Hurdles for implementation of primary prevention strategies for Chronic Kidney Disease

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**Consultant:** Amgen, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Janssen, Lilly, MSD, Novartis, Novo Nordisk, Roche, Sanofi and Servier.

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**Member of KDIGO CKD in Diabetes Guidelines**
**Member of ADA-KDIGO Consensus Report: Diabetes Management in CKD**
Outline

• Unmet need in CKD
• Evidence for CKD and CVD prevention
• Barriers to CKD Care
• Potential solution – CKD Model of Care
• Summary
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• Unmet need in CKD
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The prevalence of undiagnosed CKD in type 2 diabetes has been decreasing, but is still over 50% in patients with CKD stage G3a.

The index date for CKD stage was the first serum creatinine measurement leading to an eGFR <60 mL/min/1.73 m².


In the UK, only 39.5% of patients with microalbuminurinia had a code for microalbuminurinia on their record.

*The index date for CKD stage was the first serum creatinine measurement leading to an eGFR <60 mL/min/1.73 m² eGFR, estimated glomerular filtration rate

Despite universal recommendations, screening of at-risk individuals is inadequate, which may contribute to the lack of diagnosis of CKD stage 3.

**Percentage of at-risk patients adequately tested**

<table>
<thead>
<tr>
<th>At-risk defined as</th>
<th>Adequate CKD screening</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM + HTN</td>
<td>Presence of test results for eGFR and urine albumin:creatinine ratio each year</td>
<td>38.0</td>
</tr>
<tr>
<td>DM</td>
<td></td>
<td>26.2</td>
</tr>
<tr>
<td>HTN</td>
<td></td>
<td>8.8</td>
</tr>
</tbody>
</table>

**Prevalence of diagnosed and undiagnosed CKD cases in patients with CKD stage 3**

- Ravera M, et al. (2005): 89.2%
- Diamantidis CJ, et al. (2010–2011): 80.9%
- REVEAL-CKD LCED (2015–2020): 61.8%
- REVEAL-CKD: 38.2%
- TriNetX (2015–2020): 64.3%

*At-risk patients defined as having a diagnosis of diabetes or high blood pressure. Adequate CKD screening defined as presence of test results for eGFR and urine albumin:creatinine ratio each year. This study shows the frequency of guideline-recommended CKD screening among patients at risk in a retrospective data set from a US clinical laboratory to identify where education efforts may be needed. From a chart review on a random sample of 152 patients selected from the 6895 patients with eGFR <60 mL/min/1.73 m² in Rochester, NY, USA between 2003–2004. Of the 152 patients sampled, 85 patients had CKD stage 3: 12 with a confirmed diagnosis and 73 with an unconfirmed diagnosis. 39,525 patients with serum creatinine measurements from the Italian hypertensive population followed up by family practitioners in 2005. Based on a cohort of 206,036 Medicare beneficiaries, of which 79,649 had lab-identified CKD stage 3 with ≥2 qualifying lab results 90 days apart indicating CKD, between 2010 and 2011. 23,541 patients from the Explorys Linked Claims-EMR Data database with two consecutive eGFR readings indicating CKD stage 3 >90 to ≤730 days apart (2015–2020); 250,879 patients from TriNetX, a global federated research network providing statistics on electronic health records, with two consecutive eGFR readings indicating CKD stage 3, >90 to ≤730 days apart (2015–2020)."
Diabetes, heart and kidneys interconnected: CKD seen as a cinderella

**CKD**
- CKD is a major cause of cardiovascular morbidity and mortality
- Coexistence of diabetes leads to elevated risk of CVD

**Hypertension**
- Hypertension is a powerful and independent risk factor for CKD
- CKD causes hypertension

**T2DM**
- Diabetes is the commonest cause of CKD
- CKD worsens glycaemic control

**CVD**
- Up to 75% of CVD in diabetes may be attributable to hypertension

**ESRD**
- End stage renal disease

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**References**
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Interventions to slow chronic kidney disease (CKD) progression and/or reduce cardiovascular risk

<table>
<thead>
<tr>
<th>G1</th>
<th>G2</th>
<th>G3a</th>
<th>G3b</th>
<th>G4</th>
<th>G5</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>A2</td>
<td>A3</td>
<td>A1</td>
<td>A2</td>
<td>A3</td>
</tr>
</tbody>
</table>

- Lifestyle modification
- Smoking cessation
- RAS inhibition
- Optimize blood pressure control
- Statins
- Optimize glycemic control
- SGLT2 inhibitors
- GLP-1 receptor agonists
- Treat metabolic acidosis
- Treat underlying cause, avoid nephrotoxins, and adjust medication dosages

