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Impact of the KidneyWise toolkit on chronic kidney disease referral practices in Ontario primary care: a prospective evaluation

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Abstract

Objectives: Chronic kidney disease (CKD) is common; therefore, coordination of care between primary care and nephrology is important. Ontario Renal Network's KidneyWise toolkit was developed to provide guidance on the detection and management of people with CKD in primary care (www.kidneywise.ca). The aim of this study was to evaluate the impact of the April 2015 KidneyWise toolkit release on the characteristics of primary care referrals to nephrology.

Design and Setting: prospective pre-post design conducted at two nephrology sites (community site: Trillium Health Partners in Mississauga, Ontario, Canada, and academic site: St Joseph's Healthcare in Hamilton, Ontario, Canada). Referrals were compared during the 3-month time period immediately prior to, and during a 3-month period one-year after, the toolkit release.

Primary and Secondary Outcome Measures: The primary outcome was the change in proportion of referrals for CKD that met Kidneywise criteria. Additional secondary referral and quality of care outcomes were also evaluated. Multivariable logistic regression was used to evaluate pre-selected variables for their independent association with meeting Kidneywise criteria.

Results: The proportion of referrals for CKD among people who met the KidneyWise referral criteria did not significantly change from pre- to post-KidneyWise implementation (44.7% vs 45.8% respectively, adjusted odds ratio (OR) 1.16; 95% C.I. 0.85-1.59, p=0.36). The significant independent predictors of meeting KidneyWise referral criteria were: academic site, increased age, and use of the KidneyWise referral form.

Conclusions: We did not observe any change in the proportion of appropriate referrals for CKD at two large nephrology centres one year after implementation of the KidneyWise toolkit.

Strengths and limitations of this study:

- A prospective study conducted in two large nephrology centres
- Pre-specified primary and secondary objectives utilizing multiple imputation to account for incomplete data.
- Relatively short time period (one-year) in which to observe changes in referral characteristics
- No information available on patients who were not referred.

Key words: chronic kidney disease, primary care, proteinuria, knowledge translation.

Abbreviations: ACR - albumin-creatinine ratio; CKD – chronic kidney disease; DM – diabetes mellitus; eGFR – estimated glomerular filtration rate; KFRE – kidney failure risk equation; SJHH – St. Joseph's Healthcare Hamilton; OR – odds ratio; ORN – Ontario Renal Network; THP – Trillium Health Partners

Background

Chronic kidney disease (CKD), defined by the persistence of an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73m^2 and/or albuminuria (urine albumin-creatinine ratio [ACR] of greater than 3.0 mg/mmol), affects 10-12% of adults in Canada.[1] A number of guidelines make recommendations on the timing of referral of persons with CKD from primary care to nephrology.[2–4] Late referral may lead to unplanned initiation of renal replacement therapy and other adverse outcomes.[5,6] Conversely, early referral may not be feasible when considering the availability of nephrology services and furthermore, may be unnecessary or does not improve outcomes.[7–10] Regardless of the timing of referrals, enhanced CKD care and improved coordination between primary care and nephrology are important for people with CKD.

The Ontario Renal Network's (ORN) KidneyWise (www.kidneywise.ca; Supplementary Appendix)[2,11] toolkit was developed in 2015 in an effort to provide succinct guidance for the detection and management of CKD in the primary care setting, incorporating recommendations from a number of relevant guideline documents.[3,12,13] We implemented knowledge translation strategies to coincide with the release of the toolkit to promote uptake, including: development of a web-based platform and mobile application, presentations at accredited local, provincial, and national primary care medical conferences, as well as dissemination from regional nephrology primary care programs to referring primary care providers. Embedded within the toolkit is a standardized referral form which mirrors the nephrology referral criteria outlined in the toolkit.

The objective of this study was to evaluate the impact of the KidneyWise toolkit release on referral characteristics and quality of care at two sites in Ontario, Canada. We hypothesized that dissemination of the toolkit would lead to: i) an increased proportion of referrals which met Kidneywise

referral criteria for CKD (low eGFR or proteinuria); and ii) improvement in the quality of CKD-relevant care in people with CKD who had been referred.

Methods

KidneyWise toolkit

The ORN, a provincial agency, oversees and funds kidney care services in Ontario. There are 27 regional programs that provide general nephrology, multidisciplinary kidney care clinics, and dialysis services to those in need in their respective regions. One of its priorities is to improve quality and coordination of CKD care in primary care which led to the development of the Kidneywise toolkit. Embedded within the KidneyWise toolkit were recommended criteria for referral to nephrology; those specifically for CKD (low eGFR and/or proteinuria) were any of: i) eGFR < 30 ml/min/1.73m^2; ii) urine ACR > 60 mg/mmol; iii) eGFR 30-44 ml/min/1.73m^2 and urine ACR 30-59 mg/mmol; or iv) eGFR < 60 ml/min/1.73m^2 with a decline of > 5 ml/min/1.73m^2 over a 6-month time period.

Study Design and Population

The study was a prospective pre-post design. Nephrology referrals received at two sites (Trillium Health Partners [THP] in Mississauga, Ontario, Canada and St Joseph's Healthcare Hamilton [SJHH] in Hamilton, Ontario, Canada) were evaluated during two 3-month time periods. The first time period occurred from January-March 2015, immediately prior to the toolkit release. The second period occurred one year after the toolkit release (April-June 2016). THP is a community-based centre and is the sole nephrology provider in Mississauga, a city with a population of 713,000. SJHH, an academic centre affiliated with McMaster University, is similarly the sole provider for a city with a population of about 537,000. Both centres have an estimated referral base of about 1 million people. At SJHH, all referrals are triaged centrally at a single location; therefore, all referrals were captured during the conduct of the

study. Conversely, at THP, referrals could either go to a central location at the hospital or directly to private nephrologist offices. In this study, only the central location referrals at THP were captured.

Toolkit Dissemination

Dissemination of the toolkit incorporated a number of passive and active strategies to promote uptake. At a provincial and national level, one of the authors [AKG] presented KidneyWise at a number of accredited primary care medical conferences; additionally, a paper version of the toolkit was handed out to conference attendees. Physician leaders from each of the regional nephrology programs in the province were informed in person of the contents of KidneyWise and were encouraged to promote its dissemination in their local regions. A web-based platform and mobile application were also developed and their use encouraged at the same conferences. At both sites, a copy of the toolkit was sent to referring physicians encouraging use of the KidneyWise referral form with future requests. Many of the nephrologists at the two sites also embedded statements within their consultation letters that encouraged use of the KidneyWise toolkit. Finally, KidneyWise was frequently promoted by two authors [KSB and AKG] on Twitter©.

Outcomes

Relevant data was extracted from referrals onto paper case report forms. The primary outcome was the change in the proportion of referrals for CKD (low eGFR and/or proteinuria) meeting Kidneywise criteria before and after the Toolkit introduction. Although the KidneyWise toolkit recommends two eGFR and ACR values at least three months apart to confirm chronicity, the primary outcome for the purposes of this study was based on a single value.

Pre-specified secondary referral outcomes included: i) change in the proportion of appropriate referrals for low eGFR (< 30 ml/min/1.73m^2); ii) change in the proportion of appropriate referrals for proteinuria (urinary ACR > 60 mg/mmol); iii) change in the proportion of appropriate referrals for low eGFR or proteinuria which provided at least one urine ACR value (actual, not estimated); iv) change in the proportion of appropriate referrals for low eGFR or proteinuria which provided at least one urinalysis; and v) change in the proportion of late referrals (defined here as eGFR < 15 ml/min/1.73m^2 and/or a two-year kidney failure risk[14] [$KFRE_2$] > 10%).

Secondary pre-specified quality of care outcomes which aligned with the recommendations in the toolkit were as follows: i) change in the proportion of persons referred who were on an ace inhibitor or angiotensin receptor blocker (all referrals and those with diabetes mellitus [DM]; and ii) change in the proportion of persons referred who were on a statin (all referrals and those with a primary prevention indication [e.g. CKD with DM, CKD without DM and ≥ 50 years of age]).

Statistical Analysis

Assuming that the baseline proportion of referrals that met Kidneywise criteria was 50% (based on a previous audit conducted at the SJHH site) and that the toolkit would lead to a relative 20% increase in this proportion (i.e. to an absolute value of 60%), 519 referrals would be required during each time period to detect a significant difference (alpha 0.05) with 90% power. Assuming that more than 2,000 referrals are received at the two sites over a one-year period (the SJHH site received ~ 2,000 referrals the previous year), a three-month collection period pre and post-toolkit introduction was considered sufficient to achieve the required sample size.

Continuous variables were described as means and standard deviations (SD) or medians and interquartile ranges and categorical variables expressed as proportions. Where required, urine protein

based on dipstick or 24-hour urine protein was converted to approximate urine ACR as previously described.[14,15] Data were assumed to be missing at random for logistic regression analyses; multiple imputation was performed (set of 15) using Markov Chain Monte Carlo procedures assuming a multivariate normal distribution. A two-sided p-value <0.05 was regarded as significant without adjustment for multiple comparisons. For the primary and secondary outcomes, the pre-post difference in proportion of categorical variables was assessed by calculating the odds ratio (OR) and its associated 95% confidence interval (C.I.) using logistic regression, adjusted for referral site. An additional analysis conducted for the primary outcome using mixed effects logistic regression (site as a random intercept) did not materially change the original estimates and are therefore not reported here. The differences between normally and non-normally distributed continuous variables were assessed using the Student's t-test and Wilcoxin rank-sum test, respectively.

Multivariable analysis of predictors of a referral meeting KidneyWise criteria were carried out using the following pre-selected variables based on clinical plausibility: age, sex, presence of DM, referral site, time period (pre versus post), and use of the KidneyWise referral form (the latter during the second time period only). All statistical analyses were performed using Stata v15.1.

Results

There were 1,043 referrals combined over the two time periods; 69.2% were at the academic site (SJHH) and 40.2% during the first time-period (Table 1). The mean age of persons referred was 63 years and was significantly higher at the academic site compared to the community site (64 ± 18.2 vs 60 ± 20.2; p=0.001). The proportion with DM was similar at the two sites (43.0% overall) with greater ethnic diversity at the community site. Overall, the severity of CKD in people referred was higher at the academic site with a lower eGFR (low eGFR referrals: median 33.1 vs 40.4 ml/min/1.73m^2, p<0.001),

higher ACR (proteinuria referrals: 59.0 vs 31.7 mg/mmol, p=0.044), and higher $KFRE_5$ (low eGFR referrals: 5.0% vs 1.8%; p<0.001). The differences noted between the two time-periods in the demographics of people referred, as well as the referral indication, were driven by the substantial increase in referrals from the community site during the post-KidneyWise time period (see Table S1). Sixty-three of 624 referrals (10.1%) used the KidneyWise referral form post-KidneyWise, all at the academic site.

Primary Outcome

The proportion of referrals for CKD that met the KidneyWise referral criteria between the two time periods did not significantly change from pre- to post-KidneyWise implementation (44.7% vs 45.8% respectively, adjusted OR 1.16; 95% C.I. 0.85-1.59, p=0.36; Table 2).

Secondary outcomes

The proportion of referrals for proteinuria with a urine ACR > 60 mg/mmol significantly increased post-KidneyWise implementation (32.6% vs 45.7%; adjusted OR 2.04 [95% C.I. 1.06-4.01]; p=0.032, Table 2). The proportion of referrals for CKD that provided a urine ACR also significantly increased post-KidneyWise (25.8% vs 43.8%; adjusted OR 1.45, [95% C.I. 1.06-1.97], p=0.02). There were no significant differences in any of the other referral outcomes between the two time periods (Table 2).

The proportion of people referred who were on an ace inhibitor or angiotensin receptor blocker and had an indication was 75.3% overall (Table 3), and was not significantly different before and after KidneyWise implementation (76.4% vs 74.8%; adjusted OR 0.80 [95% C.I. 0.62-1.23], p=0.47).

Similarly, the proportion of those on a statin with an indication did not significantly change from pre- to post-implementation (71.0% vs 65.8% respectively, adjusted OR 0.77 [95% C.I. 0.54-1.10]; p=0.16).

The significant independent predictors of received referrals meeting KidneyWise criteria were: academic site, increased age, and use of the KidneyWise referral form (Table 4). Referrals that utilized the KidneyWise referral form had a lower eGFR, higher ACR, and higher kidney failure risk compared to those that did not use the form (Table 5).

