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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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Speakers' Bureau: AstraZeneca, Berlin-Chemie AG / Menarini Group, Boehringer Ingelheim, Janssen, Lilly, MSD, Napp, Novartis, Novo Nordisk, Roche and Sanofi

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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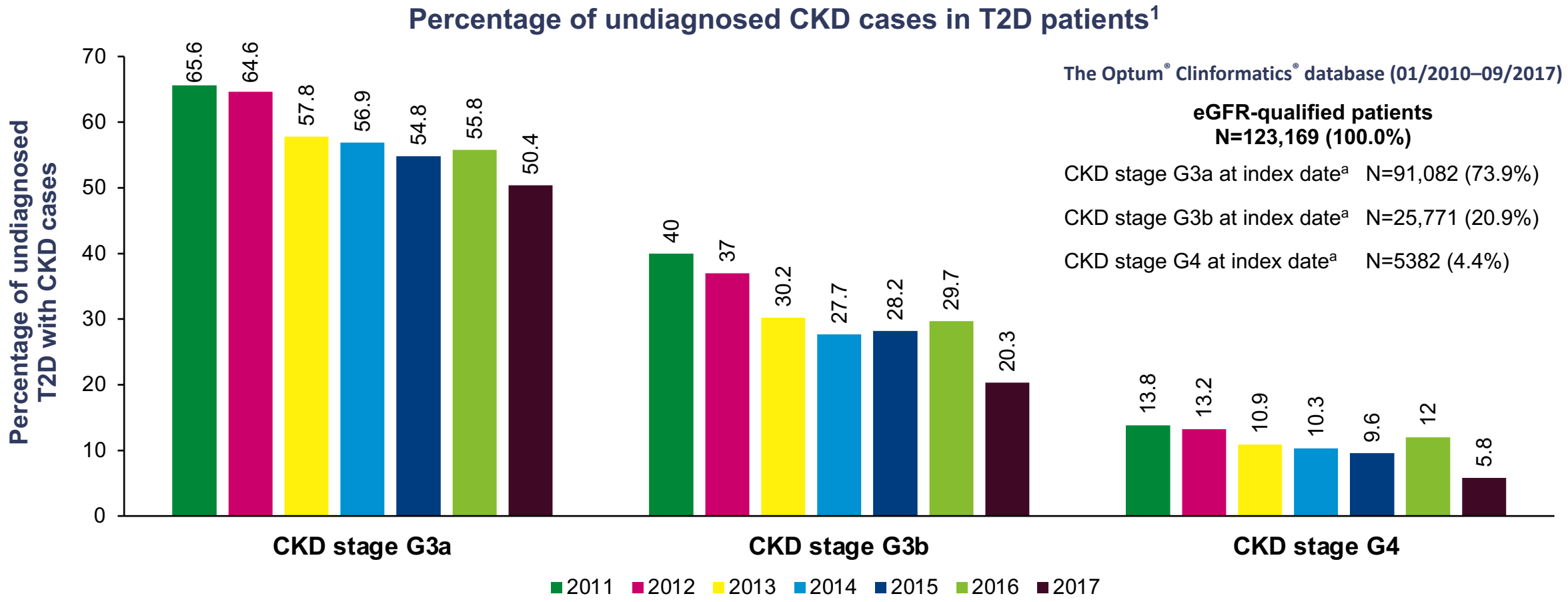
The prevalence of undiagnosed CKD in type 2 diabetes has been decreasing, but is still over 50% in patients with CKD stage G3a



In the UK, only 39.5% of patients with microalbuminuria had a code for microalbuminuria on their record[2]

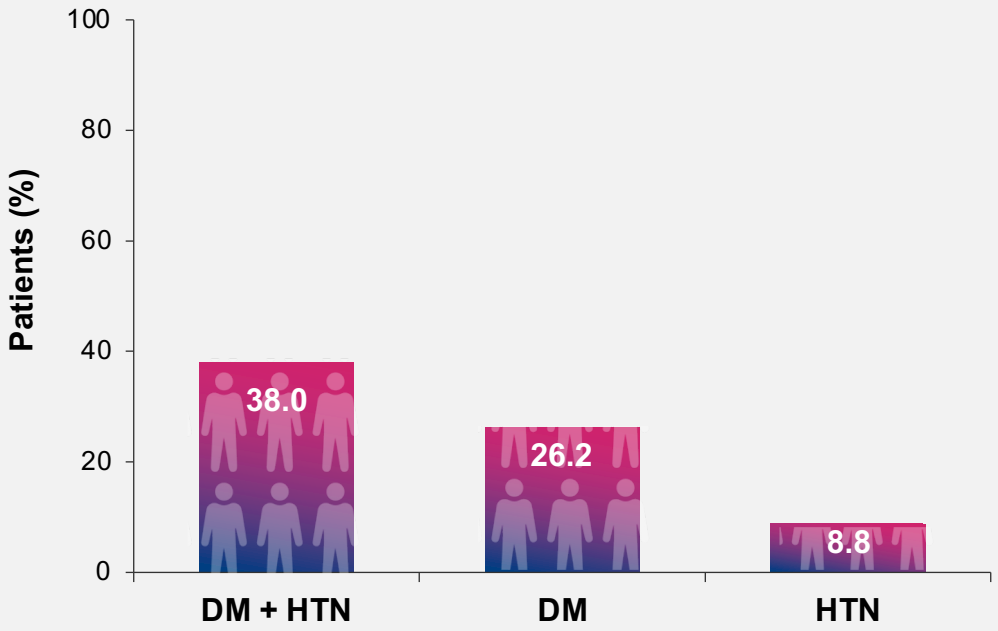
[a]The index date for CKD stage was the first serum creatinine measurement leading to an eGFR <60 mL/min/1.73 m^2

eGFR, estimated glomerular filtration rate

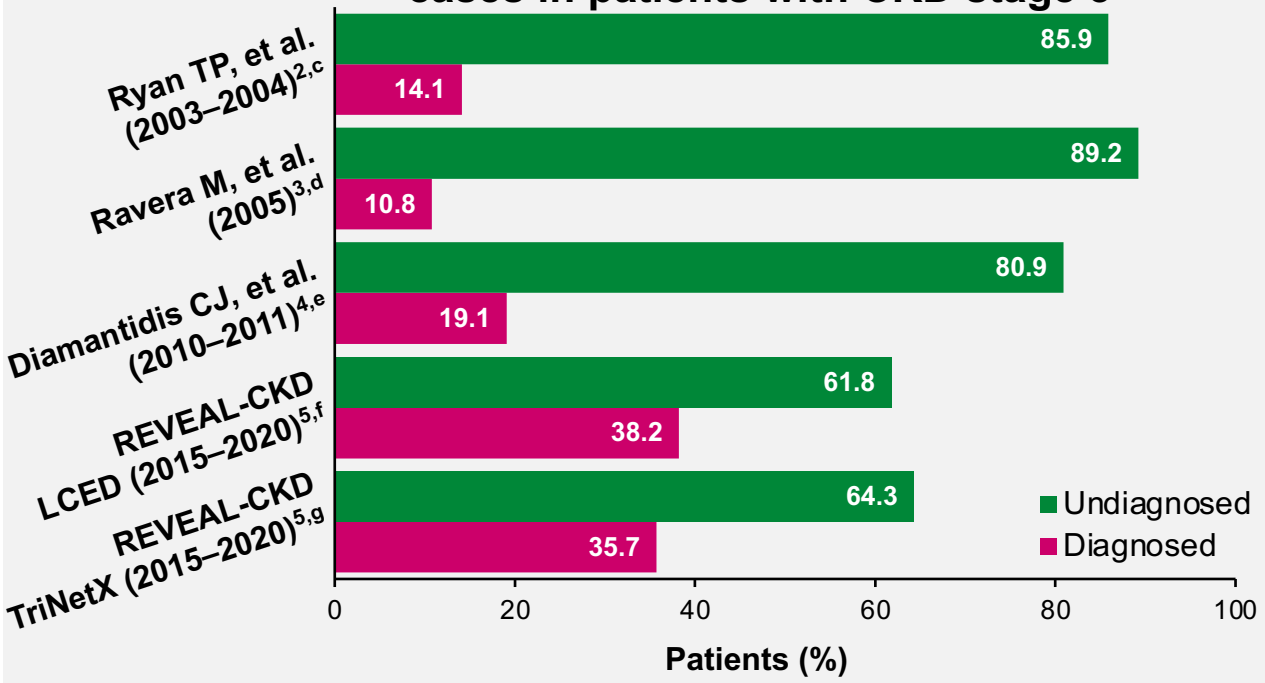
1. Bakris GF, et al. Presented at the National Kidney Foundation 2019 Spring Clinical Meetings; May 8th–12th, 2019; Boston, MA, USA; Poster 308; 2. Willis A, et al. *Diabetes Care* 2020. doi:10.2337/dc19-2243 [Epub ahead of print]

