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# The incidence, frequency rate and length of stay for all-cause hospitalisation in adults with impaired fasting glucose (IFG) and diabetes mellitus: a longitudinal study

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| Complete List of Authors: | Sajjad, Muhammad<br>Holloway, Kara; Deakin University - Geelong Waterfront Campus, Department of Medicine<br>de Abreu, Lelia; Deakin University - Geelong Waterfront Campus, Department of Medicine<br>Mohebbi, Mohammadreza; Deakin University, Biostatistics Unit, Faculty of Health<br>Kotowicz, Mark; Barwon Health, Department of Endocrinology and Diabetes<br>Pedler, Daryl; Deakin University - Geelong Waterfront Campus, Department of Medicine<br>Pasco, Julie; The University of Melbourne, Clinical and Biomedical Sciences: Barwon Health |
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**Full title:** The incidence, frequency rate and length of stay for all-cause hospitalisation in adults with impaired fasting glucose (IFG) and diabetes mellitus: a longitudinal study

Muhammad A. Sajjad,[1] Kara L. Holloway,[1] Lelia L. F. de Abreu,[1] Mohammadreza Mohebbi,[1] Mark A. Kotowicz,[1,2,3] Daryl Pedler,[1] and Julie A. Pasco,[1,2,3]

[1]*Deakin University, Geelong, VIC 3220, Australia*

[2]*Department of Medicine-Western Health, Melbourne Medical School, The University of Melbourne, St Albans, VIC 3010, Australia*

[3]*University Hospital Geelong, Barwon Health, Geelong, VIC 3220, Australia*

**Corresponding author:** Muhammad A. Sajjad. Epi-Centre for Healthy Ageing, IMPACT Strategic Research Centre, Deakin University, PO Box 281 (Barwon Health), Geelong, Victoria 3220, Australia.

Email address: msajjad@barwonhealth.org.au

Telephone: +61 342153339

Fax: +61 342153491

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## Abstract

**Objective:** To determine whether adults with normoglycaemia, impaired fasting glucose (IFG) and diabetes differed according to the incidence, frequency, length and reasons for hospitalisation.

**Design:** Longitudinal observational cohort study.

**Setting:** Barwon Statistical Division, Geelong, Australia.

**Participants:** Cohort included 971 men and 924 women, aged 20+yr, participating in the Geelong Osteoporosis Study. Glycaemic status was assessed at cohort entry using fasting plasma glucose, use of anti-hyperglycaemic medication and/or self-report.

**Primary and secondary outcome measures:** Primary outcome measure was any admission to the major tertiary public hospital in the study region over the follow-up period. Secondary outcome measures were frequency rate and length of hospital stay.

**Results:** Over a median follow-up of 7.4 years (IQR 5.3-9.6), participants with diabetes, compared to those with normoglycaemia, were twice as likely to be hospitalised (OR 2.07, 95% CI 1.42-3.02), had a higher frequency rate (IRR 1.61, 95% CI 1.17-2.23), and longer hospital stay (3$^{rd}$ quartile difference 7.7, 95% CI 1.3-14.1 and 9$^{th}$ decile difference 16.2, 95% CI 4.2-28.3). IFG group was similar to normoglycaemia for the incidence, frequency and length of hospitalisation. Cardiovascular disease-related diagnoses were the most common primary reasons for hospitalisation across all glycaemic categories.

**Conclusions:** Our results show increased incidence, frequency and length of all-cause hospitalisation in adults with diabetes as compared to normoglycaemia, however we did not detect any associations for IFG. Interventions should focus on preventing IFG-to-diabetes progression and reducing cardiovascular risk in IFG and diabetes.

**Keywords:** Diabetes mellitus; hospitalisation; impaired fasting glucose; health service utilisation.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- Longitudinal cohort design with long term follow-up.
- Randomly selected sample of general population, including both men and women.
- Robust method of identification of normoglycaemia, impaired fasting glucose and diabetes mellitus.
- Hospitalisation data were limited to the only tertiary public hospital in the study region.

## INTRODUCTION

The rapid increase in the prevalence of diabetes mellitus poses a significant challenge for health planners globally. Diabetes causes deterioration in physical health, mental wellbeing and quality of life, resulting in adverse outcomes including increased risk of hospitalisation.[1 2] According to the Australian Institute of Health and Welfare (AIHW), diabetes is one of the major causes of Potentially Preventable Hospitalisations (PPHs) in Australia, where hospitalisation may be avoidable through timely and adequate non-hospital care.[3-5]

It has been reported that people with diabetes have higher rates of hospitalisation as compared to those without the condition.[6-9] Previous research, however, has mainly focused on individuals with a diagnosis of diabetes. The association of intermediate deteriorations in glucose metabolism such as Impaired Fasting Glucose (IFG) and the risk of hospitalisation remains largely unexplored. IFG represents levels of Fasting Plasma Glucose (FPG) that are above normal (100 mg/dL or 5.5 mmol/L) but below the diagnostic threshold for diabetes (126 mg/dL or 7.0 mmol/L).[1] IFG is known to increase the risk of cardiovascular disease in addition to being a risk factor for diabetes.[10 11] As evidence builds for IFG as a disease condition rather than just a risk factor for diabetes, investigating adverse outcomes including hospitalisations in this grouping is warranted. The aim of this study was to compare the incidence and frequency rate of all-cause hospitalisation and length of hospital stay between adults with normoglycaemia, IFG and diabetes mellitus over a median period of 7.4 years. Moreover, we aimed to highlight primary reasons for hospitalisations for individuals in different glycaemic categories.

## METHODS

### Study Design and participants

We utilised data from the Geelong Osteoporosis Study, a longitudinal cohort study including 3034 residents of the Barwon Statistical Division (BSD), located in south-eastern Australia, with a population of around 280,000. A detailed cohort profile, recruitment strategy and methodology have been described elsewhere.[12] In brief, during 1993-1997, an age-stratified sample of 1494 women aged 20-94 years was recruited from the Commonwealth electoral rolls with an overall participation of 77.1%. Of the original sample, 881 women participated in the 10-year follow-up commencing 2004 and an additional 246 women aged 20-29 years were recruited in 2006-2008. Of these two groups, we included 924 women for whom glycaemic status could be confirmed based on FPG measurement, self-reported diabetes and/or use of anti-hyperglycaemic agents.

Similarly, during 2001-2006, 1540 men were recruited and assessed, followed by a 5-year reassessment commencing 2006. We used either baseline or 5-year follow-up as the point of cohort entry depending on when FPG was measured. The final sample for this analysis included 971 men for whom we were able to ascertain glycaemic status using FPG measurement, self-report and/or use of anti-hyperglycaemic agents.

### Baseline measures

Cohort entry or 'baseline' was defined as the point when glycaemic status was confirmed and the follow-up was up to December 31, 2012 or date of death where applicable. At baseline, body weight and height were measured using electronic scales and a wall mounted stadiometer, respectively. Venous blood was collected after an overnight fast and FPG was measured using an adaptation of the hexokinase-glucose-6-phosphate dehydrogenase

method.[13] Participants were categorised into diabetes, IFG and normoglycaemia according to the 2003 American Diabetes Association's diagnostic criteria where diabetes was defined as FPG ≥ 7.0 mmol/L (126 mg/dL), self-report of diabetes, or use of anti-hyperglycaemic agents. IFG was considered present if FPG level was between 5.5 and 6.9 mmol/L (100-125 mg/dL). Participants with a FPG level ≤ 5.5 mmol/L in the absence of self-reported diabetes or use of anti-hyperglycaemic agents were classified as having normoglycaemia.

A series of questionnaires was administered seeking information on socio-demographic characteristics, use of medications and supplements, physical activity, alcohol consumption, and cigarette smoking.[12]

Levels of physical activity were determined using a multiple choice question with responses ranging from 'very active and active' (aggregated as 'high mobility') to 'sedentary, limited, inactive, chair/bedridden, and bedfast' (aggregated as 'low mobility'). Frequency of alcohol consumption was measured using the Cancer Council Victoria Dietary Questionnaire for Epidemiological Studies (DQESV2).[14] The Australian National Health and Medical Research Council guidelines were used to classify alcohol consumption into a binary variable; 'low use' (≤ 2 standard drinks/day) and 'high use' (>2 standard drinks/day), where a standard drink equals 10 grams of alcohol.[15] The Australian Bureau of Statistics Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD) was derived from the participants' area of residence, as an indicator of socioeconomic status.[16]

**Outcome measures**

Our primary outcome measure was any hospitalisation to the University Hospital Geelong (UHG) during the follow-up period; women (median follow-up 7.1 years, inter-quartile range 5.7-8.5) and men (median follow-up 8.3 years, inter-quartile range 5.6-11.0). Baseline data were linked to the admissions data using unique identification codes used by the hospital. The

UHG is the largest public hospital and the only health service in the study region classified as a "principal referral hospital" according to the Australian hospitals peer-group classification.[17] It has 370 inpatient beds, 24 Intensive Care Unit beds and had the only 24-hour Emergency Department in the region during the study period. It provides a full spectrum of care including community care, aged care, rehabilitation, mental health, emergency and acute care.[18]

**Reasons for hospitalisation**

Australian hospitals use an alphanumeric coding system for diseases and external causes of injury, referred to as the tenth revision of the International Classification of Diseases, Australian Modification (ICD-10-AM).[19] It comprises three, four and five character categories, structured by body system and etiology and is updated regularly.[19] We classified primary diagnoses into broad categories by aggregating individual disease codes, for instance, primary ICD-10 diagnoses codes of I21.0 'acute transmural myocardial infarction (MI) of anterior wall', I21.1 'acute transmural MI of inferior wall', and I21.4 'acute sub-endocardial MI', were combined as a single category of I21 'acute MI'.

**Deaths**

All deaths during the follow-up period were confirmed using the National Deaths Index, a national register maintained by the AIHW containing records of all deaths registered in Australia since 1980.[20]

**Ethics approval**

The study was approved by the Barwon Health Human Research Ethics Committee. All participants provided informed consent.

**Statistical analysis**

We used t-tests for continuous data and Chi-square tests for categorical data to compare baseline characteristics of participants in different glycaemic categories (normoglycaemia, IFG and diabetes).

