CKD-CHECK toolkit to improve doctors' practice in managing chronic kidney disease rapid progressors: a pilot study in primary care setting

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ABSTRACT

Introduction: Chronic kidney disease (CKD) rapid progression is associated with higher risk of end-stage kidney disease and higher mortality rate. Monitoring and recognition of CKD rapid progression is still lacking, however interventions have been shown to improve this. Thus, this study aimed to evaluate the acceptability and feasibility of CKD-CHECK toolkit and preliminary measure the outcome of the CKD-CHECK toolkit in assisting primary care doctor to order further tests for CKD rapid progressors and trigger appropriate nephrology referral.

Materials and Methods: The CKD-CHECK (CKD-CHECK EGFR Chart in Kidney disease) is a toolkit that was developed to auto-generate patients' eGFR trend using a line graph, displaying the trend visually over a year. It identifies patients with rapid CKD progression, triggers the doctors to order appropriate tests (proteinuria quantification or renal imaging) and helps in decision making (continued monitoring at primary care level or referral to nephrologist). The toolkit was piloted among medical officers practising in a hospital-based primary care clinic treating patients with eGFR<60ml/min/1.73m^2 using an interventional before-after study design from February to May 2022. In the pre-intervention period, the CKD patients were managed based on standard practice. The doctors then used the CKD-CHECK toolkit on the same group of CKD patients during the intervention period. The feasibility and acceptability of the toolkit was assessed at the end of the study period using the Acceptability of Intervention Measure (AIM) and Feasibility of Intervention Measure (FIM) questionnaires. All patients' clinical data and referral rate were collected retrospectively through medical files and electronic data systems. Comparison between the pre- and post-intervention group were analysed using paired t-test and McNemar test, with statistical significance p value of <0.05.

Results: A total of 25 medical officers used the toolkit on 60 CKD patients. The medical officers found the CKD-CHECK toolkit to be highly acceptable and feasible in primary care setting. The baseline characteristics of the patients were a mean age of 72 years old, predominantly females and Chinese ethnicity. Majority of the CKD patients had diabetes mellitus, hypertension and dyslipidemia. The numbers of CKD rapid progressors was similar (26.7% in the pre-intervention group vs 33.3% in the post-intervention group). There were no significant differences in terms of proteinuria assessment and ultrasound kidney for CKD rapid progressors before and after the intervention. However, a significant number of CKD rapid progressors were referred to nephrologists after the use of CKD-CHECK toolkit (p=0.016).

Conclusions: CKD-CHECK toolkit is acceptable and feasible to be used in primary care. Preliminary findings show that the CKD-CHECK toolkit improved the primary care doctor's referral of rapid CKD progressors to nephrologists.

KEYWORDS:
CKD rapid progressor, CKD toolkit, nephrology, primary care, feasibility, acceptability

INTRODUCTION

Chronic kidney disease (CKD) is defined as evidence of kidney damage with or without estimated Glomerular Filtration Rate (eGFR) less than 60ml/min/1.73m^2 that is present more than three months.[1] It is associated with increased risks for all-cause mortality and caused impairment in quality of life.[2] Globally, the prevalence of CKD in 2017 is 9.1% and has resulted in 1.2 million deaths.[3] In Malaysia, its prevalence has increased from 9.07% in the year 2011 to 15.48% in the year 2018.[4] There were almost 40,000 patients in Malaysia who required dialysis in 2016.[5] It is estimated that this figure will reach up to 106,249 cases in year 2040.[6] In term of economic burden, the total annual expenditure of end stage renal disease (ESRD) by the public sector in Malaysia has increased 94% from Malaysian Ringgit (MYR) 572 million purchasing power parity in 2010 to MYR1.12 billion in 2016.[7]

Numerous studies have reported that CKD patients did not follow the same decline rate in their eGFR.[8,9] A prospective study conducted at primary care looking into the five-year outcomes of CKD has reported that change in eGFR at year 1 significantly influenced CKD progression.[10] CKD patients who experience loss of eGFR of more than 5 ml/min/1.73 m^2 per

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year are referred as CKD rapid progressors.[1] The prevalence of CKD rapid progressors in primary care ranged from 25 - 40%.[11,12] These individuals faced higher risk to progress to end stage renal disease, requiring dialysis and had a greater mortality rate compared to those with a slower decline in their eGFR.[9,10] Given this scenario, some guidelines have highlighted the rapid decline in eGFR rate as a criterion for nephrology referral.[1,13] However, up to 40% of CKD rapid progressors were not referred to nephrologists by primary care doctors.[12] These late referrals to nephrologist have been linked to higher risk of unplanned dialysis, hospitalisation rate and increased treatment cost.[14] Conversely, those rapid progressors who were referred early to nephrologists exhibited a slower decline in their GFR rate and experienced better health outcomes.[15]

Based on a previous study, primary care doctors in Malaysia had an average of 40 consultations per day, with each consultation lasting less than 15 minutes.[16] However, the patients managed by primary care doctors in public clinics were more chronic and complex compared to those who visited private sectors.[17] Other than time factors, up to 51% of primary care doctors were found lacking in knowledge and familiarity with the CKD guideline.[18] This limits their ability to integrate CKD care into practice. All these led to therapeutic inertia in which the doctors failed to identify CKD rapid progressors and refer them to nephrologist earlier.[19]

Interventions such as automated reporting of eGFR with creatinine have been introduced more than a decade ago in assisting the doctors for recognising CKD. The eGFR value would be included in the test report whenever creatinine test was ordered. However, not all laboratories in Malaysia provide automated eGFR report, especially in government primary care clinics.[20] eGFR value needs to be manually calculated by the primary care doctors and documented in the patient's medical record.[21]

Furthermore, the findings on the improvement of CKD detection and appropriate nephrology referrals using automated reporting of eGFR were inconsistent. A study done by Akbari et al., reported that the number of appropriate referrals to nephrologist increased by 43.2% after the introduction of automatic reporting of the eGFR.[22] However, the appropriateness of nephrology referrals in Australia has fallen significantly from 74.3% before the eGFR reporting to 65.2% thereafter.[23] Similar findings were shown in a Canadian study which reported that up to 62.7% of nephrology referrals were considered as inappropriate and has contributed to longer clinic appointment waiting time.[24] In the United Kingdom, the ASSIST-CKD program used software to create a five-year graph of all the eGFR results for patients with eGFR less than 50ml/min/1.73m^2.[25] The graphs were reviewed by laboratory staff, renal pharmacist or renal nurse to determine if the patient sustained a rapid decline in their eGFR. For patients who met the criteria, the printed report was sent to the respective general practitioners (GP). This report included the patient's graph, ways to contact nephrologists and how to make the nephrology referral. A total of 90% of GPs found that the eGFR graphs were helpful and up to 48% of GP had referred a patient on receipt of a graph to a nephrologist. Similarly, intervention that use trigger tool to notify the doctors of a falling eGFR trend have received positive feedback from doctors.[26]

In view of the potential benefit of tools in assisting CKD rapid progression identification and management, this study's aims were twofold. Firstly, we aim to assess the acceptability and feasibility of the newly developed CKD-CHECK toolkit, a tool that auto-generates a graph showing visual representation of the patient's eGFR trend. Second, we aim to preliminary measure the outcome of the CKD-CHECK toolkit to improve the management of CKD rapid progressors in a primary care clinic, in terms of improving further test for these patients and subsequently aid in appropriate referral of rapid progressors to nephrologists.

MATERIALS AND METHODS

This pilot study was a single arm, pre- and post-intervention study that was conducted at a university-based primary care clinic in Kuala Lumpur, Malaysia between the period of February to August 2022. The pre-intervention period started from February to March 2022. The intervention was subsequently introduced in April 2022. This was a clinic-wide intervention study where all medical officers practising during the study period received training to use the toolkit. The medical officers used the toolkit on patients until August 2022.