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[1,a,b]



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

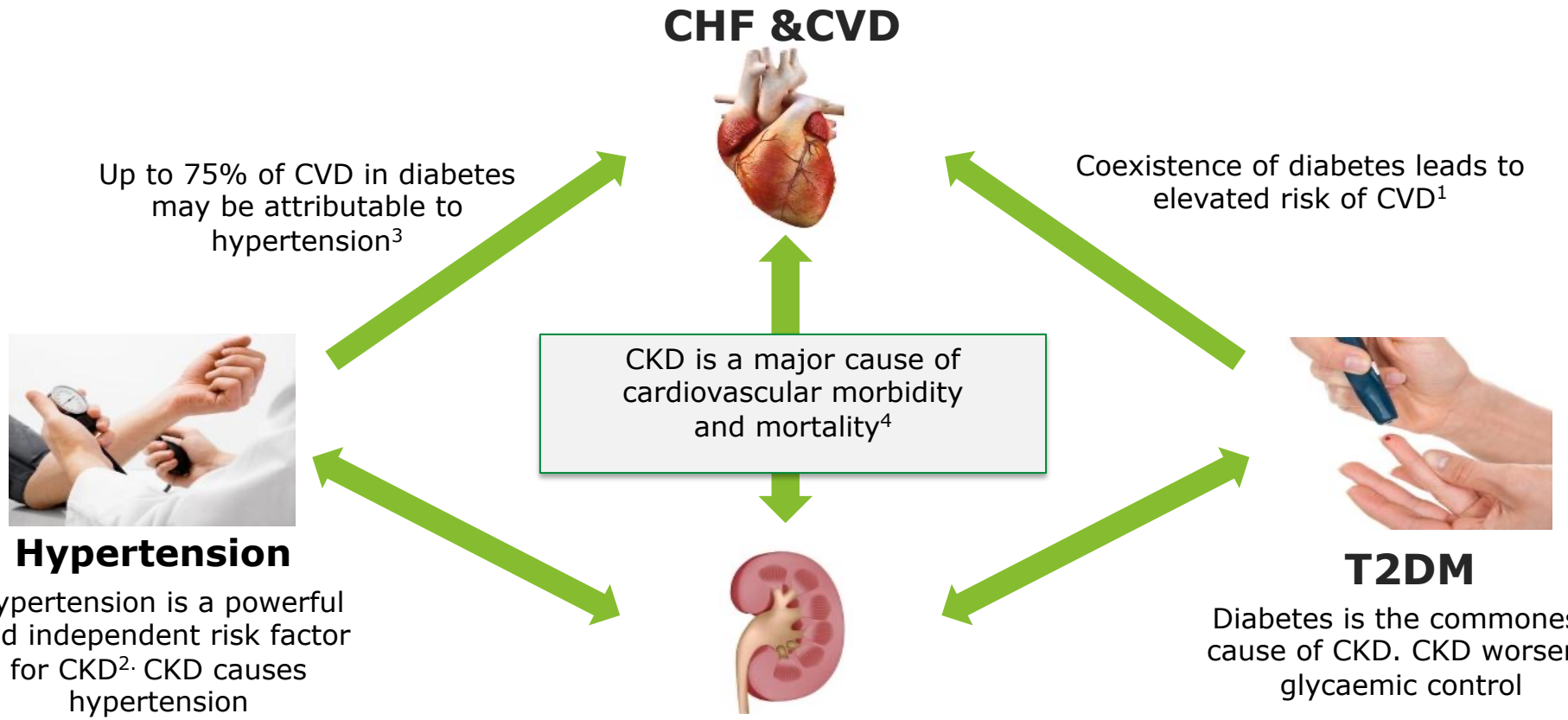


[a]At-risk patients defined as having a diagnosis of diabetes or high blood pressure; [b]Adequate CKD screening defined as presence of test results for eGFR and urine albumin:creatinine ratio each year. This study shows the frequency of guideline-recommended CKD screening among patients at risk in a retrospective data set from a US clinical laboratory to identify where education efforts may be needed; [c]From a chart review on a random sample of 102 patients selected from the 6895 patients with eGFR <60 mL/min/1.73 m^2 in Rochester, NY, USA between 2003–2004. Of the 102 patients sampled, 85 patients had CKD stage 3: 12 with a confirmed diagnosis and 73 with an unconfirmed diagnosis; [d]39,525 patients with serum creatinine measurements from the Italian hypertensive population followed up by family practitioners in 2005; [e]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; [f]23,614 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); [g]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)

CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension

1. Ennis J, et al. Presented at National Kidney Foundation 2020 Spring Clinical Meetings; March 25th–29th, 2020; poster; 2. Ryan TP, et al. *Am J Med* 2007;120:981–986; 3. Ravera M, et al. *Am J Kidney Dis* 2011;57:71–77; 4. Diamantidis CJ, et al. *BMC Nephrol* 2019;20:357; 5. Sultan AA, et al. Presented at American Diabetes Association Virtual 81st Scientific Sessions; June 25th–29th, 2021; poster 988

Diabetes, heart and kidneys interconnected: CKD seen as a cinderella



CKD: chronic kidney disease

CVD: cardiovascular disease
T2DM: type 2 diabetes mellitus

ESRD: end stage renal disease

Spoelstra-de Man AM, et al. Diabetes Care 2001;24:2097–2101
Retnakaran R, et al. Diabetes 2006;55:1832–1839
Sowers JR, et al. Hypertension 2001;37:1053-1059
Dusing R. Business briefing: european endocrine review 2006. Available at: http://www.touchbriefings.com/pdf/1711/Dusing.pdf (last accessed October 2013)