For the analysis of association between glycaemic status and the incidence of all-cause hospitalisation, Chi-square test followed by incident odds ratio (OR) and 95% confidence intervals (CI) have been reported for examining bivariate association. A set of tri-variate analyses was performed to examine the impact of each potential risk factor above and beyond the glycaemic category association with the study outcomes. Tri-variate logistic regressions for all-cause hospitalisation, tri-variate Poisson regressions for hospitalisation frequency rate and two-way ANOVAs on rank of hospital length of stay were implemented. Odds ratios, risk ratios and partial eta squared effect size have been used to illustrate the impact of potential risk factors. Partial eta squared values of 0.009, 0.0588 and 0.1379 were considered as benchmarks for small, medium and large effect sizes, respectively.[21] Logistic regression was performed to evaluate the association after adjusting for covariates and interactions and model adjusted OR and 95% CI are reported. Rate of hospitalisation was calculated as frequency of hospitalisation divided by total person-years of follow-up for normoglycaemia, IFG and diabetes groups. Chi-square test followed by incident risk ratio (IRR) and its 95% CI were illustrated for examining bivariate associations. Poisson regression with glycaemic status as factor and the frequency as the outcome and total person-years of follow-up as the offset was implemented for multivariate analysis. Medians and inter quartile ranges (IQR) of length of stay were reported in the three groups. In order to deal with positively skewed nature of hospital length of stay and possible outliers, a non-parametric median-based regression based on L1-norm estimation[22 23] was performed as multivariate model. Simultaneous quantile regression on median, 3rd quartile and 9$^{th}$ decile using bootstrapping

technique for estimating standard errors[24] was used to analyse the relationship between glycaemic status and upper quartile and last decile of length of all-cause hospitalisation.

Only the variables that showed significant associations at 0.1 level in the bivariate chi-square analyses were included in the multivariate models. Two-way interactions were also examined. A backward variable selection approach with p-entry=0.1 and p-exit=0.05 was implemented to obtain the final models.

Statistical analyses were conducted using Stata software version 14 (Stata Corp, College Station, TX, USA) and Minitab statistical software package (Version 17; Minitab, State College, PA, USA)

## RESULTS

Table 1 shows baseline characteristics of participants by glycaemic status. In men, 615 (63.3%) had normoglycaemia, 275 (28.3%) had IFG and 81 (8.3%) had diabetes. In women, 694 (75.1%) had normoglycaemia, 159 (17.2%) had IFG and 71 (7.6%) had diabetes.

For both men and women, those with diabetes were older and had higher BMI as compared to normoglycaemia group. Women with diabetes were more likely to have 'low mobility' at baseline as compared to those with normoglycaemia. Participants with normoglycaemia, IFG and diabetes did not differ significantly at baseline in terms of current smoking status and socioeconomic status.

**Table 1:** Descriptive statistics of men and women at baseline by glycaemic status (normoglycaemia, IFG and diabetes). Data presented as median (inter-quartile range) or n (%)

| **MEN** | **Total (n=971)** | **Normoglycaemia (n=615)** | **IFG (n=275)** | **Diabetes (n=81)** | **p value** |
|---|---|---|---|---|---|
| Age (years) | 56.9 (28.0, 84.0) | 52.0 (24.0, 80.0) | 62.0 (40.0, 84.0) | 67.0 (53.0, 81.0) | **<0.001** |
| BMI[a] | 26.9 (21.9, 31.9) | 26.3 (21.6, 31.0) | 28.0 (23.1, 32.9) | 28.6 (24.3, 32.9) | **<0.001** |
| Current smoking | 141 (14.5) | 98 (15.9) | 33 (12.0) | 10 (12.3) | 0.25 |
| High alcohol use | 233 (23.9) | 138 (22.4) | 82 (29.8) | 13 (16.0) | **0.008** |
| Low mobility | 292 (30.0) | 180 (29.2) | 85 (30.9) | 27 (33.3) | 0.7 |
| IRSAD[b] | | | | | |
| 1 | 166 (17.0) | 96 (15.6) | 49 9 (17.8) | 21 (25.9) | 0.39 |
| 2 | 204 (21.0) | 126 (20.4) | 59 (21.4) | 19 (23.4) | |
| 3 | 189 (19.4) | 126 (20.4) | 52 (18.9) | 11 (13.5) | |
| 4 | 201 (20.7) | 131 (21.3) | 58 (21.0) | 12 (14.8) | |
| 5 | 211 (21.7) | 136 (22.1) | 57 (20.7) | 18 (22.2) | |
| Person-years of follow-up | 7324.0 | 4644.1 | 2113.6 | 617.7 | |
| **WOMEN** | **Total (n=924)** | **Normoglycaemia (n=694)** | **IFG (n=159)** | **Diabetes (n=71)** | **p value** |
| Age (years) | 53.0 (25.0, 81.0) | 49.0 (20.0, 78.0) | 63.0 (41.0, 85.0) | 66.0 (46.0, 86.0) | **<0.001** |
| BMI[a] | 26.3 (19.1, 33.5) | 25.6 (19.3, 31.9) | 29.5 (22.3, 36.7) | 31.5 (21.4, 41.6) | **<0.001** |
| Current smoking | 109 (11.7) | 83 (11.9) | 21 (13.2) | 5 (7.0) | 0.44 |
| High alcohol use | 55 (5.9) | 45 (6.4) | 9 (5.6) | 1 (1.4) | 0.24 |
| Low mobility | 202 (22.0) | 121 (17.5) | 48 (30.3) | 33 (48.5) | **<0.001** |
| IRSAD[b] | | | | | |
| 1 | 150 (16.2) | 97 (13.9) | 37 (23.2) | 16 (22.5) | 0.41 |
| 2 | 186 (20.1) | 145 (20.8) | 30 (18.8) | 11 (15.4) | |
| 3 | 213 (23.0) | 162 (23.3) | 33 (20.7) | 18 (25.3) | |
| 4 | 187 (20.2) | 141 (20.3) | 32 (20.1) | 14 (19.7) | |
| 5 | 188 (20.3) | 149 (21.4) | 27 (16.9) | 12 (16.9) | |
| Person-years of follow-up | 6434.1 | 4843.1 | 1104.4 | 486.6 | |

[a]Body Mass Index (kg/m$^2$). [b]Index of Relative Socioeconomic Advantage and Disadvantage.

**Incidence of all-cause hospitalisation**

Bivariate analyses showed that men with IFG were almost 50% more likely to be admitted (OR 1.48, 95% CI 1.11-1.98, p=0.006) and men with diabetes were more than 3 times more likely to be hospitalised (OR 3.17, 95% CI 1.93-5.1, p<0.001) compared to men with normoglycaemia.

Similarly, women with IFG and diabetes were also more likely to be hospitalised as compared to normoglycaemia, (OR 1.48, 95% CI 1.05-2.10, p=0.025) and (OR 3.14, 95% CI 1.86-5.28, p<0.001) respectively.

After accounting for glycaemic category through tri-variate analyses for both men and women in the study, older age and lower socioeconomic status were associated with increased risk of all-cause hospitalisation (Table 2). In addition, a higher BMI in men and low mobility in women were associated with increased risk of all-cause hospitalisation after adjusting for glycaemic category (Table 2).

**Table 2:** Evaluating the impact of potential risk factors at baseline on hospitalisation outcome association with glycaemic category using tri-variate regressions between variables in men and women.

| | All-cause hospitalisation by glycaemic category | | | All-cause hospitalisation OR[1] (95% CI) | p value | Hospitalisation frequency rate IRR[2] (95% CI) | p value | Hospital length of stay partial eta squared[3] | p value |
|---|---|---|---|---|---|---|---|---|---|
| **Men** | **Normoglycaemia n=615** | **IFG n=275** | **Diabetes n=81** | | | | | | |
| Admitted n (%) | 246 (40.00) | 137 (49.80) | 55 (67.90) | - | - | - | - | - | - |
| Age in years mean (SD) | 51.43 (16.89) | 60.01 (14.01) | 65.74(9.74) | 1.05 (1.04-1.06) | **<0.001** | 1.04 (1.03-1.05) | **<0.001** | 0.160 | **<0.001** |
| BMI kg/m$^2$ mean (SD) | 26.56 (3.74) | 28.42 (4.24) | 29.04 (4.30) | 1.04 (1.01-1.08) | **0.008** | 1.04 (1.01-1.08) | **0.006** | 0.011 | **0.001** |
| Current smoker n (%) | 33 (33.70) | 17 (51.50) | 4 (40.00) | 0.74 (0.51-1.07) | 0.115 | 1.07 (0.69-1.66) | 0.731 | 0.004 | 0.063 |
| High alcohol use n (%) | 53 (38.40) | 35 (42.70) | 9 (69.20) | 0.83 (0.61-1.12) | 0.238 | 0.74 (0.56-0.99) | **0.045** | 0.002 | 0.160 |
| Low mobility n (%) | 69 (38.30) | 44 (51.80) | 27 (66.70) | 0.96 (0.73-1.27) | 0.966 | 1.40 (1.05-1.87) | **0.021** | <0.001 | 0.723 |
| IRSAD | - | - | - | 0.89 (0.81-0.97) | **0.016** | 0.81 (0.74-0.89) | **<0.001** | 0.007 | **0.010** |
| **Women** | **Normoglycaemia n=694** | **IFG n=159** | **Diabetes n=71** | | | | | | |
| Admitted n (%) | 277 (39.90) | 79 (49.70) | 48 (67.60) | - | - | - | - | - | - |
| Age in years mean (SD) | 49.53 (18.26) | 61.83 (14.73) | 65.03 (13.11) | 1.03 (1.02-1.03) | **<0.001** | 1.03 (1.02-1.03) | **<0.001** | 0.098 | **<0.001** |
| BMI kg/m$^2$ mean (SD) | 26.59 (5.16) | 30.16 (5.98) | 31.23 (7.19) | 1.00 (0.97-1.02) | 0.781 | 1.01 (0.98-1.04) | 0.434 | 0.001 | 0.433 |
| Current smoking n (%) | 34 (41.00) | 21 (38.10) | 5 (80.00) | 0.96 (0.64-1.45) | 0.859 | 0.84 (0.58-1.19) | 0.336 | 0.001 | 0.437 |
| High alcohol use n (%) | 15 (33.30) | 3 (33.30) | 0 (0.00) | 0.65 (0.36-1.17) | 0.155 | 0.49 (0.29-0.82) | **0.007** | 0.001 | 0.278 |
| Low mobility n (%) | 82 (67.80) | 25 (52.1) | 27 (81.80) | 2.99 (2.14-4.18) | **<0.001** | 2.53 (1.69-3.74) | **<0.001** | 0.089 | **<0.001** |
| IRSAD | - | - | - | 0.86 (0.78-0.95) | **0.004** | 0.90 (0.81-1.00) | 0.069 | 0.009 | **0.004** |

1. Tri-variate logistic regression

2. Tri-variate Poisson regression

3. Two-way ranked ANOVA

IFG, Impaired Fasting Glucose; BMI, Body Mass Index; IRSAD, Index for Relative Socioeconomic Advantage and Disadvantage; OR, Odds ratio; IRR, Incident Rate Ratio.

A significant age-sex interaction was observed and, therefore, included in the multivariate models (OR 1.3, 95% CI 1.0-1.6, p=0.04). After adjustments for age, sex and socioeconomic status, participants with diabetes were twice likely to be hospitalised for any cause, as compared to normoglycaemia (OR 2.0, 95% CI 1.4-3.0, p<0.001). Having IFG at baseline was not significantly associated with the incidence of all-cause hospitalisation (OR 1.1, 95% CI 0.8-1.4, p=0.38).