Discussion

Implementation of the KidneyWise toolkit was not associated with an increased proportion of referrals that met KidneyWise referral criteria or improvement in quality of CKD care delivered in primary care. Utilization of the KidneyWise referral form, a surrogate measure of KidneyWise awareness, appeared to be restricted to the academic site's catchment area.

A number of studies have examined the characteristics of primary care referrals to nephrology, including the appropriateness of referrals.[16–20] In many of these studies, the introduction of automated eGFR has led to an increased volume of referrals, many deemed perhaps unnecessary. Similar to the present findings, Akbari and colleagues found that at an academic centre in Ottawa, Ontario, only 55% of referrals were considered necessary using similar criteria to those used in KidneyWise (eGFR < 30 ml/min/1.73m^2, ACR > 60 mg/mmol, or 20% decline in eGFR over one year).[16] Another study found that despite the implementation of an educational intervention prior to eGFR reporting, referral volume increased.[17] Conversely, a targeted educational intervention in nine primary care and five nephrology practices demonstrated an increase in the proportion of patients with an eGFR < 30 ml/min/1.73m^2 who were referred to nephrology.[21]

Interventions in primary care to influence physician behavior have had mixed results. A previous

systematic review found that the use of structured referral forms and the involvement of consultants in educational activities, both techniques employed here, improved referral appropriateness.[22] More recent trials have found that the use of peer comparison with active choice framing, accountable justification, and/or audit and feedback reporting increased appropriate prescribing behavior in primary care.[23–25] The knowledge translation strategies employed here were primarily passive and may have been less effective than more active strategies.[26,27] It should be noted that CKD severity was higher at the academic site and similarly, utilization of the KidneyWise referral form was only observed at the academic site. There may be local differences in referral patterns of primary care providers and/or the earnestness and methods with which nephrologists encouraged appropriate referral at the two sites.

We observed that the proportion of referrals for proteinuria meeting Kidneywise criteria increased post-implementation, as did the proportion of CKD referrals that provided an ACR. The effect size was large and the time interval between the two time periods relatively short; suggesting that this observation is likely due to dissemination of Kidneywise rather than other secular phenomena.

Feedback from referring primary care providers at a number of KidneyWise presentations indicated that incorporation of KidneyWise into their office-based electronic medical record (EMR) systems to facilitate appropriate and timely referrals would be vital to changing their behavior and improving workflow. To that end, work has been completed to facilitate KidneyWise incorporation into one of the major EMR systems in Canada.[28]

Appropriate utilization of ace inhibitors or angiotensin receptor blockers in patients referred to nephrology was already quite high at baseline, similar to what has been previously described in a Canadian jurisdiction.[29] On the other hand, use of statins was more modest, again consistent with previous work.[29,30] While we did not see any change in the use of statins post-KidneyWise, there would appear to be an opportunity to improve statin utilization in those with increased cardiovascular risk.

This study has limitations that require consideration. We do not have information on patients who may have met KidneyWise referral criteria but were not referred. Only two sites were included in this study, however, they both have large catchment areas and are likely to be representative of other urban centres in Ontario. As already outlined, the strategies employed to promote uptake of KidneyWise may have been ineffective despite evidence that a majority of primary care providers were aware of KidneyWise.[31] Additional time may have been required to realize the full impact of the KidneyWise toolkit on referral patterns. A recent one-month audit (September 2018) at the SJHH site revealed that 68% of referrals for CKD met KidneyWise criteria, up from 44.6% previously. Additionally, 23% of referrals during this time period utilized the KidneyWise referral form, implying increased awareness of the toolkit over time. Nevertheless, interventions such as electronic decision support tools that promote desired behaviors may be required to substantially improve referral practices and/or quality of CKD care.[32] Finally, a large increase in referral number was observed at the community site, reflecting local changes in how referrals were directed to the central location, rather than necessarily a substantial overall increase in the number of referrals received.

In summary, we did not observe any change in the proportion of referrals for CKD that met KidneyWise referral criteria at two large nephrology centres in Ontario, Canada one year after implementation of the toolkit. We did, however, observe an increase in referrals for proteinuria that met Kidneywise criteria suggesting some impact of KidneyWise dissemination on referral patterns. Future efforts, including incorporation of KidneyWise into electronic medical record systems, will require careful evaluation to determine whether such strategies may prove effective in improving the appropriateness of primary care referrals to nephrology.

Competing interests statement: KSB is a paid Provincial Medical Lead at the ORN. AGK is a former paid Provincial Medical Lead at the ORN. PGB is a paid Provincial Medical Director of the ORN. DP has received research support from: Amgen, Otsuka, Pfizer, Sanofi, Servier, and Bausch Health; speaking fees/honoraria from: Ardeane Healthcare Solutions; and consulting fees from: Amgen, Otsuka, Pfizer, Sanofi, and Servier. PB, AOM, DMN, AXG, AA, and DP do not have any competing interests to declare.

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Author contributions: KSB, PB, AKG, DP: conceived of the study. KSB and AOM: drafted the manuscript. AOM, DMN, AXG contributed substantially to the analytical approach. KSB: conducted the data analyses. AA, PGB: contributed to the interpretation of the data. All authors contributed substantially to the revision of the manuscript and provide final approval of this version.

Ethics approval: The study protocol was approved by the Hamilton Integrated Research Ethics Board (Study ID3: 14-847-C) and the Trillium Health Partners Research Ethics Board (ID#: 682).

Data sharing statement: Data can be made available upon request from readers

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Table 1. Baseline characteristics of the patients referred.

	Academic site	Community site	P value	Pre-KidneyWise	Post-KidneyWise	P value
N - (%)	722 (69.2)	321 (30.8)		419 (40.2)	624 (59.8)	
Age, Mean (SD)	64.2±18.1	60.0±20.2	0.001	64.1±17.2	62.0±19.9	0.077
Female – no. (%)	326 (45.2)	145 (45.8)	0.892	197 (47.0)	274 (44.2)	0.375
DM - no. (%)	313 (44.7)	124 (39.2)	0.115	179 (45.2)	258 (41.6)	0.270
Race - no. (%)						
Caucasian	420 (58.1)	145 (45.2)	<0.001	218 (52.0)	347 (55.6)	0.011
Black African	18 (2.5)	19 (5.9)		8 (1.9)	26 (4.2)	
Asian	13 (1.8)	22 (6.9)		9 (2.2)	26 (4.2)	
Hispanic	6 (0.83)	3 (0.93)		3 (0.72)	6 (0.96)	
Mid-east/Arabian	12 (1.7)	23 (7.2)		5 (1.2)	30 (4.8)	
Indigenous	6 (0.83)	0 (0)		3 (0.72)	3 (0.48)	
Indian sub-continent	19 (2.6)	42 (13.1)		20 (4.8)	41 (6.6)	
Other/Unknown	228 (31.6)	67 (20.9)		153 (36.6)	142 (22.8)	
Reason for referral – no. (%)						
CKD	427 (59.1)	138 (43.0)	<0.001	233 (55.6)	332 (53.2)	<0.001
Proteinuria/DM	129 (17.9)	65 (20.3)		89 (21.2)	105 (16.8)	
Hypertension	32 (4.4)	12 (3.7)		28 (6.7)	16 (2.6)	
Stones	17 (2.4)	35 (10.9)		8 (1.9)	44 (7.1)	
Hematuria	13 (1.8)	21 (6.5)		4 (0.95)	30 (4.8)	
GN/Nephrotic syndrome	13 (1.8)	11 (3.4)		8 (1.9)	20 (3.2)	
AKI	22 (3.1)	11 (3.4)		13 (3.1)	20 (3.2)	
Other	65 (9.0)	28 (8.7)		36 (8.6)	57 (9.1)	
eGFR, ml/min/1.73m^2 – median (IQR)						
All (N=889)	40.2 (29.4-66.4)	53.9 (38.8-85.3)	<0.001	43.8 (30.5-71.5)	44.7 (31.6-74.6)	0.406
Low eGFR (N=510)	33.1 (26.9-41.8)	40.4 (30.5-49.6)	<0.001	33.5 (27.0-43.8)	35.8 (28.3-44.4)	0.307
Urine ACR, mg/mmol – median (IQR)						
All (N=616)	9.2 (1.0-74.0)	3.4 (1.0-17.8)	0.002	9.3 (2.0-61.1)	4.0 (1.0-45.4)	<0.001
Low eGFR or proteinuria (N=481)	11.0 (1.2-81.1)	5.0 (1.7-43.2)	0.072	12.1 (2.5-76.2)	5.7 (1.0-67.7)	0.012
Proteinuria (N=170)	59.0 (15.9-121.4)	31.7 (6.2-89.2)	0.044	30.0 (11.1-89.2)	32.4 (11.4-118.2)	0.318
$KFRE_2$, % – median (IQR)						
All (N=582)	0.60 (0.041-2.5)	0.16 (0.0042-0.77)	<0.001	0.56 (0.021-2.4)	0.44 (0.051-1.62)	0.879
Low eGFR (N=213)	1.6 (0.57-4.7)	0.57 (0.23-1.5)	<0.001	1.4 (0.47-4.3)	1.1 (0.37-3.4)	0.306
$KFRE_5$, % – median (IQR)						
All (N=582)	1.8 (0.13-7.7)	0.51 (0.013-2.4)	<0.001	1.05 (0.046-6.3)	1.3 (0.062-5.1)	0.879
Low eGFR (N=213)	5.0 (1.8-14.0)	1.8 (0.72-4.5)	<0.001	4.3 (1.4-12.9)	3.3 (1.2-10.2)	0.306

Missing values: female – 4; DM – 27; race - 272. Not provided: eGFR – 154; urine ACR: 427. Not calculable: $KFRE_2$/$KFRE_5$ – 461.

Abbreviations: yr - year; DM - diabetes mellitus; CKD - chronic kidney disease; DMN - diabetic nephropathy; GN - glomerulonephritis; AKI - acute kidney injury; eGFR - estimated glomerular filtration rate; ml - millilitres; min - minutes; m - metres; ACR - urine albumin-creatinine ratio; IQR – interquartile range; mg - milligrams; mmol - millimoles; $KFRE_2$ - 2-yr kidney failure risk; $KFRE_5$ - 5-yr kidney failure risk.

Table 2. Primary and secondary referral outcomes of patients referred.

	No. of patients/Total no. (%)				
	Overall	**Pre-Kidneywise**	**Post-Kidneywise**	**Adjusted Odds Ratio§**	**P value**
		Primary outcome			
Kidneywise criteria met†	344/759 (45.3)	144/322 (44.7)	200/437 (45.8)	1.16 (0.85-1.59)	0.36
		Secondary outcomes			
eGFR<30 ml/min/1.73m^2 ‡	177/565 (30.6)	76/233 (32.6)	101/332 (30.4)	1.01 (0.69-1.49)	1.00
ACR > 60 mg/mmol¶	77/194 (39.7)	29/89 (32.6)	48/105 (45.7)	2.04 (1.06-4.01)	0.032
eGFR 30-44 ml/min/1.73m^2 & ACR 30-59 mg/mmol †	7/759 (0.92)	3/322 (0.93)	4/437 (0.92)	1.12 (0.18-7.84)	1.00
eGFR decline ≥ 5 ml/min/1.73m^2 in 6-months‡	66/565 (11.7)	27/233 (11.6)	39/332 (11.8)	1.02 (0.58-1.81)	1.00
$KFRE_2$ ≥ 10% or eGFR < 15 ml/min/1.73m^2 ‡	36/759 (4.7)	19/322 (5.9)	17/437 (3.9)	0.54 (0.25-1.11)	0.099
$KFRE_5$ > 5%‡	126/302 (41.7)	52/111 (46.9)	74/191 (38.7)	0.86 (0.51-1.44)	0.62
ACR provided†	355/759 (46.8)	132/322 (41.0)	223/437 (51.0)	1.45 (1.06-1.97)	0.018
Urinalysis provided†	317/759 (41.8)	123/322 (38.2)	194/437 (44.4)	1.22 (0.90-1.68)	0.22
ORN form used	-	-	63/624 (10.1)	-	-

† Restricted to referrals for low eGFR and/or proteinuria.
‡ Restricted to referrals for low eGFR.
¶ Restricted to referrals for proteinuria.
§ Models adjusted for referral site. Referent is pre-KidneyWise time period.
Abbreviations: eGFR - estimated glomerular filtration rate; ACR - urine albumin-creatinine ratio; $KFRE_2$ - 2-yr kidney failure risk; $KFRE_5$ - 5-yr kidney failure risk; ml - millilitres; min - minutes; m - metres; mg - milligrams; mmol – millimoles.

