the patient sought follow-up care, and to record results of follow-up tests. In order to maximize data acquisition, a minimum of 8 attempts over eight weeks were undertaken for participants who were difficult to reach or who delayed seeking follow-up care. This study was approved by the hospital Research Ethics Board.

This study was powered to identify at least 10 diabetic patients with incidental findings of elevated RPG. Based on previously reported studies, we anticipated a 20% prevalence of new diagnosis of diabetes. With worst case scenario expectations of 50% of charts with RPG>7.0 mmol/l meeting exclusion criteria, 50% compliance with first telephone interview, and 80% participation in second telephone interview, we aimed to analyze at least 250 ED visits with RPG>7mmol/l.

Outcome Measures:

The primary outcome measure was the proportion of ED patients with RPG over 7.0 mmol/l) and no previous diagnosis of IGM who were diagnosed with diabetes or pre-diabetes as defined by secondary testing by family physicians with the OGTT or FPG. The secondary outcomes were: (1) characteristics (by age, gender, BMI, language) of the patient population presenting with elevated RPG; and (2) patient compliance when this population was encouraged to seek appropriate follow-up care.

Data Analysis:

Data was entered into Microsoft Office Excel 2007 and transferred to SPSS version 17.0 for statistical analysis. Independent T-tests were used to compare means for continuous variables, and chi square tests for categorical variables.

Results:

During the one month study period (March, 2010), 3470 patients visited the TWH ED. 33% (n=1149) of these patients had RPG measured and of these patients 24% (n=278) had RPG over 7.0 mmol/l. After the first telephone follow-up, 31% (n=88 / 278) of the patients met inclusion criteria to participate in the study. (See Figure 1 for flow diagram of subjects.)

Mean RPG of enrolled subjects was approximately 8.4 mmol/l and BMI approximately 28 kg/m^2. Patients who were not contactable did not significantly differ by age or gender from those that were (data not shown). The majority of these patients spoke English (77%, n 68), followed by Portuguese (10%, n=9) and the others (13%, n=11) spoke one of 14 different languages. (See Table 1 - Baseline characteristics).

73% of patients (n = 64) followed up with their FP. There were no significant differences in age, BMI or initial RPG between those who sought follow-up and those that did not. After eight weeks and up to eight telephone attempts, 27.3 % (24/88) were either unreachable or had not followed up with their family doctor.

73% of patients (n=64/88) who participated in telephone follow-up saw their FP for blood-work. The FP subsequently diagnosed impaired glucose metabolism in 12.5% (n=11/88 study participants meeting inclusion criteria, or 17.1 % (11/64) of those following up with the FP), with institution of dietary and lifestyle modifications in 11.4 % (n=10/88), and oral hypoglycemic agent (OHGA) in 1.1 % (n=1/88). There were no significant differences in baseline characteristics (Age, BMI, RPG) between those who were diagnosed with IGM versus those that were not (see: Table 2)

The family physician did not perform confirmatory testing (i.e. 75 G OGTT) in 7% (n=6/88) of the patients who brought them the letter mailed from the ED advising confirmatory testing.

Discussion:

Approximately 1 in 8 people without previously diagnosed diabetes who completed follow-up were found to have IGM. RPG as a screening tool for diabetes in the acute care setting has been criticized on the grounds that transient stress-induced hyperglycemia and the non-fasting state act as confounders that make the interpretation of this test difficult. Despite this, many studies have shown that when using an appropriate cut-off, RPG can reliably detect a significant portion of undiagnosed diabetes with acceptable specificity <15,16,17,18,19,20>. George et al. <19> found that over half of the patients presenting to the ED with undiagnosed diabetes and random capillary blood glucose (RCBG) over 7.0mmol/l fulfilled criteria for IGM. This substantial number may be an underestimate as the researchers only used fasting plasma glucose and not the OGTT test for diagnosing IGM, thus missing people with impaired glucose tolerance. Charfen et al.<14> also found that amongst ED visitors with undiagnosed diabetes, 66% of those with two or more diabetes risk factors or RPG over 7.0mmol/l (or over 7.8mmol/l if food was ingested within 2hrs of the test) fulfilled criteria for IGM. Ziemer et alanalyzed the sensitivity and specificity of various RPG cut-offs and found that a cut-off of 7.0mmol/l has 93% specificity and 40% sensitivity for identifying diabetes. <19>

A finding of IGM in 1 in 8 people with previously undiagnosed diabetes is significant given the substantial burden that diabetes has at the individual and community levels. This screening effort did present some cost to the patients and the health-care system, including use of resources, clinician time and potential psychological stress in patients. One consideration to optimize cost versus benefit is to improve the yield of screening by targeting patients with risk factors for T2DM and/or those who do not regularly access primary care.

Age and BMI are important risk factors for diabetes <3,15,16>. In our study, there was a nonsignificant trend towards a slightly higher age and BMI for people with impaired glucose tolerance, which is in keeping with findings from other studies. The lack of significant difference in our study may reflect a study sample size limitation.

A challenge in using the ED to screen for diabetes is the need for follow-up by patients with their FPs. Lack of follow-up has consistently been identified as a problem in other studies, often trending towards half of patients not following up <15,17,18>. The high follow-up rate in our study may be attributable to a more health-conscious Canadian population or may likely be due to a substantial number of reminder telephone calls (minimum of 8) from the study researchers to patients delaying follow-up. Poor follow-up has often been cited as an argument against using the ED for routine screening <15,17,18>. Suggestions for improvement include investigators notifying the FPs directly, ED diabetic teaching, and reminders to patients to seek follow-up care.