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Diabetes, CKD and CVD Multimorbidity Paradigm: Potential for fragmented care
Primary Care Barriers to Management of CKD

**PATIENT LEVEL**
- Low awareness of CKD
- Poor adherence

**PROVIDER**
- Knowledge
- Familiarity with guidelines,
- Difficulty managing risk factors
- Belief they are unable to improve CKD

**HEALTH CARE SYSTEM**
- Poor electronic medical records
- Limited time
- Limited resources

Primary Care Barriers to Nephrology Referrals

1. Patient lack of trust to establish relationship with nephrologist
2. Lack of timely and adequate information exchange
3. Limited access to nephrologist
4. Unclear, delineation of rules and responsibilities
5. Poor working relationships with nephrologist

CKD is a multiple long term condition (multimorbidity)\textsuperscript{1}

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**Concordant physical conditions (%)**

- Hypertension (71.2)
- Heart failure (13.0)
- Diabetes (24.3)
- Coronary heart disease (36.3)
- Peripheral vascular disease (6.6)
- Atrial fibrillation (12.1)
- Stroke and transient ischaemic attack (19.4)

**Discordant physical conditions (%)**

- Rheumatological conditions (14.9)
- Inflammatory bowel disease (1.4)
- Painful conditions (29.4)
- Thyroid disorders (14.8)
- Chronic liver disease (6.3)
- Psoriasis or eczema (1.3)
- Viral hepatitis (8.1)
- Chronic obstructive pulmonary disease (11.5)
- New diagnosis of cancer in last 5 years (16.0)
- Prostate disorders (3.6)
- Diverticular disease of intestine (16.7)
- Migraine (5.6)
- Dyspepsia (13.7)
- Asthma (7.2)
- Blindness and low vision (3.0)
- Irritable bowel disease (6.5)
- Constipation (12.0)
- Bronchiectasis (6.5)
- Hearing loss (10.9)
- Chronic sinusitis (6.7)
- Gout (6.4)
- Epilepsy (1.0)
- Multiple sclerosis (6.2)
- Parkinson’s disease (6.7)

**Mental health conditions (%)**

- Schizophrenia or bipolar affective disorder (1.5)
- Depression (17.7)
- Learning disability (6.2)
- Anxiety and associated anxiety disorders (6.2)
- Anorexia or bulimia (6.2)
- Other psychoactive substance misuse (1.3)
- Alcohol problems (2.5)
- Dementia (6.0)

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\textsuperscript{a}Disease labels show percentage of people with CKD who also have this disease. CKD = chronic disease.

**Adjusted odds ratio with 95% CI (log scale)**

Age-, sex-, and deprivation-adjusted odds ratios for physical and mental comorbidities.\textsuperscript{a}

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Khunti K et al BMJ 2023
McRae C et al. BJGP 2021;71(704):e243-e249
CKD and Concordant physical MLTCs

Age-, sex-, and deprivation-adjusted odds ratios for physical and mental comorbidities.\(^a\)

\(^a\)Disease labels show percentage of people with CKD who also have this disease. CKD = chronic disease.
CKD and Discordant physical MLTCs

Age-, sex-, and deprivation-adjusted odds ratios for physical and mental comorbidities. \(^a\)

\(^a\)Disease labels show percentage of people with CKD who also have this disease. CKD = chronic disease.
CKD and Mental health MLTCs

Age-, sex-, and deprivation-adjusted odds ratios for physical and mental comorbidities.\textsuperscript{a}

\textsuperscript{a}Disease labels show percentage of people with CKD who also have this disease. CKD = chronic disease.
## CKD and MLTCs

Number of comorbidities by CKD status, \( N = 1\,274\,374 \)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CKD (N= 33 567)</th>
<th>Without CKD (N= 1 240 807)</th>
<th>Unadjusted OR (95% CI)</th>
<th>aOR (95% CI)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean comorbidities, n (SD)</td>
<td>3.8 (2.2)</td>
<td>1.2 (1.6)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Total comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>614 (1.8)</td>
<td>598 194 (48.2)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1</td>
<td>3553 (10.6)</td>
<td>278 807 (22.5)</td>
<td>12.4 (11.4 to 13.5)</td>
<td>6.5 (6.0 to 7.1)</td>
</tr>
<tr>
<td>2–3</td>
<td>12 472 (37.2)</td>
<td>248 971 (20.1)</td>
<td>48.8 (45.0 to 53.0)</td>
<td>15.2 (14.0 to 16.5)</td>
</tr>
<tr>
<td>4–6</td>
<td>13 000 (38.7)</td>
<td>99 779 (8.0)</td>
<td>126.9 (117.0 to 137.7)</td>
<td>26.6 (24.4 to 28.9)</td>
</tr>
<tr>
<td>( \geq 7 )</td>
<td>3928 (11.7)</td>
<td>15 056 (1.2)</td>
<td>254.2 (233.1 to 277.2)</td>
<td>41.9 (38.3 to 45.8)</td>
</tr>
</tbody>
</table>
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Effects of an Electronic Software “Prompt” With Health Care Professional Training on CV and Renal Complications (GP-Prompt Study)

2,721 patients
2 years of FU

Benefits

Prespecified outcomes

TC <4.0 mmol
Coding for microalbuminuria
Increased with intensive intervention vs with control.