Table 3. Quality of care outcomes at the time of referral.

	No. of patients/Total no. (%)				
	Overall	**Pre-implementation**	**Post-implementation**	**Adjusted Odds Ratio§**	**P value**
On an ACEI or ARB (missing: 103)					
Low eGFR or proteinuria referral	438/683 (64.1)	177/267 (66.3)	261/416 (62.7)	0.87 (0.62, 1.23)	0.473
DM/ACR>3 or no DM/ACR>30	238/316 (75.3)	84/110 (76.4)	154/206 (74.8)	0.96 (0.52, 1.73)	1.00
On a statin (missing: 103)					
Low eGFR or proteinuria referral	433/688 (62.9)	175/269 (65.1)	258/419 (61.6)	0.86 (0.61, 1.21)	0.405
DM and/or CKD/age>49	440/649 (67.8)	174/245 (71.0)	266/404 (65.8)	0.77 (0.54, 1.10)	0.16

§ Models adjusted for referral site. Referent is pre-KidneyWise time period.

Abbreviations: ACEI – angiotensin converting enzyme inhibitor; ARB - angiotensin receptor blocker; DM - diabetes mellitus; ACR - urine albumin creatinine ratio; CKD - chronic kidney disease, no. – number.

Table 4. Multivariable predictors of a referral meeting KidneyWise referral criteria.				
	Met KidneyWise referral criteria			
	Odds ratio (95% C.I.)	P value	Odds ratio (95% C.I.)	P value
Time period	1.18 (0.87-1.59)	0.292	-	-
Site	0.59 (0.41-0.83)	0.002	0.60 (0.44-0.82)	0.001
Age	1.23 (1.12-1.35)	<0.001	1.32 (1.21-1.43)	<0.001
Male sex	1.25 (0.93-1.68)	0.142	1.16 (0.88-1.52)	0.303
DM	1.05 (0.78-1.43)	0.736	1.18 (0.89-1.56)	0.253
KidneyWise referral form	-	-	2.09 (1.21-3.61)	0.008

1st model inclusive of both time periods. Second model includes only the post-implementation time period.

Abbreviations: DM – diabetes mellitus; C.I. – confidence interval.

Table 5. Referral form characteristics and use of ORN referral form.

	Kidneywise form used		Kidneywise form not used		P value
	N (%)	Median (IQR)	N (%)	Median (IQR)	
eGFR, ml/min/1.73m^{2}†	37 (7.3)	30.8 (24.8-37.1)	473 (92.7)	35.2 (27.6-44.6)	0.039
Urine ACR, mg/mmol‡	14 (8.2)	93.8 (76.9-153.4)	156 (91.8)	39.5 (10.8-100.2)	0.009
$KFRE_2$, %†	32 (10.6)	2.6 (0.65-7.8)	270 (89.4)	1.1 (0.35-3.4)	0.019
$KFRE_5$, %†	32 (10.6)	7.8 (2.0-22.4)	270 (89.4)	3.4 (1.1-10.3)	0.019

† Restricted to referrals for low eGFR.

‡ Restricted to referrals for proteinuria.

Abbreviations: eGFR - estimated glomerular filtration rate; ACR - urine albumin-creatinine ratio; $KFRE_2$ - 2-yr kidney failure risk; $KFRE_5$ - 5-yr kidney failure risk; ml - millilitres; min - minutes; m - metres; mg - milligrams; mmol - millimoles.

Appendix

1. Supplemental Tables:

Table S1. Distribution of referrals between the two sites and time periods.

	Pre-Kidneywise	Post-Kidneywise	Total
Academic site (SJHH) – no. (%)	345 (33.1)	377 (36.1)	722 (69.2)
Community site (THP) – no. (%)	74 (7.1)	247 (23.7)	321 (30.8)
Total – no. (%)	419 (40.2)	624 (59.8)	1043 (100)

Abbreviations: SJHH – St. Joseph's Healthcare Hamilton, no. – number; THP – Trillium Health Partners.

2. Kidneywise toolkit:

Ontario Renal Network

Kidney Wise
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Introduction to the KidneyWise Clinical Toolkit

The Ontario Renal Network (ORN), a division of Cancer Care Ontario (CCO) and an agency of the provincial government, is responsible for overseeing and funding the delivery of chronic kidney disease (CKD) services across Ontario. By establishing consistent standards and guidelines, based on the best available evidence, along with information systems that measure performance, the ORN supports a continuously improving kidney care system in Ontario.

The KidneyWise Clinical Toolkit, developed by the ORN for primary care providers (PCPs), is intended to help with the identification, detection, and management of CKD.

The Toolkit is designed to help PCPs determine which patients are at high risk of developing CKD, and provides recommendations on how to properly diagnose and best manage the disease in order to reduce the risk of further progression.

The KidneyWise Clinical Toolkit has three components:

1. An evidence-based **Clinical Algorithm** that helps with identification, detection, and management of CKD, and recommends which patients might benefit from referral to a nephrologist.
2. The **Evidence Summary** offers PCPs further clinical detail regarding the Algorithm content including references to clinical guidelines that were used in the development of the Toolkit.
3. The **Outpatient Nephrology Referral Form** provides PCPs with referral guidance by outlining clinical scenarios which would require consultation with a nephrologist, as well as the appropriate investigations that should accompany the referral.

How can I get it?

To access the KidneyWise Clinical Toolkit, please visit **kidneywise.ca**.

Also available for iPhone and Android.

Any questions?
Please contact us directly at **kidneywise@renalnetwork.on.ca**.

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Ontario
Cancer Care Ontario

BMJ Open

Ontario Renal Network

Identification, Detection, and Management of CKD in Primary Care

Kidney Wise
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IDENTIFY

Identify patients in your practice with elevated risk of CKD based on the following:

- Hypertension
- Diabetes mellitus
- Age 60–75 with cardiovascular disease (CV)

DETECT

- CKD detection should be done in the absence of acute intercurrent illness. Low eGFR (estimated Glomerular Filtration Rate) in such scenarios may reflect acute kidney injury and require more rapid evaluation
- Test with eGFR and urine ACR (Albumin to Creatinine Ratio)
- Note: eGFR calculation needs to be adjusted for black patients (multiply eGFR by 1.21)
- If eGFR < 60ml/min/1.73m^2, repeat test in 3 months, or sooner if clinical concern dictates (i.e. rapid decline from previous eGFR result or very low eGFR)
- If urine ACR ≥ 3mg/mmol on initial testing, repeat 1 or 2 more times over the next 3 months (at least 2 out of 3 random urine ACRs must be elevated in order to be considered abnormal)
- Always consider reversible causes prior to re-testing (e.g. recent treatments with NSAIDs, recent use of contrast dye for diagnostic imaging, BPH/urinary retention)

Results after 3 months

Box A **eGFR < 30 or ACR > 60**

- Patient has CKD
- Based on above parameters, consider seeking consultation from nephrology

Work-up

- For low eGFR: Urine R+M, CBC, electrolytes, Ca, PO_4^{3-}, Albumin, PTH
- For albuminuria: Urine R+M, electrolytes

Box B **eGFR 30–59 and/or ACR 3–60**

- Patient has CKD
- See Manage box below for management
- Check urine R+M, electrolytes
- **Follow eGFR & urine ACR every 6 months**

- eGFR < 60 and decline ≥ 5ml/min within 6 months (confirmed on repeat testing within 2 to 4 weeks), or
- eGFR < 30 or ACR > 60, or
- eGFR < 45 and urine ACR between 30 and 60 on 2 occasions, at least 3 months apart
- Inability to achieve blood pressure targets, or
- Significant K^+ disorder, RBC casts or hematuria (> 20 RBC/hpf)

Box C **eGFR ≥ 60 and ACR < 3**

- Patient does **not** have CKD
- Re-test annually for patients with diabetes, less frequently otherwise, unless clinical circumstances dictate more frequent testing

- If eGFR stable for 2 years, **follow eGFR and urine ACR every 12 months**

REFER TO NEPHROLOGIST While waiting for consultation, see MANAGE box below for management

MANAGE

Implement measures to modify CV risk factors

- Lifestyle modification, smoking cessation
- Lipid management for patients with CKD (see KDIGO guidelines for further details):
  - **If with diabetes, age >18 → treat with a statin***
  - **If without diabetes, age ≥ 50 → treat with a statin***
  - **If without diabetes, age 18–49, has known coronary artery disease, prior stroke, or 10-year Framingham risk >10% → treat with a statin***
- For patients with diabetes, target HbA1c to appropriate level (see CDA guidelines)

*Contraindications: active liver disease, high alcohol consumption or pregnancy. Women with childbearing potential should only use a statin if there is reliable contraception.

Minimize further kidney injury

- If possible, avoid nephrotoxins such as NSAIDs, IV and intra-arterial contrast, etc. (if eGFR < 60)
- If contrast is necessary, consider oral hydration, withholding diuretics
- Refer to Sick Day Medication List (see Evidence Summary)

Implement measures to slow rate of CKD progression

BP and RAAS blockade (repeat creatinine and potassium 2 weeks after initiation of ACEI or ARB use):

- If with diabetes, target BP < 130/80, otherwise target BP < 140/90
- If with diabetes and with ACR > 3, start use of an ACEI or ARB as first-line therapy. If BP already < 130/80, use ACEI or ARB cautiously, monitoring for signs and symptoms of hypotension
- If without diabetes, ACR > 30 and BP > 140/90, start use of an ACEI or ARB as first-line therapy

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Evidence Summary for KidneyWise Clinical Algorithm

PURPOSE

The KidneyWise Clinical Algorithm was created as a resource for primary care providers to aid in the identification, detection, and management of chronic kidney disease (CKD). Note, the clinical algorithm may not apply in the following situations:

- Frail and elderly patients or those with a short life expectancy
- When clinical circumstances warrant investigation for suspected acute kidney injury (i.e. volume depletion, urinary obstruction, etc.)
- When an eGFR (estimated Glomerular Filtration Rate) is necessary in prescribing medications that require dose adjustment for reduced kidney function (e.g. new oral anticoagulants, certain antibiotics)

KEY ELEMENTS

IDENTIFY

Diabetes mellitus (DM) is the leading cause of CKD and end-stage renal disease (ESRD) in Canada. Hypertension (HTN) is an important risk factor for CKD and its progression, although it is uncommon as the sole cause if blood pressure is well controlled. Other risk factors listed for CKD are based on epidemiologic findings (e.g. age 60–75 with cardiovascular disease). First Nations, Inuit and Métis patients are at particularly high risk of developing ESRD, although this risk is primarily mediated through an increased risk for DM and HTN.

DETECT

Most relevant guidelines, including Kidney Disease Improving Global Outcomes (KDIGO)[1], recommend testing with both an eGFR and a urine ACR (Albumin to Creatinine Ratio), as both measures are independent risk factors for progression to ESRD. An eGFR with a value < 60[a] should be repeated if < 60[a], as many patients will have a value above on repeat testing. Consider the possibility of a reversible cause for a low eGFR, including dehydration (i.e. recent gastrointestinal illness or excess diuretic use), or the concomitant use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). The diagnosis of CKD requires evidence of chronicity (i.e. at least 3 months with an eGFR < 60[a]). The urine ACR should be repeated if abnormal; confirmation requires at least 2 of 3 values to be elevated.

Patients with an eGFR ≥ 60[a] and an ACR < 3[b] can be re-screened at an interval commensurate with the underlying risk factor. Re-testing annually in patients with DM is reasonable. Patients with HTN may require less frequent testing, depending on patient age, the presence of other co-morbidities, and the degree of blood pressure control. It is important to note that a substantial proportion of otherwise healthy elderly individuals will have an eGFR < 60[a] due to normal aging (40% of women > 75 years of age and 30% of men > 80 years of age).

MANAGE

Review of the KDIGO Clinical Practice Guideline for Lipid Management in CKD[2], Canadian Hypertension Education Program (CHEP)[3], and Canadian Diabetes Association (CDA)[4] clinical practice guidelines is recommended for detailed advice regarding hyperlipidemia, hypertension, and glycemic control, respectively.