Eligibility Criteria

The inclusion criteria of this study include medical officers who were practising at the university-based primary care clinic during study period and clinically managed CKD patients. The medical officers would use the CKD-CHECK toolkit on patients with the following characteristics: patients aged 18 years old and above, eGFR<60ml/min/1.73m^2, have been followed up at least a year at the clinic, had at least two recorded serum creatinine results, minimum three months apart throughout a year and had not been referred to a nephrologist. Patients who were pregnant and had acute kidney injury for the past 3 months were excluded from this study. Acute kidney injury was defined as an increase an increase in serum creatinine of at least 26.5µmol/L within 48 hours or by a 50% increase in serum creatinine from baseline within 7 days, or a urine volume of less than 0.5ml/kg/h for at least six hours.[1] For this initial pilot study we focused the toolkit to be used on only patients diagnosed with CKD stage 3 and below.

Sample Size Calculation and Justification

In this study, we aimed to assess the acceptability and feasibility of CKD-CHECK toolkit among medical officers and preliminary measure the outcome of the CKD-CHECK toolkit in assisting medical officers to manage CKD rapid progressors. Considering the limited availability of medical officers within the study setting, all medical officers (n=25) were recruited to answer the questionnaire on acceptability and feasibility of CKD-CHECK toolkit.

The secondary objective of this study was to preliminary measure the outcome of CKD-CHECK toolkit in assisting medical officers to manage CKD rapid progressors. In order to establish the required sample size for statistical analysis,

based on recommendations for pilot studies by Whitehead et al.[27], and considering a drop-out rate of 20%, a total of 60 patients were assessed by the medical officers using convenience sampling method.

Standard Practice

All CKD patients were managed according to Malaysian Clinical Practice Guideline (CPG) on CKD 2018.[13] The medical officers traced the patient's blood and urine test results through online laboratory system. eGFR values of each patient were calculated manually by entering the patient's gender, age and creatinine level using online eGFR calculators. These values were documented in patient's case note. Renal profile and albuminuria were monitored at least annually in CKD patients. Urine test for proteinuria would be repeated 3 to 6 months later if the initial result was abnormal. Subsequently, patient's GFR and albuminuria categories were documented in the case note, based on KDIGO guideline.[1] The frequency of follow up of each patient was determined by their risk of CKD progression. For CKD patient who experienced rapid loss of eGFR more than 5ml/min/1.73m^2, renal imaging would be ordered by the medical officer. The renal imaging would be carried out at tertiary centre, located 2km distance from the clinic. For those CKD patients who met the criteria of nephrology referrals, such as rapidly declining eGFR more than 5ml/min/1.73m^2 and eGFR <30ml/min/1.73m^2, the medical officers would arrange for nephrology clinic referral at the tertiary hospital.

Intervention

A review of the literature was done to look at current tools available to assist doctors in identifying CKD and monitor eGFR progression.[22-26,28] Our toolkit was developed based on the favourable outcome of the ASSIST CKD study[25] which generates eGFR trend over time. Other factors that were associated with CKD rapid progression and may influence decision making were also derived from literature including age, gender, co-morbidities, medications, HbA1C value, proteinuria and renal imaging.[13,29] In order to develop the content of the CKD-CHECK toolkit, expert input was sought from a Family Medicine Specialist and nephrologist. To reach the aim of easier identification of CKD rapid progressors, we deemed having a visual representation of the eGFR trend using a line graph was ideal as it is simple to interpret, shows a trend over time, produces trends and patterns and will aid in decision making.[25,26] The content of the CKD-CHECK toolkit consist of three sections.

Section A of CKD-CHECK gathered information on the background of the patient and their medical history. This includes the patient's registration number, race, comorbidity and their medications. The comorbidities listed were diabetes mellitus (DM), hypertension (HPT), dyslipidaemia, cardiovascular disease and stroke. If the patient had another medical illness other than what had been listed, the doctors elaborated further at the provided empty column. The medication history of the patient was gathered by ticking at the relevant checkbox if the patient was on angiotensin converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers (ARBs), statin or aspirin. If the patient was not on any of the listed medications, the checkboxes remain unticked.

Section B consists of a table which included date, the patient's age, gender, serum creatinine level, calculated eGFR value, lowest eGFR level and difference between highest and lowest eGFR value. This section required the doctor to input the patient's age (in year) and creatinine level (µmol/l) according to date. A warning message would pop out if the doctors keyed in the value outside the normal range. The normal range of age was set between 19-90 years old while the creatinine level was between 50-900 µmol/l. The eGFR values were calculated automatically using the 2021 CKD-EPI creatinine equation,[30] which equals to 142 × min (Standardised Scr/K, 1) α × max (Standardised Scr/K, 1) -1.200 × 0.9938 age × 1.012 (if female), where Scr is serum creatinine (mg/dl), κ is 0.7 for females and 0.9 for males, α is -0.241 for females and -0.302 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. The lowest eGFR level and the differences between the highest and lowest eGFR were calculated and shown in the table. A line graph with the time length (in month) at the x-axis and eGFR value (ml/min/1.73m^2) at the y-axis was plotted automatically next to the table. This section aims to aid the doctors to take note if the patient had rapid decline of eGFR level based on the graph.

Section C of CKD-CHECK listed two referral criteria to nephrologists based on CKD-CHECK: 'eGFR≤30ml/min/1.73m^2' and 'loss of eGFR ≥5ml/min/1.73m^2 in a year'. The patient met the criteria of 'eGFR≤30 ml/min/1.73m^2' if the column of lowest eGFR value shown in the table was ≤30ml/min/1.73m^2. A column written 'CAUTION' would appear next to it, together with the following message 'please order urinalysis, proteinuria quantification, USG KUB to look for reversible causes, please refer nephrologist if no evidence of obstruction on USG KUB'. If the differences between the highest and lowest eGFR of patient was ≥5, a column written 'CAUTION' would appear next to the criteria of 'loss of eGFR≥5ml/min/1.73m^2 in a year'. A message would appear as 'if the eGFR trend is dropping, please order urinalysis, proteinuria quantification, USG KUB to look for reversible causes, please refer to a nephrologist if no evidence of obstruction on USG KUB'. Some patients could have experienced acute kidney injury in the past but already recovered from it, their line graph would dip before returning to baseline kidney function. Since the toolkit was unable to exclude those eGFR values, the medical officers were reminded to review the line graph and manage accordingly. If the patient did not meet either criterion, a column of 'CONTINUE MONITORING' would appear. The doctor can print out this CKD-CHECK and attach it with the written referral letter to the nephrologist. The toolkit has 2 versions depending on the gender of the patient. The example of CKD-CHECK for male and female CKD patients are shown in Figures 1 and 2.

This CKD-CHECK toolkit was made available on the Google Sheet® platform. For testing this initial concept of the CKD-CHECK toolkit, Google Sheet® was used as it was easily accessible by the doctors from each consultation rooms' computer, was relatively easy to use and was free. The CKD-CHECK toolkit may later be integrated in the electronic medical record or lab system if found to be beneficial. After the toolkit was developed, it underwent evaluation of its

content by two experts consisting of another Family Medicine Specialist familiar with the clinic's set-up and managing CKD and by a nephrologist practicing in a university-based tertiary hospital. No major changes were made to the toolkit.

Outcome Measures

The primary outcome measures of this study were to evaluate the acceptability and feasibility of our CKD-CHECK toolkit among medical officers. Acceptability was defined as the perception among medical officers that the intervention is satisfactory while feasibility was defined as the extent to which CKD-CHECK toolkit can be successfully used in primary care setting.[31]

We measured the acceptability of the CKD-CHECK toolkit using the Acceptability of Intervention Measure (AIM) questionnaire. This questionnaire has been validated and has shown good reliability with a Cronbach alpha of 0.85.[31] Medical officers were asked to what extent they agreed with the following statements using a 5-point Likert scale (1=completely disagree to 5=completely agree): (1) CKD-CHECK toolkit meets my approval, (2) CKD-CHECK toolkit is appealing to me, (3) I like CKD-CHECK toolkit, (4) I welcome CKD-CHECK toolkit. The total score for each construct fell within the range of 4-20, with higher scores indicating a greater perception of acceptability of the CKD-CHECK toolkit.