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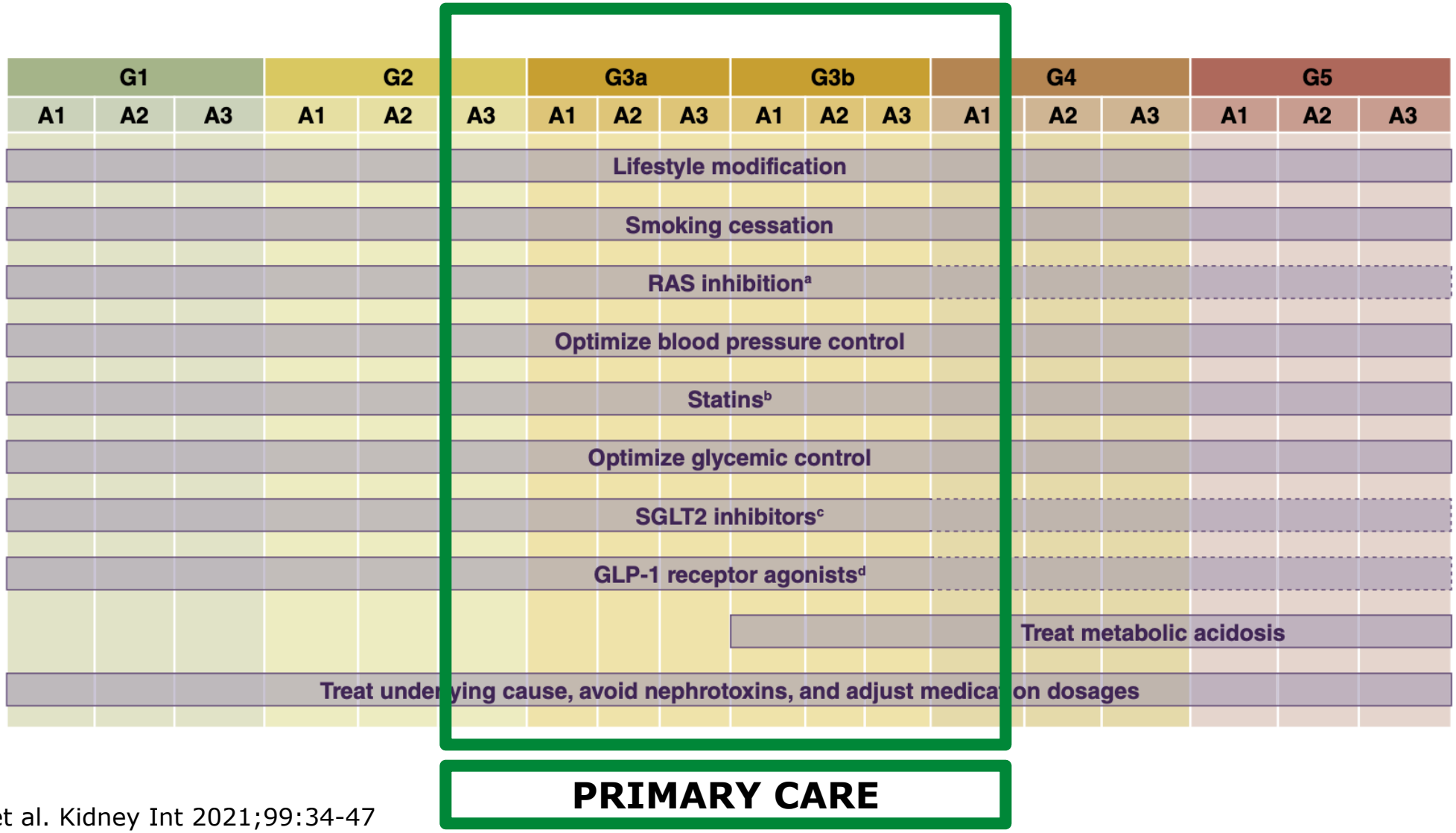
Interventions to slow chronic kidney disease (CKD) progression and/or reduce cardiovascular risk



Shlipak, M. G et al. Kidney Int 2021;99:34-47

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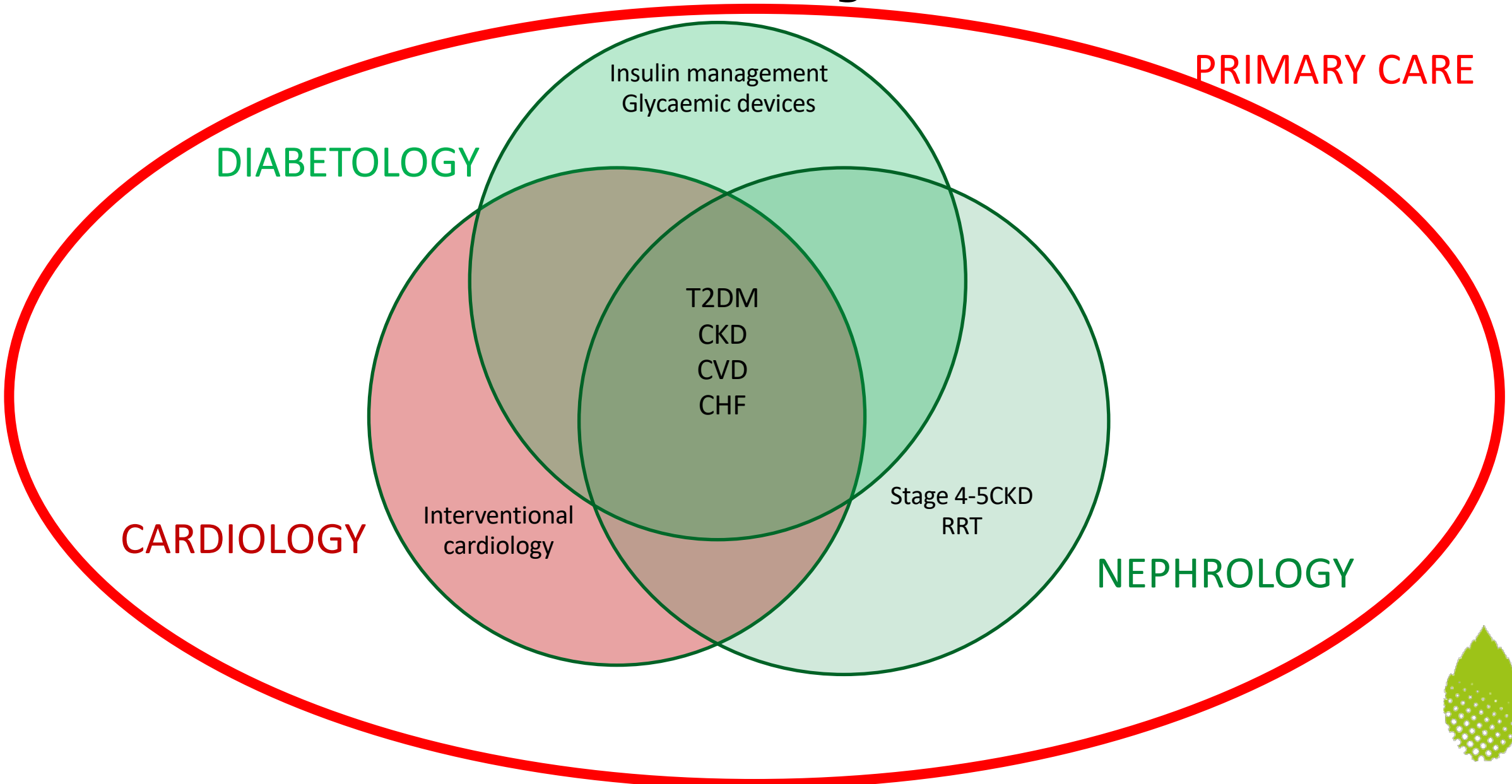
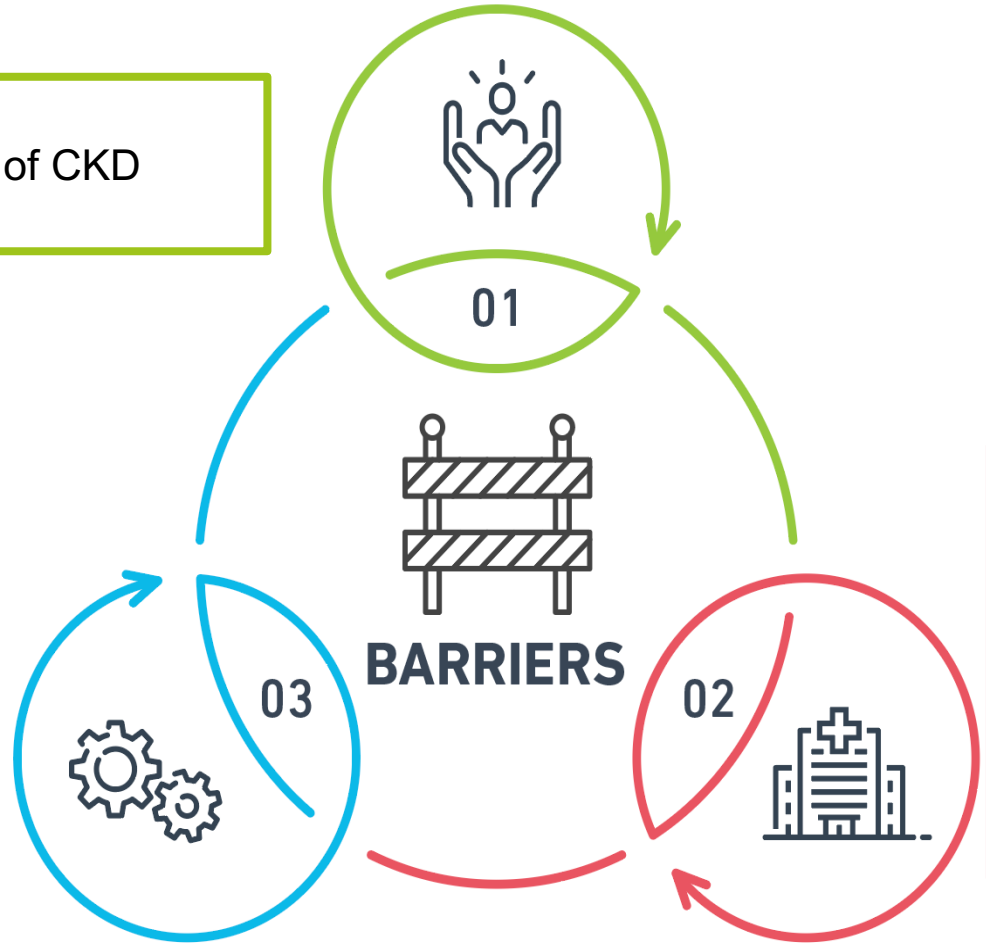
Diabetes, CKD and CVD Multimorbidity Paradigm: Potential for fragmented care