**Frequency rate of all-cause hospitalisation**

In men, rate of hospitalisation was 0.43 per person per year for those with diabetes (95% CI 0.32-0.57), 0.21 per person per year in IFG (95% CI 0.17-0.27) and 0.19 per person per year in those with normoglycaemia (95% CI 0.15-0.23). The rate of hospitalisation was 0.50 per person per year for women with diabetes (95% CI 0.30-0.84), 0.24 per person per year for those with IFG (95% CI 0.18-0.31) and 0.16 per person per year in those with normoglycaemia (95% CI 0.14-0.19). In men, older age, BMI, high alcohol use, low mobility and low socioeconomic status were associated with higher rate of hospitalisation (Table 2). In women, older age, high alcohol use and low mobility were associated with higher frequency of hospitalisation (Table 2).

In the final multivariate model, the rate of all-cause hospitalisation was significantly higher in the diabetes group, as compared to normoglycaemia (IRR 1.6, 95% CI 1.1-2.2, p<0.05). The IFG group was not significantly different from normoglycaemia in terms of the rate of all-cause hospitalisation (IRR 0.9, 95% CI 0.7-1.1, p=0.67).

**Length of hospital stay**

The effect sizes of individual baseline characteristics on the hospital length of stay based on two-way ranked ANOVA are illustrated in Table 2. For men, older age, higher BMI and

lower socioeconomic status were associated with increased length of hospital stay (Table 2). Older age had a large effect on length of hospital stay, while high BMI and low socioeconomic status had medium and small effects respectively (partial eta squared=0.160, 0.011 and 0.007) (Table 2).

Median regression analysis did not show a difference between the glycaemic categories in terms of median length of hospital stay (Table 3). In additional analysis, 3rd quantile and 9th decile comparison was performed showing that having diabetes at baseline was associated with an increased duration of hospital stay (3rd quartile difference 7.7, 95% CI 1.3-14.1, p=0.01) and (9th decile difference 16.2, 95% CI 4.2-28.3, p=0.008) in patients with longer than median length of stay. Hence, in participants that spent longer than the median length of stay in the hospital, having diabetes was associated with increased length of hospital stay.

**Table 3:** Relationship between glycaemic status and all-cause hospitalisation (multivariate model), presented for men, women and total sample.

| | All-cause hospitalisation OR (95% CI) | Hospitalisation frequency IRR (95% CI) | Hospitalisation length in days Median (95% CI) | Hospitalisation length in days 3rd quartile (95% CI) | Hospitalisation length in days 9th decile (95% CI) |
|---|---|---|---|---|---|
| **Men** | | | | | |
| Normoglycaemia | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| IFG | 1.08 (0.79-1.48, p=0.592) | 0.85 (0.65-1.12, p=0.271) | 0.00 (-0.13-(-0.12), p=0.882) | 0.24 (-1.20-1.70, p=0.739) | -0.31 (-6.70-6.06, p=0.922) |
| Diabetes | **1.90 (1.11-3.24, p=0.018)** | 1.34 (0.95-1.88, p=0.090) | 2.47 (-1.73-6.68, p=0.249) | **10.46 (1.44-19.48, p=0.023)** | **21.55 (1.39-41.72, p=0.036)** |
| Age (years) | - | - | 0.00 (-0.00-0.01, p=0.107) | **0.13 (0.09-0.18, p=0.0001)** | **0.25 (0.04-0.45, p=0.016)** |
| Age category (40-60) | 1.42 (0.96-2.10, p=0.075) | **1.91 (1.14-3.19, p=0.013)** | - | - | - |
| (>60) | **4.73 (3.22-6.93, p<0.001)** | **4.59 (2.92-7.21, p<0.001)** | | | |
| BMI (kg/m$^2$) | **1.03 (0.99-1.07, p=0.052)** | **1.03 (1.00-1.06, p=0.033)** | | - | - |
| Current smoking | - | - | 0.02 (-0.09-0.03, p=0.370) | - | - |
| High alcohol use | | | 0.01 (-0.06-0.03, p=0.557) | -0.56 (-1.33-0.20, p=0.152) | **-6.67(-12.84-(-0.49), p=0.034** |
| IRSAD | - | **0.84 (0.77-0.91, p<0.001)** | 0.01 (-0.02-0.00, p=0.37) | - | |
| **Women** | | | | | |
| Normoglycaemia | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| IFG | 1.10 (0.75-1.60, p=0.614) | 1.10 (0.79-1.54, p=0.557) | 0.00 (-0.16-0.15, p=0.944) | -0.6 (-2.77-1.49, p=0.557) | 1.20 (-6.75-9.16, p=0.766) |
| Diabetes | **2.32 (1.34-4.02, p=0.003)** | 2.12 (1.12-4.03, p=0.021) | 0.76 (-1.06-2.59, p=0.414) | 4.30 (-3.19-11.8, p=0.260) | 14.41 (-3.91-32.74, p=0.123) |
| Age (years) | - | - | 0.00 (0.00-0.00, p=0.155) | **0.09 (0.04-0.14, p=0.001)** | **0.32 (0.24-0.40, p=0.001)** |
| Age category (40-60) | 1.03 (0.72-1.47, p=0.845) | 1.30 (0.83-2.04, p=0.238) | - | - | - |
| (60-80) | **2.51 (1.73-3.64, p<0.001)** | **2.73 (1.84-4.06, p<0.001)** | | | |
| (>80) | **7.22 (3.58-14.56, p<0.001)** | **3.06 (2.08-4.52, p<0.001)** | | | |
| BMI | - | - | 0.00 (0.00-0.00, p=0.748) | - | - |
| Current smoking | - | - | 0.01 (-0.07-0.05, p=0.697) | - | - |
| High alcohol use | - | 0.55 (0.34-0.89, p=0.017) | 0.00 (-0.03-0.03, p=0.890) | - | - |
| IRSAD | **0.86 (0.78-0.95, p=0.005)** | | 0.01 (-0.03-0.00, p=0.231) | -0.37 (-0.66-(-0.08), p=0.01) | **-0.81 (-1.36-(-.0.24), p=0.004)** |
| **Total** | | | | | |
| Normoglycaemia | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| IFG | 1.11 (0.87-1.40, p=0.380) | 0.95 (0.77-1.18, p=0.671) | 0.00 (-0.05-0.05, p=1.000) | 0.00 (-0.61-0.61, p=1.000) | 0.00 (-2.22-2.22, p=1.000) |
| Diabetes | **2.07 (1.42-3.02, p<0.001)** | **1.61 (1.17-2.26, p=0.003)** | 1.70 (-0.05-3.47, p=0.058) | **7.77 (1.39-14.16, p=0.017)** | **16.29 (4.20-28.38, p=0.008)** |
| Age category | **1.78 (1.49-2.12, p<0.001)** | **1.82 (1.49-2.24, p<0.001)** | 0.00 (-0.00-0.08, p=1.000) | **1.93 (0.89-2.97, p=0.001)** | **8.33 (5.63-11.04, p<0.001)** |
| Sex (male) | **0.52 (0.29-0.95, p=0.033)** | 0.71 (0.33-1.52, p=0.391) | -0.13(-0.30-0.02, p=0.095) | **-1.55 (-2.98- (-0.12, p=0.033)** | -2.21 (-5.65-1.21, p=0.206) |
| Sex-age interaction | **1.31 (1.02-1.69, p=0.034)** | 1.19 (0.90-1.57, p=0.210) | 0.13 (-0.02-0.30, p=0.095) | **1.55 (0.13-2.97, p=0.032)** | 2.08 (-1.11-5.28, p=0.201) |
| BMI | - | 1.02 (0.99-1.04, p=0.069) | 0.00 (-0.00-0.00, p=1.000) | - | - |
| Current smoking | - | - | 0.00 (-0.00-0.00, p=1.000) | | |
| High alcohol use | - | **0.78 (0.61-0.99, p=0.045)** | 0.00 (-0.00-0.00, p=1.000) | - | - |
| IRSAD | **0.89 (0.83-0.95, p=0.002)** | **0.88 (0.82-0.94, p<0.001)** | 0.00 (-0.00-0.00, p=1.000) | -0.05 (-0.16-0.04, p=0.274) | **-1.08 (-1.65-(-5.09), p<0.001** |

IFG, Impaired Fasting Glucose; BMI, Body Mass Index; IRSAD, Index for Relative Socioeconomic Advantage and Disadvantage; OR, Odds ratio; IRR, Incident Rate Ratio.

**Reasons for hospitalisation**

Figures 1 and 2 show the 10 most common primary reasons for hospitalisation by glycaemic category for men and women in the study respectively.

Among men with diabetes, the most commonly encountered diagnosis was 'angina pectoris', with 20.0% of the group having at least one hospitalisation primarily for the condition. It was followed by 'type 2 diabetes mellitus' (14.5%). 'Pain in throat and chest' was the most common reason for hospitalisation for men in the IFG (14.6%) and normoglycaemia (9.8%) groups.

In women with diabetes, 'type 2 diabetes mellitus' was the most commonly documented primary reason for hospitalisation in women with diabetes (12.5%), followed by 'heart failure' (10.4%). For the IFG and normoglycaemia groups, 'pain in throat and chest' was the most common reason for hospitalisation, 11.4% and 11.6% respectively.