ACE inhibitors (ACEI) or angiotensin receptor blockers (ARB), but not both, are recommended as outlined for most CKD patients who also have albuminuria; for normotensive patients with diabetes with an elevated ACR (> 3[b]), an ACEI or ARB can be considered although careful monitoring for signs or symptoms of hypotension is advised. Most patients with DM and an elevated ACR will have hypertension in the absence of any anti-hypertensive therapy. For patients without diabetes with a blood pressure > 140/90 and an ACR > 30[b], an ACEI or ARB should be used as first-line therapy. CKD patients who require statin therapy should be treated regardless of baseline lipid status and do not routinely require follow-up measurement of lipid levels. Patients with a non-renal indication for one of these agents (i.e. heart failure) should be treated accordingly.

It is recommended that a serum potassium and creatinine be repeated approximately 2 weeks after any initiation or dose increase of an ACEI or ARB to monitor for the development of hyperkalemia and/or a substantial decrease in eGFR. An increase in serum creatinine of up to 30% after initiation of an ACEI or ARB is not associated with an increased risk of worsening long-term kidney function. Larger increases may suggest excessive diuretic use and/or underlying renovascular disease.

Note, given the high risk of influenza-related complications among CKD patients, primary care providers should recommend they receive the seasonal influenza vaccine on an annual basis[5].

SICK DAY MEDICATION LIST

If patients with CKD are unable to maintain adequate fluid intake during an illness, it is recommended that potentially nephrotoxic or renally excreted drugs should be withheld until the patient has recovered. As outlined in the CDA guidelines, this can be recalled by referring to the acronym **SADMAN** (**S**ulfonylureas, **A**CEI, **D**iuretics, **M**etformin, **A**RB, **N**SAIDs).

Adapted from: Change in appropriate referrals to nephrologists after the introduction of automatic reporting of the estimated glomerular filtration rate. Akbari A., Grimshaw J., Stacey D, et al. CMAJ 2012. DOI: 10.1503/cmaj.110678

[a] units for eGFR are ml/min/1.73m^2
[b] units for ACR are mg/mmol
[1] Kidney Disease Improving Global Outcomes CKD Guidelines 2012. **http://kdigo.org/home/guidelines/ckd-evaluation-management/**
[2] Kidney Disease Improving Global Outcomes Clinical Practice Guideline for Lipid Management in CKD 2013. **http://kdigo.org/home/guidelines/lipids/**
[3] Canadian Hypertension Education Program Guidelines 2014. **http://www.hypertension.ca/en/chep**
[4] Canadian Diabetes Association Clinical Practice Guidelines 2013. **http://guidelines.diabetes.ca/Browse.aspx**
[5] Public Health Agency of Canada 2013. **http://www.phac-aspc.gc.ca/index-eng.php**

Ontario Renal Network

Kidney Wise
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Outpatient Nephrology Referral Form for Primary Care Providers

To our primary care provider colleagues:

Please find an Outpatient Nephrology Referral Form developed by the Ontario Renal Network (ORN). Recommended reasons for referral of patients with nephrological problems are outlined, and these closely mirror the ORN's KidneyWise Clinical Algorithm and Evidence Summary. While patients (and their primary care providers) often want to arrange a timely appointment so that their clinical concerns can be addressed and/or alleviated quickly, most nephrologists will triage referred patients based on level of need. Those patients who are at high risk of progressing to end-stage renal disease and/or who may require a renal biopsy for diagnosis are usually seen more urgently.

Typical indications include:

- Very low renal function (eGFR < 20 ml/min/1.73m^2, confirmed on repeat testing)
- Rapidly declining renal function (eGFR decline ≥ 10 ml/min/1.73m^2 within 2 to 4 weeks, confirmed on repeat testing)
- Nephrotic syndrome (edema with severe proteinuria – i.e. urine ACR > 150 mg/mmol or 24-hour urine protein > 3.5 g/day and serum albumin < 25 g/L)
- Suspected glomerulonephritis or renal vasculitis (hematuria with > 20 RBC/hpf or RBC casts associated with proteinuria, declining renal function and/or positive immune markers)

Please note that the use of NSAIDs should be discontinued prior to confirming very low or rapidly declining renal function, as this is a common reversible cause of a decline in eGFR. Also, note that initiating the use of an ACEI or ARB may cause a reversible decline in eGFR (up to 30%) that does not necessarily warrant referral.

If you feel that circumstances warrant referral of a patient with CKD who does not meet the recommended referral criteria on the Outpatient Nephrology Referral Form, particularly in younger patients, contact your local nephrology group for further advice. If you feel your patient needs to be seen within 24 hours, contact the nephrologist on call in your region for further discussion.

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The KidneyWise Clinical Toolkit helps primary care providers identify, detect, and manage chronic kidney disease (CKD).

The KidneyWise Clinical Toolkit helps to:

- Determine which patients are at high risk of developing CKD
- Provide recommendations on how to properly diagnose and best manage the disease to reduce risk for further progression
- Guide clinicians on which patients might benefit from referral to nephrology

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CLINIC INFORMATION HERE

Patient Information (please fill in or affix label):

NAME: _____ DOB: ____/____/____ (DD/MM/YY)

ADDRESS: _____

PHONE #: _____ HEALTH CARD #: _____

ALT. CONTACT INFO: _____

Outpatient Nephrology Referral Form

Date of referral: ____/____/____ (DD/MM/YY) Is this a re-referral? ☐ Yes ☐ No

Name of nephrologist seen previously: _____

Recommended Reason for Referral:

- ◯ eGFR < 30 ml/min/1.73m^2 on 2 occasions, at least 3 months apart
- ◯ eGFR < 45 ml/min/1.73m^2 and urine ACR between 30 and 60 mg/mmol on 2 occasions, at least 3 months apart
- ◯ Rapid deterioration in renal function (eGFR < 60 ml/min/1.75m^2 and decline of 5 ml/min within 6 months, confirmed on repeat testing within 2 to 4 weeks on 2 occasions)
- ◯ Proteinuria (urine ACR > 60 mg/mmol on at least 2 of 3 occasions)
- ◯ Hematuria (> 20 RBC/hpf or RBC casts)
- ◯ Resistant or suspected secondary hypertension
- ◯ Suspected glomerulonephritis/renal vasculitis
- ◯ Metabolic work-up for recurrent renal stones
- ◯ Other: _____

Additional comments:

Co-morbid Conditions:

◯ Diabetes mellitus ◯ Coronary artery disease ◯ Hypertension ◯ Frailty ◯ Peripheral vascular disease
◯ Previous stroke ◯ Cognitive impairment

Lab Values:
Please fill out below if applicable; refer to the ORN KidneyWise Clinical Algorithm for suggested investigations

Date #1: (DD/MM/YY)	eGFR:	Creatinine:	Urine ACR:
Date #2: (DD/MM/YY)	eGFR:	Creatinine:	Urine ACR:
HbA1c:	Hgb:	K^+:	Ca^{2+}:
PO_4^{3-}:	Albumin:	PTH:	Hematuria (dipstick):
Other (or attach):			

Current Medications:

Referring practitioner/address/phone/fax:	**Referring billing #:**
	Signature:

Kidney Wise
Detect + Protect

Please send the completed referral form to a local nephrologist in your region.
Do not forward this form to CCO/Ontario Renal Network. If you need to access contact information for a local nephrologist, please visit http://www.cpso.on.ca/public-register/all-doctors-search?term

Ontario Renal Network

Ontario Renal Network: BACKGROUNDER

Chronic kidney disease (CKD) is a serious, lifelong condition. People with advanced CKD often require complex and intensive care from a multidisciplinary team of healthcare professionals. Approximately 12,000 people in Ontario have CKD requiring pre-dialysis care. An additional 10,500 Ontarians with advanced CKD require dialysis. The need for dialysis has been gradually rising for more than a decade and is expected to continue climbing in the foreseeable future. This trend is largely driven by changing demographics and the increasing prevalence of risk factors associated with CKD, such as diabetes, hypertension and aging.

In 2009, Ontario's Ministry of Health and Long-Term Care transferred oversight and coordination of kidney care services to the Ontario Renal Network (ORN). The ORN, a division of CCO and an agency of the provincial government, manages the delivery of chronic kidney disease services. Our decisions and advice are based on the best evidence available, enabling us to provide effective planning, programs and funding to support a continuously improving kidney care system in Ontario. ORN improves the healthcare system by engaging people with chronic kidney disease and their families, along with health care providers, in the design, delivery and evaluation of care. Person-centered care helps improve the patient experience while enabling the system to deliver better outcomes and value.

ORN consists of a vast array of partners including healthcare professionals, Regional Renal Program staff, partner health agencies and organizations, patients and families, and many others. The provincial office works closely with all our regional partners in planning, delivering, funding, and monitoring CKD care across the province. In total, 26 Regional Renal Programs provide dialysis and other kidney care services within approximately 100 facilities (including hospitals and community-based facilities). Other community partners such as long-term care homes and independent health facilities also provide kidney care services to many patients.

ORN recently released the Ontario Renal Plan II 2015-2019 (ORP II), the provincial roadmap to guide how regional partners will work over the next four years to continue to improve the lives of those living with CKD. It builds on the foundation laid by the first strategic plan and addresses patient care across the kidney care journey, from early detection through dialysis, palliative care and transplant.

Patients and their families are at the heart of all three goals. ORP II reframes the way we think about kidney care and the roles of everyone involved. Our focus shifts beyond dialysis to kidney health; beyond medical treatments to quality of life; beyond making decisions for patients to empowering them to make choices with their care teams. With a strong infrastructure in place, ORPII represents a significant shift for the Ontario Renal Network towards person-centred care. See the change at www.renalnetwork.on.ca/orp

www.renalnetwork.on.ca
information@renalnetwork.on.ca

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	-	
		(*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	2	
Objectives	3	State specific objectives, including any prespecified hypotheses	2	Final paragraph
Methods				
Study design	4	Present key elements of study design early in the paper	5	2nd paragraph
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	2nd paragraph
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5	2nd paragraph
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	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	6	1st paragraph
Bias	9	Describe any efforts to address potential sources of bias		All referrals captured
Study size	10	Explain how the study size was arrived at	7	Statistical analysis section

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7	Statistical analysis section
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7	Statistical analysis section
		(*b*) Describe any methods used to examine subgroups and interactions	7	2nd paragraph
		(*c*) Explain how missing data were addressed	8	1st paragraph
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A	
		(*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	9	1st paragraph and Table 1
		(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	9	1st paragraph and Table 1
		(b) Indicate number of participants with missing data for each variable of interest		Table 1 - footnote
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		Table 2-3
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	9-10	1º and 2º outcome sections & Tables 2-3
		(*b*) Report category boundaries when continuous variables were categorized	N/A	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses		Table 4-5
Discussion				
Key results	18	Summarise key results with reference to study objectives	Discussion section	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	1	Limitations section
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion section	
Generalisability	21	Discuss the generalisability (external validity) of the study results	1	Limitations section
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	Title page	

*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.

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Impact of the KidneyWise toolkit on chronic kidney disease referral practices in Ontario primary care: a prospective evaluation

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Impact of the KidneyWise toolkit on chronic kidney disease referral practices in Ontario primary care: a prospective evaluation

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Abstract

Objectives: Chronic kidney disease (CKD) is common; therefore, coordination of care between primary care and nephrology is important. Ontario Renal Network's KidneyWise toolkit was developed to provide guidance on the detection and management of people with CKD in primary care (www.kidneywise.ca). The aim of this study was to evaluate the impact of the April 2015 KidneyWise toolkit release on the characteristics of primary care referrals to nephrology.

Design and Setting: prospective pre-post design conducted at two nephrology sites (community site: Trillium Health Partners in Mississauga, Ontario, Canada, and academic site: St Joseph's Healthcare in Hamilton, Ontario, Canada). Referrals were compared during the 3-month time period immediately prior to, and during a 3-month period one-year after, the toolkit release.

Primary and Secondary Outcome Measures: The primary outcome was the change in proportion of referrals for CKD that met Kidneywise criteria. Additional secondary referral and quality of care outcomes were also evaluated. Multivariable logistic regression was used to evaluate pre-selected variables for their independent association with referrals that met Kidneywise criteria.