A further challenge in using the ED for screening is poor follow-up by physicians. In the current study, 7% of FPs did not do further testing despite patient request. In a pilot study be

Hewat et al, the proportion was 50%. <18>.This phenomenon may be attributable to the controversial role for RPG in screening for diabetes and this stresses the importance of FP education to ensure improved collaboration with the ED. A study by Ginde et al <21>showed that in a U.S. ED setting, elevated RPG was often overlooked and not communicated to patients by ED physicians. This supports the argument that ED physician education would also be an essential component of an ED diabetes screening program.

Limitations:

A small sample size may have precluded determination of significant differences between groups. As the study was performed at a single site, generalization to the Canadian urban ED population should be viewed cautiously. However, similar studies from other parts of the world support these findings and suggest that a finding of high RPG should prompt further outpatient evaluation for diabetes.

Logistics of the study and health privacy concerns precluded collection of follow-up test results (i.e. HbA1c, FPG and OGTT) directly from the FPs as opposed to the participants of the study. It would also have been informative to analyze presenting complaints to the ED and time of last meal to determine other contributors to increased RPG. (We note that a proportion of RPG samples collected may have in fact been fasting for 8 hours at the time that blood was drawn in the ED, and thus in fact serve as a fasting plasma glucose). A thorough analysis of diabetes risk factors would have been beneficial, as would determining which patients had FPs prior to and after the study.

Conclusions:

This was the first study looking at the use of the Canadian ED as a screening point for diabetes. This pilot study suggests that the ED has good potential to screen for T2DM, and supports the use of RPG as an opportunistic screening tool. For ED screening to be effective, good collaboration with FPs is essential. Further multi-centered large scale studies are required to form a more conclusive opinion with regards to the widespread use of Canadian EDs as a screening point.

Contributorship: SMF was senior responsible author, designed the trial and implemented the plan. BB and JV performed chart review and telephone interview. SF and BB analyzed the data. SF, BB, and JV drafted the manuscript. SF revised the draft paper.

Data sharing: Data published in this study will be made freely available upon request, free of charge, in the format of an Excel spreadsheet, stripped of patient identifiers.

Competing Interests: None

Funding: None

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Figure 1

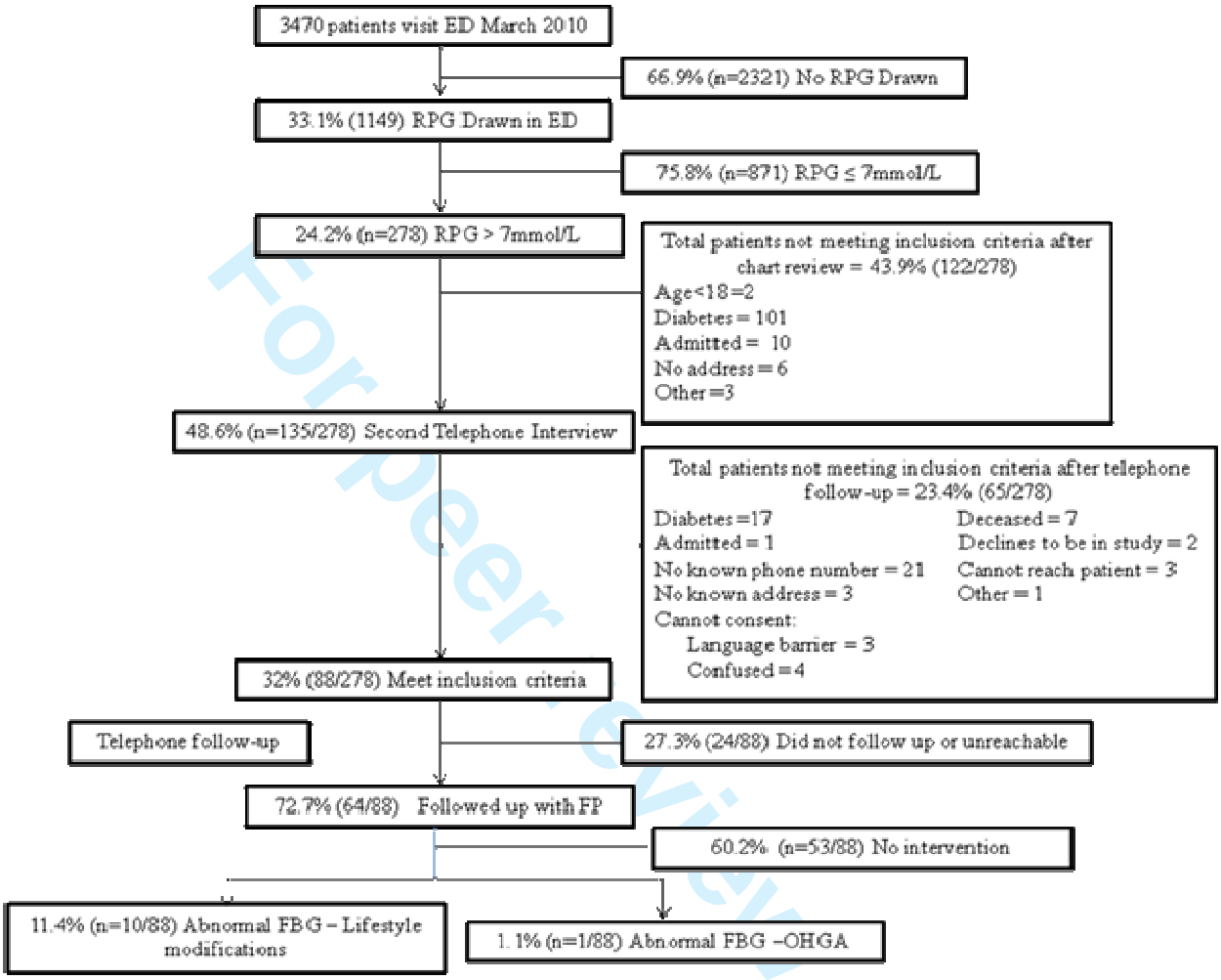

Figure 1. Consort diagram. ED = Emergency Department; RPG = Random plasma glucose; OHGA = Oral hypoglycemic agent; FBG = Fasting blood glucose; FP = family physician