Primary Care Barriers to Management of CKD

PATIENT LEVEL
- Low awareness of CKD
- Poor adherence

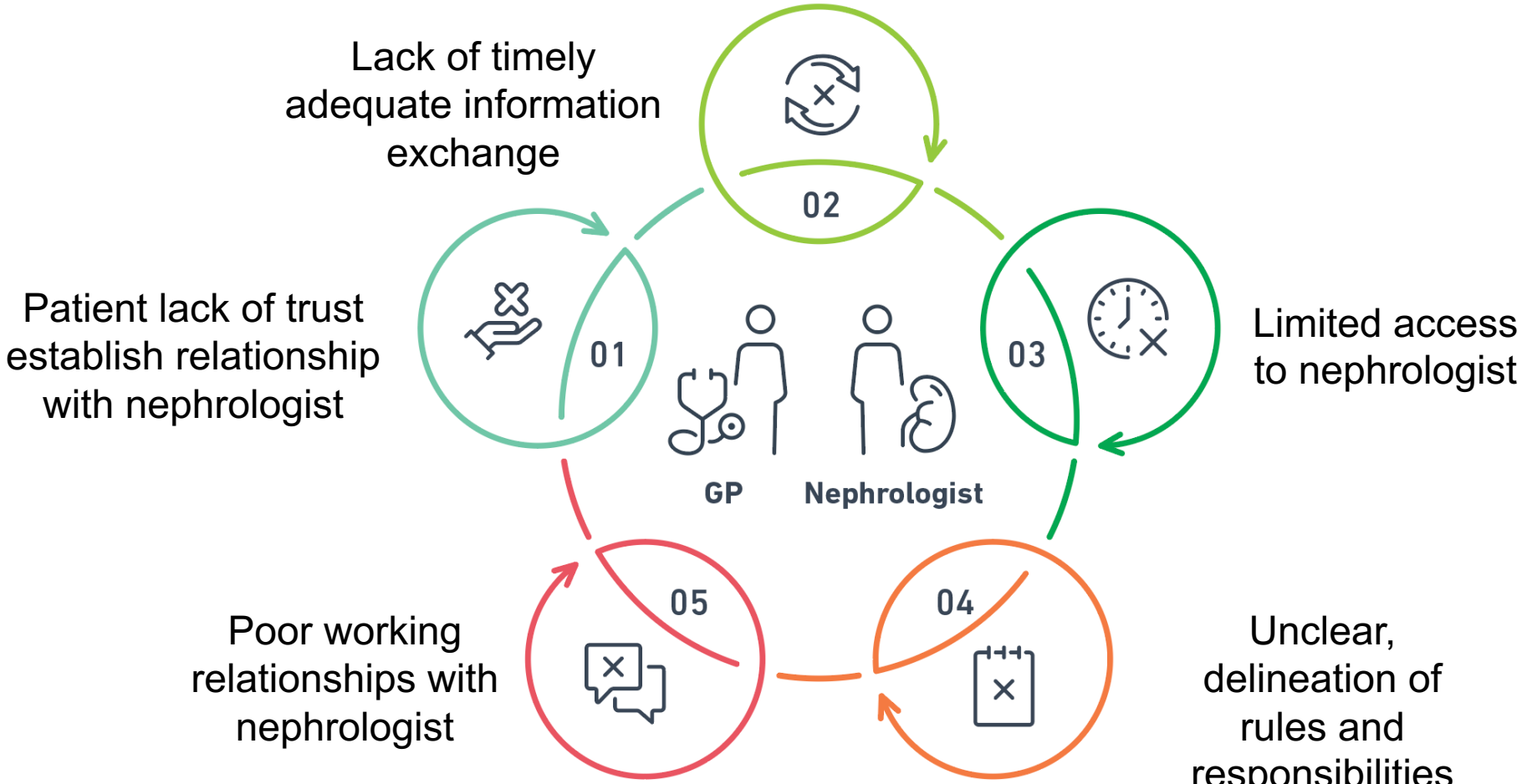


HEALTH CARE SYSTEM
- Poor electronic medical records
- Limited time
- Limited resources

