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Tan, Wei Beng; Szücs, Anna; Burkill, Sarah M; Ong, Shih Hui; Young, Doris; Goh, Lay Hoon

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Nephrologist referrals of elderly CKD patients in Singapore: A cross-sectional study

Wei Beng Tan, MBChB (UK), MRCGP (UK), DRCOG (UK), DGFM (Singapore), GDip (Family Practice Dermatology, Singapore), M. Med (Family Medicine, Singapore).

Job Title: Family Physicians, Associate Consultant, National University Polyclinics, National University Health System.

ORCID number: 0000-0002-6361-6780

Address: National University Polyclinics, 1 Jurong East Street 21, Singapore 609606

Anna Szücs M.D.

Job Title: Postdoctoral Research Fellow, Division of Family Medicine, Department of Medicine, National University of Singapore

ORCID number: 0000-0001-6356-4178

Address: NUS Yong Loo Lin School of Medicine NUHS Tower Block, 1E Kent Ridge Road Level 11, Singapore 119228

Sarah M Burkill PHD

Job title: Postdoctoral Research Fellow

ORCID number: 0000-0002-8988-4724

Address: Saw Swee Hock School of Public Health, Tahir Foundation Building, National University of Singapore, 12 Science Drive 2, #10-01, Singapore 117549

Ong Shih Hui, Master in Public Health (Singapore).

Job title: Assistant Director, Regional Health System Office, National University Health System, Singapore.

Address: Alexandra Hospital, Blk 20, 378 Alexandra Rd, Singapore 159964

Doris Young, MBBS (Australia), MD (Australia), FRACGP,

Professor,

Division of Family Medicine, Yong Loo Lin School of Medicine, National University of Singapore

ORCID number: N/A

Address: NUS Yong Loo Lin School of Medicine NUHS Tower Block, 1E Kent Ridge Road Level 11, Singapore 119228

Goh Lay Hoon, MBBS (Singapore), M. Med (Family Medicine, Singapore), MClin Epid (Australia)

Job title: Senior Consultant, Department of Family Medicine, National University Health System, Senior Consultant, National University Polyclinics, Assistant Professor, Division of Family Medicine, Yong Loo Lin School of Medicine, National University of Singapore

ORCID number: 0000-0003-1536-3050

Address: NUS Yong Loo Lin School of Medicine NUHS Tower Block, 1E Kent Ridge Road Level 11, Singapore 119228

Correspondence: wei_beng_tan@nuhs.edu.sg

Background:

Chronic kidney disease (CKD) is common in the elderly population. By 2035, approximately one-quarter of Singapore residents are expected to have CKD. Many of these patients are not referred to nephrologists.

Aim:

We aimed to compare the characteristics of elderly (≥ 65 years old) patients with stage 3B CKD and above in the referral and non-referral groups.

Design and settings

A cross-sectional study in the primary care organisation National University Polyclinics (NUP), Singapore.

Method:

Retrospective data were extracted from the electronic health records of CKD patients (≥ 65 years old) with stage 3B CKD and above.

Results:

From 1 January to 31 December 2018, a total of 1,536 patients aged 65 years or older were diagnosed with stage 3B CKD or above (non-referral group = 1,179 vs. referral group = 357). The mean patient age in the non-referral group (78.3 years) was older than that in the referral group (75.9 years) ($P < 0.001$). Indian elderly patients were referred more compared to their Chinese counterparts ($P = 0.008$). The non-referral group was prescribed significantly less fibrate, statins, insulin, sulfonylureas, dipeptidyl peptidase-4 inhibitors, and antiplatelet than the referral group ($P < 0.05$), but only the difference in fibrates remained significant on subsequent multivariate analysis.

Conclusions:

This study demonstrates that there is a considerable number of elderly CKD patients exclusively managed in the primary care setting (n = 1,179) and that referrals primarily depend on demographic factors, namely age and ethnicity, rather than medical determinants of CKD severity or case complexity.

Keywords:

CKD, elderly, primary health care, referral, nephrology, family medicine, population health.

How this fits in

This study reflects a vital role of family physicians in managing elderly CKD patients and highlights the need to review the referral process among this diverse group of patients. We recommend multidisciplinary collaboration between family physicians and nephrologists to refine the referral criteria to determine who truly needs early referrals to a nephrologist, and to develop guidelines to optimise the primary care management and monitoring of CKD patients, especially of those who are not referred and treated conservatively.