Table 1. Baseline characteristics of participants included in final data analysis

Age, BMI and RPG by gender			
	Female (n=39)	**Male (n=49)**	**Range**
Age (years)	59.03 ± 19.40	61.71 ± 16.99	21 to 92
BMI (kg/m^2)	27.56 ± 6.22	27.98 ± 6.01	17.75 to 58.00
Random Plasma Glucose (mmol/l)	8.40 ± 2.46	8.37 ± 1.19	7.10 to 21.00

 P values were calculated with t-tests
∞Plus-minus values are means ± SD
*n=9 of BMI missing data secondary to patients not disclosing weight and/or height

Table 2. Baseline characteristics of patients diagnosed with IGM versus not diagnosed

Age, BMI and RPG in patients diagnosed with IGM vs patients not diagnosed with IGM		
	Diagnosed with IGM (n=11)	**Not diagnosed with IGM (n=53)**
Age (years)	66.73 ± 12.59	59.48 ± 18.10
BMI (kg/m^2)	27.45 ± 4.17	24.73 ± 9.85
Random Plasma Glucose (mmol/l)	8.61 ± 1.03	8.42 ± 2.05

∞Plus-minus values are means ± SD
*n=24/88 of missing data secondary to patients not reachable or did not follow-up with Fp after eight weeks.

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Article Summary

Article Focus

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- We followed up on patients in the emergency department who were noted to have a random (nonfasting) plasma glucose > 7.0 mmol/l

- We hypothesized that a proportion of these patients would have previously undetected diabetes or impaired glucose metabolism.

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- Approximately 1 in 8 people without previously diagnosed diabetes who completed follow-up were found to have IGM.

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Screening initiatives for diabetes have generally focused on the primary care setting and the use of fasting plasma glucose and oral glucose tolerance tests (OGTT). <12> More recently, glycated hemoglobin (HbA1C) has been accepted as an alternative diagnostic test for T2DM. The Canadian Task Force on Preventive Health Care advises HbA1C testing every 3-5 years for routine screening of adults at high risk of diabetes. <13> However, an estimated 15.3% of the Canadian population does not have a family physician (FP) and these patients as well as those who do not visit their FP routinely are being missed by the current screening practices <14>.

Several studies have characterized the emergency department (ED) as a promising venue for diabetes screening, particularly of benefit for those individuals who do not have access to routine primary care. It is estimated that half of all ED patients have a random plasma glucose (RPG) drawn and there is emerging support of RPG as an opportunistic screening tool in the ED. RPG

has a moderate correlation with HbA1c, and has been used to identify a significant portion of patients in EDs with undiagnosed impaired glucose metabolism (IGM) <15,16,17,18,19>.

There have been no studies that have looked at RPG screening for diabetes in Canadian EDs. The primary objective of this study was to determine if RPG collected in a Canadian ED is a useful way to screen for patients at risk for IGM who may otherwise not be identified. There are currently no guidelines for using RPG as a screening tool. In this study, a screening threshold of RPG > 7.0 mmol/l was selected to minimize false positives yet provide adequate sensitivity to prompt further confirmatory testing for prediabetes and diabetes. This selection was based on studies including that by Ziemer et al. which explored the sensitivity and specificity of various RPG cut-offs and found that a cut-off of 7.0 mmol/l was provided 93% specificity and 40% sensitivity for identifying diabetes.<19>

Methods:

Study Design: Retrospective cohort study

Setting: ED in Toronto Western Hospital (TWH), an urban teaching hospital in downtown Toronto that sees more than 40,000 emergency visits annually.

Participants:

Using electronic chart review, we retrospectively identified patients visiting the ED over a one month period who had a random plasma glucose drawn in the ED. Patients 18 years of age and older with RPG >7.0 mmol/l, with access to telephone services, and who were able to provide verbal consent and were willing to complete follow-up testing (see below) were included in the study. Patients were excluded from the study if they: (1) had known IGM or a prior history of diabetes, (3) were on diabetic medication, (4) were admitted to hospital, (5) were deceased, or (6) were unable to provide informed consent as they were non-English speaking or confused.

Methods:

The hospital electronic patient record data was searched retrospectively for ED visits during a one month period in cases where RPG was sampled and was >7.0 mmol/l. Flagged charts were reviewed by the researchers (BB) to identify inclusion/exclusion criteria and for recording of additional demographic information (i.e. age, gender, language). A letter of introduction to the study (with opt-out option) was mailed to patients meeting inclusion criteria. The letter also included the level of the patient's elevated RPG, with instructions to follow-up with their family doctor for further diabetic screening. Within two to four weeks of posting the letter these patients were contacted by telephone by one of the researchers (JVP, BB, AS). If the patient provided verbal consent, a brief standardized telephone interview was conducted, and the patient was advised to seek confirmatory testing with a primary care providor. A second post-

intervention phone follow-up was made to determine if the patient sought follow-up care, and to record results of follow-up tests. In order to maximize data acquisition, a minimum of 8 attempts over eight weeks were undertaken for participants who were difficult to reach or who delayed seeking follow-up care. This study was approved by the hospital Research Ethics Board.