The feasibility of the CKD-CHECK toolkit was assessed using the Feasibility of Intervention Measure (FIM) questionnaire. This questionnaire has been validated and has shown good reliability with a Cronbach's alpha of 0.89.[31] Medical officers were requested to indicate their level of agreement with the following statements, utilising a 5-point Likert scale ranging from 1 (completely disagree) to 5 (completely agree): (1) CKD-CHECK seems implementable, (2) CKD-CHECK toolkit seems possible, (3) CKD-CHECK toolkit seems doable, (4) CKD-CHECK toolkit seems easy to use. Each construct's total score ranged from 4-20, with higher scores indicating a better perception of the CKD-CHECK toolkit's feasibility. In addition, a section was included for the medical officers to give their feedback and suggestions on how to improve the toolkit.

For the secondary objective of this study which is the preliminary measure the outcome of the CKD-CHECK toolkit, the outcome measures included the following:

Appropriate proteinuria assessment requested by medical officers for CKD rapid progressors. It is recommended that albuminuria is monitored at least annually in CKD patients according to guideline.[1] An abnormal urine test for proteinuria should be repeated after 3 to 6 months.[13] The appropriateness of ordering urine test for proteinuria was determined when the medical officers requested the urine test for patients who had not done it in the previous one year or repeated the urine test for patients who had proteinuria. The urine tests include urine full examination microscopy examination (UFEME), urine albumin: creatinine ratio (UACR) or urine protein: creatinine index (UPCI).

Appropriate renal imaging orders for CKD rapid progressors: Renal imaging is indicated for CKD patients who experienced rapid loss of eGFR more than 5ml/min/1.73m^2.[13] The appropriateness of ordering renal imaging for CKD rapid progressor was determined if patients who met the above criteria were or were not ordered for renal imaging and if there was any documentation of such request in the medical records.

Appropriate nephrology referral of CKD rapid progressors by medical officers: The criteria of nephrology referrals include rapidly declining eGFR>5ml/min/1.73m^2 and eGFR<30 ml/min/1.73m^2.[13] The referral of CKD patients to nephrologist was considered appropriate if such criteria were met.

Study Flow

All the medical officers were given a talk on CKD management based on the latest local guideline before the study initiation. During the pre-intervention period, the CKD patients were managed according to the standard practices by medical officers. The medical officers were instructed to mark the patient's name on the attendance list if they met the study's inclusion criteria. The study site investigator then recorded all the highlighted names on a weekly basis for data collection at a later stage. The data collection period for the pre intervention period was set at two months. A total of 77 patients were identified, however four patients who had nephrology follow up were excluded. A yellow sticker was placed on the continuation sheet inside the medical record as identification of the pre-intervention group. Subsequently, a briefing and demonstration on how to use the CKD-CHECK toolkit was given to the same group of medical officers. A soft copy of the user guide manual on how to use the toolkit was also distributed to each medical officer. The toolkit needed to be used during their consultation with the same group of CKD patients. The medical officers accessed the toolkit by logging in Google drive with the provided username and password. They were required to make a copy the toolkit and rename the file using patient's registration number. Once the new toolkit was opened, the medical officers entered the patient's relevant information such as patient's registered number, age, co-morbidities, and medications. They were required to enter the patient's available serum creatinine level within the past one year, with retrospective input from the day of encounter. All the serum creatinine values were traced from the online laboratory system. The toolkit would then generate the patient's eGFR trend via a line graph and be used by the medical officers to aid their decision making. The data collection period for the post intervention period was set at 6 months. Throughout follow-up, five CKD patients defaulted their clinic appointment and eight patients were not accessed by using CKD-CHECK toolkit. At the end of the study period, questionnaires were collected from medical officers. Figure 3 summarises the flow of this study.

Data Collection

Secondary data of the patients assessed using the CKD-CHECK toolkit by the medical officers were extracted retrospectively from the medical records, online laboratory system and drug prescription system at the end of study period. Information such as the patient's socio-demographic characteristics and medical comorbidities were obtained from their medical records. Medication recorded includes antihypertensive medication (ACE inhibitors, ARBs, beta

Table I: The baseline sociodemographic and clinical characteristics of patients evaluated using the CKD-CHECK toolkit (N = 60)

Variables	Category	n (%)	Mean (SD)
Age (years)			72.58 (SD±8.62)
Gender	Male	28 (46.7)	
	Female	32 (53.3)	
Ethnicity	Malay	22 (36.7)	
	Chinese	34 (56.7)	
	Indian	4 (6.7)	
Comorbidities	Diabetes mellitus	52 (86.7)	
	Hypertension	60 (100.0)	
	Dyslipidaemia	57 (95.0)	
	Ischemic heart disease	9 (15.0)	
	Stroke	1 (1.7)	
	Benign prostatic hyperplasia	2 (3.3)	
	Congestive heart failure	3 (5.0)	
	Gout	6 (10.0)	

SD – Standard Deviation

Table II: The baseline medication, laboratory data and ultrasound of patients evaluated using the CKD-CHECK toolkit (N = 60)

Variables	n (%)
Angiotensin-converting enzyme (ACE) inhibitors	37 (61.7)
Angiotensin receptor blockers (ARBs)	14 (23.3)
Beta blockers	27 (45.0)
Calcium channel blockers	32 (53.3)
Loop diuretics	14 (23.3)
Thiazide diuretics	14 (23.3)
Alpha blocker	4 (6.7)
Metformin	28 (46.7)
Sulphonylurea	19 (31.7)
Dipeptidyl peptidase IV (DPP IV) inhibitors	8 (13.3)
Sodium-glucose cotransporter-2 (SGLT2) inhibitors	6 (10.0)
Insulin	25 (41.7)
Statin	56 (93.3)
Aspirin	26 (43.3)
Baseline proteinuria	40 (66.7)
Baseline renal imaging	29 (48.3)

Table III: Clinical and laboratory data of patients evaluated using the CKD-CHECK toolkit (n=60)

Variables	Category	Group		*p* value
		Pre-intervention (n=60) n (%)	Post-intervention (n=60) n (%)	
Systolic BP (mmHg)		136.42 (SD±14.60)	134.45 (SD±13.32)	0.390[a]
Diastolic BP (mmHg)		74.25 (SD±9.27)	73.35 (SD±9.81)	0.498[a]
HbA1c (%) (n=52)		7.71 (SD±1.47)	7.81 (SD±1.56)	0.624[a]
eGFR (ml/min/1.73m2)		45.47 (SD±8.09)	40.72 (SD±7.96)	<0.001[a]*
CKD rapid progressors	Yes	16 (26.7)	20 (33.3)	0.125[b]
	No	44 (73.3)	40 (66.7)	

[a] Paired t-test, [b] McNemar test, *significant as p<0.05; SD – Standard Deviation.