Introduction

Chronic kidney disease (CKD) is one of the common presentations among the older population in the primary care setting[1–3]. In the United States, the Third National Health and Nutrition Examination Survey (NHANES III) conducted between 1988 and 1994 demonstrated that 7.6% of individuals aged 60–69 years and 25.9% of those aged at least 75 years had a glomerular filtration rate (GFR) of 15–60 ml per minute per 1.73 m^2 compared to only 1.8% of those aged 40–59 years and 0.2% of those aged less than 40 years[4]. In France, an epidemiological survey of the Île-de-France area showed that the incidence rate among patients above 75 years was almost seven times that of patients aged 20–39 years (619 versus 92 new cases/million population) and more than double that of patients aged 40–59 years (619 versus 264 new cases/million population)[5]. In Singapore, it is projected that from 2007 to 2035, the number of residents with CKD will increase from 316,521 to 887,870, indicating an increase in prevalence from 12.2% to 24.3%[6]. By 2035, approximately one-quarter of Singapore residents are expected to have CKD. This trend will likely affect how we manage CKD patients in the primary care community[6].

CKD management has become part of multi-chronic disease management for family physicians in Singapore. With the introduction of CKD classification by *Kidney Disease: Improving Global Outcomes* (KDIGO)[7], the resultant increasing awareness of CKD among primary care settings had a significant impact on referral patterns to renal medical services with increased referral rates as reported in Boston, USA[8] and Brisbane, Australia[9]. However, comparative studies contrasting the characteristics of elderly CKD patients between referral and non-referral groups in the primary care setting are lacking.

In Singapore, National University Polyclinics (NUP) is the public primary care provider of the Western cluster health care system known as the National University Health System (NUHS). It offers subsidized family medical care services to communities in Western Singapore. In April 2017, the Holistic Approach in Lowering and Tracking CKD (HALT-CKD) programme was launched by the Ministry of Health, aiming to 1) recruit and track all patients with stage 1–4 CKD from any cause; 2) slow down CKD progression with control of risk factors and Renin Angiotensin System (RAS) blockade in all stages of CKD; and 3) encourage shared-care collaboration between primary health care and nephrologists at stage 3B–4 CKD[10]. This programme recommends that patients with stage 3B CKD or above be referred to nephrologists at secondary care hospitals. This is to provide the patients with early access to further investigations by nephrologists and preparation for renal replacement therapies to reduce morbidity, mortality and hospitalisation rates[11,12]. However, many elderly patients are

managed by the primary care team and are not referred to renal physicians. The factors contributing to the referral preferences are not well studied.

The objective of the study was to compare the characteristics of the elderly (≥ 65 years) CKD 3B, 4, and 5 patients who were referred to nephrologists to those who were not referred at NUP in Singapore from 1 January 2018 until 31 December 2018. The null hypothesis is that there is no significant difference in CKD severity, socio-demographic factors, comorbidities, or medication between the referral and the non-referral groups.

Methodology

We defined CKD as per the KDIGO classification[7], and the elderly patients as those aged 65 years and above[13]. We collected retrospective data on all elderly patients with stage 3B CKD and above at five NUP polyclinics (Bukit Batok, Choa Chu Kang, Clementi, Jurong, and Pioneer) between 1 January 2018 and 31 December 2018 using the NUP electronic record system. As the CKD status can be confirmed only with two consecutive estimated GFRs (eGFR mL/min/1.73 m^2) 90 days apart, data extraction was performed from 1 October 2017 until 31 December 2018. Estimated Glomerular Filtration Rate (eGFR) results are reported based on CKD-EPI Equation: Serum Creatinine (µmol/L), age (years), gender. Albuminuria-proteinuria categories were defined based on the albumin-to-creatinine ratio (ACR), and when not available, based on the protein-to-creatinine ratio (PCR), following the cut-off values of the KDIGO classification[7]: ACR < 3 mg/mmol or PCR < 15 mg/mmol – *Normal to mildly increased*; ACR of 3-30 mg/mmol or PCR of 15-50 mg/mmol – *Moderately increased*; ACR > 300 mg/mmol or PCR > 50 mg/mmol – *Severely increased*.