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

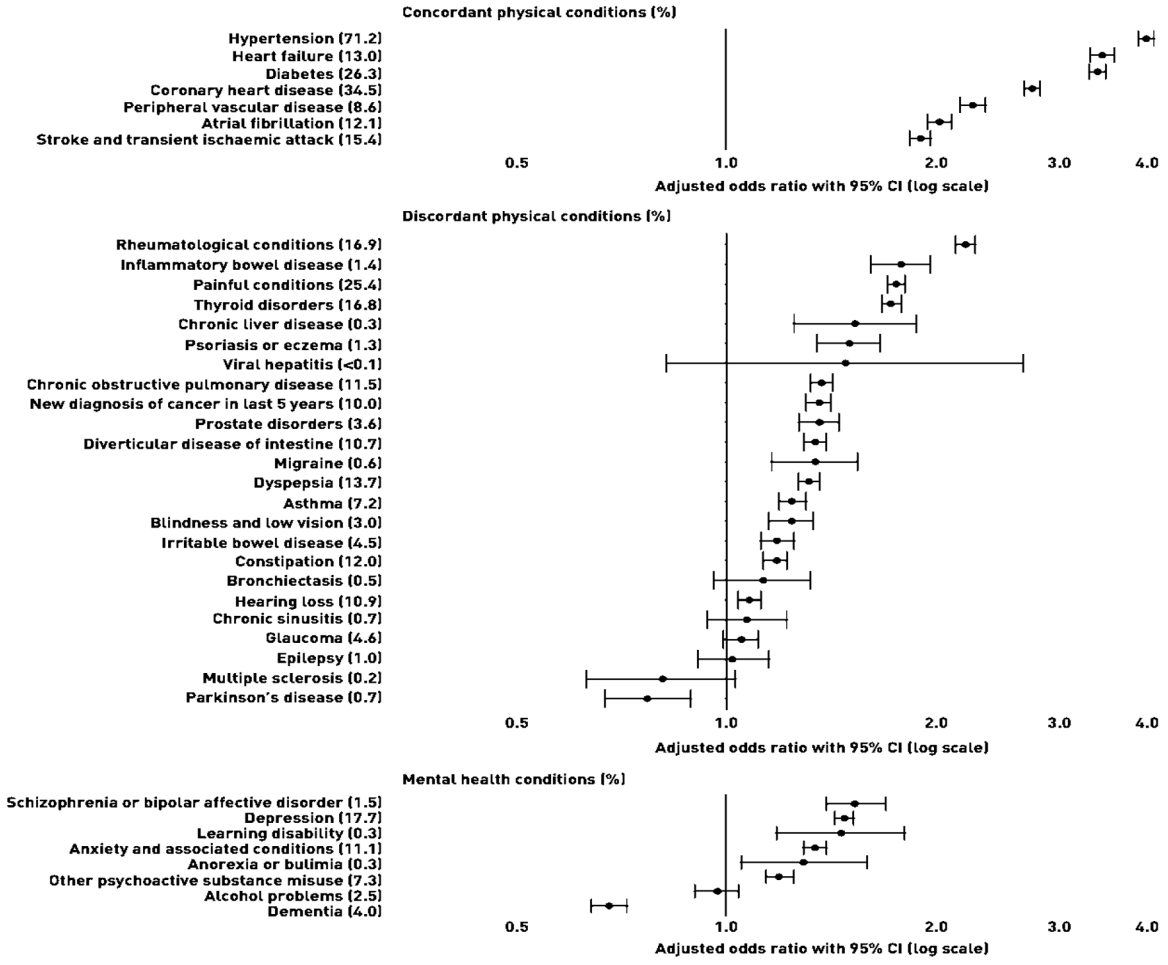
Neale et al. BMC Nephrology (2020) 21:83

Primary Care Barriers to Nephrology Referrals



Greer RC et al. Gen Intern Med. 2019 Jul;34(7):1228-1235.

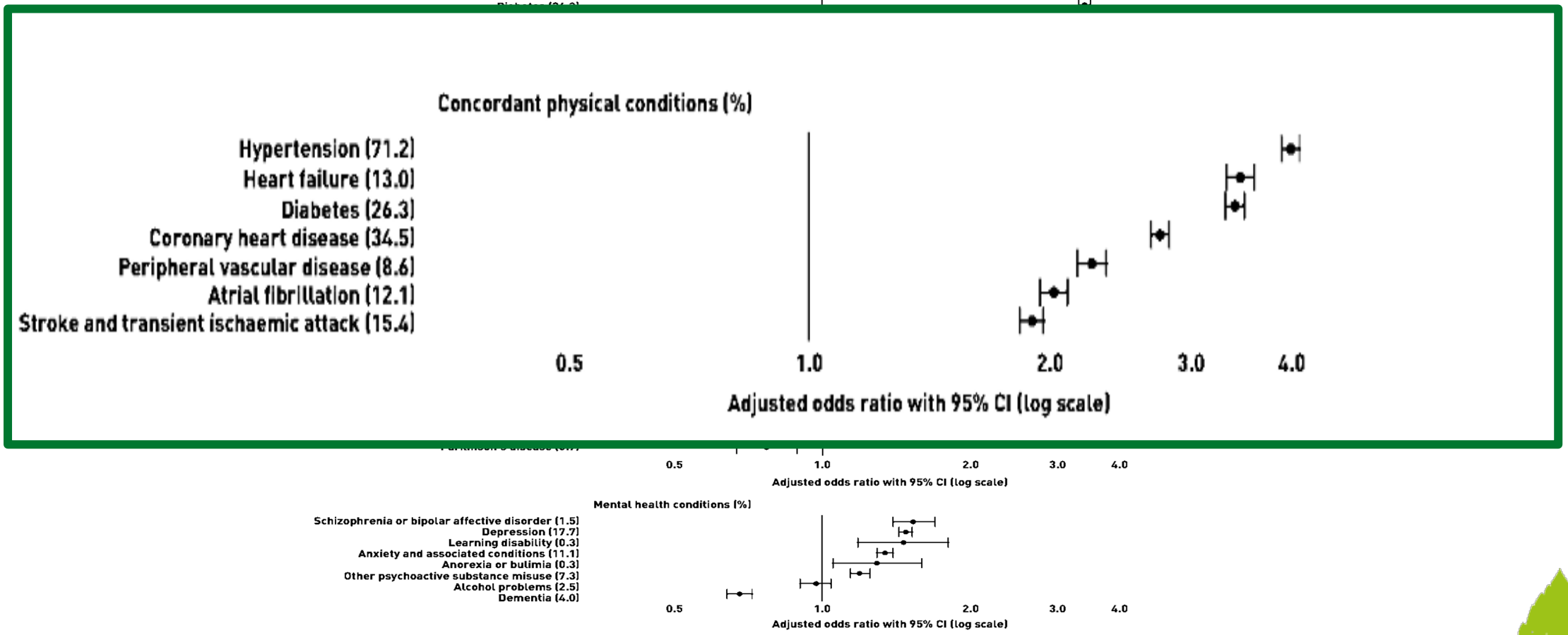
CKD is a multiple long term condition(multimorbidity)[1]



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.