Table IV: Comparison of outcome measures pre and post intervention among CKD rapid progressors (n=16)

Variables	Category	Group		*p* value
		Pre-intervention (n=16) n (%)	Post-intervention (n=16) n (%)	
Appropriate proteinuria assessment for CKD rapid progressor	Yes	9 (56.3)	10 (62.5)	>0.999[a]
	No	7 (43.7)	6 (37.5)	
Appropriate order renal imaging for CKD rapid progressor	Yes	4 (25.0)	5 (31.3)	>0.999[a]
	No	12 (75.0)	11 (68.8)	
Appropriate nephrology referral for CKD rapid progressor	Yes	3 (18.8)	10 (62.5)	0.016[a]*
	No	13 (81.3)	6 (37.5)	

[a]McNemar test, *significant as p<0.05

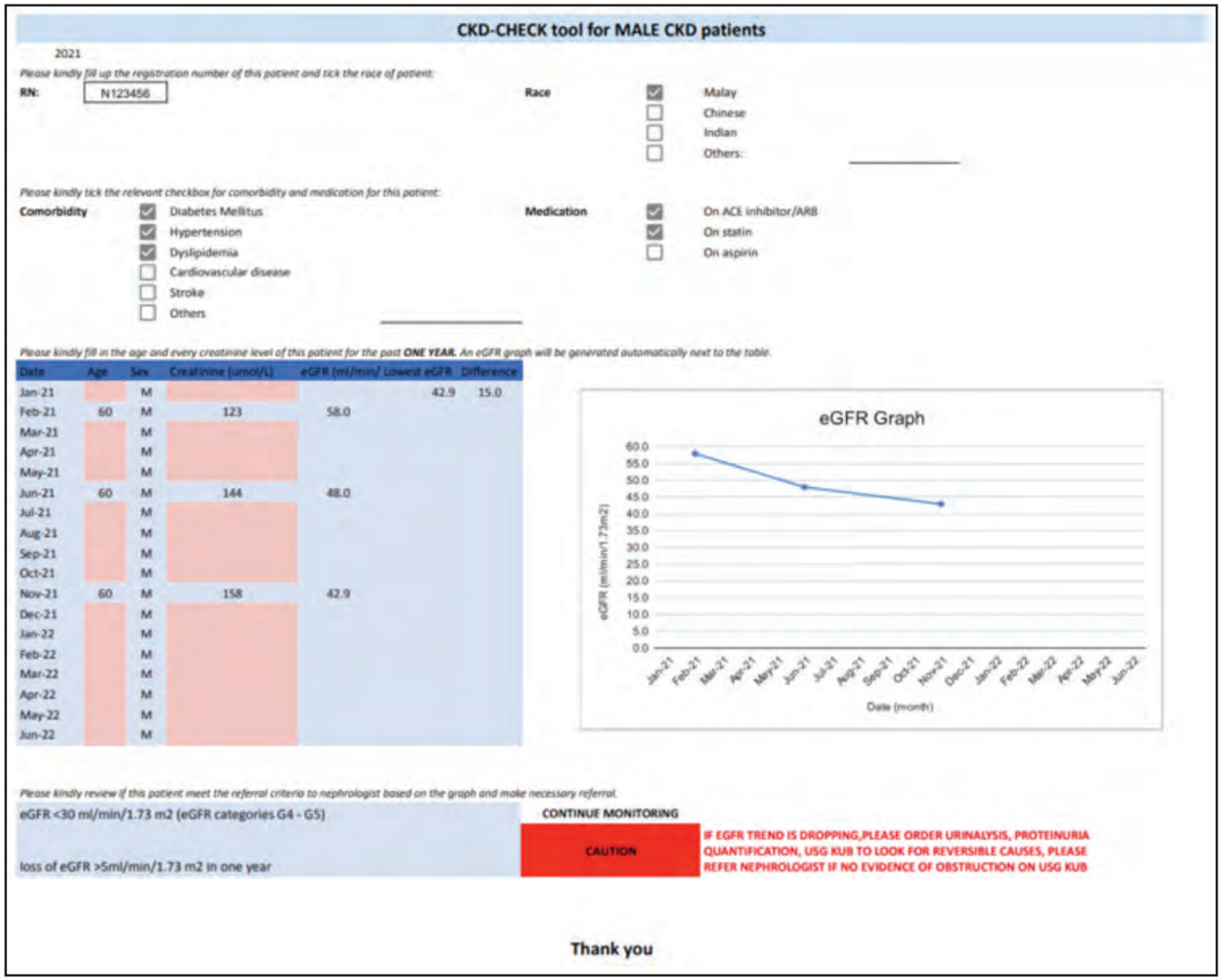

Fig. 1: Example of CKD-CHECK toolkit for male CKD patient.

blockers, calcium channel blockers, loop diuretics, thiazide diuretics and alpha blocker), oral hypoglycaemic agents (metformin, sulphonylurea, dipeptidyl peptidase IV [DPP IV] inhibitors, sodium-glucose cotransporter-2 [SGLT2] inhibitors), insulin, statin and aspirin. The patient's creatinine level for the past 1 year, most recent HbA1c level and urine test for proteinuria were obtained through the online laboratory system. eGFR values were calculated based on the most recent serum creatinine level available during clinic visit. Baseline urine test for proteinuria is defined as a test that was carried out within a year from the current visit was recorded. Baseline ultrasound kidney, bladder and ureter (KUB) refer to any renal imaging that was performed at any time before the current follow-up visit. Any subsequent management of the patient's post intervention including ordering of urine test for proteinuria, renal imaging and

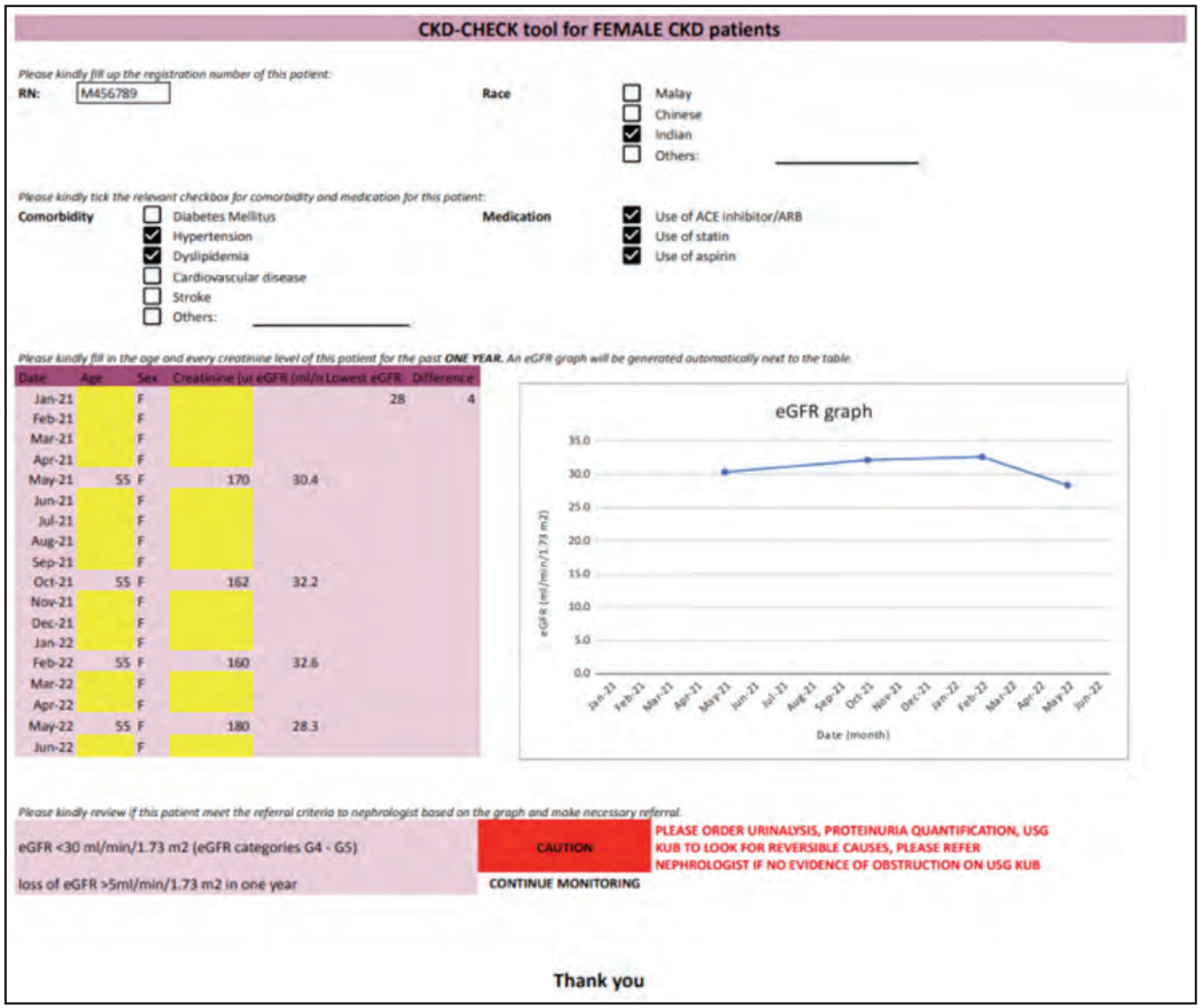

Fig. 2: Example of CKD-CHECK toolkit for female CKD patient.

referral to the nephrologist by medical officers were collected from medical records and online laboratory systems. At the end of the study period, the medical officers were required to complete a post-intervention questionnaire consisting of the AIM and FIM that was given via Google Form. They were required to provide feedback on improvement of CKD-CHECK toolkit.