The inclusion criteria were as follows:

1. Patient age: ≥ 65 years

2. The stages of CKD in patients were confirmed when there were two eGFRs in mL/min/1.73 m^2 90 days apart, defined as:

    Stage 3B (eGFR: 30–44 mL/min/1.73 m^2)

    Stage 4 (eGFR: 15–29 mL/min/1.73 m^2)

    Stage 5 (eGFR: <15 mL/min/1.73 m^2)

The exclusion criteria were as follows:

1. Patients with stages 1–3A CKD or an unknown CKD stage/status (lack of two consecutive eGFR results at least 90 days apart).

The following data was extracted from the electronic record for all eligible patients: demographics (age, sex, ethnicity, and smoking), comorbidities (diabetes mellitus, hypertension, dyslipidaemia, ischaemic heart disease, cerebrovascular disease, and peripheral vascular disease), and medications as of the date where CKD status was established [angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), statins, fibrates, biguanides, sulfonylureas, loop / potassium-sparing diuretics, insulin and antiplatelets].

We compared the characteristics of patients between those who were referred by the family physicians to nephrologists and those who were not.

Statistical analysis: We performed statistical analysis using STATA version 16.0 and R version 3.6.1. We used Chi-square tests for categorical variables; t-tests for continuous variables in bivariate comparisons between referral and non-referral groups; and two-way ANOVA to assess the mean number of comorbid diseases by age group in referral vs non-referral groups. In our further confirmatory analysis, we ran a stepwise logistic regression predicting referral with a first model containing only CKD status and albuminuria-proteinuria, as these two factors determine prognosis in the KDIGO classification[7]. The subsequent models included variables that were significant in the bivariate analysis, entered hierarchically by category (sociodemographic factors, comorbidities, medication). Missing values were handled by listwise deletion (we performed complete case analysis).

Results

From 1 January to 31 December 2018, a total of 1,536 patients aged 65 years or older were diagnosed with stage 3B or above CKD (Table 1). There were 1,179 patients in the non-referral group and 357 in the referral group. Data on blood pressure was missing in four participants (0.27% of the total sample). HbA1c data was missing in 50 out of 1,097 patients with diabetes mellitus (4.56%). Thirty-three patients (2.15% of the total sample) had a PCR but no ACR value: 19 patients (1.61%) of the non-referral group and 14 patients (3,92%) of the referral group. Values for both ACR and PCR were missing in 183 patients (11.91% of the total sample), 154 from the non-referral group (13.06%) and 29 from the referral group (8.12%).

The bivariate analysis indicated a significant difference in age between those who were not referred and those who were referred (means: 78.3 vs 75.9 years), regardless of age being coded as a continuous or a categorical variable (both $P < 0.001$). The Chi-square test was significant with respect to ethnicities ($P = 0.017$; Table 1). There was no significant difference between the non-referral and referral groups on CKD severity (Table 2) or comorbidities (Table

3). The groups differed for the following medications: fibrates, statins, insulin, sulfonylureas, dipeptidyl peptidase-4 (DPP-4) inhibitors, and antiplatelets (Table 4).

Logistic regression did not find significant associations between referrals and CKD status or albuminuria-proteinuria (Table 5). In Model 2, additionally testing socio-demographic variables, the older age groups, namely 80-84 years (OR: 0.43, P < 0.001), 85-89 years (OR: 0.49, P = 0.003), and ≥ 90 years (OR: 0.41, P = 0.015) were less likely to be referred than 65–69-year-olds. With respect to ethnicity, both Indians and the ethnicities grouped under "Others" had significantly higher odds to be referred than Chinese (resp. OR = 2.18 P = 0.008 and OR = 2.74 P = 0.007). These effects of age and ethnicity remained significant in Model 3, where medications were additionally included. However, of the drugs that were significant in the bivariate analysis, only fibrates remained weakly significant in the multivariate analysis (OR = 1.68, P = 0.049).

Discussion

Summary

This study demonstrates that primary care services such as NUP in Western Singapore manage a considerable number of elderly CKD patients instead of referrals to nephrologists (n = 1,179, 77%). It is noteworthy that the HALT-CKD programme's recommendation includes referral for patients with stage 3B CKD, which contrasts with the KDIGO guidelines that recommend referral to kidney specialists for patients who have stage 4 or 5 CKD[14]. However, our study showed that CKD severity or comorbidities may not contribute to patient referrals.