Microalbuminuria with T2D identifies an increased risk of cardiorenal complications.

Tight & targeted control of modifiable CV risk factors can reduce CV complications & mortality, although it remains therapeutic inertia in identifying and treating these high-risk patients.

Improvements in lipid profile and coding MA can benefit patients with diabetes to alter the high risk of atherosclerotic CV events.

Association of continuity of primary care & outcomes in people with CKD


86,475 people with CKD

<table>
<thead>
<tr>
<th>Level of continuity</th>
<th>HIGH (51.3%)</th>
<th>MODERATE (30.0%)</th>
<th>POOR (18.7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OUTCOMES</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cause hospitalisation</td>
<td>1.0</td>
<td>1.28 (1.25-1.32)</td>
<td>1.52 (1.47-1.57)</td>
</tr>
<tr>
<td>All cause ED visits</td>
<td>1.0</td>
<td>1.42 (1.39-1.46)</td>
<td>1.78 (1.73-1.83)</td>
</tr>
<tr>
<td>RAAS inbitors prescribed</td>
<td>1.0</td>
<td>0.99 (0.96-1.02)</td>
<td>1.03 (0.98-1.07)</td>
</tr>
<tr>
<td>Statins prescribed</td>
<td>1.0</td>
<td>0.89 (0.84-0.95)</td>
<td>0.8 (0.74-0.86)</td>
</tr>
</tbody>
</table>
### Barriers & solutions to the uptake SGLT-2 inhibitors in clinical practice

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complexity of current guidelines pertaining to SGLT-2 inhibitor use</td>
<td>Improve clarity of guidelines and provide further information on how and when best to apply them</td>
</tr>
<tr>
<td>Safety concerns regarding adverse events associated with SGLT-2 inhibitors and lack of communication between clinicians</td>
<td>Improve clinician and patient education regarding benefits and risks; implement streamlined care pathways with collaborative care models with joint visits with clinicians from different relevant specialties</td>
</tr>
<tr>
<td>Patient characteristics affecting prescription rates</td>
<td>Highlight benefits and risks to patients and facilitate diabetes self-management; improve clinician awareness of implicit biases regarding patient characteristics; seek to remove financial barriers and patient out-of-pocket costs</td>
</tr>
<tr>
<td>Higher comparative cost of SGLT-2 inhibitors versus other glucose-lowering medications</td>
<td>Payers and guideline formulary committees should consider increased quality-adjusted life years associated with the cardiovascular and renal benefits of SGLT-2 inhibitors</td>
</tr>
</tbody>
</table>

A summary of barriers to the uptake of sodium-glucose co-transporter-2 (SGLT-2) inhibitors in clinical practice and proposed solutions.

Khunti K et al. DOM 2022;24:1187-1196
Influence of early referral to a nephrologist on kidney function decline in patients with diabetes and CKD

Better blood pressure control, slower eGFR decline, higher use of RAASi as well as less use of NSAIDs in CKD patients when treated by nephrologists

<table>
<thead>
<tr>
<th></th>
<th>Nephrologist care</th>
<th>PCP care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Final</td>
</tr>
<tr>
<td>n/o patients</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>62.5 ± 9.3</td>
<td></td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td>14.7 ± 8.4</td>
<td>14.2 ± 8.0</td>
</tr>
<tr>
<td>Duration of hypertension</td>
<td>10.6 ± 9.9</td>
<td>10.3 ± 8.8</td>
</tr>
<tr>
<td>sysBP</td>
<td>140 ± 30</td>
<td>130 ± 21</td>
</tr>
<tr>
<td>diaBP</td>
<td>76 ± 14</td>
<td>70 ± 10</td>
</tr>
<tr>
<td>Albuminuria</td>
<td>158 (62-451)</td>
<td>216 (97-619)</td>
</tr>
<tr>
<td>eGFR</td>
<td>83.8 ± 26.1</td>
<td>80.4 ± 35.5</td>
</tr>
<tr>
<td>Use of ACEs</td>
<td>25 (48)</td>
<td>44 (90)</td>
</tr>
<tr>
<td>Use ARBs</td>
<td>1 (2)</td>
<td>22 (45)</td>
</tr>
<tr>
<td>Use of Statins</td>
<td>2 (4)</td>
<td>21 (43)</td>
</tr>
<tr>
<td>Use of NSAIDs</td>
<td>6 (11)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