Data Analysis

Descriptive statistics were used to describe the implementation outcome measures: the acceptability (AIM) and feasibility (FIM) of using the tool, and socio-demographic and clinical characteristics of the patients assessed. Categorical data were described in absolute numbers (n) and percentages (%). Continuous variables were presented using mean and standard deviation (SD). Paired t-test was used to compare the mean of pre- and post-intervention groups. We compared secondary outcome measures of investigations ordered and nephrology referrals before and after the intervention using the McNemar test for matched pairs. All data analysis was done using the Statistical Package for Social Sciences (SPSS) version 27. (SPSS Inc., Chicago, IL, USA). All probability values are two-sided, and a level of significance of less than 0.05 (p-value<0.05) were considered as statistically significant.

Ethical Consideration

Any CKD patients who met the criteria for nephrology referral but missed during follow-up were recorded in the medical records, for the doctors to refer them accordingly.

RESULTS

A total of 25 medical officers were involved in this study. More than two-thirds were females (76%) and the mean age of the medical officers were 36.68 years. Up to 80% of them had been practising in primary care clinics for more than 6 years, with the minimum years of practice being 3 years and maximum being 11 years. The responses of medical officers on acceptability and feasibility of CKD-CHECK toolkit

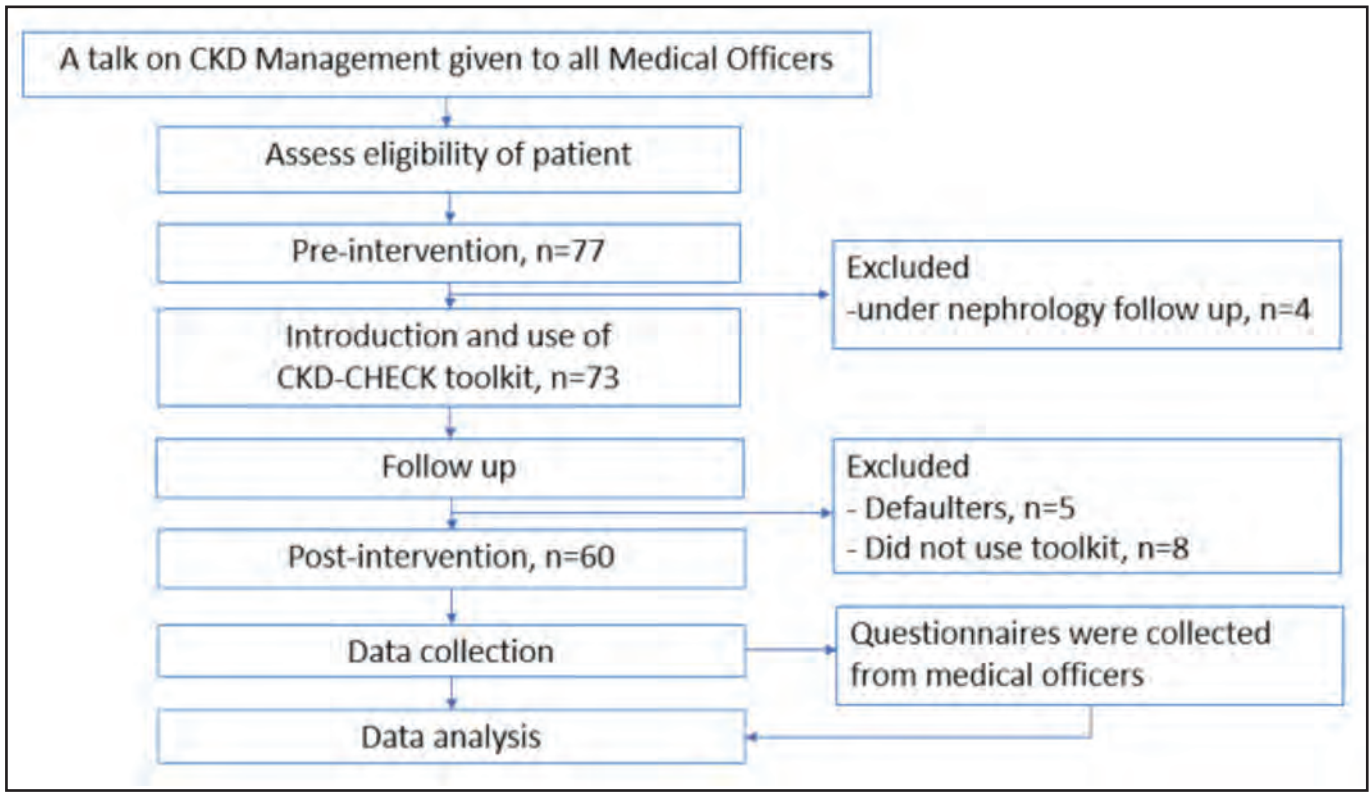

Fig. 3: Study flow chart.

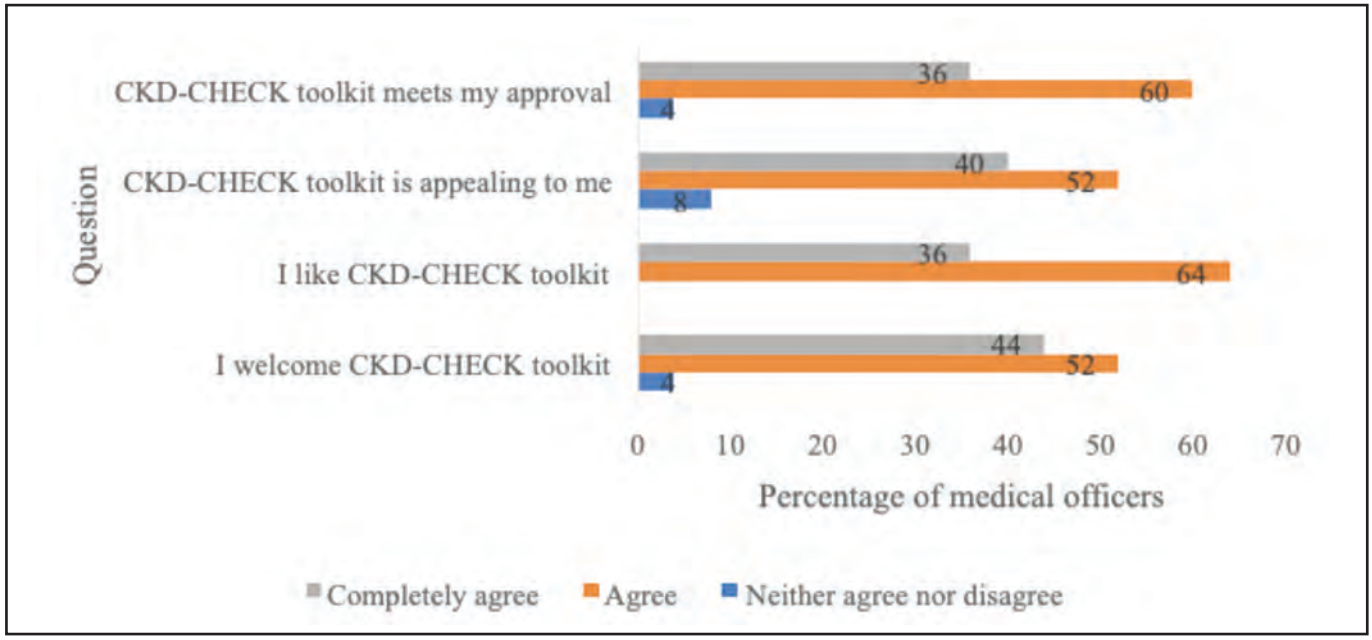

Fig. 4: Acceptability of CKD-CHECK TOOLKIT among medical officers using the AIM.