On the other hand, we found that patients above 80 years were less likely to be referred. Additionally, among ethnicities, Indian patients were more likely referred than Chinese patients. Other studies also highlighted age and ethnicities as possible implicit factors affecting treatment processes in healthcare management[15,16]. Differences in age groups and ethnicities may suggest underlying socio-cultural factors affecting patients' preferences and the family physician's beliefs, attitude and understanding in managing elderly CKD patients. In the case of age, the non-referral could arise from a shared decision made between the family physicians and the "older" elderly CKD patients to favour continued management in the community. Furthermore, language barriers may influence referrals, as most physicians at NUP are English-speaking and of Chinese ethnicity. Although English is the main language, the heterogenous socio-cultural backgrounds of Singaporean patients likely played a role in the dynamic interaction among elderly patients, their caregivers, and family physicians.

Bivariate analysis also suggested that more referral group patients were taking fibrates, statins, insulin, sulfonylureas, dipeptidyl peptidase-4 inhibitors, and antiplatelets than the non-referral group. However, only a weak difference in fibrates remained in the multivariate analysis. It is therefore possible that the initial bivariate differences found in medications were confounded by age. As the referral group of CKD patients was comparatively younger than the non-referral group, their chronic diseases were likely to be treated with more aggressive treatments.

Strengths and limitations

This study is one of the first retrospective cross-sectional studies to investigate elderly CKD patients enrolled in a single primary care organisation with a diverse mix of ethnicities in Southeast Asia. It highlights the role of age and ethnicity in the decision to refer elderly CKD patients to a nephrologist, demonstrating the real-life management of elderly CKD patients in the community.

Further qualitative studies to account for these differences are warranted to gain insights into the reasons underlying the decisions in the referral process involving primary care physicians, patients, and their families.

This study did not investigate whether the non-referral group could be further divided into subgroups, i.e., those who were already followed by a nephrologist before the study period, declined referral to a nephrologist, defaulted to hospital follow-ups, were discharged from the hospital and/or were treated at private health sectors. While duplicate follow-ups for CKD by NUP and nephrologists are likely avoided by most patients due to unnecessary costs, it cannot be excluded that more patients from older age groups have seen a nephrologist in the past, as they had likely had CKD for a longer time than the younger patients. Data collection was done in a cross-sectional manner over the course of one year and did not contain outcome data; future research into outcomes for those who are referred and those who are not referred would provide useful insights. We did not study changes in GFR or albuminuria-proteinuria. Finally, data on both ACR and PCR was missing in approximately one tenth of the sample, which reduced the power of the analyses to detect differences in albuminuria-proteinuria.

Comparing with existing literature

Torreggiani et al. 2021 showed that 70% of their hospital renal clinic outpatients were aged 60 and above and 25% were aged 80 or older[17]. However, in their study, only approximately 50% of these patients had stage 3B CKD or above[17]. This contrasts with our study population, where the NUP local guidelines do not recommend referral to a nephrologist below stage 3B. Torreggiani et al. 2021 also revealed that the majority of the causes of CKD are multifactorial diseases, nephroangiosclerosis, and diabetes-associated kidney disease, particularly the

variant with low proteinuria (diabetes-vascular), which increases with age[17]. This variant accounts for over 80% of the diagnoses in patients aged 80 or older. Unlike outpatient nephrologist clinics, where causes of kidney diseases can be confirmed using hospital diagnostic support such as renal biopsy and imaging, almost all CKD patients in primary care in Singapore are diagnosed biochemically and with an ultrasound scan to rule out underlying obstructive nephropathy.

Conservative management of CKD is gradually recognised as a viable therapeutic alternative for patients with advanced CKD[18,19]. Early detection leads to early management of the associated risk factors to optimise medical care in the elderly population[5,6]. Most of these risk factors can be identified and managed in the primary care setting. In the United Kingdom, Mclure retrospectively studied 124 patients in the hospital setting who were ≥ 80 years of age and had stage 4 (115 patients) or 5 (9 patients) CKD[20]. Forty-seven percent of their patients were discharged to the primary care with median time to death being 3.57 years vs 2.66 years for those who remained in the nephrologist follow-up. This study suggests that the majority of elderly patients can be safely and appropriately managed in the primary care setting.