**DISCUSSION**

This study reports that, compared to normoglycaemia, having diabetes is associated with a higher incidence, frequency rate, and longer duration of hospitalisation. During the follow-up, 68.0% of participants with diabetes had at least one hospitalisation as compared to 50.0% with IFG and 40.0% with normoglycaemia. The incidence of hospitalisation was twice in those with diabetes as compared to normoglycaemia. Previous studies reporting hospitalisation rates have varied depending on the study population and duration of follow-up. Only one study in the literature has examined hospitalisations in the Australian population with diabetes.[25] The study followed individuals aged 45 years and over, with and without diabetes, for a year, reporting that 32.8% of participants with diabetes had one or more hospitalisations as compared to 24.2% of those with normoglycaemia.[25] Similar studies have

been performed in other countries, for example, a New Zealand study conducted over a three-year period reported an all-cause hospitalisation rate of 43.5% in those with diabetes.[26] An Italian study showed an even higher proportion of participants with diabetes (55.0%) being hospitalised at least once over a 4.5 year follow-up.[7]

There are a number of factors which could explain the higher risk of hospitalisation in people with diabetes. Comorbid coronary heart disease, stroke, depression, musculoskeletal disease and cancer are common in people with diabetes and can increase the risk of hospitalisation.[27] [28] In addition, diabetes shares common risk factors with other chronic diseases (particularly cardiovascular disease) such as obesity, physical inactivity and unhealthy diet. In our study, half of the 10 most common primary reasons for hospitalisation in participants with diabetes were related to complications and/or diagnoses related to cardiovascular disease. This is consistent with studies showing that a significant proportion of morbidity and mortality associated with diabetes is due to cardiovascular disease.[10] Some recent studies have reported a decline in incident cardiovascular disease in people with diabetes, however, the risk is still double that of those with normoglycaemia.[29]

In our sample, older age was independently associated with both having diabetes and the risk of hospitalisation. Elderly patients with diabetes often present with multiple and advanced complications and are more likely to be readmitted and spend longer in hospital beds as compared to younger counterparts.[30]

Other factors predisposing people with diabetes to hospitalisation are related to disease management that involves maintaining a balance between lowering blood glucose levels and preventing hypoglycaemic events. One of the goals of management is achieving tight glycaemic control (FPG < 6 mmol/L); while this has been shown to reduce microvascular complications, it may simultaneously increase the incidence of hypoglycaemic events.[6]

Therefore, the benefits of obtaining optimum blood glucose levels have to be weighed against the risk of severe hypoglycaemic episodes that could result in frequent Emergency Department visits and hospital admissions.[31] Furthermore, optimal diabetes care requires active involvement by the patients and their ability to navigate the health system, hence, health literacy plays a key role. Health outcomes are poorer in population sub-groups with diabetes having low health literacy levels such as migrants from non-English speaking backgrounds and indigenous people.[32 33]

In our study, 14.5% of men and 12.5% of women with diabetes had a hospitalisation specifically for a diagnosis or complication related to diabetes mellitus. Other studies have reported higher proportions of diabetes-related hospitalisations in the group with diabetes ranging from 18.8% to 33.0% per year.[6 9 25 26] This could be explained by the fact that our sample was derived from general population which may be healthier than clinical samples used in other studies. It might also be a "healthy participant bias" where individuals with less severe disease agree to participate in research resulting in an underestimation of the outcome. It could also have resulted from not being able to capture admissions to private hospitals and smaller hospitals in the study region. Furthermore, definitions of diabetes-related hospitalisations are inconsistent between countries and thus, comparisons need to be made cautiously. In Australia, diabetes coding standards have changed significantly over the last decade making it problematic to compare diabetes-related hospitalisation rates over time.[4] Nonetheless, our results highlight an opportunity to devise interventions aimed specifically at reducing or delaying complications in those with diabetes. Previous evidence suggests that microvascular complications can be reduced by up to 50-60% and macrovascular complications by 40-45% with improved outpatient management.[9] The Diabetes Control and Complications Trial demonstrated that intensive diabetes treatment delayed the onset of complications in adolescents and young adults with type 1 diabetes mellitus.[31] The trial

concluded that intensive therapy aimed at achieving non-diabetic glucose levels slowed the progression of diabetic retinopathy, nephropathy, and neuropathy.[31] Similarly, the United Kingdom Prospective Diabetes Study showed a substantial decrease in microvascular complications of type 2 diabetes through intensive blood glucose control[34] and Steno study showed reduced rates of cardiovascular-related mortality with multifactorial intervention.[35]

We did not detect an association between IFG and the incidence, frequency rate and length of all-cause hospitalisation. To our knowledge, this is the first study to investigate the relationship between IFG and hospitalisation, thus comparable data are not available. Studies have reported a moderate increase in the risk of cardiovascular disease in the 'pre-diabetes' group as compared to normoglycaemia, which increases significantly once diabetes develops.[36] The authors of this study have previously identified predictors of progression from IFG to diabetes.[37] The greatest reductions in the occurrence of diabetes have been achieved through intensive lifestyle interventions for weight loss (5-10% of body weight), dietary modification, and physical activity (~30 minutes/day). Pharmacological therapy such as Metformin has also shown some promise, particularly in the younger and obese individuals.[38] Our results further signify the need for identifying those with IFG in the community, and developing and implementing targeted interventions to prevent or delay diabetes.

This study has a number of distinct advantages over previous studies that have explored the relationship between diabetes and hospital admissions. Our sample comprised randomly selected community-dwelling adults living in a well-defined area. Previous studies have used self-report,[25] hospital admissions data,[9 26 39] general practice registers[6 40] or data from diabetes clinics[7] to identify individuals with diabetes. We used a more robust method for identifying diabetes using a combination of FPG measurement, self-report and/or use of anti-hyperglycaemic medication. Through this approach, we were able to identify individuals with

dysglycaemia, even in the absence of fully developed diabetes. Finally, we followed participants for hospital admissions over a longer period as compared to previous studies,[25 26]

Our study has some limitations. First, we obtained linked hospital admissions data from one major public hospital in the study region. It is possible that some of our participants were admitted to a private hospital or a smaller hospital. We consider this unlikely as UHG is the only major tertiary hospital in the study area and our sample was derived from a region in the immediate vicinity of the hospital. Second, although our study region (BSD) is considered to have a stable population, it is still possible that some of the participants might have moved intercity or interstate during the follow-up period. Finally, we did not differentiate between the types of diabetes at baseline and are, therefore, unable to comment on the proportion of different types of diabetes in our sample.

## CONCLUSION

Our study confirms existing evidence showing higher risk, frequency rate and length of hospitalisation in individuals with diabetes mellitus. Further research should focus on identifying individual risk factors for hospitalisation in dysglycaemia. Strategies to reduce the need for hospitalisation should include preventing the disease itself (primary prevention), early diagnosis and treatment (secondary prevention) and preventing complications (tertiary prevention). Finally, adverse outcomes related with diabetes including hospital admissions could be reduced by preventing the progression from IFG to diabetes. We recommend screening for IFG in the population combined with targeted interventions to prevent diabetes in high risk individuals.

**Author contributions:** MAS and JAP conceived the study. MAS drafted the manuscript. MM performed the data analysis. MAS, KLH, LLFA, MM, MAK, DP and JAP critically appraised the manuscript and approved the final draft.

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**Competing interests:** None declared.

**Data sharing statement:** Data are available upon request.

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**Figure legend**

Figure 1: Reasons for hospitalisation by glycaemic category (% of men)

Figure 2: Reasons for hospitalisation by glycaemic category (% of women)

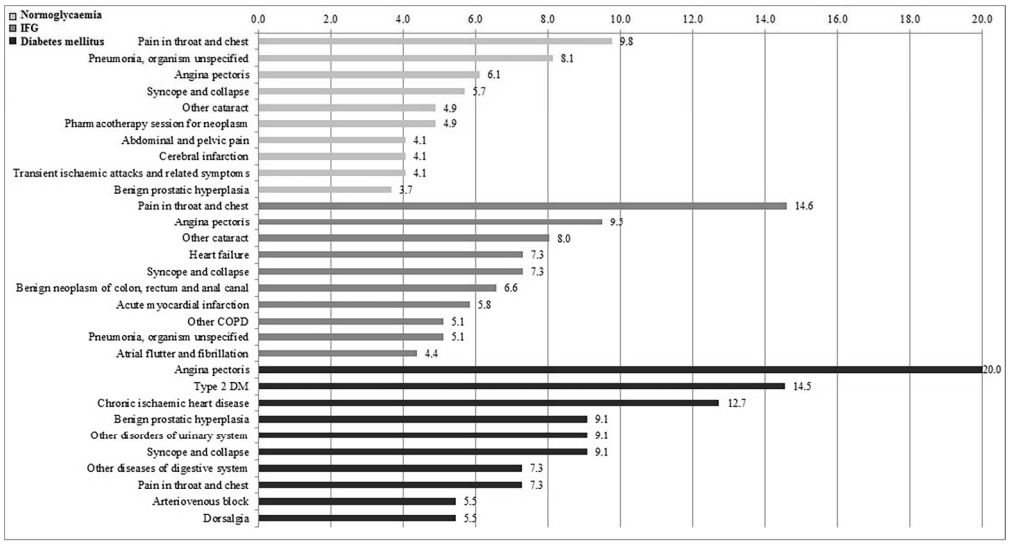


Figure 1: Reasons for hospitalisation by glycaemic category (% of men)

209x112mm (300 x 300 DPI)

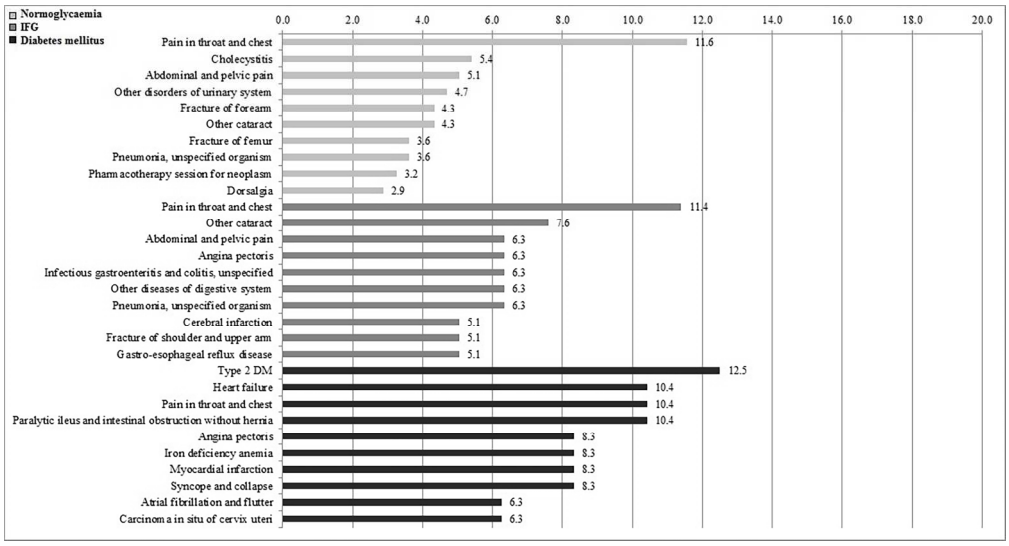


Figure 2: Reasons for hospitalisation by glycaemic category (% of women)

209x112mm (300 x 300 DPI)

**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies***

| Section/Topic | Item # | Recommendation | Reported on page # |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1,2 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 4 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 1,2,5 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | 5,6,7 |
| | | (*b*) For matched studies, give matching criteria and number of exposed and unexposed | n/a |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5,6,7 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 5,6,7 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 6,7,19,20 |
| Study size | 10 | Explain how the study size was arrived at | 5 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 8,9 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 8,9 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 8,9 |
| | | (*c*) Explain how missing data were addressed | 8,9 |
| | | (*d*) If applicable, explain how loss to follow-up was addressed | 20 |
| | | (*e*) Describe any sensitivity analyses | n/a |
| **Results** | | | |

| | | | |
|---|---|---|---|
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 5 |
| | | (b) Give reasons for non-participation at each stage | n/a |
| | | (c) Consider use of a flow diagram | n/a |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 10 |
| | | (b) Indicate number of participants with missing data for each variable of interest | n/a |
| | | (c) Summarise follow-up time (eg, average and total amount) | 10 |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | 11,12,13,14,15 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 11,12,13,14,15 |
| | | (*b*) Report category boundaries when continuous variables were categorized | 11,12,13,14,15 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 12,13,14 |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 11,12,13,14,15 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 16 |
| **Limitations** | | | |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 16,17,18,18,20 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 19,20,21 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 21 |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

# Comparison of incidence, rate and length of all-cause hospital admissions between adults with normoglycaemia, impaired fasting glucose and diabetes: a retrospective cohort study in Geelong, Australia

| | |
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| Secondary Subject Heading: | Epidemiology, Health services research |
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| | |

**Full title:** Comparison of incidence, rate and length of all-cause hospital admissions between adults with normoglycaemia, impaired fasting glucose and diabetes: a retrospective cohort study in Geelong, Australia.