questionnaire are shown in Figures 4 and 5 respectively. In terms of acceptability of CKD-CHECK toolkit, more than 90% of medical officers found the toolkit to be appealing, met their approval and they welcomed CKD-CHECK toolkit. All of them like this toolkit. For feasibility of CKD-CHECK toolkit, all medical officers agreed that CKD-CHECK toolkit seems possible and easy to use. 96% of them agreed that the CKD-CHECK toolkit seems implementable. Only 8% of medical officers neither agree nor disagree that CKD-CHECK toolkit was doable. The mean score for both FIM and AIM were 17.4 out of 20, indicating a high-level perception of acceptability and feasibility of the CKD-CHECK toolkit among medical officers in this university-based primary care clinic. Regarding the feedback from medical officers, most of them

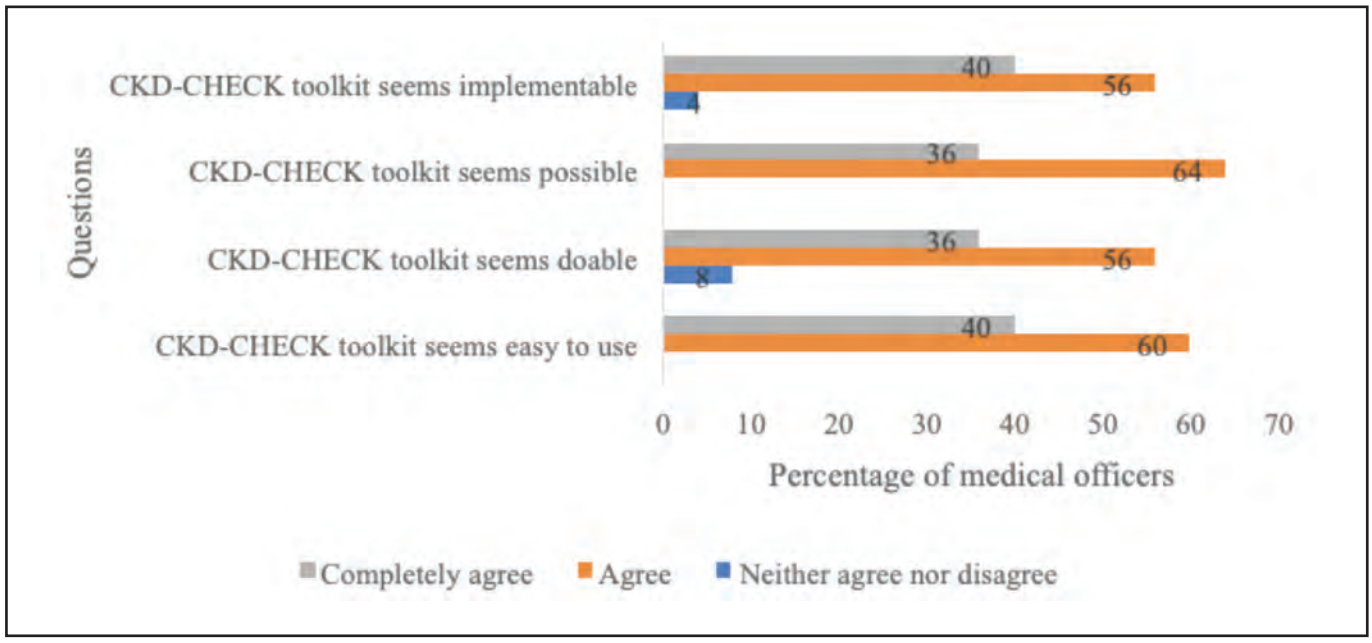

Fig. 5: Feasibility of the CKD-CHECK toolkit among medical officers using the FIM.

thought that CKD-CHECK toolkit helped them in monitoring eGFR progression and it was user friendly. However, a few medical officers preferred less data to be entered by them.

The medical officers used the CKD-CHECK toolkit on the same 60 patients seen during the pre-intervention period. No data was missed during the post-intervention period. The baseline sociodemographic and clinical characteristics of patients are shown in Tables I to III. Most of the patients were female, of Chinese ethnicity and had comorbid of DM, HPT and dyslipidaemia. The most commonly used medications among CKD patients were ACE inhibitors, CCB and statins.

For clinical and investigation data, the blood pressure and HbA1c of the patients before and after intervention showed no significant difference (Table III). The mean eGFR values of the patients have declined, where it was significantly lower during post-intervention period (40.72ml/min/1.72m^2- stage 3b) as compared to pre-intervention period (45.47ml/min/1.72m^2- stage 3a), with p<0.001. The proportion of CKD rapid progressors is similar pre-intervention (26.7%) and post-intervention (33.2%), and the difference was not significant.

Table IV shows the comparison between the pre- and post-intervention period for the secondary outcome measures among CKD rapid progressors. There were no significant differences in terms of proteinuria assessment and requests of renal imaging for CKD rapid progressors before and after the intervention. In terms of nephrology referral, a significant number of CKD rapid progressors were referred appropriately. However, despite the use of the CKD-CHECK toolkit, 37.5% of patients were still not referred. Based on the review of the medical files, the most common reasons for not referring in ranking order were doctors choosing to continue to monitor CKD trend (n=2), awaiting patients to perform renal imaging (n=2) and patients refusing to be seen by nephrologists (n=2).

DISCUSSION

The aims of this study were to assess the acceptability and feasibility of the newly developed CKD-CHECK toolkit and also to preliminarily explore the outcome of the toolkit to aid primary care doctors in their clinical decision making on whether to order further tests and make appropriate referrals of CKD rapid progressors to the nephrology clinic. The CKD-CHECK toolkit utilised a simple Google sheet to auto-generate a line graph showing the patient's eGFR trend once their serum creatinine levels were inserted. The visual depiction of the eGFR trend, along with the tool indicating when the eGFR trend meets the criteria for rapid progression, serves as a prompt for primary care doctors to take appropriate management actions. It is important to recognise the eGFR trend as several studies[8,9] have found that not all the CKD patients progress in a similar pattern. Due to the high morbidity and mortality rates among CKD rapid progressors, early identification of this group of patients has become important.