Results: The proportion of referrals for CKD among people who met the KidneyWise referral criteria did not significantly change from pre- to post-KidneyWise implementation (44.7% vs 45.8% respectively, adjusted odds ratio (OR) 1.16; 95% C.I. 0.85-1.59, p=0.36). The proportion of referrals for CKD that provided a urine ACR significantly increased post-KidneyWise (25.8% vs 43.8%; adjusted OR 1.45, [95% C.I. 1.06-1.97], p=0.02). The significant independent predictors of meeting KidneyWise referral criteria were: academic site, increased age, and use of the KidneyWise referral form.

Conclusions: We did not observe any change in the proportion of appropriate referrals for CKD at two large nephrology centres one year after implementation of the KidneyWise toolkit.

Strengths and limitations of this study:

- A prospective study conducted in two large nephrology centres
- Pre-specified primary and secondary objectives utilizing multiple imputation to account for incomplete data.
- Relatively short time period (one-year) in which to observe changes in referral characteristics
- No information available on patients who were not referred.

Key words: chronic kidney disease, primary care, proteinuria, knowledge translation.

Abbreviations: ACR - albumin-creatinine ratio; C.I. – confidence interval; CKD – chronic kidney disease; CSN – Canadian Society of Nephrology; DM – diabetes mellitus; eGFR – estimated glomerular filtration rate; KDIGO – Kidney Disease: Improving Global Outcomes; KFRE – kidney failure risk equation; SJHH – St. Joseph's Healthcare Hamilton; OR – odds ratio; ORN – Ontario Renal Network; THP – Trillium Health Partners

Background

Chronic kidney disease (CKD), defined by the persistence of an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73m^2 and/or albuminuria (urine albumin-creatinine ratio [ACR] of greater than 3.0 mg/mmol), affects 10-12% of adults in Canada.[1] A number of guidelines make recommendations on the timing of referral of persons with CKD from primary care to nephrology, although it is unclear how familiar primary care providers are with these.[2–6] Late referral may lead to unplanned initiation of renal replacement therapy and other adverse outcomes.[7,8] Conversely, early referral may not be feasible when considering the availability of nephrology services and furthermore, may be unnecessary and/or may not improve outcomes.[9-12] Regardless of the timing of referrals, enhanced CKD care and improved coordination between primary care and nephrology are important for people with CKD.

The Ontario Renal Network's (ORN) KidneyWise (www.kidneywise.ca; Supplementary Appendix)[2,13] toolkit was developed in 2015 in an effort to provide succinct guidance for the detection and management of CKD in the primary care setting, incorporating recommendations from a number of relevant guideline documents.[3,14,15] We implemented knowledge translation strategies to coincide with the release of the toolkit to promote uptake, including: development of a web-based platform and mobile application, presentations at accredited local, provincial, and national primary care medical conferences, as well as dissemination from regional nephrology primary care programs to referring primary care providers. Embedded within the toolkit is a standardized referral form which mirrors the nephrology referral criteria outlined in the toolkit.

The objective of this study was to evaluate the impact of the KidneyWise toolkit release on referral characteristics and quality of care at two sites in Ontario, Canada. We hypothesized that dissemination of the toolkit would lead to: i) an increased proportion of referrals which met

Kidneywise referral criteria for CKD (low eGFR or proteinuria); and ii) improvement in the quality of CKD-relevant care in people with CKD who had been referred.

Methods

KidneyWise toolkit

The ORN, a provincial agency, oversees and funds kidney care services in Ontario. There are 27 regional programs that provide general nephrology, multidisciplinary kidney care clinics, and dialysis services to those in need in their respective regions. One of its priorities is to improve quality and coordination of CKD care in primary care which, through the efforts of a small working group of nephrologists and primary care providers, led to the development of the Kidneywise toolkit.[2,13] Embedded within the KidneyWise toolkit are recommended criteria for referral to nephrology; , adapted from several existing guidelines, with an emphasis on the Canadian Society of Nephrology (CSN) recommendation.[3,5-6] As a result, an eGFR less than 30 ml/min/1.73m^2 or urine ACR greater than 60 mg/mmol were two key referral criteria that were common to KidneyWise and the CSN recommendations. Concerns were raised by the working group that some patients may be at higher risk of progression but who would not meet either criteria. Therefore, KidneyWise also recommended referral for those with an eGFR 30-44 ml/min/1.73m^2 and urine ACR 30-59 mg/mmol. Finally, with respect to evidence of rapid progression, we noted substantial variation in the guidelines, ranging from a five[3] to a 15 ml/min/1.73m^2 decline over one year.[6] Balancing out the need for more timely referral for those with evidence of rapid progression, while avoiding an excessive volume of referrals, we recommended referral for those with an eGFR less than 60 ml/min.173m^2 and a decline of at least 5 ml/min/1.73m^2 over six months.

Study Design and Population

The study was a prospective pre-post design. Nephrology referrals received at two sites (Trillium Health Partners [THP] in Mississauga, Ontario, Canada and St Joseph's Healthcare Hamilton [SJHH] in Hamilton, Ontario, Canada) were evaluated during two 3-month time periods. The first time period occurred from January-March 2015, immediately prior to the toolkit release. The second period occurred one year after the toolkit release (April-June 2016). THP is a community-based centre and is the sole nephrology provider in Mississauga, a city with a population of 713,000. SJHH, an academic centre affiliated with McMaster University, is similarly the sole provider for a city with a population of about 537,000. Both centres have an estimated referral base of about 1 million people. At SJHH, all referrals are triaged centrally at a single location; therefore, all referrals were captured during the conduct of the study. Conversely, at THP, referrals could either go to a central location at the hospital or directly to private nephrologist offices. In this study, only the central location referrals at THP were captured.

Toolkit Dissemination

Dissemination of the toolkit incorporated a number of passive and active strategies to promote uptake. At a provincial and national level, one of the authors [AKG] presented KidneyWise at a number of accredited primary care medical conferences; additionally, a paper version of the toolkit was handed out to conference attendees. Physician leaders from each of the regional nephrology programs in the province were informed in person of the contents of KidneyWise and were encouraged to promote its dissemination in their local regions. A web-based platform and mobile application were also developed and their use encouraged at the same conferences. At both sites, a copy of the toolkit was sent to referring physicians encouraging use of the KidneyWise referral form with future requests. Many of the nephrologists at the two sites

also embedded statements within their consultation letters that encouraged use of the KidneyWise toolkit. Finally, KidneyWise was frequently promoted by two authors [KSB and AKG] on Twitter©.

Outcomes

Relevant data was extracted from referrals onto paper case report forms. The primary outcome was the change in the proportion of referrals for CKD (low eGFR and/or proteinuria) meeting Kidneywise criteria before and after the Toolkit introduction. Although the KidneyWise toolkit recommends two eGFR and ACR values at least three months apart to confirm chronicity, the primary outcome for the purposes of this study was based on a single value. The rationale for this was the observed high background referral rate providing only a single eGFR and/or proteinuria measure. A sensitivity analysis was also performed for the primary outcome using the stricter requirement for two qualifying values.

Pre-specified secondary referral outcomes included: i) change in the proportion of appropriate referrals for low eGFR (< 30 ml/min/1.73m^2); ii) change in the proportion of appropriate referrals for proteinuria (urinary ACR > 60 mg/mmol); iii) change in the proportion of appropriate referrals for low eGFR or proteinuria which provided at least one urine ACR value (actual, not estimated); iv) change in the proportion of appropriate referrals for low eGFR or proteinuria which provided at least one urinalysis; and v) change in the proportion of late referrals (defined here as eGFR < 15 ml/min/1.73m^2 and/or a two-year kidney failure risk[14] [KFRE$_2$] > 10%).

Secondary pre-specified quality of care outcomes which aligned with the recommendations in the toolkit were as follows: i) change in the proportion of persons referred

who were on an ace inhibitor or angiotensin receptor blocker (all referrals and those with diabetes mellitus [DM]; and ii) change in the proportion of persons referred who were on a statin (all referrals and those with a primary prevention indication [e.g. CKD with DM, CKD without DM and ≥ 50 years of age]).

Statistical Analysis

Assuming that the baseline proportion of referrals that met Kidneywise criteria was 50% (based on a previous audit conducted at the SJHH site) and that the toolkit would lead to a relative 20% increase in this proportion (i.e. to an absolute value of 60%), 519 referrals would be required during each time period to detect a significant difference (alpha 0.05) with 90% power. Assuming that more than 2,000 referrals are received at the two sites over a one-year period (the SJHH site received ~ 2,000 referrals the previous year), a three-month collection period pre and post-toolkit introduction was considered sufficient to achieve the required sample size.

Continuous variables were described as means and standard deviations (SD) or medians and interquartile ranges and categorical variables expressed as proportions. Where required, urine protein based on dipstick or 24-hour urine protein was converted to approximate urine ACR as previously described.[16,17] Data were assumed to be missing at random for logistic regression analyses; multiple imputation was performed (set of 15) using Markov Chain Monte Carlo procedures assuming a multivariate normal distribution. A two-sided p-value <0.05 was regarded as significant without adjustment for multiple comparisons. For the primary and secondary outcomes, the pre-post difference in proportion of categorical variables was assessed by calculating the odds ratio (OR) and its associated 95% confidence interval (C.I.) using logistic regression, adjusted for referral site. An additional analysis conducted for the primary outcome

using mixed effects logistic regression (site as a random intercept) did not materially change the original estimates and are therefore not reported here. The differences between normally and non-normally distributed continuous variables were assessed using the Student's t-test and Wilcoxin rank-sum test, respectively.

Multivariable analysis of predictors of a referral meeting KidneyWise criteria were carried out using the following pre-selected variables based on clinical plausibility: age, sex, presence of DM, referral site, time period (pre versus post), and use of the KidneyWise referral form (the latter during the second time period only). All statistical analyses were performed using Stata v15.1.

Patient and Public Involvement

Patients were not directly involved in this study.

Results

There were 1,043 referrals combined over the two time periods; 69.2% were at the academic site (SJHH) and 40.2% during the first time-period (Table 1). The mean age of persons referred was 63 years and was significantly higher at the academic site compared to the community site (64 ± 18.2 vs 60 ± 20.2; p=0.001). The proportion with DM was similar at the two sites (43.0% overall) with greater ethnic diversity at the community site. Overall, the severity of CKD in people referred was higher at the academic site with a lower eGFR (low eGFR referrals: median 33.1 vs 40.4 ml/min/1.73m^2, p<0.001), higher ACR (proteinuria referrals: 59.0 vs 31.7 mg/mmol, p=0.044), and higher $KFRE_5$ (low eGFR referrals: 5.0% vs 1.8%; p<0.001). The differences noted between the two time-periods in the demographics of

people referred, as well as the referral indication, were driven by the substantial increase in referrals from the community site during the post-KidneyWise time period (see Table S1). Sixty-three of 624 referrals (10.1%) used the KidneyWise referral form post-KidneyWise, all at the academic site.

Primary Outcome

The proportion of referrals for CKD that met the KidneyWise referral criteria between the two time periods did not significantly change from pre- to post-KidneyWise implementation (44.7% vs 45.8% respectively, adjusted OR 1.16; 95% C.I. 0.85-1.59, p=0.358; Table 2). Using the stricter requirement for two eGFR and/or ACR values meeting referral criteria did not alter the conclusions, although the proportion meeting criteria was substantially lower during both time periods (21.4% vs 24.5% respectively, adjusted OR 1.26; 95% C.I. 0.87-1.82, p=0.237).

Secondary outcomes

The proportion of referrals for proteinuria with a urine ACR > 60 mg/mmol significantly increased post-KidneyWise implementation (32.6% vs 45.7%; adjusted OR 2.04 [95% C.I. 1.06-4.01]; p=0.032, Table 2). The proportion of referrals for CKD that provided a urine ACR also significantly increased post-KidneyWise (25.8% vs 43.8%; adjusted OR 1.45, [95% C.I. 1.06-1.97], p=0.0179). An exploratory analysis conducted by forcing use of the KidneyWise referral form into the model suggested that this effect was largely explained by the latter (post-KidneyWise time period: adjusted OR 1.20 [95% C.I. 0.88-1.63], p=0.255; KidneyWise referral form: adjusted OR 4.24 [95% C.I. 2.13-8.44], p<0.001). There were no significant differences in any of the other referral outcomes between the two time periods (Table 2).

The proportion of people referred who were on an ace inhibitor or angiotensin receptor blocker and had an indication was 75.3% overall (Table 3), and was not significantly different before and after KidneyWise implementation (76.4% vs 74.8%; adjusted OR 0.96 [95% C.I. 0.52-1.73], p=1.000). Similarly, the proportion of those on a statin with an indication did not significantly change from pre- to post-implementation (71.0% vs 65.8% respectively, adjusted OR 0.77 [95% C.I. 0.54-1.10]; p=0.158).