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]
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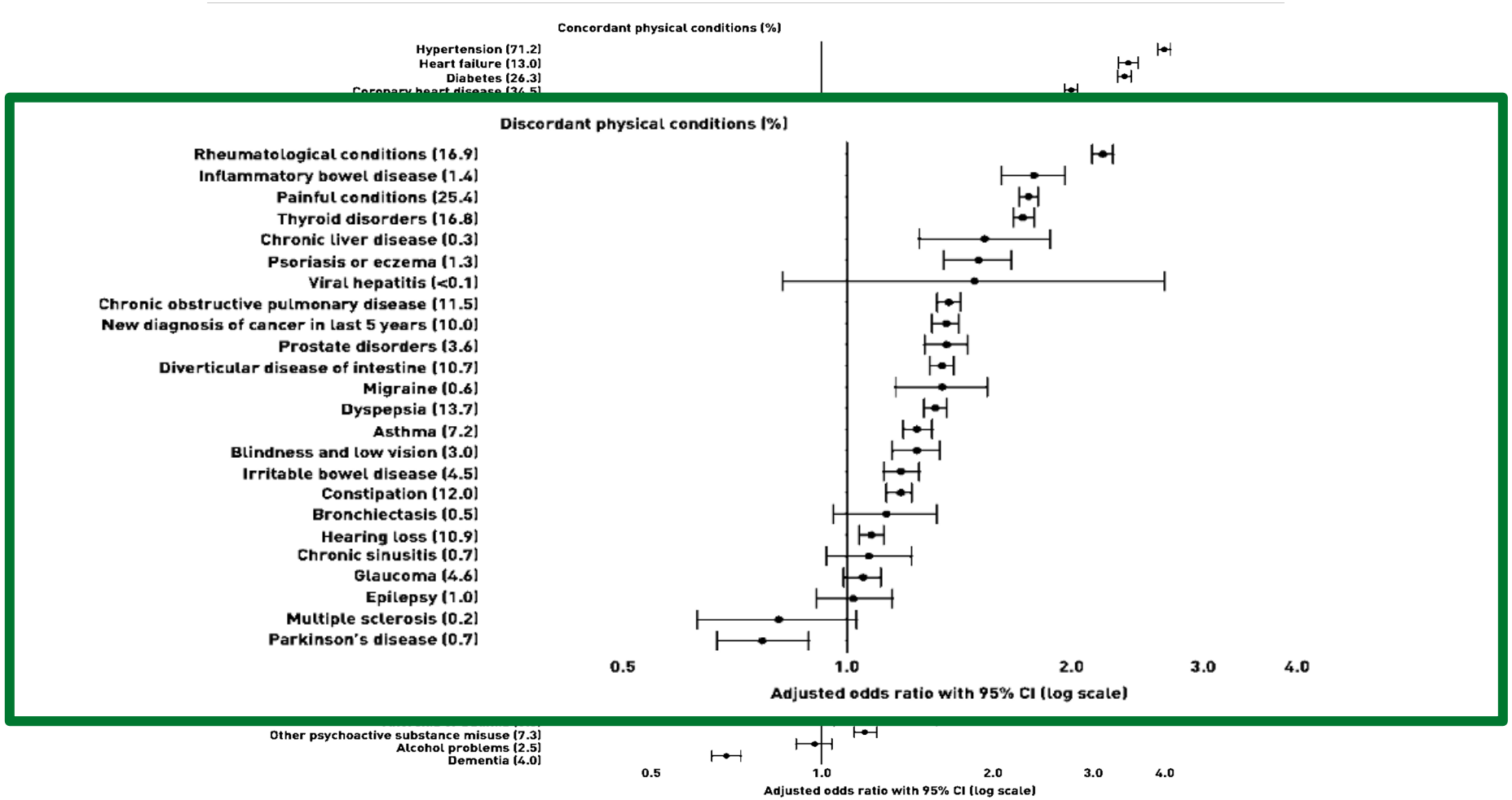
McRae C et al. *BJGP* 2021;71(704):e243-e249

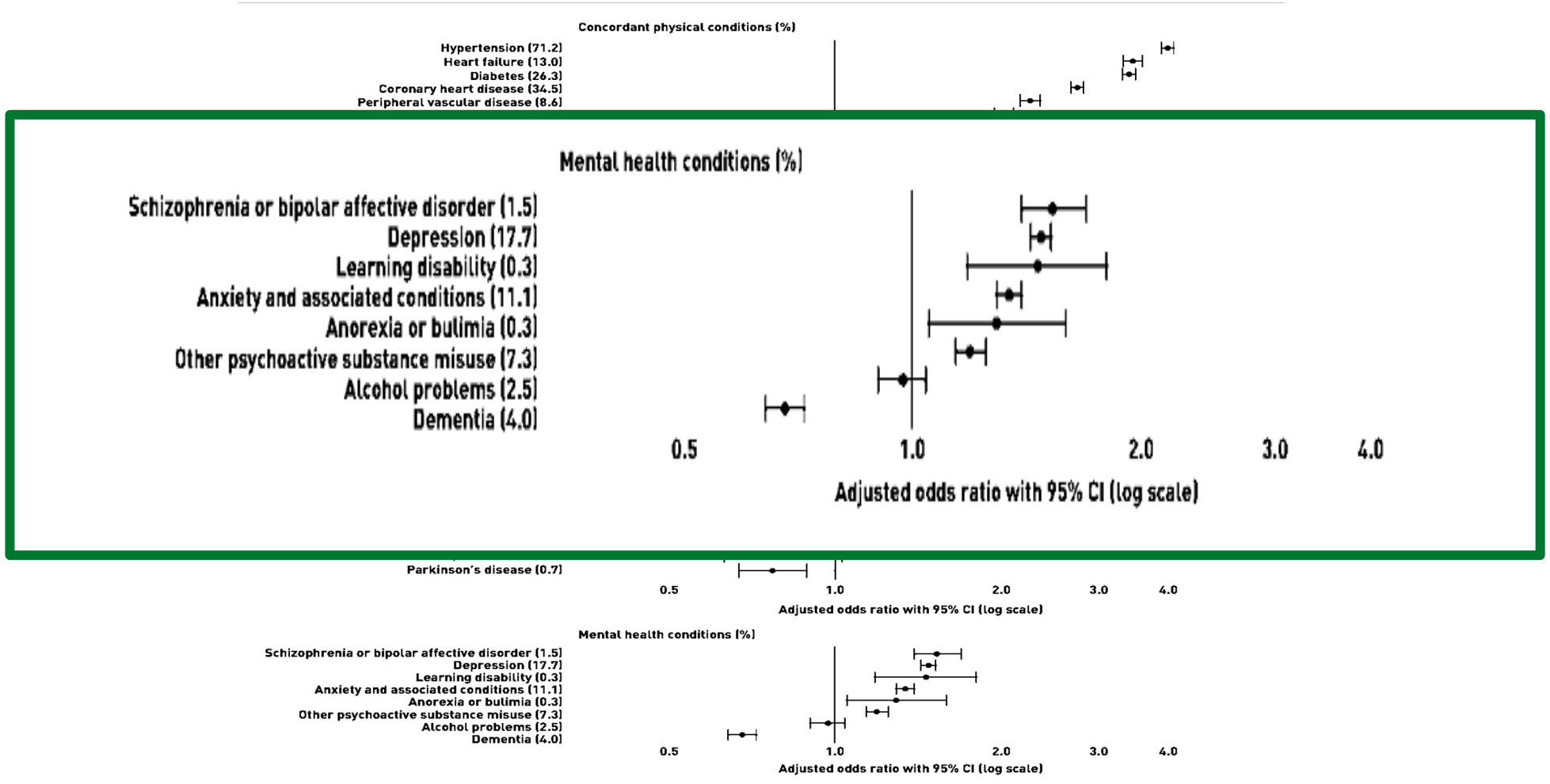
CKD and Discordant physical MLTCs



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.