This study was powered to identify at least 10 diabetic patients with incidental findings of elevated RPG. Based on previously reported studies, we anticipated a 20% prevalence of new diagnosis of diabetes. With worst case scenario expectations of 50% of charts with RPG>7.0 mmol/l meeting exclusion criteria, 50% compliance with first telephone interview, and 80% participation in second telephone interview, we aimed to analyze at least 250 ED visits with RPG>7mmol/l.

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The primary outcome measure was the proportion of ED patients with RPG over 7.0 mmol/l) and no previous diagnosis of IGM who were diagnosed with diabetes or pre-diabetes as defined by secondary testing by family physicians with the OGTT or FPG. The secondary outcomes were: (1) characteristics (by age, gender, BMI, language) of the patient population presenting with elevated RPG; and (2) patient compliance when this population was encouraged to seek appropriate follow-up care.

Data Analysis:

Data was entered into Microsoft Office Excel 2007 and transferred to SPSS version 17.0 for statistical analysis. Independent T-tests were used to compare means for continuous variables, and chi square tests for categorical variables.

Results:

During the one month study period (March, 2010), 3470 patients visited the TWH ED. 33% (n=1149) of these patients had RPG measured and of these patients 24% (n=278) had RPG over 7.0 mmol/l. After the first telephone follow-up, 31% (n=88 / 278) of the patients met inclusion criteria to participate in the study. (See Figure 1 for flow diagram of subjects.)

Mean RPG of enrolled subjects was approximately 8.4 mmol/l and BMI approximately 28 kg/m^2. Patients who were not contactable did not significantly differ by age or gender from those that were (data not shown). The majority of these patients spoke English (77%, n 68), followed by Portuguese (10%, n=9) and the others (13%, n=11) spoke one of 14 different languages. (See Table 1 - Baseline characteristics).

73% of patients (n = 64) followed up with their FP. There were no significant differences in age, BMI or initial RPG between those who sought follow-up and those that did not. After eight weeks and up to eight telephone attempts, 27.3 % (24/88) were either unreachable or had not followed up with their family doctor.

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The family physician did not perform confirmatory testing (i.e. 75 G OGTT) in 7% (n=6/88) of the patients who brought them the letter mailed from the ED advising confirmatory testing.

Discussion:

Approximately 1 in 8 people without previously diagnosed diabetes who completed follow-up were found to have IGM. RPG as a screening tool for diabetes in the acute care setting has been criticized on the grounds that transient stress-induced hyperglycemia and the non-fasting state act as confounders that make the interpretation of this test difficult. Despite this, many studies have shown that when using an appropriate cut-off, RPG can reliably detect a significant portion of undiagnosed diabetes with acceptable specificity <15,16,17,18,19,20>. George et al. <19> found that over half of the patients presenting to the ED with undiagnosed diabetes and random capillary blood glucose (RCBG) over 7.0mmol/l fulfilled criteria for IGM. This substantial number may be an underestimate as the researchers only used fasting plasma glucose and not the OGTT test for diagnosing IGM, thus missing people with impaired glucose tolerance. Charfen et al.<14> also found that amongst ED visitors with undiagnosed diabetes, 66% of those with two or more diabetes risk factors or RPG over 7.0mmol/l (or over 7.8mmol/l if food was ingested within 2hrs of the test) fulfilled criteria for IGM. Ziemer et alanalyzed the sensitivity and specificity of various RPG cut-offs and found that a cut-off of 7.0mmol/l has 93% specificity and 40% sensitivity for identifying diabetes. <19>

A finding of IGM in 1 in 8 people with previously undiagnosed diabetes is significant given the substantial burden that diabetes has at the individual and community levels. This screening effort did present some cost to the patients and the health-care system, including use of resources, clinician time and potential psychological stress in patients. One consideration to optimize cost versus benefit is to improve the yield of screening by targeting patients with risk factors for T2DM and/or those who do not regularly access primary care.

Age and BMI are important risk factors for diabetes <3,15,16>. In our study, there was a nonsignificant trend towards a slightly higher age and BMI for people with impaired glucose tolerance, which is in keeping with findings from other studies. The lack of significant difference in our study may reflect a study sample size limitation.

A challenge in using the ED to screen for diabetes is the need for follow-up by patients with their FPs. Lack of follow-up has consistently been identified as a problem in other studies, often trending towards half of patients not following up <15,17,18>. The high follow-up rate in our study may be attributable to a more health-conscious Canadian population or may likely be due to a substantial number of reminder telephone calls (minimum of 8) from the study researchers to patients delaying follow-up. Poor follow-up has often been cited as an argument against using the ED for routine screening <15,17,18>. Suggestions for improvement include investigators notifying the FPs directly, ED diabetic teaching, and reminders to patients to seek follow-up care.

A further challenge in using the ED for screening is poor follow-up by physicians. In the current study, 7% of FPs did not do further testing despite patient request. In a pilot study by Hewat et al, the proportion was 50%. <18>.This phenomenon may be attributable to the controversial role for RPG in screening for diabetes and this stresses the importance of FP education to ensure improved collaboration with the ED. A study by Ginde et al <21>showed that in a U.S. ED setting, elevated RPG was often overlooked and not communicated to patients by ED physicians. This supports the argument that ED physician education would also be an essential component of an ED diabetes screening program.

Limitations:

A small sample size may have precluded determination of significant differences between groups. As the study was performed at a single site, generalization to the Canadian urban ED population should be viewed cautiously. For example, regional variations in practices and guidelines for ordering blood tests in the ED, reasons for patient presentation to the ED, and premorbid health status (i.e. prevalence of obesity diabetic risk factors) will impact generalizability of these results. However, similar studies from other parts of the world support these findings and suggest that a finding of high RPG should prompt further outpatient evaluation for diabetes.