Muhammad A. Sajjad,[1] Kara L. Holloway,[1] Lelia L. F. de Abreu,[1] Mohammadreza Mohebbi,[2] Mark A. Kotowicz,[1,3,4] Daryl Pedler,[1] and Julie A. Pasco,[1,3,4]

[1]*Deakin University, Geelong, VIC 3220, Australia*

[2]*Biostatistics Unit, Faculty of Health, Deakin University, Geelong, VIC 3220, Australia*

[3]*Department of Medicine-Western Health, Melbourne Medical School, The University of Melbourne, St Albans, VIC 3010, Australia*

[4]*University Hospital Geelong, Barwon Health, Geelong, VIC 3220, Australia*

**Corresponding author:** Muhammad A. Sajjad. Epi-Centre for Healthy Ageing, IMPACT Strategic Research Centre, Deakin University, PO Box 281 (Barwon Health), Geelong, Victoria 3220, Australia.

Email address: msajjad@BarwonHealth.org.au

Telephone: +61 342153339

Fax: +61 342153491

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Number of Figures: 2

## ABSTRACT

**Objective:** To determine whether adults with normoglycaemia, impaired fasting glucose (IFG) and diabetes differed according to the incidence, rate, length and primary reasons for hospital admission.

**Design:** Retrospective cohort study.

**Setting:** Barwon Statistical Division, Geelong, Australia.

**Participants:** Cohort included 971 men and 924 women, aged 20+yr, participating in the Geelong Osteoporosis Study. Glycaemic status was assessed at cohort entry using fasting plasma glucose, use of anti-hyperglycaemic medication and/or self-report.

**Primary and secondary outcome measures:** Primary outcome measure was any admission to the major tertiary public hospital in the study region over the follow-up period. Secondary outcome measures were admission rate and length (days).

**Results:** Over a median follow-up of 7.4 years (IQR 5.3-9.6), participants with diabetes, compared to those with normoglycaemia, were twice as likely to be hospitalised (OR 2.07, 95% CI 1.42-3.02), had a higher admission rate (IRR 1.61, 95% CI 1.17-2.23), and longer hospital stay (3$^{rd}$ quartile difference 7.7, 95% CI 1.3-14.1 and 9$^{th}$ decile difference 16.2, 95% CI 4.2-28.3). IFG group was similar to normoglycaemia for the incidence, rate and length of admission. Cardiovascular disease-related diagnoses were the most common primary reasons for hospitalisation across all glycaemic categories.

**Conclusions:** Our results show increased incidence, rate and length of all-cause hospital admission in adults with diabetes as compared to normoglycaemia, however we did not detect any associations for IFG. Interventions should focus on preventing IFG-to-diabetes progression and reducing cardiovascular risk in IFG and diabetes.

**Keywords:** Diabetes mellitus; hospitalisation; impaired fasting glucose; health service utilisation.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- Retrospective cohort design with long term follow-up.
- Randomly selected sample of general population, including both men and women.
- Robust method of identification of normoglycaemia, impaired fasting glucose and diabetes mellitus.
- To our knowledge, this is the first study to investigate the relationship between impaired fasting glucose and hospitalisation.
- Hospital admissions data were limited to the only tertiary public hospital in the study region.

## INTRODUCTION

The rapid increase in the prevalence of diabetes mellitus poses a significant challenge for health planners globally. Diabetes causes deterioration in physical health, mental wellbeing and quality of life, resulting in adverse outcomes including increased risk of hospitalisation.[1 2] According to the Australian Institute of Health and Welfare (AIHW), diabetes is one of the major causes of Potentially Preventable Hospitalisations (PPHs) in Australia, where hospitalisation may be avoidable through timely and adequate non-hospital care.[3-5]

It has been reported that people with diabetes have higher rates of hospitalisation as compared to those without the condition.[6-9] Previous research, however, has mainly focused on individuals with a diagnosis of diabetes. The association of intermediate deteriorations in glucose metabolism such as Impaired Fasting Glucose (IFG) and the risk of hospitalisation remains largely unexplored. IFG represents levels of Fasting Plasma Glucose (FPG) that are above normal (100 mg/dL or 5.5 mmol/L) but below the diagnostic threshold for diabetes (126 mg/dL or 7.0 mmol/L).[1] IFG is known to increase the risk of cardiovascular disease in addition to being a risk factor for diabetes.[10 11] As evidence builds for IFG as a disease condition rather than just a risk factor for diabetes, investigating adverse outcomes including hospitalisations in this grouping is warranted. The aim of this study was to compare the incidence, rate and length of all-cause hospital admissions between adults with normoglycaemia, IFG and diabetes mellitus over a median period of 7.4 years. Moreover, we aimed to highlight primary reasons for hospital admissions for individuals in different glycaemic categories.

## METHODS

### Study design and participants

We retrospectively analysed data from the Geelong Osteoporosis Study, a longitudinal cohort study including 3034 residents of the Barwon Statistical Division (BSD), located in south-eastern Australia, with a population of around 280,000. A detailed cohort profile, recruitment strategy and methodology have been described elsewhere.[12] In brief, during 1993-1997, an age-stratified sample of 1494 women aged 20-94 years was recruited from the Commonwealth electoral rolls with an overall participation of 77.1%. Of the original sample, 881 women participated in the 10-year follow-up commencing 2004 and an additional 246 women aged 20-29 years were recruited in 2006-2008. Of these two groups, we included 924 women for whom glycaemic status could be confirmed based on FPG measurement, self-reported diabetes and/or use of anti-hyperglycaemic agents.

Similarly, during 2001-2006, 1540 men were recruited and assessed, followed by a 5-year reassessment commencing 2006. We used either baseline or 5-year follow-up as the point of cohort entry depending on when FPG was measured. The final sample for this analysis included 971 men for whom we were able to ascertain glycaemic status using FPG measurement, self-report and/or use of anti-hyperglycaemic agents.

### Baseline measures

Cohort entry or 'baseline' was defined as the point when glycaemic status was confirmed and the follow-up was up to December 31, 2012 or date of death where applicable. At baseline, body weight and height were measured using electronic scales and a wall mounted stadiometer, respectively. Venous blood was collected after an overnight fast and FPG was measured using an adaptation of the hexokinase-glucose-6-phosphate dehydrogenase

method.[13] Participants were categorised into normoglycaemia, IFG and diabetes according to the 2003 American Diabetes Association's diagnostic criteria where diabetes was defined as FPG ≥ 7.0 mmol/L (126 mg/dL), self-report of diabetes, or use of anti-hyperglycaemic agents. IFG was considered present if FPG level was between 5.5 and 6.9 mmol/L (100-125 mg/dL). Participants with a FPG level ≤ 5.5 mmol/L in the absence of self-reported diabetes or use of anti-hyperglycaemic agents were classified as having normoglycaemia.

A series of questionnaires was administered seeking information on socio-demographic characteristics, use of medications and supplements, physical activity, alcohol consumption, and cigarette smoking.[12]

Levels of physical activity were determined using a multiple choice question with responses ranging from 'very active and active' (aggregated as 'high mobility') to 'sedentary, limited, inactive, chair/bedridden, and bedfast' (aggregated as 'low mobility'). Frequency of alcohol consumption was measured using the Cancer Council Victoria Dietary Questionnaire for Epidemiological Studies (DQESV2).[14] The Australian National Health and Medical Research Council guidelines were used to classify alcohol consumption into a binary variable; 'low use' (≤ 2 standard drinks/day) and 'high use' (>2 standard drinks/day), where a standard drink equals 10 grams of alcohol.[15] The Australian Bureau of Statistics Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD) was derived from the participants' area of residence, as an indicator of socioeconomic status.[16]

**Outcome measures**

Our primary outcome measure was any hospital admission, planned or unplanned, to the University Hospital Geelong (UHG) during the follow-up period; women (median follow-up 7.1 years, inter-quartile range 5.7-8.5) and men (median follow-up 8.3 years, inter-quartile range 5.6-11.0). Secondary outcomes included admission rate based on the total number of

hospital admissions over the follow-up period and length of admission in days, calculated from the admission and discharge dates, considering each admission as a separate occasion. Baseline data were linked to the admissions data using unique identification codes used by the hospital, referred to as Unit Record numbers or UR numbers.

The UHG is the largest public hospital and the only health service in the study region classified as a "principal referral hospital" according to the Australian hospitals peer-group classification.[17] It has 370 inpatient beds, 24 Intensive Care Unit beds and had the only 24-hour Emergency Department in the region during the study period. It provides a full spectrum of care including community care, aged care, rehabilitation, mental health, emergency and acute care.[18]

**Primary reasons for hospital admission**

Australian hospitals use an alphanumeric coding system for diseases and external causes of injury, referred to as the tenth revision of the International Classification of Diseases, Australian Modification (ICD-10-AM).[19] It comprises three, four and five character categories, structured by body system and etiology and is updated regularly.[19] We classified primary diagnoses into broad categories by aggregating individual disease codes, for instance, primary ICD-10 diagnoses codes of I21.0 'acute transmural myocardial infarction (MI) of anterior wall', I21.1 'acute transmural MI of inferior wall', and I21.4 'acute sub-endocardial MI', were combined as a single category of I21 'acute MI'.

**Deaths**

All deaths during the follow-up period were confirmed using the National Deaths Index, a national register maintained by the AIHW containing records of all deaths registered in

Australia since 1980.[20] To identify deaths, a combination of surname, first and second given names, address, date of birth, and date of last contact with the study were used.

**Potential confounders**

The risk of hospital admission in diabetes is reported to vary by age,[4] sex,[4 9] unhealthy weight,[21] cigarette smoking,[22] physical inactivity,[22] and socioeconomic deprivation.[23] In addition, high alcohol use may cause difficulties in management of diabetes, resulting in early onset of complications.[23] Hence, we included these potential confounders in our analyses to investigate the relationship between glycaemic status and hospitalisation outcomes. Furthermore, due to previously reported differences in hospitalisation patterns between men and women with diabetes,[4 9] we stratified our cohort by sex, in addition to reporting findings for the overall sample.