McRae C et al. *BJGP* 2021;71(704):e243-e249

CKD and Mental health MLTCs



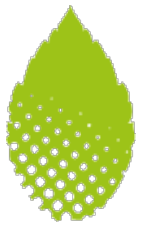
Age-, sex-, and deprivation-adjusted odds ratios for physical and mental comorbidities.[a]
[a]Disease labels show percentage of people with CKD who also have this disease. CKD = chronic disease.

McRae C et al. *BJGP* 2021;71(704):e243-e249

CKD and MLTCs

Number of comorbidities by CKD status, *N* = 1 274 374

Characteristic	CKD (N= 33 567)	Without CKD (N= 1 240 807)	Unadjusted OR (95% CI)	aOR (95% CI)a
Mean comorbidities, n (SD)	3.8 (2.2)	1.2 (1.6)	–	–
Total comorbidities, n (%)				
0	614 (1.8)	598 194 (48.2)	1.00	1.00
1	3553 (10.6)	278 807 (22.5)	12.4 (11.4 to 13.5)	6.5 (6.0 to 7.1)
2–3	12 472 (37.2)	248 971 (20.1)	48.8 (45.0 to 53.0)	15.2 (14.0 to 16.5)
4–6	13 000 (38.7)	99 779 (8.0)	126.9 (117.0 to 137.7)	26.6 (24.4 to 28.9)
≥7	3928 (11.7)	15 056 (1.2)	254.2 (233.1 to 277.2)	41.9 (38.3 to 45.8)



McRae C et al. *BJGP* 2021;71(704):e243-e249

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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

GP-Prompt Study

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.

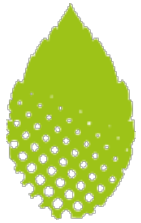
Improvements in lipid profile and coding MA can benefit patients with diabetes to alter the high risk of atherosclerotic CV events.

Willis A et al. *Diabetes Care* 2020;43(8):1893–1901

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

86,475 people with CKD

Level of continuity	HIGH (51.3%)	MODERATE (30.0%)	POOR (18.7%)
OUTCOMES			–
All cause hospitalisation	1.0	1.28 (1.25-1.32)	1.52 (1.47-1.57)
All cause ED visits	1.0	1.42 (1.39-1.46)	1.78 (1.73-1.83)
RAAS inbitors prescribed	1.0	0.99 (0.96-1.02)	1.03 (0.98-1.07)
Statins prescribed	1.0	0.89 (0.84-0.95)	0.8 (0.74-0.86)



Chong C et al. Annals Fam Med 2022;20:237-245

Barriers & solutions to the uptake SGLT-2 inhibitors in clinical practice

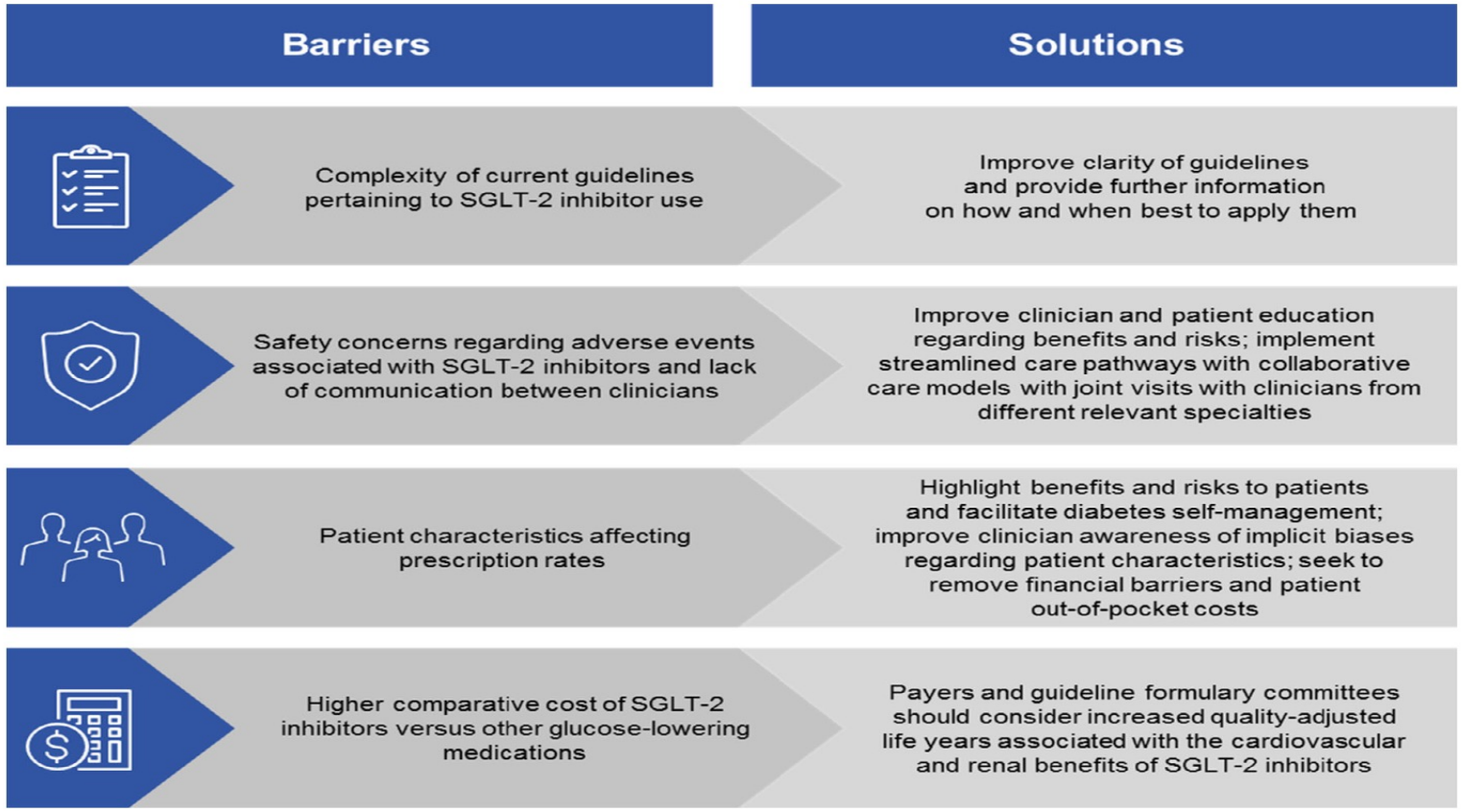


FIGURE 5 A summary of barriers to the uptake of sodium-glucose co-transporter-2 (SGLT-2) inhibitors in clinical practice and proposed solutions