Although there are several toolkits on monitoring of CKD progression available, our toolkit is different as eGFR trend of CKD patient is represented in a line graph, generated automatically in Google sheet and interpreted directly by the respective doctor. A reminder would pop out if the doctors entered the value outside the normal range that was preset in the toolkit. This has reduced the chances that the graph could have been plotted wrongly by the doctors.[32] Despite this additional measure, we acknowledge that transcriptional errors may still occur and not be detected if the incorrect values lie within the normal ranges. Our toolkit's feature of direct interpretations of eGFR graph by the treating doctor is crucial in deciding the subsequent management of CKD patients. In a previous study, the graph was interpreted by the other health personnel before it was sent to the treating doctor.[25] This might prolong the patient's waiting time for subsequent appropriate management and nephrology referral. Besides notifying the doctors on patient's falling

eGFR trend,[26] our toolkit also has a trigger tool that provides guidance to doctors on subsequent management before nephrology referral was made. At the time of writing, a web-based app for use by healthcare workers and supported by the Malaysian Society of Nephrology (myCKDCPG) had been recently released which provides easy reference to the Malaysian CKD clinical practice guideline. It also uses a similar eGFR slope calculator and decision aid tool and utilises the Kidney Failure Risk Equation (KFRE), a widely used tool to predict risk of patients developing ESRD. Another app, The Care for Kidney app, supported by the National Kidney Foundation, has also been made available, although this app focuses on patients as the utiliser. It has a section where the patient can input their own eGFR value and a graph can be generated. These new developments support the benefits of utilising eGFR trend monitoring through a graph similar to the CKD-CHECK toolkit.

Our toolkit was highly accepted and deemed feasible by medical officers in this university-based primary care clinic. This is consistent with study findings that majority of primary healthcare providers prefer supportive technology to assist them in managing CKD patients.[33] The possible reasons may be because our tool has the potential to provide good quality nephrology referral by including sequential eGFR results and the indication for referrals,[34] facilitating collaboration between primary care doctors and nephrologists in managing CKD rapid progressors. Furthermore, the implementation of our tool did not require any additional cost, allows repetitive use and only require an easy access to the network.

In our study, the mean eGFR value of our CKD patients declined significantly during the pre-intervention to post-intervention period. This was consistent with study findings that nearly half of their CKD patients experienced decline in their eGFR, but with different rates of eGFR decline.[8] Our data was comparable with a study done by Go et al that 23% of diabetic patients and 15.3% of non-diabetic patients experienced rapid decline in their eGFR.[11] Since the majority of our CKD patients were having diabetes, they were more likely to experience rapid progression of CKD. In contrast to a study conducted in Hong Kong, only 10% of their CKD patients progress rapidly.[8]

Looking at the practice of the doctors with regards to CKD management, the testing rate of proteinuria among our CKD rapid progressors did not defer after the use of CKD-CHECK toolkit. A study in the United States that used automated electronic medical record alerts for healthcare providers has also reported similar findings.[35] In contrast to another study, the implementation of a CKD checklist in a primary care clinic has reported that patients in the intervention group had higher testing rates of albuminuria.[36] The possible explanation of low testing of proteinuria in our study could be due to our healthcare providers prioritise monitoring other parameters such as eGFR. In addition, our CKD patients might feel a financial burden with the total cost for blood and urine test and opted not to proceed with urine test for proteinuria.

In our study, a third of our patients met the criteria to proceed with renal imaging. An evaluation of new referrals to the nephrology outpatient department for renal ultrasounds also indicated that only 40% of the ultrasound requests meet the guidelines' requirements.[37] However, there was no significant improvement in ordering renal imaging for CKD rapid progressors after the use of CKD-CHECK toolkit. We hypothesised that logistics and scheduling issues could be the one of the reasons why the renal imaging was not requested for CKD rapid progressors. In our clinic setting, the ultrasound would be done in a different centre and required additional appointments for the patient. This is challenging particularly for patients who require multiple appointments or who have mobility issues. Thus, may result in delays or difficulties in accessing the necessary imaging services.

The preliminary finding from this pilot study shows improvement in nephrology referral from 18.8-62.5% when comparing the primary care doctors' practice before and after using the CKD-CHECK toolkit. This significant improvement of detection of CKD rapid progressors and subsequent referral is promising as previously there may have been gaps in practice of doctors to recognise the rapid CKD progressor as one of the important criteria for nephrology referral. A study conducted in Canada by Akbari has shown that the total number of nephrology referrals increased by 43% after automatic reporting of the eGFR.[22] In our study, unfortunately there were still 37.5% of rapid progressors not being referred to nephrologists despite the use of our toolkit. This was relatively lower compared to a study finding which reported that 54.6% of patients who met criteria were not referred to nephrologists.[38] The reasons for missed referral from our study were the decision by doctors to continue monitoring eGFR trend, awaiting results of renal imaging prior to referral and refusal of some patients to be referred to the nephrologists. A systematic review looking at delayed referral of CKD patients to nephrology revealed that they were more likely to be in the older age group and having multiple comorbidities.[39] Fear and denial from the CKD patients themselves were some of the factors that led to late referral to nephrologist.[40] Missing the diagnosis of rapid CKD progression despite the use of this toolkit could still be a possible reason for missed referral, although this was not specifically looked at in our study. An additional factor that may contribute to the non-referral of CKD rapid progressors, despite being identified by our toolkit, could be the higher threshold among doctors in a university-based primary care clinic for referring patients to nephrologists. This could be attributed to the ease of communication with the nephrology team for any consultation, which enhances the doctors' confidence in delaying referrals to nephrologists.

The limitation of our study includes the utilisation of an external system (Google sheet) for graph creation and data entry, which may introduce additional complexity to the current workflow. All the data needs to be entered manually by the doctors and typo errors could possibly occur. While Google sheet allows free access initially, subscription may be required in the future to accommodate large data storage. The initial concept of the CKD-CHECK toolkit on Google sheet may later be utilised in the electronic medical records system or lab system. The passive use of this toolkit by medical officers which they need to key in the data manually by themselves could be another limitation. As this was a single-arm study design, there was also presence of possible

unidentified confounders in this study. The awareness of medical officers on nephrology referral could have increased with the use of CKD-CHECK, contributing to a higher number of nephrology referrals. Ideally, a proper assessment should be carried out to ensure all doctors have a homogenous understanding about CKD management. Regarding our toolkit, since this toolkit focuses only on eGFR trend of CKD patients, a revised version should include albuminuria or proteinuria results. To further help the decision making by doctors, a scoring system that predicts the need for renal replacement therapy in the future- Kidney Failure Risk Estimate (KFRE) could potentially be incorporated in the toolkit based on the already entered data in the toolkit. Since this study was conducted at a single-centre university based primary care clinic, the findings may not be generalisable to other settings. For future research purposes, a qualitative study should be carried out to get the feedback from medical doctors on the feasibility of the toolkit in other clinic settings. A two-arms, multicentre study with cross-over design using CKD-CHECK toolkit then should be conducted to fully determine its effectiveness.

CONCLUSION

This pilot study has demonstrated that the CKD-CHECK toolkit was deemed feasible and acceptable to be used by our primary care doctors. Initial preliminary findings of the effectiveness of the toolkit seems promising but further larger scale studies would need to be conducted before this tool can be used in clinical practice. Once fully tested, the CKD-CHECK toolkit has the potential to be incorporated into the electronic health data system, making it accessible by all healthcare clinics and tertiary hospitals.

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This study was self-funded, and we declare no conflicts of interest.

ETHICAL APPROVAL

This study was approved by the Universiti Kebangsaan Malaysia (UKM) Research Ethics Committee and Institute of Medical Research Ethics Committee (FF-2022-010).