**Ethics approval**

The study was approved by the Barwon Health Human Research Ethics Committee. All participants provided informed consent.

**Statistical analysis**

We used t-tests for continuous data and Chi-square tests for categorical data to compare baseline characteristics of participants in different glycaemic categories (normoglycaemia, IFG and diabetes).

For the analysis of association between glycaemic status and the incidence of all-cause hospital admission, Chi-square test followed by incidence difference (i.e. risk difference) and 95% confidence intervals (CI) have been reported for examining bivariate association (i.e. the outcome and glycaemic status as exposure of interest). A set of tri-variate analyses (i.e. the outcome and glycaemic status as exposure of interest and one potential confounder) was

performed to examine the impact of each potential risk factor above and beyond the glycaemic category association with the study outcomes. We used (i) tri-variate logistic regressions for admission incidence, (ii) tri-variate Poisson regressions for admission rate and (iii) two-way ANOVAs on rank of admission length. Odds ratios, risk ratios and partial eta squared effect size were used to illustrate the impact of potential risk factors, respectively. Partial eta squared values of 0.009, 0.0588 and 0.1379 were considered as benchmarks for small, medium and large effect sizes, respectively.[24] Multivariate logistic regression was performed to evaluate the association of admission incidence and glycaemic status after adjusting for potential confounders that were significant at 0.1 level in tri-variate analyses and two-way interactions of confounders and glycaemic status; model adjusted OR and 95% CI are reported. Admission rate was calculated as frequency of hospitalisation divided by total person-years of follow-up for normoglycaemia, IFG and diabetes groups. Chi-square test followed by incidence rate ratio (IRR) and its 95% CI were illustrated for examining bivariate associations. Poisson regression with glycaemic status as factor and the frequency as the outcome and total person-years of follow-up as the offset was implemented for multivariate analysis. All potential confounders that were significant at 0.1 from the Poisson tri-variate analyses were included in the primary multivariate Poisson regression model. Sensitivity of the Poisson models against any deviations from model assumptions, including zero inflation was examined by implementing negative binomial regression models.

Medians and inter-quartile ranges of admission length were reported in the three groups. In order to deal with positively skewed nature of admission length and possible outliers, a non-parametric median-based regression based on L1-norm estimation[25 26] was performed as multivariate model. Simultaneous quantile regression on median, 3rd quartile and 9$^{th}$ decile using bootstrapping technique for estimating standard errors[27] was used to analyse the relationship between glycaemic status and upper quartile and last decile of admission length.

Similarly, all potential confounders that were significant at 0.1 from the two-way ranked ANOVA analyses were included in the primary multivariate linear regression model. Backward variable selection approach with p-entry=0.1 and p-exit=0.05 was implemented to all multivariate models obtain the final models.

Statistical analyses were conducted using Stata software version 14 (Stata Corp, College Station, TX, USA) and Minitab statistical software package (Version 17; Minitab, State College, PA, USA)

## RESULTS

Table 1 shows baseline characteristics of participants by glycaemic status. In men, 615 (63.3%) had normoglycaemia, 275 (28.3%) had IFG and 81 (8.3%) had diabetes. In women, 694 (75.1%) had normoglycaemia, 159 (17.2%) had IFG and 71 (7.6%) had diabetes.

For both men and women, those with diabetes were older and had higher BMI as compared to normoglycaemia group. Women with diabetes were more likely to have 'low mobility' at baseline as compared to those with normoglycaemia. Participants with normoglycaemia, IFG and diabetes did not differ significantly at baseline in terms of current smoking status and socioeconomic status.

**Table 1:** Descriptive statistics of men and women at baseline by glycaemic status (normoglycaemia, IFG and diabetes). Data presented as median (inter-quartile range) or n (%)

| **MEN** | **Total (n=971)** | **Normoglycaemia (n=615)** | **IFG[c] (n=275)** | **Diabetes (n=81)** | **p value** |
|---|---|---|---|---|---|
| Age (years) | 56.9 (28.0, 84.0) | 52.0 (24.0, 80.0) | 62.0 (40.0, 84.0) | 67.0 (53.0, 81.0) | **<0.001** |
| BMI[a] | 26.9 (21.9, 31.9) | 26.3 (21.6, 31.0) | 28.0 (23.1, 32.9) | 28.6 (24.3, 32.9) | **<0.001** |
| Current smoking | 141 (14.5) | 98 (15.9) | 33 (12.0) | 10 (12.3) | 0.25 |
| High alcohol use | 233 (23.9) | 138 (22.4) | 82 (29.8) | 13 (16.0) | **0.008** |
| Low mobility | 292 (30.0) | 180 (29.2) | 85 (30.9) | 27 (33.3) | 0.7 |
| IRSAD[b] | | | | | |
| 1 | 166 (17.0) | 96 (15.6) | 49 9 (17.8) | 21 (25.9) | 0.39 |
| 2 | 204 (21.0) | 126 (20.4) | 59 (21.4) | 19 (23.4) | |
| 3 | 189 (19.4) | 126 (20.4) | 52 (18.9) | 11 (13.5) | |
| 4 | 201 (20.7) | 131 (21.3) | 58 (21.0) | 12 (14.8) | |
| 5 | 211 (21.7) | 136 (22.1) | 57 (20.7) | 18 (22.2) | |
| Person-years of follow-up | 7324.0 | 4644.1 | 2113.6 | 617.7 | |
| **WOMEN** | **Total (n=924)** | **Normoglycaemia (n=694)** | **IFG[c] (n=159)** | **Diabetes (n=71)** | **p value** |
| Age (years) | 53.0 (25.0, 81.0) | 49.0 (20.0, 78.0) | 63.0 (41.0, 85.0) | 66.0 (46.0, 86.0) | **<0.001** |
| BMI[a] | 26.3 (19.1, 33.5) | 25.6 (19.3, 31.9) | 29.5 (22.3, 36.7) | 31.5 (21.4, 41.6) | **<0.001** |
| Current smoking | 109 (11.7) | 83 (11.9) | 21 (13.2) | 5 (7.0) | 0.44 |
| High alcohol use | 55 (5.9) | 45 (6.4) | 9 (5.6) | 1 (1.4) | 0.24 |
| Low mobility | 202 (22.0) | 121 (17.5) | 48 (30.3) | 33 (48.5) | **<0.001** |
| IRSAD[b] | | | | | |
| 1 | 150 (16.2) | 97 (13.9) | 37 (23.2) | 16 (22.5) | 0.41 |
| 2 | 186 (20.1) | 145 (20.8) | 30 (18.8) | 11 (15.4) | |
| 3 | 213 (23.0) | 162 (23.3) | 33 (20.7) | 18 (25.3) | |
| 4 | 187 (20.2) | 141 (20.3) | 32 (20.1) | 14 (19.7) | |
| 5 | 188 (20.3) | 149 (21.4) | 27 (16.9) | 12 (16.9) | |
| Person-years of follow-up | 6434.1 | 4843.1 | 1104.4 | 486.6 | |

[a]Body Mass Index (kg/m$^2$). [b]Index of Relative Socioeconomic Advantage and Disadvantage. [c]Impaired Fasting Glucose

**Incidence of all-cause hospital admission (admission incidence)**

Bivariate analyses showed that men with IFG had 10% more admission incidence (risk difference 0.10, 95% CI 0.02-0.17, p=0.006) and men with diabetes had almost 40% more admission incidence (risk difference 0.28, 95% CI 0.17-0.39, p<0.001), compared to men with normoglycaemia.

Similarly, women with IFG and diabetes were also more likely to be admitted as compared to normoglycaemia, (risk difference 0.10, 95% CI 0.01-0.18, p=0.024) and (risk difference 0.28, 95% CI 0.16-0.39, p<0.001), respectively.

After accounting for glycaemic category through tri-variate analyses for both men and women in the study, older age and lower socioeconomic status were associated with increased admission incidence (Table 2). In addition, a higher BMI in men and low mobility in women were associated with increased admission incidence after adjusting for glycaemic category (Table 2).

**Table 2:** Evaluating the impact of potential confounders at baseline on hospitalisation outcome association with glycaemic category using tri-variate regressions (i.e. one confounder at a time) between variables in men and women.

| | All-cause hospital admission by glycaemic category | | | Admission incidence OR[1] (95% CI) | p value | Admission rate IRR[2] (95% CI) | p value | Admission length (days) partial eta squared[3] | p value |
|---|---|---|---|---|---|---|---|---|---|
| **Men** | **Normoglycaemia n=615** | **IFG n=275** | **Diabetes n=81** | | | | | | |
| Admitted n (%) | 246 (40.00) | 137 (49.80) | 55 (67.90) | - | - | - | - | - | - |
| Age in years mean (SD) | 51.43 (16.89) | 60.01 (14.01) | 65.74(9.74) | 1.05 (1.04-1.06) | **<0.001** | 1.04 (1.03-1.05) | **<0.001** | 0.160 | **<0.001** |
| BMI kg/m$^2$ mean (SD) | 26.56 (3.74) | 28.42 (4.24) | 29.04 (4.30) | 1.04 (1.01-1.08) | **0.008** | 1.04 (1.01-1.08) | **0.006** | 0.011 | **0.001** |
| Current smoker n (%) | 33 (33.70) | 17 (51.50) | 4 (40.00) | 0.74 (0.51-1.07) | 0.115 | 1.07 (0.69-1.66) | 0.731 | 0.004 | 0.063 |
| High alcohol use n (%) | 53 (38.40) | 35 (42.70) | 9 (69.20) | 0.83 (0.61-1.12) | 0.238 | 0.74 (0.56-0.99) | **0.045** | 0.002 | 0.160 |
| Low mobility n (%) | 69 (38.30) | 44 (51.80) | 27 (66.70) | 0.96 (0.73-1.27) | 0.966 | 1.40 (1.05-1.87) | **0.021** | <0.001 | 0.723 |
| IRSAD | - | - | - | 0.89 (0.81-0.97) | **0.016** | 0.81 (0.74-0.89) | **<0.001** | 0.007 | **0.010** |
| **Women** | **Normoglycaemia n=694** | **IFG n=159** | **Diabetes n=71** | | | | | | |
| Admitted n (%) | 277 (39.90) | 79 (49.70) | 48 (67.60) | - | - | - | - | - | - |
| Age in years mean (SD) | 49.53 (18.26) | 61.83 (14.73) | 65.03 (13.11) | 1.03 (1.02-1.03) | **<0.001** | 1.03 (1.02-1.03) | **<0.001** | 0.098 | **<0.001** |
| BMI kg/m$^2$ mean (SD) | 26.59 (5.16) | 30.16 (5.98) | 31.23 (7.19) | 1.00 (0.97-1.02) | 0.781 | 1.01 (0.98-1.04) | 0.434 | 0.001 | 0.433 |
| Current smoking n (%) | 34 (41.00) | 21 (38.10) | 5 (80.00) | 0.96 (0.64-1.45) | 0.859 | 0.84 (0.58-1.19) | 0.336 | 0.001 | 0.437 |
| High alcohol use n (%) | 15 (33.30) | 3 (33.30) | 0 (0.00) | 0.65 (0.36-1.17) | 0.155 | 0.49 (0.29-0.82) | **0.007** | 0.001 | 0.278 |
| Low mobility n (%) | 82 (67.80) | 25 (52.1) | 27 (81.80) | 2.99 (2.14-4.18) | **<0.001** | 2.53 (1.69-3.74) | **<0.001** | 0.089 | **<0.001** |
| IRSAD | - | - | - | 0.86 (0.78-0.95) | **0.004** | 0.90 (0.81-1.00) | 0.069 | 0.009 | **0.004** |

1. Tri-variate logistic regression
2. Tri-variate Poisson regression
3. Two-way ranked ANOVA

IFG, Impaired Fasting Glucose; BMI, Body Mass Index; IRSAD, Index of Relative Socioeconomic Advantage and Disadvantage; OR, Odds ratio; IRR, Incidence Rate Ratio.