However, there are reported challenges that affect the delivery of CKD care in primary care[21]. These include suboptimal screening/monitoring of CKD risk factors[22,23], infrequent discussions between providers and patients regarding CKD[20], suboptimal albuminuria testing[23,24], suboptimal blood pressure control[23], suboptimal renin-angiotensin blockade in CKD patients with proteinuria[25,26], limited knowledge of CKD risk factors[27,28] and poor awareness of Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines[29–32]. Our study shows that 381 (33%) of patients in the non-referral group and 106 (30%) of patients in the referral group were not prescribed a reno-protective ACEI or ARB. This may be explained by the average blood pressure readings of respectively 133/67 mmHg and 134/68 mmHg in the two groups (Table 3). Lowering blood pressure further could be contraindicated in these elderly groups of patients. However, among the diabetic elderly CKD patients, the diabetic control was good, with both groups showing HbA1c < 8.0% (Table 3).

Implications for Research and/or practice

This study highlights that family physicians at NUP managed 77% of the total elderly CKD patients with stage 3B, 4 and 5 diseases. This reflects a vital role of family physicians in managing the elderly with severe CKD. This study highlights the need to review the referral process in this diverse group of patients and to better understand the role of socio-demographic factors in this context. We recommend multidisciplinary collaboration between family physicians and nephrologists to refine the referral criteria to detect patients who truly need early referrals to nephrologists and to develop guidelines to optimise primary care

management and monitoring of CKD patients, especially for those who are not referred and treated conservatively.

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Ethics: Ethics approval was obtained from the ethics committee of the Domain Specific Review Board of the National Healthcare Group.

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Table 1. Patient demographics

	Non-referral group	Referral group	P value
Sex (n(%))			
Female	621 (52.67)	188 (52.66)	
Male	558 (47.33)	169 (47.34)	0.997
Age group (n(%))			
65–69	167 (14.16)	77 (21.57)	
70–74	226 (19.17)	74 (20.73)	
75–79	258 (21.88)	107 (29.97)	
80–84	267 (22.65)	52 (14.57)	
85–89	177 (15.01)	35 (9.80)	
90+	84 (7.12)	12 (3.36)	<0.001
Age (mean (SD))	78.35 (7.51)	75.88 (6.83)	<0.001
Ethnicity (n(%))			
Chinese	907 (76.93)	250 (70.03)	
Indian	48 (4.07)	21 (5.88)	
Malay	204 (17.30)	72 (20.17)	
Others	20 (1.70)	14 (3.92)	0.017
Smoking status (n(%))			
Ex-smoker	39 (3.31)	16 (4.48)	
Non-smoker	1,089 (92.37)	317 (88.80)	
Current smoker	51 (4.33)	24 (6.72)	0.097

*P value is taken from chi-square test for categorical, and t-test for continuous variables.

Table 2. Comparison of indicators of CKD severity (CKD status and albuminuria-proteinuria) of non-referral and referral groups

	Non-referral group (n(%))	**Referral group (n(%))**	**P value**
CKD status			
CKD 3B	856 (72.60)	249 (69.75)	
CKD 4	279 (23.66)	96 (26.89)	
CKD 5	44 (3.73)	12 (3.36)	0.453
Albuminuria-proteinuria*			
Normal to mildly increased	290 (74.94)	97 (25.06)	
Moderately increased	402 (78.67)	109 (21.33)	
Severely increased	333 (73.19)	122 (26.81)	0.126

P value is taken from chi-square tests.

*Albuminuria-proteinuria data (ACR or PCR) was available for 1353 patients, 1025 in the non-referral and 328 in the referral group.

Table 3. Comparison of patient comorbidities between non-referral and referral groups.

	Non-referral group	Referral group	P value
Diagnoses (n(%))			
Diabetes mellitus	837 (70.99)	260 (72.83)	0.544
Hypertension	1,165 (98.81)	348 (97.48)	0.117
Hyperlipidaemia	1,155 (98.00)	351 (98.30)	0.837
Gout	233 (19.80)	65 (18.21)	0.566
Ischaemic heart disease	296 (25.11)	91 (25.49)	0.939
Peripheral vascular disease	93 (7.89)	25 (7.00)	0.662
Stroke	268 (22.73)	72 (20.17)	0.343
Dementia	93 (7.89)	25 (7.00)	0.662
Mean number of comorbid diagnoses (mean (SD))	4.51 (1.01)	4.46 (1.00)	0.443
Mean number of comorbid diagnoses by age group (mean (SD))			
65–69	4.54 (1.01)	4.34 (1.01)	0.136
70–74	4.48 (1.01)	4.61 (1.01)	0.352
75–79	4.55 (1.01)	4.41 (1.01)	0.218
80–84	4.52 (1.01)	4.31 (1.01)	0.172
85–89	4.50 (1.01)	4.71 (1.01)	0.258
90+	4.39 (1.01)	4.83 (1.01)	0.158
Blood pressure (mean (SD))*			
Systolic	133.33 (16.24)	134.17 (14.54)	0.357
Diastolic	67.71 (9.41)	68.55 (8.94)	0.125
HbA1c (mean (SD))**	7.35 (1.34)	7.46 (1.46)	0.261

P value is taken from chi-square test for categorical, unpaired t-test for continuous variables, and two-way ANOVA for the mean number of comorbid diagnoses by age group.