Logistics of the study and health privacy concerns precluded collection of follow-up test results (i.e. HbA1c, FPG and OGTT) directly from the FPs as opposed to from the participants of the study. It would also have been informative to analyze presenting complaints to the ED and time of last meal to determine other contributors to increased RPG. (We note that a proportion of RPG samples collected may have in fact been fasting for 8 hours at the time that blood was drawn in the ED, and thus in fact serve as a fasting plasma glucose). Analysis of diabetes risk factors would have been beneficial, as would determining which patients had FPs prior to and after the

study. It is possible that patients who did not follow-up with their family physician are a selected subgroup with different risk factors and disease prevalence from those who did follow-up.

While excluding patients who were admitted to the ED likely removed the majority of the more acutely ill patients with febrile illnesses, we felt that it would be worthwhile to include patients despite elevated temperature, despite the potential for more 'false positive' random blood glucose results. Stratification of patients by reason of ED visit might prove useful for subgroup analysis in future studies.

Conclusions:

This was the first study looking at the use of the Canadian ED as a screening point for diabetes. This pilot study suggests that the ED has good potential to screen for T2DM, and supports the use of RPG as an opportunistic screening tool. For ED screening to be effective, good collaboration with FPs is essential. Further multi-centered large scale studies are required to form a more conclusive opinion with regards to the widespread use of Canadian EDs as a screening point.

Contributorship: SMF was senior responsible author, designed the trial and implemented the plan. BB and JV performed chart review and telephone interview. SF and BB analyzed the data. SF, BB, and JV drafted the manuscript. SF revised the draft paper.

Prior Publication:

This study was published in Can J Emerg Med in **Abstract** form:

Baswick B, Scott A, Vallipuram J, Friedman SM. Incidental findings of elevated random plasma glucose in the ED as a prompt for outpatient diabetes screening. [abstract] Can J Emerg Med May, 2011: 13(3) PP204-205

Funding Statement:

- This research received no specific grant from any funding agency in the public, commercial or not-for-profit sector.

Data sharing

Data published in this study will be made freely available upon request, free of charge, in the format of an Excel spreadsheet, stripped of patient identifiers.

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Figure legend

Figure 1. Consort diagram. ED = Emergency Department; RPG = Random plasma glucose; OHGA = Oral hypoglycemic agent; FBG = Fasting blood glucose; FP = family physician

Table 1. Baseline characteristics of participants included in final data analysis

Age, BMI and RPG by gender			
	Female (n=39)	**Male (n=49)**	**Range**
Age (years)	59.03 ± 19.40	61.71 ± 16.99	21 to 92
BMI (kg/m^2)	27.56 ± 6.22	27.98 ± 6.01	17.75 to 58.00
Random Plasma Glucose (mmol/l)	8.40 ± 2.46	8.37 ± 1.19	7.10 to 21.00

 P values were calculated with t-tests
∞Plus-minus values are means ± SD
*n=9 of BMI missing data secondary to patients not disclosing weight and/or height

Table 2. Baseline characteristics of patients diagnosed with IGM versus not diagnosed

Age, BMI and RPG in patients diagnosed with IGM vs patients not diagnosed with IGM		
	Diagnosed with IGM (n=11)	**Not diagnosed with IGM (n=53)**
Age (years)	66.73 ± 12.59	59.48 ± 18.10
BMI (kg/m^2)	27.45 ± 4.17	24.73 ± 9.85
Random Plasma Glucose (mmol/l)	8.61 ± 1.03	8.42 ± 2.05

∞Plus-minus values are means ± SD
*n=24/88 of missing data secondary to patients not reachable or did not follow-up with Fp after eight weeks.

Nov 18, 2013

Dear Editors,

Kindly accept the following REVISED research manuscript for publication as per your request.

Manuscript ID bmjopen -2013-003486

Incidental Findings of Elevated Random Plasma Glucose in the ED as a Prompt for Outpatient Diabetes Screening: A Retrospective Study

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Contributorship: SMF was senior responsible author, designed the trial and implemented the plan. BB and JV performed chart review and telephone interview. SF and BB analyzed the data. SF, BB, and JV drafted the manuscript. SF revised the draft paper.

Prior Publication:

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Funding Statement:

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Word Count**:** 3150 Words

Sincerely,

Steven Marc Friedman, MD

Abstract

Objective: To determine if Random Plasma Glucose (RPG) collected in ED patients without known impaired glucose metabolism (IGM) is a useful screen for diabetes or pre-diabetes.

Design: Retrospective cohort study

Setting: Emergency Department (ED) of a Canadian teaching hospital over one month.

Participants: Adult ED patients with RPG over 7.0 mmol/l were recruited for participation. Exclusion criteria included known diabetes, hospital admission, and inability to consent. Subjects were contacted by mail, encouraged to follow-up with their family physician (FP) for further testing, and subsequently interviewed.

Outcome Measures: The primary outcome measure was the proportion of ED patients with RPG over 7.0 mmol/l) and no previous diagnosis of IGM who were diagnosed with diabetes or pre-diabetes as defined by secondary testing by FP with OGTT or FPG. Secondary outcomes included patient characteristics (age, gender, BMI, language) and (2) compliance with advice to seek appropriate follow-up care.

Results: Random plasma glucose (RPG) was drawn on approximately one third (33%, n=1149) of the 3470 ED patients in March 2010. RPG over 7.0 mmol/l was detected in 24% (n=278) and after first telephone follow-up, 32% (n=88/278) met inclusion criteria and were advised to seek confirmatory testing. 41.0% (n=114/278) were excluded for known diabetes. 73% of patients contacted (n=64/88) followed up with their FP. 12.5% (n=11/88) had abnormal fasting plasma glucose, and of these 11% (n=10/88) were encouraged to initiate lifestyle modifications, and 1% (n=1/88) was started on an oral hypoglycemic agent. For 7% (n=6/88) of the patients, FP's declined to do follow-up fasting bloodwork.