A significant age-sex interaction was observed and, therefore, included in the multivariate models (OR 1.3, 95% CI 1.0-1.6, p=0.04). After adjustments for age, sex and socioeconomic status, participants with diabetes were twice likely to be hospitalised for any cause, as compared to normoglycaemia (OR 2.0, 95% CI 1.4-3.0, p<0.001). Having IFG at baseline was not significantly associated with admission incidence (OR 1.1, 95% CI 0.8-1.4, p=0.38).

**Admission rate**

Overall, 50.6% of the participants with diabetes were admitted more than once over the follow-up period, compared with 30.8% and 22.0% of those with IFG and normoglycaemia, respectively. In men, admission rate was 0.43 per person per year for those with diabetes (95% CI 0.32-0.57), 0.21 per person per year in IFG (95% CI 0.17-0.27) and 0.19 per person per year in those with normoglycaemia (95% CI 0.15-0.23). Admission rate was 0.50 per person per year for women with diabetes (95% CI 0.30-0.84), 0.24 per person per year for those with IFG (95% CI 0.18-0.31) and 0.16 per person per year in those with normoglycaemia (95% CI 0.14-0.19). In men, older age, BMI, high alcohol use, low mobility and low socioeconomic status were associated with higher admission rate (Table 2). In women, older age, high alcohol use and low mobility were associated with higher admission rate (Table 2).

In the final multivariate model, admission rate was significantly higher in the diabetes group, as compared to normoglycaemia (IRR 1.6, 95% CI 1.1-2.2, p<0.05). The IFG group was not significantly different from normoglycaemia in terms of admission rate (IRR 0.9, 95% CI 0.7-1.1, p=0.67).

**Admission length (days)**

The effect sizes of individual baseline characteristics on admission length based on two-way ranked ANOVA are illustrated in Table 2. For men, older age, higher BMI and lower socioeconomic status were associated with increased admission length (Table 2). Older age had a large effect on admission length, while high BMI and low socioeconomic status had medium and small effects respectively (partial eta squared=0.160, 0.011 and 0.007) (Table 2).

Median regression analysis did not show a difference between the glycaemic categories in terms of median admission length (Table 3). In additional analysis, 3rd quartile and 9th decile comparison was performed showing that having diabetes at baseline was associated with an increased admission length (3rd quartile difference 7.7, 95% CI 1.3-14.1, p=0.01) and (9th decile difference 16.2, 95% CI 4.2-28.3, p=0.008) in patients with longer than median admission length. Hence, in participants that spent longer than the median admission length in the hospital, having diabetes was associated with longer hospital stay.

**Table 3:** Relationship between glycaemic status and all-cause hospital admission (multivariate model), presented for men, women and total sample.

| | All-cause hospital admission incidence OR (95% CI) | Admission rate IRR (95% CI)[1] | Admission length (days) Median (95% CI) | Admission length (days) 3rd quartile (95% CI) | Admission length (days) 9th decile (95% CI) |
|---|---|---|---|---|---|
| **Men** | | | | | |
| Normoglycaemia | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| IFG | 1.08 (0.79-1.48, p=0.592) | 0.85 (0.65-1.12, p=0.271) | 0.00 (-0.13-(-0.12), p=0.882) | 0.24 (-1.20-1.70, p=0.739) | -0.31 (-6.70-6.06, p=0.922) |
| Diabetes | **1.90 (1.11-3.24, p=0.018)** | 1.34 (0.95-1.88, p=0.090) | 2.47 (-1.73-6.68, p=0.249) | **10.46 (1.44-19.48, p=0.023)** | **21.55 (1.39-41.72, p=0.036)** |
| Age (years) | - | - | 0.00 (-0.00-0.01, p=0.107) | **0.13 (0.09-0.18, p=0.0001)** | **0.25 (0.04-0.45, p=0.016)** |
| Age category (40-60) | 1.42 (0.96-2.10, p=0.075) | **1.91 (1.14-3.19, p=0.013)** | - | - | - |
| (>60) | **4.73 (3.22-6.93, p<0.001)** | **4.59 (2.92-7.21, p<0.001)** | | | |
| BMI (kg/m$^2$) | **1.03 (0.99-1.07, p=0.052)** | **1.03 (1.00-1.06, p=0.033)** | | - | - |
| Current smoking | - | - | 0.02 (-0.09-0.03, p=0.370) | - | - |
| High alcohol use | | | 0.01 (-0.06-0.03, p=0.557) | -0.56 (-1.33-0.20, p=0.152) | **-6.67(-12.84-(-0.49), p=0.034** |
| IRSAD | - | **0.84 (0.77-0.91, p<0.001)** | 0.01 (-0.02-0.00, p=0.37) | - | |
| **Women** | | | | | |
| Normoglycaemia | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| IFG | 1.10 (0.75-1.60, p=0.614) | 1.10 (0.79-1.54, p=0.557) | 0.00 (-0.16-0.15, p=0.944) | -0.6 (-2.77-1.49, p=0.557) | 1.20 (-6.75-9.16, p=0.766) |
| Diabetes | **2.32 (1.34-4.02, p=0.003)** | 2.12 (1.12-4.03, p=0.021) | 0.76 (-1.06-2.59, p=0.414) | 4.30 (-3.19-11.8, p=0.260) | 14.41 (-3.91-32.74, p=0.123) |
| Age (years) | - | - | 0.00 (0.00-0.00, p=0.155) | **0.09 (0.04-0.14, p=0.001)** | **0.32 (0.24-0.40, p=0.001)** |
| Age category (40-60) | 1.03 (0.72-1.47, p=0.845) | 1.30 (0.83-2.04, p=0.238) | - | - | - |
| (60-80) | **2.51 (1.73-3.64, p<0.001)** | **2.73 (1.84-4.06, p<0.001)** | | | |
| (>80) | **7.22 (3.58-14.56, p<0.001)** | **3.06 (2.08-4.52, p<0.001)** | | | |
| BMI | - | - | 0.00 (0.00-0.00, p=0.748) | - | - |
| Current smoking | - | - | 0.01 (-0.07-0.05, p=0.697) | - | - |
| High alcohol use | - | 0.55 (0.34-0.89, p=0.017) | 0.00 (-0.03-0.03, p=0.890) | - | - |
| IRSAD | **0.86 (0.78-0.95, p=0.005)** | | 0.01 (-0.03-0.00, p=0.231) | -0.37 (-0.66-(-0.08), p=0.01) | **-0.81 (-1.36-(-.0.24), p=0.004)** |
| **Total** | | | | | |
| Normoglycaemia | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| IFG | 1.11 (0.87-1.40, p=0.380) | 0.95 (0.77-1.18, p=0.671) | 0.00 (-0.05-0.05, p=1.000) | 0.00 (-0.61-0.61, p=1.000) | 0.00 (-2.22-2.22, p=1.000) |
| Diabetes | **2.07 (1.42-3.02, p<0.001)** | **1.61 (1.17-2.26, p=0.003)** | 1.70 (-0.05-3.47, p=0.058) | **7.77 (1.39-14.16, p=0.017)** | **16.29 (4.20-28.38, p=0.008)** |
| Age category | **1.78 (1.49-2.12, p<0.001)** | **1.82 (1.49-2.24, p<0.001)** | 0.00 (-0.00-0.08, p=1.000) | **1.93 (0.89-2.97, p=0.001)** | **8.33 (5.63-11.04, p<0.001)** |
| Sex (male) | **0.52 (0.29-0.95, p=0.033)** | 0.71 (0.33-1.52, p=0.391) | -0.13(-0.30-0.02, p=0.095) | **-1.55 (-2.98- (-0.12, p=0.033)** | -2.21 (-5.65-1.21, p=0.206) |
| Sex-age interaction | **1.31 (1.02-1.69, p=0.034)** | 1.19 (0.90-1.57, p=0.210) | 0.13 (-0.02-0.30, p=0.095) | **1.55 (0.13-2.97, p=0.032)** | 2.08 (-1.11-5.28, p=0.201) |
| BMI | - | 1.02 (0.99-1.04, p=0.069) | 0.00 (-0.00-0.00, p=1.000) | - | - |
| Current smoking | - | - | 0.00 (-0.00-0.00, p=1.000) | | |
| High alcohol use | - | **0.78 (0.61-0.99, p=0.045)** | 0.00 (-0.00-0.00, p=1.000) | - | - |
| IRSAD | **0.89 (0.83-0.95, p=0.002)** | **0.88 (0.82-0.94, p<0.001)** | 0.00 (-0.00-0.00, p=1.000) | -0.05 (-0.16-0.04, p=0.274) | **-1.08 (-1.65-(-5.09), p<0.001** |

IFG, Impaired Fasting Glucose; BMI, Body Mass Index; IRSAD, Index of Relative Socioeconomic Advantage and Disadvantage; OR, Odds ratio; IRR, Incidence Rate Ratio.

1. Results from Poisson models; sensitivity of the Poisson models against any deviations from model assumptions, including zero inflation, was examined by implementing negative binomial regression models and there were negligible changes in RRs, 95% CIs and p-values.

**Primary reasons for hospital admission**

Figures 1 and 2 show the 10 most common primary reasons for hospitalisation by glycaemic category for men and women in the study, respectively.

Among men with diabetes, the most commonly encountered diagnosis was 'angina pectoris', with 20.0% of the group having at least one hospitalisation primarily for the condition. It was followed by 'type 2 diabetes mellitus' (14.5%). 'Pain in throat and chest' was the most common reason for hospitalisation for men in the IFG (14.6%) and normoglycaemia (9.8%) groups.

In women with diabetes, 'type 2 diabetes mellitus' was the most commonly documented primary reason for hospitalisation (12.5%), followed by 'heart failure' (10.4%). For the IFG and normoglycaemia groups, 'pain in throat and chest' was the most common reason for hospitalisation, 11.4% and 11.6% respectively.