REFERENCES

1. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco ALM, De Jong PE, et al. Kidney Disease: Improving Global Outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl 2013; 3(1): 1-150.
2. Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, et al. Chronic kidney disease and mortality risk: a systematic review. J Am Soc Nephrol 2006;17(7): 2034-47.
3. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020; 395(10225): 709-33.
4. Saminathan TA, Hooi LS, Mohd Yusoff MF, Ong LM, Bavanandan S, Rodzlan Hasani WS, et al. Prevalence of chronic kidney disease and its associated factors in Malaysia; findings from a nationwide population-based cross-sectional study. BMC Nephrol 2020; 21(1): 344.
5. Wong HS, Goh BL. 24th Report of the Malaysian Dialysis and Transplant Registry. 2016. The National Renal Registry.
6. Bujang MA, Adnan TH, Hashim NH, Mohan K, Kim Liong A, Ahmad G, et al. Forecasting the incidence and prevalence of patients with end-stage renal disease in Malaysia up to the year 2040. Int J Nephrol 2017; 2017: 2735296.
7. Ismail H, Abdul Manaf MR, Abdul Gafor AH, Mohamad Zaher ZM, Ibrahim AIN. Economic burden of ESRD to the Malaysian health care system. Kidney Int Rep 2019; 4(9): 1261-70.
8. Jiang G, Luk AOY, Tam CHT, Xie F, Carstensen B, Lau ESH, et al. Progression of diabetic kidney disease and trajectory of kidney function decline in Chinese patients with type 2 diabetes. Kidney Int 2019; 95(1): 178-87.
9. Santos J, Oliveira P, Severo M, Lobato L, Cabrita A, Fonseca I. Different kidney function trajectory patterns before dialysis in elderly patients: clinical implications and outcomes. Ren Fail 2021; 43(1): 1049-59.
10. Shardlow A, McIntyre NJ, Fluck RJ, McIntyre CW, Taal MW. Chronic Kidney Disease in primary care: outcomes after 5 years in a prospective cohort study. PLoS Med 2016; 13(9): e1002128.
11. Go AS, Yang J, Tan TC, Cabrera CS, Stefansson BV, Greasley PJ, et al. Contemporary rates and predictors of fast progression of chronic kidney disease in adults with and without diabetes mellitus. BMC Nephrol 2018; 19(1): 146.
12. Koraishy FM, Hooks-Anderson D, Salas J, Scherrer JF. Rate of renal function decline, race and referral to nephrology in a large cohort of primary care patients. Fam Pract 2017; 34(4): 416-22.
13. Kementerian Kesihatan Malaysia. Clinical Practice Guidelines - Management of Chronic Kidney Disease. 2nd Edition. Clinical Practice Guideline.
14. Smart NA, Dieberg G, Ladhani M, Titus T. Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease. Cochrane Database Syst Rev 2014; (6): CD007333.
15. Jones C, Roderick P, Harris S, Rogerson M. Decline in kidney function before and after nephrology referral and the effect on survival in moderate to advanced chronic kidney disease. Nephrol Dial Transplant 2006; 21(8): 2133-43.
16. Ab Rahman N, Husin M, Dahian K, Mohamad Noh K, Atun R, Sivasampu S. Job satisfaction of public and private primary care physicians in Malaysia: analysis of findings from QUALICO-PC. Hum Resour Health 2019; 17: 82.
17. Mimi O, Tong S, Nordin S, Teng C, Khoo E, Abdul-Rahman A, et al. A comparison of morbidity patterns in public and private primary care clinics in Malaysia. Malays Fam Physician 2011; 6(1): 19-25.
18. Abdel-Kader K, Greer RC, Boulware LE, Unruh ML. Primary care physicians' familiarity, beliefs, and perceived barriers to practice guidelines in non-diabetic CKD: a survey study. BMC Nephrol 2014; 15: 64.
19. Phillips LS, Branch WT, Cook CB, Doyle JP, El-Kebbi IM, Gallina DL, et al. Clinical inertia. Ann Intern Med 2001; 135(9): 825-34.
20. Sthaneshwar P, Lai LC, Raja Azzidin RE, Mohd Hussain B, Anas SS, Supremaniam S, et al. A national audit of estimated glomerular filtration rate and proteinuria and the MACD CKD task force recommendations. Malays J Pathol 2021; 43(1): 41-8.
21. Jamaluddin J, Mohamed Yassin MS, Jamil SN, Mohamed Kamel MA, Yusof MY. A clinical audit of the diagnosis and management of chronic kidney disease in a primary care clinic. Malays Fam Physician 2021; 16(3): 68-76.
22. Akbari A, Swedko PJ, Clark HD, Hogg W, Lemelin J, Magner P, et al. Detection of chronic kidney disease with laboratory reporting of estimated glomerular filtration rate and an educational program. Arch Intern Med 2004; 164(16): 1788-92.

23. Noble E, Johnson DW, Gray N, Hollett P, Hawley CM, Campbell SB, et al. The impact of automated eGFR reporting and education on nephrology service referrals. Nephrol Dial Transplant 2008; 23(12): 3845-50.
24. Hingwala J, Bhangoo S, Hiebert B, Sood MM, Rigatto C, Tangri N, et al. Evaluating the implementation strategy for estimated glomerular filtration rate reporting in Manitoba: the effect on referral numbers, wait times, and appropriateness of consults. Can J Kidney Health Dis 2014; 1: 9.
25. Barton AL, Mallard AS, Patterson A, Thomas N, Dickinson S, Gallagher H. The cornish experience of the ASSIST-CKD project. Ann Clin Biochem 2018; 55(1): 100-6.
26. Thomas N, Rajabzadeh V, Hull S. Using chronic kidney disease trigger tools for safety and learning: a qualitative evaluation in East London primary care. Br J Gen Pract 2019; 69(687): e715-23.
27. Whitehead AL, Julious SA, Cooper CL, Campbell MJ. Estimating the sample size for a pilot randomised trial to minimise the overall trial sample size for the external pilot and main trial for a continuous outcome variable. Stat Methods Med Res 2016; 25(3): 1057-73.
28. Rousselot N, Tombrey T, Zongo D, Mouillet E, Joseph JP, Gay B, et al. Development and pilot testing of a tool to assess evidence-based practice skills among French general practitioners. BMC Med Educ 2018; 18(1): 254.
29. Ali I, Chinnadurai R, Ibrahim ST, Green D, Kalra PA. Predictive factors of rapid linear renal progression and mortality in patients with chronic kidney disease. BMC Nephrol 2020; 21(1): 345.
30. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New creatinine- and cystatin c-based equations to estimate GFR without race. N Engl J Med 2021; 385(19): 1737-49.
31. Weiner BJ, Lewis CC, Stanick C, Powell BJ, Dorsey CN, Clary AS, et al. Psychometric assessment of three newly developed implementation outcome measures. Implement Sci 2017; 12(1): 108.
32. Guppy M, Glasziou P, Beller E, Flavel R, Shaw JE, Barr E, et al. Kidney trajectory charts to assist general practitioners in the assessment of patients with reduced kidney function: a randomised vignette study. BMJ Evid Based Med 2022; 27(5): 288-95.
33. Neale EP, Middleton J, Lambert K. Barriers and enablers to detection and management of chronic kidney disease in primary healthcare: a systematic review. BMC Nephrol 2020; 21(1): 83.
34. Wright J, Glenister KM, Thwaites R, Terry D. The importance of adequate referrals for chronic kidney disease. Aust J Gen Pract 2018; 47(1-2): 58-62.
35. Abdel-Kader K, Fischer GS, Li J, Moore CG, Hess R, Unruh ML. Automated clinical reminders for primary care providers in the care of CKD: a small cluster-randomised controlled trial. Am J Kidney Dis 2011; 58(6): 894-902.
36. Mendu ML, Schneider LI, Aizer AA, Singh K, Leaf DE, Lee TH, et al. Implementation of a CKD checklist for primary care providers. Clin J Am Soc Nephrol 2014; 9(9): 1526-35.
37. Shahzad V, Redahan L, McDonald K. An audit of renal ultrasounds for new referrals to the nephrology outpatients service. J Kidney Care 2022; 7(5): 232-4.
38. Navaneethan SD, Kandula P, Jeevanantham V, Nally Jr JV, Liebman SE. Referral patterns of primary care physicians for chronic kidney disease in general population and geriatric patients. Clin Nephrol 2010; 73(4): 260-7.
39. Navaneethan SD, Aloudat S, Singh S. A systematic review of patient and health system characteristics associated with late referral in chronic kidney disease. BMC Nephrol 2008; 9: 3.
40. Okaka EI, Adejumo OA, Akinbodewa AA. Late referral and associated factors among chronic kidney disease outpatients in Southern Nigeria. Ann Afr Med 2020; 19(1): 47-52.