Conclusion: Elevated RPG in the ED is useful for identification of patients at risk for IGM and in need of further diabetic screening. Emergency physicians should advise patients with elevated RPG to consider screening for diabetes. For ED screening to be successful, patient education and collaboration with family physicians is essential.

Keywords: Diabetes Mellitus, Type 2, Emergency Medicine, Screening, Blood Glucose

Article Summary

Article Focus

- An estimated 15.3% of the Canadian population does not have a family physician (FP) and these patients as well as those who do not visit their FP routinely are being missed by diabetes current screening practices

- We followed up on patients in the emergency department who were noted to have a random (nonfasting) plasma glucose > 7.0 mmol/l

- We hypothesized that a proportion of these patients would have previously undetected diabetes or impaired glucose metabolism.

Key Messages

- Approximately 1 in 8 people without previously diagnosed diabetes who completed follow-up were found to have IGM.

- When using an appropriate cut-off, RPG (random plasma glucose) can reliably detect a significant portion of undiagnosed diabetes with acceptable specificity

- This pilot study suggests that the ED has good potential to screen for T2DM, and supports the use of RPG as an opportunistic screening tool

Strengths and Limitations of the Study

- A small sample size may have precluded determination of significant differences between subgroups.

- Logistics of the study and health privacy concerns precluded collection of follow-up test results (i.e. HbA1c, FPG and OGTT) directly from the FPs as opposed to from participants of the study.

- As the study was performed at a single site, generalization to the Canadian urban ED population should be viewed cautiously.

Introduction

Approximately 300 million adults are affected with diabetes worldwide, and this number is expected to rise to 439 million over the next 2 decades <1>. In Canada, an estimated 2.8 million people have been diagnosed with diabetes <2> and approximately 6% of the population may be living with undiagnosed diabetes and pre-diabetes <3>. Diabetes is a cause of significant morbidity and mortality; it is a major contributor to cardiovascular and cerebrovascular disease, and is the leading cause of blindness, end-stage renal failure and non-traumatic amputations in Canadians <4>. In 2010, the estimated cost of diabetes to the Canadian economy was $6.3 billion annually, and this is expected to nearly triple over the next decade <5>.

Approximately 90% of diabetes in the population is type II diabetes (T2DM) <6>, which has a prolonged asymptomatic period of 5-12 years <7>. During this time hyperglycemia develops insidiously and causes significant functional changes to various target tissues. <7,8> At time of diagnosis, about 20% to 30% have developed diabetes related complications <8>. Screening tests for diabetes allow diagnosis during the asymptomatic diabetic and pre-diabetic stages, and can contribute to reduced morbidity and mortality. The implementation of lifestyle and pharmacological interventions during the pre-diabetic stage can prolong and even prevent the onset of diabetes <9,10>, and control of hyperglycemia during the early diabetic stage has long-term benefits in delaying the progression of complications and reducing the risk of premature death. <11>

The diagnosis of diabetes is typically made on the basis of a Fasting Plasma Glucose (FPG) > 7.0 mmol/l, or random plasma glucose (RPG) > 11.1 mmol/l with symptoms of diabetes, or a 2 hour plasma glucose >=11.1 mmol/l in a 75 G OGTT. The term “prediabetes” is a term for impaired fasting glucose or impaired glucose tolerance, which are conditions that place the patient at high risk of developing diabetes. Prediabetes is diagnosed on the basis of a fasting plasma glucose between 6.1mmol/l and 6.9 mmol/l, and warrants further confirmatory testing. <4>

Screening initiatives for diabetes have generally focused on the primary care setting and the use of fasting plasma glucose and oral glucose tolerance tests (OGTT). <12> More recently, glycated hemoglobin (HbA1C) has been accepted as an alternative diagnostic test for T2DM. The Canadian Task Force on Preventive Health Care advises HbA1C testing every 3-5 years for routine screening of adults at high risk of diabetes. <13> However, an estimated 15.3% of the Canadian population does not have a family physician (FP) and these patients as well as those who do not visit their FP routinely are being missed by the current screening practices <14>.

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Discussion:

Approximately 1 in 8 people without previously diagnosed diabetes who completed follow-up were found to have IGM. RPG as a screening tool for diabetes in the acute care setting has been criticized on the grounds that transient stress-induced hyperglycemia and the non-fasting state act as confounders that make the interpretation of this test difficult. Despite this, many studies have shown that when using an appropriate cut-off, RPG can reliably detect a significant portion of undiagnosed diabetes with acceptable specificity <15,16,17,18,19,20>. George et al. <19> found that over half of the patients presenting to the ED with undiagnosed diabetes and random capillary blood glucose (RCBG) over 7.0mmol/l fulfilled criteria for IGM. This substantial number may be an underestimate as the researchers only used fasting plasma glucose and not the OGTT test for diagnosing IGM, thus missing people with impaired glucose tolerance. Charfen et al.<14> also found that amongst ED visitors with undiagnosed diabetes, 66% of those with two or more diabetes risk factors or RPG over 7.0mmol/l (or over 7.8mmol/l if food was ingested within 2hrs of the test) fulfilled criteria for IGM. Ziemer et alanalyzed the sensitivity and specificity of various RPG cut-offs and found that a cut-off of 7.0mmol/l has 93% specificity and 40% sensitivity for identifying diabetes. <19>

A finding of IGM in 1 in 8 people with previously undiagnosed diabetes is significant given the substantial burden that diabetes has at the individual and community levels. This screening effort did present some cost to the patients and the health-care system, including use of resources, clinician time and potential psychological stress in patients. One consideration to optimize cost versus benefit is to improve the yield of screening by targeting patients with risk factors for T2DM and/or those who do not regularly access primary care.