*Blood pressure data available for 1,532 patients, 1,177 in non-referral and 355 in referral group

**HbA1c data available for 1,047/1,097 diabetes mellitus patients, 795 in non-referral and 252 in referral group

Table 4. Comparisons of patient medications between non-referral and referral groups.

	Non-referral group, n (%)	Referral group, n (%)	P value
Drugs			
Fibrates	55 (4.66)	28 (7.84)	0.020
Statins	959 (81.34)	311 (87.11)	0.012
Insulin	187 (15.86)	76 (21.29)	0.017
Biguanides	281 (23.83)	88 (24.65)	0.752
Sulfonylureas	331 (28.07)	123 (34.45)	0.021
DPP4	184 (15.61)	79 (22.13)	0.004
ARB	435 (36.90)	144 (40.34)	0.24
ACEI	363 (30.79)	107 (29.97)	0.769
CCB	472 (62.5)	707 (60.00)	0.433
Loop-diuretics	302 (25.61)	95 (26.61)	0.707
Potassium Sparing Diuretic	28 (2.37)	5 (1.40)	0.266
Alpha-blocker	42 (3.56)	6 (1.68)	0.073
Beta-blocker	490 (41.56)	157 (43.98)	0.418
Antiplatelets	408 (34.61)	147 (41.18)	0.024

P value is taken from chi-square tests.

Table 5 Logistic regression predicting likelihood of referral with all variables significant in the bivariate analysis

	Model 1		Model 2		Model 3	
	OR (95% CI)	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
CKD severity						
CKD status						
CKD_catG3b	Ref.		Ref.		Ref.	
CKD_catG4	1.23 (0.92-1.63)	0.162	1.30 (0.97-1.74)	0.081	1.30 (0.97-1.74)	0.085
CKD_catG5	1.02 (0.53-2.00)	0.943	0.99 (0.50-1.96)	0.977	0.98 (0.49-1.96)	0.961
Albuminuria-proteinuria						
Normal to mildly increased	Ref.		Ref.		Ref.	
Moderately increased	0.82 (0.60-1.12)	0.201	0.89 (0.64-1.22)	0.243	0.87 (0.63-1.21)	0.410
Severely increased	1.11 (0.81-1.51)	0.518	1.18 (0.86-1.62)	0.318	1.14 (0.83-1.58)	0.417
Socio-demographics						
Age group						
65-69 years			Ref.		Ref.	
70-74 years			0.75 (0.51-1.13)	0.168	0.77 (0.52-1.16)	0.208
75-79 years			0.97 (0.66-1.41)	0.856	1.01 (0.69-1.48)	0.962
80-84 years			0.43 (0.28-0.67)	<0.001***	0.47 (0.30-0.73)	<0.001***
85-89 years			0.49 (0.30-0.79)	0.003**	0.56(0.34-0.91)	0.020*
90 years and older			0.41 (0.20-0.84)	0.015*	0.48 (0.23-0.99)	0.046*
Ethnicity						
Chinese			Ref.		Ref.	
Indian			2.18 (1.23-3.86)	0.008**	2.07 (1.16-3.70)	0.014*
Malay			1.23 (0.88-1.70)	0.223	1.21 (0.87-1.68)	0.268
Others			2.74 (1.32-5.70)	0.007**	2.82 (1.35-5.89)	0.006**
Medication						
Fibrates					1.69 (1.00-2.83)	0.049
Statins					1.35 (0.91-2.00)	0.141
Insulin					1.01 (0.72-1.43)	0.935
Sulfonylureas					1.15 (0.85-1.54)	0.365
DPP4					1.20 (0.85-1.71)	0.295
Antiplatelets					1.23 (0.94-1.60)	0.131

Results indicate the odds of being referred. Legend: *<0.05; **<0.01 ***< 0.001

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