The significant independent predictors of received referrals meeting KidneyWise criteria were: academic site, increased age, and use of the KidneyWise referral form (Table 4). Referrals that utilized the KidneyWise referral form had a lower eGFR, higher ACR, and higher kidney failure risk compared to those that did not use the form (Table 5).

Discussion

Implementation of the KidneyWise toolkit was not associated with an increased proportion of referrals that met KidneyWise referral criteria or improvement in quality of CKD care delivered in primary care. Utilization of the KidneyWise referral form, a surrogate measure of KidneyWise awareness, appeared to be restricted to the academic site's catchment area.

It is uncertain which criteria, if any, primary care providers considered when determining whether a patient required referral prior to KidneyWise implementation. In the Canadian context, the Canadian Society of Nephrology (CSN) published a commentary on the Kidney Disease International Guideline Organization (KDIGO) which included referral recommendations.[5] These recommendations were similar to KidneyWise: eGFR less than 30 ml/min/1.73m^2 or urine ACR greater than 60 mg/mmol, but differed with respect to decline in kidney function (abrupt 20% drop versus 5 ml/min/1.73m^2 decline over 6-months). While the similarities between the

two referral guidelines might suggest that dissemination of KidneyWise would have a limited effect on referral patterns, it should be noted that the proportion of referrals for low eGFR or proteinuria that met these common referral recommendations was low. Furthermore, the authors are unaware of prior local efforts to promote the CSN referral criteria which had been published in a nephrology rather than primary care journal.

A number of studies have examined the characteristics of primary care referrals to nephrology, including the appropriateness of referrals.[18–22] In many of these studies, the introduction of automated eGFR has led to an increased volume of referrals, many deemed perhaps unnecessary. Similar to the present findings, Akbari and colleagues found that at an academic centre in Ottawa, Ontario, only 55% of referrals were considered necessary using similar criteria to those used in KidneyWise (eGFR < 30 ml/min/1.73m^2, ACR > 60 mg/mmol, or 20% decline in eGFR over one year).[18] Another study found that despite the implementation of an educational intervention prior to eGFR reporting, referral volume increased.[19] Conversely, a targeted educational intervention in nine primary care and five nephrology practices demonstrated an increase in the proportion of patients with an eGFR < 30 ml/min/1.73m^2 who were referred to nephrology.[23]

Interventions in primary care to influence physician behavior have had mixed results. A previous systematic review found that the use of structured referral forms and the involvement of consultants in educational activities, both techniques employed here, improved referral appropriateness.[24] More recent trials have found that the use of performance feedback methods, including peer comparison with active choice framing and audit and feedback reporting, as well as accountable justification, increased appropriate prescribing behavior in primary care.[25–27] The knowledge translation strategies employed here were primarily passive and may have been less

effective than more active strategies.[28,29] It should be noted that CKD severity was higher at the academic site and similarly, utilization of the KidneyWise referral form was only observed at the academic site. There may be local differences in referral patterns of primary care providers and/or the earnestness and methods with which nephrologists encouraged appropriate referral at the two sites.

We observed that the proportion of referrals for proteinuria meeting KidneyWise criteria increased post-implementation, as did the proportion of CKD referrals that provided an ACR. The effect size was large and the time interval between the two time periods relatively short; suggesting that this observation is likely due to dissemination of KidneyWise rather than other secular phenomena. The finding that use of the KidneyWise referral form was a strong predictor of CKD referrals including an ACR supports this hypothesis.

Feedback from referring primary care providers at a number of KidneyWise presentations indicated that incorporation of KidneyWise into their office-based electronic medical record (EMR) systems to facilitate appropriate and timely referrals would be vital to changing their behavior and improving workflow. To that end, work has been completed to facilitate KidneyWise incorporation into one of the major EMR systems in Canada.[30]

Appropriate utilization of ace inhibitors or angiotensin receptor blockers in patients referred to nephrology was already quite high at baseline, similar to what has been previously described in a Canadian jurisdiction.[31] On the other hand, use of statins was more modest, again consistent with previous work.[31,32] While we did not see any change in the use of statins post-KidneyWise, there would appear to be an opportunity to improve statin utilization in those with increased cardiovascular risk.

This study has limitations that require consideration. Although the total number of referrals exceeded projections for the sample size determination, only 73% of the referrals were for low eGFR and proteinuria. A post-hoc analysis indicates that we had 78% power to detect the original estimated effect size, suggesting the study may have been underpowered. However, based on the observed effect size it seems unlikely that a larger sample size would have changed our conclusions. We do not have information on patients who may have met KidneyWise referral criteria but were not referred. Only two sites were included in this study, however, they both have large catchment areas and are likely to be representative of other urban centres in Ontario. As already outlined, the strategies employed to promote uptake of KidneyWise may have been ineffective despite evidence that a majority of primary care providers were aware of KidneyWise.[33] Additional time may have been required to realize the full impact of the KidneyWise toolkit on referral patterns. A follow-up one-month audit (September 2018) at the SJHH site revealed that 68% of referrals for CKD met KidneyWise criteria, up from 44.6% previously. Additionally, 23% of referrals during this time period utilized the KidneyWise referral form, implying increased awareness of the toolkit over time. Nevertheless, interventions such as electronic decision support tools that promote desired behaviors may be required to substantially improve referral practices and/or quality of CKD care.[34] Finally, a large increase in referral number was observed at the community site, reflecting local changes in how referrals were directed to the central location, rather than necessarily a substantial overall increase in the number of referrals received.

In summary, we did not observe any change in the proportion of referrals for CKD that met KidneyWise referral criteria at two large nephrology centres in Ontario, Canada one year after implementation of the toolkit. We did, however, observe an increase in referrals for

proteinuria that met Kidneywise criteria suggesting some impact of KidneyWise dissemination on referral patterns. Future efforts, including incorporation of KidneyWise into electronic medical record systems, will require careful evaluation to determine whether such strategies may prove effective in improving the appropriateness of primary care referrals to nephrology.

Competing interests statement: KSB is a paid Provincial Medical Lead at the ORN. AGK is a former paid Provincial Medical Lead at the ORN. PGB is a paid Provincial Medical Director of the ORN. DP has received research support from: Amgen, Otsuka, Pfizer, Sanofi, Servier, and Bausch Health; speaking fees/honoraria from: Ardeane Healthcare Solutions; and consulting fees from: Amgen, Otsuka, Pfizer, Sanofi, and Servier. PB, AOM, DMN, AXG, AA, and DP do not have any competing interests to declare.

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Ethics approval: The study protocol was approved by the Hamilton Integrated Research Ethics Board (Study ID3: 14-847-C) and the Trillium Health Partners Research Ethics Board (ID#: 682).

Data sharing statement: Deidentified data (csv file) can be made available upon reasonable request from readers by emailing the corresponding author at brimbles@mcmaster.ca.

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Table 1. Baseline characteristics of the patients referred.

	Academic site	Community site	P value	Pre-KidneyWise	Post-KidneyWise	P value
N - (%)	722 (69.2)	321 (30.8)		419 (40.2)	624 (59.8)	
Age, Mean (SD)	64.2±18.1	60.0±20.2	0.001	64.1±17.2	62.0±19.9	0.077
Female – no. (%)	326 (45.2)	145 (45.8)	0.892	197 (47.0)	274 (44.2)	0.375
DM - no. (%)	313 (44.7)	124 (39.2)	0.115	179 (45.2)	258 (41.6)	0.270
Race - no. (%)						
Caucasian	420 (58.1)	145 (45.2)	<0.001	218 (52.0)	347 (55.6)	0.011
Black African	18 (2.5)	19 (5.9)		8 (1.9)	26 (4.2)	
Asian	13 (1.8)	22 (6.9)		9 (2.2)	26 (4.2)	
Hispanic	6 (0.83)	3 (0.93)		3 (0.72)	6 (0.96)	
Mid-east/Arabian	12 (1.7)	23 (7.2)		5 (1.2)	30 (4.8)	
Indigenous	6 (0.83)	0 (0)		3 (0.72)	3 (0.48)	
Indian sub-continent	19 (2.6)	42 (13.1)		20 (4.8)	41 (6.6)	
Other/Unknown	228 (31.6)	67 (20.9)		153 (36.6)	142 (22.8)	
Reason for referral – no. (%)						
CKD	427 (59.1)	138 (43.0)	<0.001	233 (55.6)	332 (53.2)	<0.001
Proteinuria/DM	129 (17.9)	65 (20.3)		89 (21.2)	105 (16.8)	
Hypertension	32 (4.4)	12 (3.7)		28 (6.7)	16 (2.6)	
Stones	17 (2.4)	35 (10.9)		8 (1.9)	44 (7.1)	
Hematuria	13 (1.8)	21 (6.5)		4 (0.95)	30 (4.8)	
GN/Nephrotic syndrome	13 (1.8)	11 (3.4)		8 (1.9)	20 (3.2)	
AKI	22 (3.1)	11 (3.4)		13 (3.1)	20 (3.2)	
Other	65 (9.0)	28 (8.7)		36 (8.6)	57 (9.1)	
eGFR, ml/min/1.73m^2 – median (IQR)						
All (N=889)	40.2 (29.4-66.4)	53.9 (38.8-85.3)	<0.001	43.8 (30.5-71.5)	44.7 (31.6-74.6)	0.406
Low eGFR (N=510)	33.1 (26.9-41.8)	40.4 (30.5-49.6)	<0.001	33.5 (27.0-43.8)	35.8 (28.3-44.4)	0.307
Urine ACR, mg/mmol – median (IQR)						
All (N=616)	9.2 (1.0-74.0)	3.4 (1.0-17.8)	0.002	9.3 (2.0-61.1)	4.0 (1.0-45.4)	<0.001
Low eGFR or proteinuria (N=481)	11.0 (1.2-81.1)	5.0 (1.7-43.2)	0.072	12.1 (2.5-76.2)	5.7 (1.0-67.7)	0.012
Proteinuria (N=170)	59.0 (15.9-121.4)	31.7 (6.2-89.2)	0.044	30.0 (11.1-89.2)	62.4 (11.4-118.2)	0.318
$KFRE_2$, % – median (IQR)						
All (N=582)	0.60 (0.041-2.5)	0.16 (0.0042-0.77)	<0.001	0.56 (0.021-2.4)	0.44 (0.051-1.62)	0.879
Low eGFR (N=213)	1.6 (0.57-4.7)	0.57 (0.23-1.5)	<0.001	1.4 (0.47-4.3)	1.1 (0.37-3.4)	0.306
$KFRE_5$, % – median (IQR)						
All (N=582)	1.8 (0.13-7.7)	0.51 (0.013-2.4)	<0.001	1.05 (0.046-6.3)	1.3 (0.062-5.1)	0.879
Low eGFR (N=213)	5.0 (1.8-14.0)	1.8 (0.72-4.5)	<0.001	4.3 (1.4-12.9)	3.3 (1.2-10.2)	0.306

Missing values: female – 4; DM – 27; race - 272. Not provided: eGFR – 154; urine ACR: 427. Not calculable: $KFRE_2$/$KFRE_5$ – 461.
Abbreviations: yr - year; DM - diabetes mellitus; CKD - chronic kidney disease; DMN - diabetic nephropathy; GN - glomerulonephritis; AKI - acute kidney injury; eGFR - estimated glomerular filtration rate; ml - millilitres; min - minutes; m - metres; ACR - urine albumin-creatinine ratio; IQR – interquartile range; mg - milligrams; mmol - millimoles; $KFRE_2$ - 2-yr kidney failure risk; $KFRE_5$ - 5-yr kidney failure risk.

Table 2. Primary and secondary referral outcomes of patients referred.