Age and BMI are important risk factors for diabetes <3,15,16>. In our study, there was a nonsignificant trend towards a slightly higher age and BMI for people with impaired glucose tolerance, which is in keeping with findings from other studies. The lack of significant difference in our study may reflect a study sample size limitation.

A challenge in using the ED to screen for diabetes is the need for follow-up by patients with their FPs. Lack of follow-up has consistently been identified as a problem in other studies, often trending towards half of patients not following up <15,17,18>. The high follow-up rate in our study may be attributable to a more health-conscious Canadian population or may likely be due to a substantial number of reminder telephone calls (minimum of 8) from the study researchers to patients delaying follow-up. Poor follow-up has often been cited as an argument against using the ED for routine screening <15,17,18>. Suggestions for improvement include investigators notifying the FPs directly, ED diabetic teaching, and reminders to patients to seek follow-up care.

A further challenge in using the ED for screening is poor follow-up by physicians. In the current study, 7% of FPs did not do further testing despite patient request. In a pilot study by

Hewat et al, the proportion was 50%. <18>.This phenomenon may be attributable to the controversial role for RPG in screening for diabetes and this stresses the importance of FP education to ensure improved collaboration with the ED. A study by Ginde et al <21>showed that in a U.S. ED setting, elevated RPG was often overlooked and not communicated to patients by ED physicians. This supports the argument that ED physician education would also be an essential component of an ED diabetes screening program.

Limitations:

A small sample size may have precluded determination of significant differences between groups. As the study was performed at a single site, generalization to the Canadian urban ED population should be viewed cautiously. For example, regional variations in practices and guidelines for ordering blood tests in the ED, reasons for patient presentation to the ED, and premorbid health status (i.e. prevalence of obesity diabetic risk factors) will impact generalizability of these results. However, similar studies from other parts of the world support these findings and suggest that a finding of high RPG should prompt further outpatient evaluation for diabetes.

Logistics of the study and health privacy concerns precluded collection of follow-up test results (i.e. HbA1c, FPG and OGTT) directly from the FPs as opposed to from the participants of the study. It would also have been informative to analyze presenting complaints to the ED and time of last meal to determine other contributors to increased RPG. (We note that a proportion of RPG samples collected may have in fact been fasting for 8 hours at the time that blood was drawn in the ED, and thus in fact serve as a fasting plasma glucose). Analysis of diabetes risk factors would have been beneficial, as would determining which patients had FPs prior to and after the study. It is possible that patients who did not follow-up with their family physician are a selected subgroup with different risk factors and disease prevalence from those who did follow-up.

While excluding patients who were admitted to the ED likely removed the majority of the more acutely ill patients with febrile illnesses, we felt that it would be worthwhile to include patients despite elevated temperature, despite the potential for more 'false positive' random blood glucose results. Stratification of patients by reason of ED visit might prove useful for subgroup analysis in future studies.

Conclusions:

This was the first study looking at the use of the Canadian ED as a screening point for diabetes. This pilot study suggests that the ED has good potential to screen for T2DM, and

supports the use of RPG as an opportunistic screening tool. For ED screening to be effective, good collaboration with FPs is essential. Further multi-centered large scale studies are required to form a more conclusive opinion with regards to the widespread use of Canadian EDs as a screening point.

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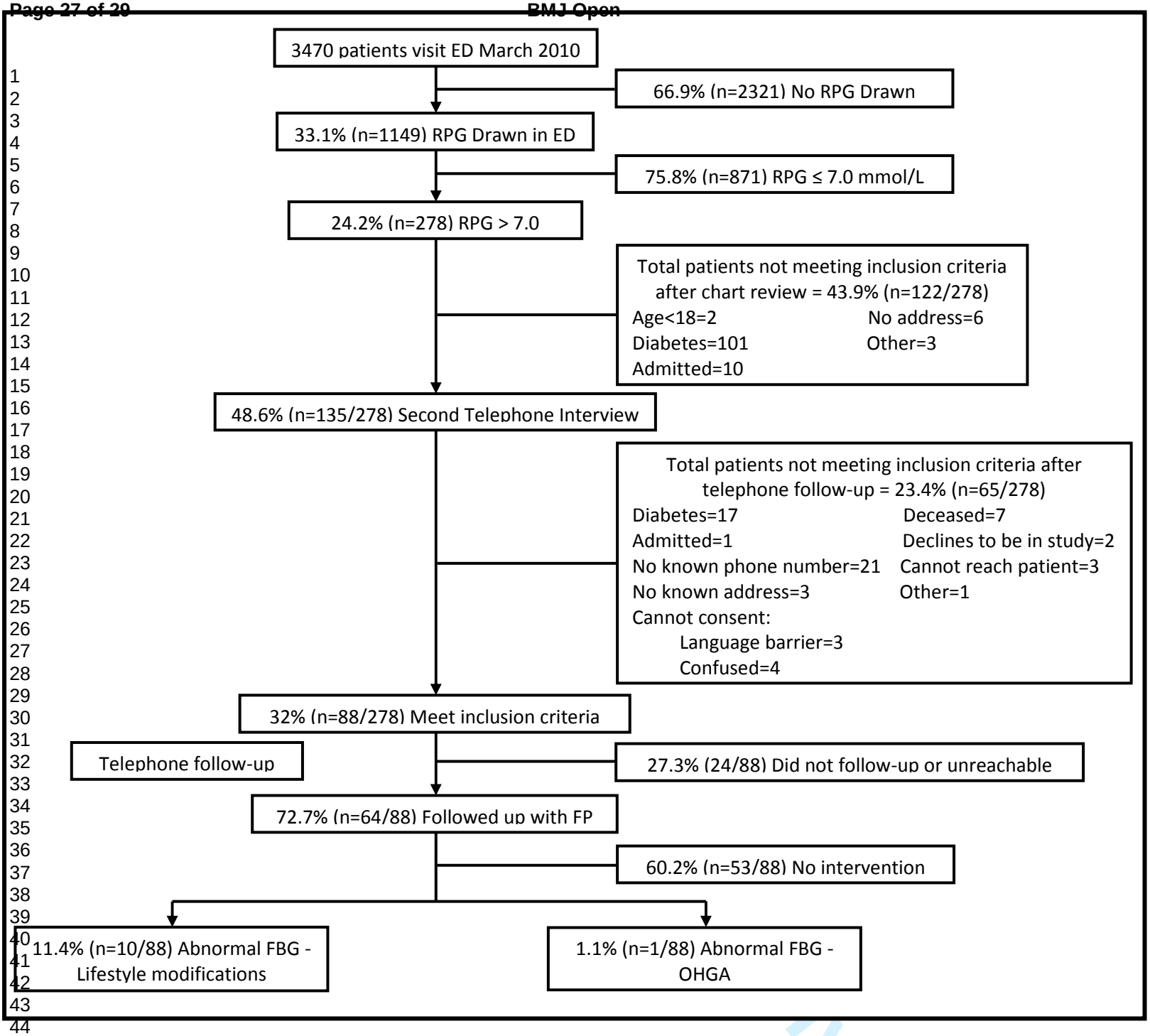