ACE, angiotensin-converting-enzyme; ARB, angiotensin-receptor-blocker, CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NSAID, non-steroidal antiinflammatory drug; RAASi, renin-angiotensin-aldosterone system inhibitor

Martinez-Ramirez HR et al. Am J Kid Dis 2006;47:78
Components of a successful cardio-renal-metabolic care model at an institutional level

Learning from models of care for diabetes: Delivery of primary care 1990s

Primary Care (63.2%)

Secondary Care (12.4%)

Shared Care (24.4%)
Delivery of primary care 2023

Primary Care (95%)

Secondary Care (5%)

Leicester Commissioning Pathway: Super Six and Necessary Nine!

DSN and Medicine management Support

EDUCATION PROGRAMME

Tiers 1&2
Primary Care
Essential and QOF

Tiers 3a
Enhanced Diabetes Care

Tier 3b
Integrated Care

Secondary Care

In patient Care
- Pregnancy
- Foot care
- Insulin pumps
- Type 1/children/transition
- Renal

Model of care is safe and cost-effective

<table>
<thead>
<tr>
<th>Clinical outcomes from the RCT. [7]</th>
<th>Mean difference (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-elective bed days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes as a primary diagnosis</td>
<td>2.20 (-0.92, 5.32)</td>
<td>0.14</td>
</tr>
<tr>
<td>Diabetes as a primary or</td>
<td>2.78 (-2.71, 8.27)</td>
<td>0.27</td>
</tr>
<tr>
<td>secondary diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First outpatient attendance</td>
<td>0.02 (-0.47, 0.52)</td>
<td>0.92</td>
</tr>
<tr>
<td>Admissions with type 2 diabetes</td>
<td>0.30 (-0.85, 1.45)</td>
<td>0.55</td>
</tr>
<tr>
<td>complications</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Cost per person/year in core practices**: £255 (95% CI 175, 380)
- **Cost per person/year in enhanced practices**: £173 (95% CI 96, 291)
- **Annual saving per patient**: -£83 (95% CI -148, -28)
- **Savings if rolled out in UK**: -£276,200,000 (95% CI -495,400,000, -94,480,000).

Significantly more patients in the intervention group with unconfirmed diagnosis of HF had improved outcomes

Khunti K et al. Heart. 2007; 93:1398-1405
Turner DR et al. Heart. 2008; 94: 1601-1606
Collaborative care approach:
Primary care, cardiology, nephrology, endocrinology

GPs and specialists must end the “them and us” divide

Clare Gerada used her final speech as chairwoman of the RCGP to call for GPs and specialists to work together to improve continuity of patient care, as Tom Moberly reports.

GPs and hospital doctors will have to change the way they work together if the health service is to improve continuity of care for patients, Clare Gerada believes.

Giving her final speech as chairwoman of the Royal College of General Practitioners at the college’s annual conference in Harrogate last week, Gerada said that the “them and us” divide between GPs and hospital specialists had ended. She now predicted that an integrated system of care, with GPs and hospitals working together, would become a thing of the past.

She said, “In future, we will be working together in one integrated system of care.”

She argued that all providers of health and social care services within a particular geographical area should pool resources with primary, community, social, and acute care funding merged into one budget. This would, she claimed, allow real integration of care.

One of the things that must change is our relationship with our specialist colleagues.

The proposals about pilot schemes to extend general practitioners’ opening hours.

The proposals outlined by Hunt spoke of his far-reaching vision for general practice moving from “reactive to proactive” service delivery. “I hope that history will judge me to be one of the most successful GPs”, he said.
Integrated multidisciplinary model of care for CKD
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Integrated care: the key to management of CKD

• Patient engagement, education and activation
  – Use of new technologies?

• Education of health care professionals
  – Breakdown of specialty barriers
  – Integration of medical workforce training

• New ways of working
  – Virtual clinics
  – New specialties (cardiorenaldiabetologist...?)
  – Primary care-based specialists?
Summary

- GPs/PCPs function as gatekeepers in the area of chronic diseases
- A greater emphasis on detecting CKD and management in primary care
- Management of CKD patients in primary care is complex and is influenced by physician-bound considerations related to individual knowledge and perception of the importance of CKD
- Strategies are needed to improve GPs/PCPs understanding of the concept of CKD by education, innovative interventions and integrated care programmes
Thank you

www.leicesterdiabetescentre.org.uk

www.facebook.com/LeicesterDiabetesCentre

@kamleshkhunti

@LDC_Tweets