	No. of patients/Total no. (%)				
	Overall	**Pre-Kidneywise**	**Post-Kidneywise**	**Adjusted Odds Ratio§**	**P value**
		Primary outcome			
Kidneywise criteria met†	344/759 (45.3)	144/322 (44.7)	200/437 (45.8)	1.16 (0.85-1.59)	0.358
		Secondary outcomes			
eGFR<30 ml/min/1.73m^2 ‡	177/565 (30.6)	76/233 (32.6)	101/332 (30.4)	1.01 (0.69-1.49)	1.000
ACR > 60 mg/mmol¶	77/194 (39.7)	29/89 (32.6)	48/105 (45.7)	2.04 (1.06-4.01)	0.0322
eGFR 30-44 ml/min/1.73m^2 & ACR 30-59 mg/mmol †	7/759 (0.92)	3/322 (0.93)	4/437 (0.92)	1.12 (0.18-7.84)	1.000
eGFR decline ≥ 5 ml/min/1.73m^2 in 6-months‡	66/565 (11.7)	27/233 (11.6)	39/332 (11.8)	1.02 (0.58-1.81)	1.000
$KFRE_2$ ≥ 10% or eGFR < 15 ml/min/1.73m^2 ‡	36/759 (4.7)	19/322 (5.9)	17/437 (3.9)	0.54 (0.25-1.11)	0.0991
$KFRE_5$ > 5%‡	126/302 (41.7)	52/111 (46.9)	74/191 (38.7)	0.86 (0.51-1.44)	0.615
ACR provided†	355/759 (46.8)	132/322 (41.0)	223/437 (51.0)	1.45 (1.06-1.97)	0.0179
Urinalysis provided†	317/759 (41.8)	123/322 (38.2)	194/437 (44.4)	1.22 (0.90-1.68)	0.215
ORN form used	-	-	63/624 (10.1)	-	-

† Restricted to referrals for low eGFR and/or proteinuria.
‡ Restricted to referrals for low eGFR.
¶ Restricted to referrals for proteinuria.
§ Models adjusted for referral site. Referent is pre-KidneyWise time period.
Abbreviations: eGFR - estimated glomerular filtration rate; ACR - urine albumin-creatinine ratio; $KFRE_2$ - 2-yr kidney failure risk; $KFRE_5$ - 5-yr kidney failure risk; ml - millilitres; min - minutes; m - metres; mg - milligrams; mmol – millimoles.

Table 3. Quality of care outcomes at the time of referral.

	No. of patients/Total no. (%)				
	Overall	Pre-implementation	Post-implementation	Adjusted Odds Ratio§	P value
On an ACEI or ARB (missing: 103)					
Low eGFR or proteinuria referral	438/683 (64.1)	177/267 (66.3)	261/416 (62.7)	0.87 (0.63-1.23)	0.473
DM/ACR>3 or no DM/ACR>30	238/316 (75.3)	84/110 (76.4)	154/206 (74.8)	0.96 (0.51-1.73)	1.000
On a statin (missing: 103)					
Low eGFR or proteinuria referral	433/688 (62.9)	175/269 (65.1)	258/419 (61.6)	0.86 (0.63-1.21)	0.405
DM and/or CKD/age>49	440/649 (67.8)	174/245 (71.0)	266/404 (65.8)	0.77 (0.52-1.10)	0.158

§ Models adjusted for referral site. Referent is pre-KidneyWise time period.

Abbreviations: ACEI – angiotensin converting enzyme inhibitor; ARB - angiotensin receptor blocker; DM - diabetes mellitus; ACR - urine albumin creatinine ratio; CKD - chronic kidney disease, no. – number.

Table 4. Multivariable predictors of a referral meeting KidneyWise referral criteria.

	Met KidneyWise referral criteria			
	Odds ratio (95% C.I.)	**P value**	**Odds ratio (95% C.I.)**	**P value**
Time period	1.18 (0.87-1.59)	0.292	-	-
Site	0.59 (0.41-0.83)	0.002	0.60 (0.44-0.82)	0.001
Age	1.23 (1.12-1.35)	<0.001	1.32 (1.21-1.43)	<0.001
Male sex	1.25 (0.93-1.68)	0.142	1.16 (0.88-1.52)	0.303
DM	1.05 (0.78-1.43)	0.736	1.18 (0.89-1.56)	0.253
KidneyWise referral form	-	-	2.09 (1.21-3.61)	0.008

1st model inclusive of both time periods. Second model includes only the post-implementation time period.
Abbreviations: DM – diabetes mellitus; C.I. – confidence interval.

Table 5. Referral form characteristics and use of ORN referral form.					
	Kidneywise form used		Kidneywise form not used		P value
	N (%)	Median (IQR)	N (%)	Median (IQR)	
eGFR, ml/min/1.73m^2†	37 (7.3)	30.8 (24.8-37.1)	473 (92.7)	35.2 (27.6-44.6)	0.039
Urine ACR, mg/mmol‡	14 (8.2)	93.8 (76.9-153.4)	156 (91.8)	39.5 (10.8-100.2)	0.009
$KFRE_2$, %†	32 (10.6)	2.6 (0.65-7.8)	270 (89.4)	1.1 (0.35-3.4)	0.019
$KFRE_5$, %†	32 (10.6)	7.8 (2.0-22.4)	270 (89.4)	3.4 (1.1-10.3)	0.019

† Restricted to referrals for low eGFR.
‡ Restricted to referrals for proteinuria.
Abbreviations: eGFR - estimated glomerular filtration rate; ACR - urine albumin-creatinine ratio; $KFRE_2$ - 2-yr kidney failure risk; $KFRE_5$ - 5-yr kidney failure risk; ml - millilitres; min - minutes; m - metres; mg - milligrams; mmol - millimoles.

Appendix

1. Supplemental Tables:

Table S1. Distribution of referrals between the two sites and time periods.

	Pre-Kidneywise	Post-Kidneywise	Total
Academic site (SJHH) – no. (%)	345 (33.1)	377 (36.1)	722 (69.2)
Community site (THP) – no. (%)	74 (7.1)	247 (23.7)	321 (30.8)
Total – no. (%)	419 (40.2)	624 (59.8)	1043 (100)

Abbreviations: SJHH – St. Joseph's Healthcare Hamilton, no. – number; THP – Trillium Health Partners.

2. Kidneywise toolkit:

Ontario Renal Network

Kidney Wise
Detect + Protect

Introduction to the KidneyWise Clinical Toolkit

The Ontario Renal Network (ORN), a division of Cancer Care Ontario (CCO) and an agency of the provincial government, is responsible for overseeing and funding the delivery of chronic kidney disease (CKD) services across Ontario. By establishing consistent standards and guidelines, based on the best available evidence, along with information systems that measure performance, the ORN supports a continuously improving kidney care system in Ontario.

The KidneyWise Clinical Toolkit, developed by the ORN for primary care providers (PCPs), is intended to help with the identification, detection, and management of CKD.

The Toolkit is designed to help PCPs determine which patients are at high risk of developing CKD, and provides recommendations on how to properly diagnose and best manage the disease in order to reduce the risk of further progression.

The KidneyWise Clinical Toolkit has three components:

1. An evidence-based **Clinical Algorithm** that helps with identification, detection, and management of CKD, and recommends which patients might benefit from referral to a nephrologist.
2. The **Evidence Summary** offers PCPs further clinical detail regarding the Algorithm content including references to clinical guidelines that were used in the development of the Toolkit.
3. The **Outpatient Nephrology Referral Form** provides PCPs with referral guidance by outlining clinical scenarios which would require consultation with a nephrologist, as well as the appropriate investigations that should accompany the referral.

How can I get it?

To access the KidneyWise Clinical Toolkit, please visit **kidneywise.ca**.

Also available for iPhone and Android.

Any questions?
Please contact us directly at **kidneywise@renalnetwork.on.ca**.

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Ontario
Cancer Care Ontario

Ontario Renal Network

Identification, Detection, and Management of CKD in Primary Care

Kidney Wise
Detect + Protect

IDENTIFY

Identify patients in your practice with elevated risk of CKD based on the following:

- Hypertension
- Diabetes mellitus
- Age 60–75 with cardiovascular disease (CV)

DETECT

- CKD detection should be done in the absence of acute intercurrent illness. Low eGFR (estimated Glomerular Filtration Rate) in such scenarios may reflect acute kidney injury and require more rapid evaluation
- Test with eGFR and urine ACR (Albumin to Creatinine Ratio)
- Note: eGFR calculation needs to be adjusted for black patients (multiply eGFR by 1.21)
- If eGFR < 60ml/min/1.73m^2, repeat test in 3 months, or sooner if clinical concern dictates (i.e. rapid decline from previous eGFR result or very low eGFR)
- If urine ACR ≥ 3mg/mmol on initial testing, repeat 1 or 2 more times over the next 3 months (at least 2 out of 3 random urine ACRs must be elevated in order to be considered abnormal)
- Always consider reversible causes prior to re-testing (e.g. recent treatments with NSAIDs, recent use of contrast dye for diagnostic imaging, BPH/urinary retention)

Results after 3 months

Box A **eGFR < 30 or ACR > 60**

- Patient has CKD
- Based on above parameters, consider seeking consultation from nephrology

Work-up

- For low eGFR: Urine R+M, CBC, electrolytes, Ca, PO_4^{3-}, Albumin, PTH
- For albuminuria: Urine R+M, electrolytes

Box B **eGFR 30–59 and/or ACR 3–60**

- Patient has CKD
- See Manage box below for management
- Check urine R+M, electrolytes
- **Follow eGFR & urine ACR every 6 months**

- eGFR < 60 and decline ≥ 5ml/min within 6 months (confirmed on repeat testing within 2 to 4 weeks), or
- eGFR < 30 or ACR > 60, or
- eGFR < 45 and urine ACR between 30 and 60 on 2 occasions, at least 3 months apart
- Inability to achieve blood pressure targets, or
- Significant K^+ disorder, RBC casts or hematuria (> 20 RBC/hpf)

Box C **eGFR ≥ 60 and ACR < 3**

- Patient does **not** have CKD
- Re-test annually for patients with diabetes, less frequently otherwise, unless clinical circumstances dictate more frequent testing

- If eGFR stable for 2 years, **follow eGFR and urine ACR every 12 months**

REFER TO NEPHROLOGIST While waiting for consultation, see MANAGE box below for management

MANAGE

Implement measures to modify CV risk factors

- Lifestyle modification, smoking cessation
- Lipid management for patients with CKD (see KDIGO guidelines for further details):
  - **If with diabetes, age >18 → treat with a statin***
  - **If without diabetes, age ≥ 50 → treat with a statin***
  - **If without diabetes, age 18–49, has known coronary artery disease, prior stroke, or 10-year Framingham risk >10% → treat with a statin***
- For patients with diabetes, target HbA1c to appropriate level (see CDA guidelines)

*Contraindications: active liver disease, high alcohol consumption or pregnancy. Women with childbearing potential should only use a statin if there is reliable contraception.

Minimize further kidney injury

- If possible, avoid nephrotoxins such as NSAIDs, IV and intra-arterial contrast, etc. (if eGFR < 60)
- If contrast is necessary, consider oral hydration, withholding diuretics
- Refer to Sick Day Medication List (see Evidence Summary)

Implement measures to slow rate of CKD progression

BP and RAAS blockade (repeat creatinine and potassium 2 weeks after initiation of ACEI or ARB use):

- If with diabetes, target BP < 130/80, otherwise target BP < 140/90
- If with diabetes and with ACR > 3, start use of an ACEI or ARB as first-line therapy. If BP already < 130/80, use ACEI or ARB cautiously, monitoring for signs and symptoms of hypotension
- If without diabetes, ACR > 30 and BP > 140/90, start use of an ACEI or ARB as first-line therapy

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Evidence Summary for KidneyWise Clinical Algorithm

PURPOSE

The KidneyWise Clinical Algorithm was created as a resource for primary care providers to aid in the identification, detection, and management of chronic kidney disease (CKD). Note, the clinical algorithm may not apply in the following situations:

- Frail and elderly patients or those with a short life expectancy
- When clinical circumstances warrant investigation for suspected acute kidney injury (i.e. volume depletion, urinary obstruction, etc.)
- When an eGFR (estimated Glomerular Filtration Rate) is necessary in prescribing medications that require dose adjustment for reduced kidney function (e.g. new oral anticoagulants, certain antibiotics)

KEY ELEMENTS

IDENTIFY

Diabetes mellitus (DM) is the leading cause of CKD and end-stage renal disease (ESRD) in Canada. Hypertension (HTN) is an important risk factor for CKD and its progression, although it is uncommon as the sole cause if blood pressure is well controlled. Other risk factors listed for CKD are based on epidemiologic findings (e.g. age 60–75 with cardiovascular disease). First Nations, Inuit and Métis patients are at particularly high risk of developing ESRD, although this risk is primarily mediated through an increased risk for DM and HTN.