**DISCUSSION**

This study reports that, compared to normoglycaemia, having diabetes is associated with a higher incidence, rate, and length of hospital admission. During the follow-up, 68.0% of participants with diabetes had at least one hospital admission as compared to 50.0% with IFG and 40.0% with normoglycaemia. The incidence of hospital admission was twice in those with diabetes as compared to normoglycaemia. Previous studies reporting admission incidence have varied depending on the study population and duration of follow-up. Only one study in the literature has examined hospitalisations in the Australian population with diabetes.[28] The study followed individuals aged 45 years and over, with and without diabetes, for a year, reporting that 32.8% of participants with diabetes had one or more hospitalisations as compared to 24.2% of those with normoglycaemia.[28] Similar studies have been performed

in other countries, for example, a New Zealand study conducted over a three-year period reported an all-cause hospitalisation rate of 43.5% in those with diabetes.[29] An Italian study showed an even higher proportion of participants with diabetes (55.0%) being hospitalised at least once over a 4.5 year follow-up.[7]

There are a number of factors which could explain the higher risk of hospitalisation in people with diabetes. Comorbid coronary heart disease, stroke, depression, musculoskeletal disease and cancer are common in people with diabetes and can increase the risk of hospitalisation.[30] [31] In addition, diabetes shares common risk factors with other chronic diseases (particularly cardiovascular disease) such as obesity, physical inactivity and unhealthy diet. In our study, half of the 10 most common primary reasons for hospitalisation in participants with diabetes were related to complications and/or diagnoses related to cardiovascular disease. This is consistent with studies showing that a significant proportion of morbidity and mortality associated with diabetes is due to cardiovascular disease.[10] Some recent studies have reported a decline in incident cardiovascular disease in people with diabetes, however, the risk is still double that of those with normoglycaemia.[32]

In our sample, older age was independently associated with both having diabetes and the risk of hospitalisation. Elderly patients with diabetes often present with multiple and advanced complications and are more likely to be readmitted and spend longer in hospital beds as compared to younger counterparts.[33]

Other factors predisposing people with diabetes to hospitalisation are related to disease management that involves maintaining a balance between lowering blood glucose levels and preventing hypoglycaemic events. One of the goals of management is achieving tight glycaemic control (FPG < 6 mmol/L); while this has been shown to reduce microvascular complications, it may simultaneously increase the incidence of hypoglycaemic events.[6]

Therefore, the benefits of obtaining optimum blood glucose levels have to be weighed against the risk of severe hypoglycaemic episodes that could result in frequent Emergency Department visits and hospital admissions.[34] Furthermore, optimal diabetes care requires active involvement by the patients and their ability to navigate the health system, hence, health literacy plays a key role. Health outcomes are poorer in population sub-groups with diabetes having low health literacy levels such as migrants from non-English speaking backgrounds and indigenous people.[35 36]

In our study, 14.5% of men and 12.5% of women with diabetes had a hospitalisation specifically for a diagnosis or complication related to diabetes mellitus. Other studies have reported higher proportions of diabetes-related hospitalisations in the group with diabetes ranging from 18.8% to 33.0% per year.[6 9 28 29] This could be explained by the fact that our sample was derived from general population which may be healthier than clinical samples used in other studies. It might also be a "healthy participant bias" where individuals with less severe disease agree to participate in research resulting in an underestimation of the outcome. It could also have resulted from not being able to capture admissions to private hospitals and smaller hospitals in the study region. Furthermore, definitions of diabetes-related hospitalisations are inconsistent between countries and thus, comparisons need to be made cautiously. In Australia, diabetes coding standards have changed significantly over the last decade making it problematic to compare diabetes-related hospitalisation rates over time.[4] Nonetheless, our results highlight an opportunity to devise interventions aimed specifically at reducing or delaying complications in those with diabetes. Previous evidence suggests that microvascular complications can be reduced by up to 50-60% and macrovascular complications by 40-45% with improved outpatient management.[9] The Diabetes Control and Complications Trial demonstrated that intensive diabetes treatment delayed the onset of complications in adolescents and young adults with type 1 diabetes mellitus.[34] The trial

concluded that intensive therapy aimed at achieving non-diabetic glucose levels slowed the progression of diabetic retinopathy, nephropathy, and neuropathy.[34] Similarly, the United Kingdom Prospective Diabetes Study showed a substantial decrease in microvascular complications of type 2 diabetes through intensive blood glucose control[37] and Steno study showed reduced rates of cardiovascular-related mortality with multifactorial intervention.[38]

We did not detect an association between IFG and the incidence, rate and length of hospital admission. To our knowledge, this is the first study to investigate the relationship between IFG and hospitalisation, thus comparable data are not available. Studies have reported a moderate increase in the risk of cardiovascular disease in the 'pre-diabetes' group as compared to normoglycaemia, which increases significantly once diabetes develops.[39] Current rates of IFG-to-diabetes progression are alarmingly high, with studies reporting development of diabetes in up to two-thirds of individuals with pre-diabetes.[39] The authors of this study have previously reported that approximately one-third of Australian women have IFG, with a six-fold higher risk of progressing to diabetes over a decade if FPG $\geq$ 6.1 mmol/L .[40] The greatest reductions in the occurrence of diabetes have been achieved through intensive lifestyle interventions for weight loss (5-10% of body weight), dietary modification, and physical activity (~30 minutes/day).[39] Pharmacological therapy such as Metformin has also shown some promise, particularly in the younger and obese individuals.[41] Our findings show that the incidence of hospital admission multiplies as IFG progresses to diabetes, which if used effectively in public health campaigns, could help reduce progression in the population.

This study has a number of distinct advantages over previous studies that have explored the relationship between diabetes and hospital admissions. Our sample comprised randomly selected community-dwelling adults living in a well-defined area. Previous studies have used self-report,[28] hospital admissions data,[9 29 42] general practice registers[6 43] or data from diabetes clinics[7] to identify individuals with diabetes. We used a more robust method for identifying

diabetes using a combination of FPG measurement, self-report and/or use of anti-hyperglycaemic medication. Through this approach, we were able to identify individuals with dysglycaemia, even in the absence of fully developed diabetes. Furthermore, we followed participants for hospital admissions over a longer period as compared to previous studies.[28 29] Finally, we used unique identifiers to capture hospital admissions and mortality data, hence, we were able to obtain this information even if we lost contact with participants over the study period. Our study has some limitations. First, we obtained linked hospital admissions data from one major public hospital in the study region. It is possible that some of our participants were admitted to a private hospital or a smaller hospital. We consider this unlikely as UHG is the only major tertiary hospital in the study area and our sample was derived from a region in the immediate vicinity of the hospital. Second, although our study region (BSD) is considered to have a stable population, it is still possible that some of the participants might have moved intercity or interstate during the follow-up period. Furthermore, the results from our study, which included mainly Caucasian individuals, may not be generalisable to other populations. Finally, we did not differentiate between the types of diabetes at baseline and are, therefore, unable to comment on the proportion of different types of diabetes in our sample.

## CONCLUSION

Our study confirms existing evidence showing higher incidence, rate and length of hospital admissions in individuals with diabetes mellitus. Further research should focus on identifying individual risk factors for hospitalisation in dysglycaemia. Strategies to reduce the need for hospitalisation should include preventing the disease itself (primary prevention), early diagnosis and treatment (secondary prevention) and preventing complications (tertiary prevention). Finally, adverse outcomes related with diabetes including hospital admissions could be reduced by preventing the progression from IFG to diabetes. We recommend

screening for IFG in the population combined with targeted interventions to prevent diabetes in high risk individuals.

**Author contributions:** MAS and JAP conceived the study. MAS drafted the manuscript. MM performed the data analysis. MAS, KLH, LLFA, MM, MAK, DP and JAP critically appraised the manuscript and approved the final draft.

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**Competing interests:** None declared.

**Data sharing statement:** Data are available upon request.

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**Figure legend**

Figure 1: Primary reasons for hospital admission by glycaemic category (% of men)

Figure 2: Primary reasons for hospital admission by glycaemic category (% of women)

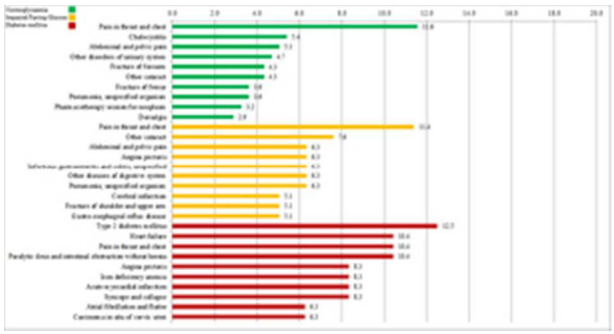

Figure 2: Primary reasons for hospital admission by glycaemic category (% of women)

25x13mm (300 x 300 DPI)

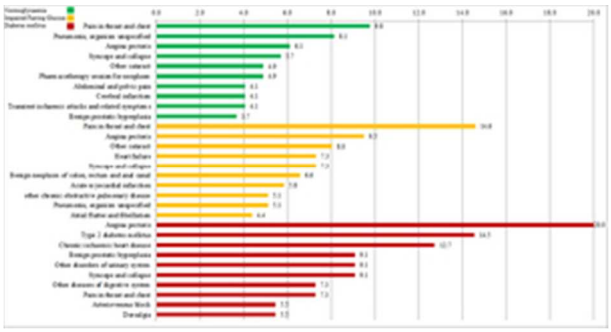

Figure 1: Primary reasons for hospital admission by glycaemic category (% of men)

25x13mm (300 x 300 DPI)

**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies***

| Section/Topic | Item # | Recommendation | Reported on page # |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1,2 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 4 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 1,2,5 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | 5,6,7 |
| | | (*b*) For matched studies, give matching criteria and number of exposed and unexposed | n/a |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5,6,7 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 5,6,7 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 6,7,19,20 |
| Study size | 10 | Explain how the study size was arrived at | 5 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 8,9 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 8,9 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 8,9 |
| | | (*c*) Explain how missing data were addressed | 8,9 |
| | | (*d*) If applicable, explain how loss to follow-up was addressed | 20 |
| | | (*e*) Describe any sensitivity analyses | n/a |
| **Results** | | | |

| | | | |
|---|---|---|---|
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 5 |
| | | (b) Give reasons for non-participation at each stage | n/a |
| | | (c) Consider use of a flow diagram | n/a |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 10 |
| | | (b) Indicate number of participants with missing data for each variable of interest | n/a |
| | | (c) Summarise follow-up time (eg, average and total amount) | 10 |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | 11,12,13,14,15 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 11,12,13,14,15 |
| | | (*b*) Report category boundaries when continuous variables were categorized | 11,12,13,14,15 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 12,13,14 |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 11,12,13,14,15 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 16 |
| **Limitations** | | | |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 16,17,18,18,20 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 19,20,21 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 21 |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.