Figure 1. Consort diagram. ED = Emergency Department; RPG = Random plasma glucose; OHGA = Oral hypoglycemic agent; FBG = Fasting blood glucose; FP = family physician

Table 1. Baseline characteristics of participants included in final data analysis

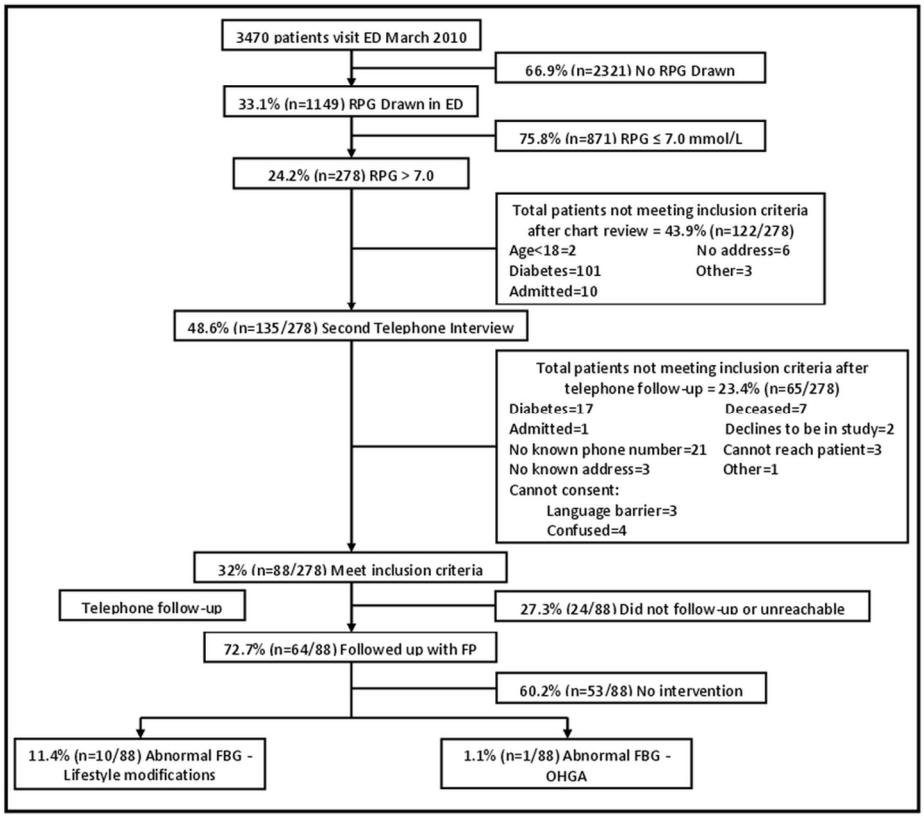
Age, BMI and RPG by gender			
	Female (n=39)	**Male (n=49)**	**Range**
Age (years)	59.03 ± 19.40	61.71 ± 16.99	21 to 92
BMI (kg/m^2)	27.56 ± 6.22	27.98 ± 6.01	17.75 to 58.00
Random Plasma Glucose (mmol/l)	8.40 ± 2.46	8.37 ± 1.19	7.10 to 21.00

 P values were calculated with t-tests
∞Plus-minus values are means ± SD
*n=9 of BMI missing data secondary to patients not disclosing weight and/or height

Table 2. Baseline characteristics of patients diagnosed with IGM versus not diagnosed

Age, BMI and RPG in patients diagnosed with IGM vs patients not diagnosed with IGM		
	Diagnosed with IGM (n=11)	**Not diagnosed with IGM (n=53)**
Age (years)	66.73 ± 12.59	59.48 ± 18.10
BMI (kg/m^2)	27.45 ± 4.17	24.73 ± 9.85
Random Plasma Glucose (mmol/l)	8.61 ± 1.03	8.42 ± 2.05

∞Plus-minus values are means ± SD
*n=24/88 of missing data secondary to patients not reachable or did not follow-up with Fp after eight weeks.



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