DETECT

Most relevant guidelines, including Kidney Disease Improving Global Outcomes (KDIGO)[1], recommend testing with both an eGFR and a urine ACR (Albumin to Creatinine Ratio), as both measures are independent risk factors for progression to ESRD. An eGFR with a value < 60[a] should be repeated if < 60[a], as many patients will have a value above on repeat testing. Consider the possibility of a reversible cause for a low eGFR, including dehydration (i.e. recent gastrointestinal illness or excess diuretic use), or the concomitant use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). The diagnosis of CKD requires evidence of chronicity (i.e. at least 3 months with an eGFR < 60[a]). The urine ACR should be repeated if abnormal; confirmation requires at least 2 of 3 values to be elevated.

Patients with an eGFR ≥ 60[a] and an ACR < 3[b] can be re-screened at an interval commensurate with the underlying risk factor. Re-testing annually in patients with DM is reasonable. Patients with HTN may require less frequent testing, depending on patient age, the presence of other co-morbidities, and the degree of blood pressure control. It is important to note that a substantial proportion of otherwise healthy elderly individuals will have an eGFR < 60[a] due to normal aging (40% of women > 75 years of age and 30% of men > 80 years of age).

MANAGE

Review of the KDIGO Clinical Practice Guideline for Lipid Management in CKD[2], Canadian Hypertension Education Program (CHEP)[3], and Canadian Diabetes Association (CDA)[4] clinical practice guidelines is recommended for detailed advice regarding hyperlipidemia, hypertension, and glycemic control, respectively.

ACE inhibitors (ACEI) or angiotensin receptor blockers (ARB), but not both, are recommended as outlined for most CKD patients who also have albuminuria; for normotensive patients with diabetes with an elevated ACR (> 3[b]), an ACEI or ARB can be considered although careful monitoring for signs or symptoms of hypotension is advised. Most patients with DM and an elevated ACR will have hypertension in the absence of any anti-hypertensive therapy. For patients without diabetes with a blood pressure > 140/90 and an ACR > 30[b], an ACEI or ARB should be used as first-line therapy. CKD patients who require statin therapy should be treated regardless of baseline lipid status and do not routinely require follow-up measurement of lipid levels. Patients with a non-renal indication for one of these agents (i.e. heart failure) should be treated accordingly.

It is recommended that a serum potassium and creatinine be repeated approximately 2 weeks after any initiation or dose increase of an ACEI or ARB to monitor for the development of hyperkalemia and/or a substantial decrease in eGFR. An increase in serum creatinine of up to 30% after initiation of an ACEI or ARB is not associated with an increased risk of worsening long-term kidney function. Larger increases may suggest excessive diuretic use and/or underlying renovascular disease.

Note, given the high risk of influenza-related complications among CKD patients, primary care providers should recommend they receive the seasonal influenza vaccine on an annual basis[5].

SICK DAY MEDICATION LIST

If patients with CKD are unable to maintain adequate fluid intake during an illness, it is recommended that potentially nephrotoxic or renally excreted drugs should be withheld until the patient has recovered. As outlined in the CDA guidelines, this can be recalled by referring to the acronym **SADMAN** (**S**ulfonylureas, **A**CEI, **D**iuretics, **M**etformin, **A**RB, **N**SAIDs).

Adapted from: Change in appropriate referrals to nephrologists after the introduction of automatic reporting of the estimated glomerular filtration rate. Akbari A., Grimshaw J., Stacey D, et al. CMAJ 2012. DOI: 10.1503/cmaj.110678

[a] units for eGFR are ml/min/1.73m^2
[b] units for ACR are mg/mmol
[1] Kidney Disease Improving Global Outcomes CKD Guidelines 2012. **http://kdigo.org/home/guidelines/ckd-evaluation-management/**
[2] Kidney Disease Improving Global Outcomes Clinical Practice Guideline for Lipid Management in CKD 2013. **http://kdigo.org/home/guidelines/lipids/**
[3] Canadian Hypertension Education Program Guidelines 2014. **http://www.hypertension.ca/en/chep**
[4] Canadian Diabetes Association Clinical Practice Guidelines 2013. **http://guidelines.diabetes.ca/Browse.aspx**
[5] Public Health Agency of Canada 2013. **http://www.phac-aspc.gc.ca/index-eng.php**

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Outpatient Nephrology Referral Form for Primary Care Providers

To our primary care provider colleagues:

Please find an Outpatient Nephrology Referral Form developed by the Ontario Renal Network (ORN). Recommended reasons for referral of patients with nephrological problems are outlined, and these closely mirror the ORN's KidneyWise Clinical Algorithm and Evidence Summary. While patients (and their primary care providers) often want to arrange a timely appointment so that their clinical concerns can be addressed and/or alleviated quickly, most nephrologists will triage referred patients based on level of need. Those patients who are at high risk of progressing to end-stage renal disease and/or who may require a renal biopsy for diagnosis are usually seen more urgently.

Typical indications include:

- Very low renal function (eGFR < 20 ml/min/1.73m^2, confirmed on repeat testing)
- Rapidly declining renal function (eGFR decline ≥ 10 ml/min/1.73m^2 within 2 to 4 weeks, confirmed on repeat testing)
- Nephrotic syndrome (edema with severe proteinuria – i.e. urine ACR > 150 mg/mmol or 24-hour urine protein > 3.5 g/day and serum albumin < 25 g/L)
- Suspected glomerulonephritis or renal vasculitis (hematuria with > 20 RBC/hpf or RBC casts associated with proteinuria, declining renal function and/or positive immune markers)

Please note that the use of NSAIDs should be discontinued prior to confirming very low or rapidly declining renal function, as this is a common reversible cause of a decline in eGFR. Also, note that initiating the use of an ACEI or ARB may cause a reversible decline in eGFR (up to 30%) that does not necessarily warrant referral.

If you feel that circumstances warrant referral of a patient with CKD who does not meet the recommended referral criteria on the Outpatient Nephrology Referral Form, particularly in younger patients, contact your local nephrology group for further advice. If you feel your patient needs to be seen within 24 hours, contact the nephrologist on call in your region for further discussion.

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Provincial Lead, Early Detection and Prevention of Progression, ORN

The KidneyWise Clinical Toolkit helps primary care providers identify, detect, and manage chronic kidney disease (CKD).

The KidneyWise Clinical Toolkit helps to:

- Determine which patients are at high risk of developing CKD
- Provide recommendations on how to properly diagnose and best manage the disease to reduce risk for further progression
- Guide clinicians on which patients might benefit from referral to nephrology

www.kidneywise.ca

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CLINIC INFORMATION HERE

Patient Information (please fill in or affix label):

NAME: _____ DOB: ____/____/____ (DD/MM/YY)

ADDRESS: _____

PHONE #: _____ HEALTH CARD #: _____

ALT. CONTACT INFO: _____

Outpatient Nephrology Referral Form

Date of referral: ____/____/____ (DD/MM/YY) Is this a re-referral? ☐ Yes ☐ No

Name of nephrologist seen previously: _____

Recommended Reason for Referral:

- ◯ eGFR < 30 ml/min/1.73m^2 on 2 occasions, at least 3 months apart
- ◯ eGFR < 45 ml/min/1.73m^2 and urine ACR between 30 and 60 mg/mmol on 2 occasions, at least 3 months apart
- ◯ Rapid deterioration in renal function (eGFR < 60 ml/min/1.75m^2 and decline of 5 ml/min within 6 months, confirmed on repeat testing within 2 to 4 weeks on 2 occasions)
- ◯ Proteinuria (urine ACR > 60 mg/mmol on at least 2 of 3 occasions)
- ◯ Hematuria (> 20 RBC/hpf or RBC casts)
- ◯ Resistant or suspected secondary hypertension
- ◯ Suspected glomerulonephritis/renal vasculitis
- ◯ Metabolic work-up for recurrent renal stones
- ◯ Other: _____

Additional comments:

Co-morbid Conditions:

◯ Diabetes mellitus ◯ Coronary artery disease ◯ Hypertension ◯ Frailty ◯ Peripheral vascular disease
◯ Previous stroke ◯ Cognitive impairment

Lab Values:
Please fill out below if applicable; refer to the ORN KidneyWise Clinical Algorithm for suggested investigations

Date #1: (DD/MM/YY)	eGFR:	Creatinine:	Urine ACR:
Date #2: (DD/MM/YY)	eGFR:	Creatinine:	Urine ACR:
HbA1c:	Hgb:	K^+:	Ca^{2+}:
PO_4^{3-}:	Albumin:	PTH:	Hematuria (dipstick):
Other (or attach):			

Current Medications:

Referring practitioner/address/phone/fax:	**Referring billing #:**
	Signature:

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Please send the completed referral form to a local nephrologist in your region.
Do not forward this form to CCO/Ontario Renal Network. If you need to access contact information for a local nephrologist, please visit http://www.cpso.on.ca/public-register/all-doctors-search?term

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Ontario Renal Network: BACKGROUNDER

Chronic kidney disease (CKD) is a serious, lifelong condition. People with advanced CKD often require complex and intensive care from a multidisciplinary team of healthcare professionals. Approximately 12,000 people in Ontario have CKD requiring pre-dialysis care. An additional 10,500 Ontarians with advanced CKD require dialysis. The need for dialysis has been gradually rising for more than a decade and is expected to continue climbing in the foreseeable future. This trend is largely driven by changing demographics and the increasing prevalence of risk factors associated with CKD, such as diabetes, hypertension and aging.

In 2009, Ontario's Ministry of Health and Long-Term Care transferred oversight and coordination of kidney care services to the Ontario Renal Network (ORN). The ORN, a division of CCO and an agency of the provincial government, manages the delivery of chronic kidney disease services. Our decisions and advice are based on the best evidence available, enabling us to provide effective planning, programs and funding to support a continuously improving kidney care system in Ontario. ORN improves the healthcare system by engaging people with chronic kidney disease and their families, along with health care providers, in the design, delivery and evaluation of care. Person-centered care helps improve the patient experience while enabling the system to deliver better outcomes and value.

ORN consists of a vast array of partners including healthcare professionals, Regional Renal Program staff, partner health agencies and organizations, patients and families, and many others. The provincial office works closely with all our regional partners in planning, delivering, funding, and monitoring CKD care across the province. In total, 26 Regional Renal Programs provide dialysis and other kidney care services within approximately 100 facilities (including hospitals and community-based facilities). Other community partners such as long-term care homes and independent health facilities also provide kidney care services to many patients.

ORN recently released the Ontario Renal Plan II 2015-2019 (ORP II), the provincial roadmap to guide how regional partners will work over the next four years to continue to improve the lives of those living with CKD. It builds on the foundation laid by the first strategic plan and addresses patient care across the kidney care journey, from early detection through dialysis, palliative care and transplant.

Patients and their families are at the heart of all three goals. ORP II reframes the way we think about kidney care and the roles of everyone involved. Our focus shifts beyond dialysis to kidney health; beyond medical treatments to quality of life; beyond making decisions for patients to empowering them to make choices with their care teams. With a strong infrastructure in place, ORPII represents a significant shift for the Ontario Renal Network towards person-centred care. See the change at www.renalnetwork.on.ca/orp

www.renalnetwork.on.ca
information@renalnetwork.on.ca

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	-	
		(*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	2	
Objectives	3	State specific objectives, including any prespecified hypotheses	2	Final paragraph
Methods				
Study design	4	Present key elements of study design early in the paper	5	2nd paragraph
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	2nd paragraph
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5	2nd paragraph
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	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	6	1st paragraph
Bias	9	Describe any efforts to address potential sources of bias		All referrals captured
Study size	10	Explain how the study size was arrived at	7	Statistical analysis section

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7	Statistical analysis section
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7	Statistical analysis section
		(*b*) Describe any methods used to examine subgroups and interactions	7	2nd paragraph
		(*c*) Explain how missing data were addressed	8	1st paragraph
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A	
		(*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	9	1st paragraph and Table 1
		(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	9	1st paragraph and Table 1
		(b) Indicate number of participants with missing data for each variable of interest		Table 1 - footnote
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		Table 2-3
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	9-10	1º and 2º outcome sections & Tables 2-3
		(*b*) Report category boundaries when continuous variables were categorized	N/A	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses		Table 4-5
Discussion				
Key results	18	Summarise key results with reference to study objectives	Discussion section	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	1	Limitations section
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion section	
Generalisability	21	Discuss the generalisability (external validity) of the study results	1	Limitations section
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	Title page	

*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.