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

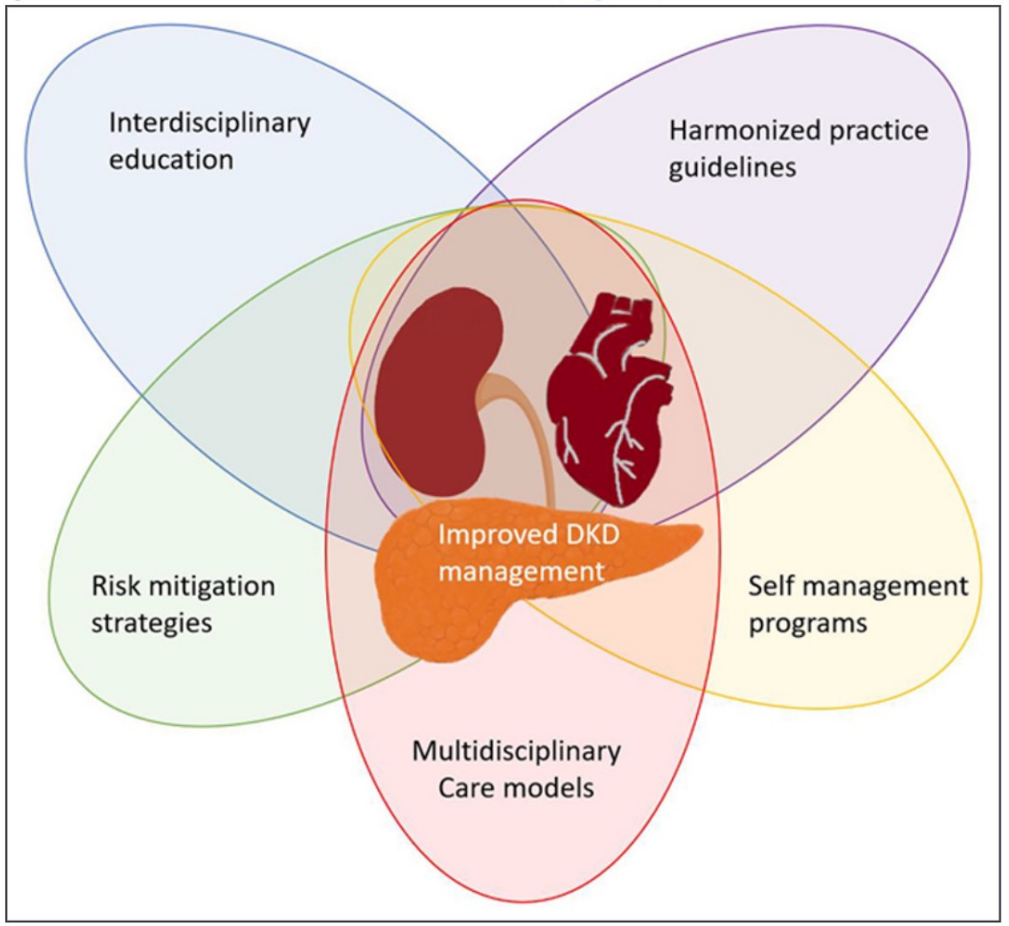
Better blood pressure control, slower eGFR decline, higher use of RAASi as well as less use of NSAIDs in CKD patients when treated by nephrologists

	Nephrologist care		PCP care	
	Baseline	Final	Baseline	Final
n/o patients	52		65	
Age	62.5 ± 9.3		62.8 ± 9.9	
Duration of diabetes	14.7 ± 8.4		14.2 ± 8.0	
Duration of hypertension	10.6 ± 9.9		10.3 ± 8.8	
sysBP	140 ± 30	130 ± 21	140 ± 19	145 ± 23
diaBP	76 ± 14	70 ± 10	79 ± 8	77 ± 11
Albuminuria	158 (62-451)	216 (97-619)	109 (50-509)	389 (92-728)
eGFR	83.8 ± 26.1	80.4 ± 35.5	78.6 ± 28.1	66.6 ± 29.9
Use of ACEs	25 (48)	44 (90)	35 (53)	37 (70)
Use ARBs	1 (2)	22 (45)	0 (0)	2 (4)
Use of Statins	2 (4)	21 (43)	10 (16)	5 (9)
Use of NSAIDs	6 (11)	0 (0)	3 (5)	17 (32)

ACE, anigotensin-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

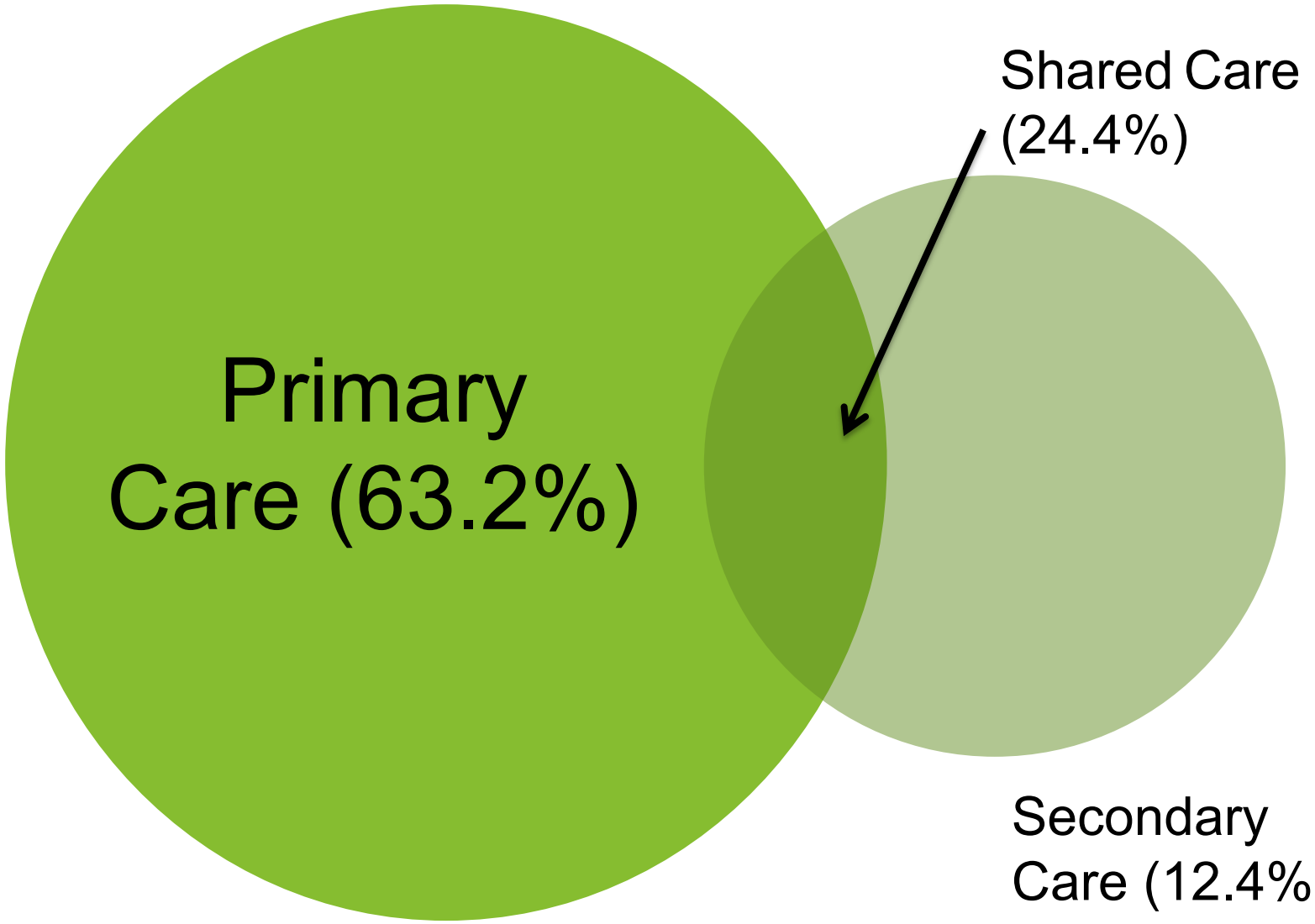
Martinez-Ramirez HR et al. Am J Kid Dis 2006;47:78

Components of a successful cardio-renal-metabolic care model at an institutional level



Rangaswami J et al Circ Cardiovasc Qual Outcomes 2020;13:e007264

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



Khunti K et al. JRSM 2000

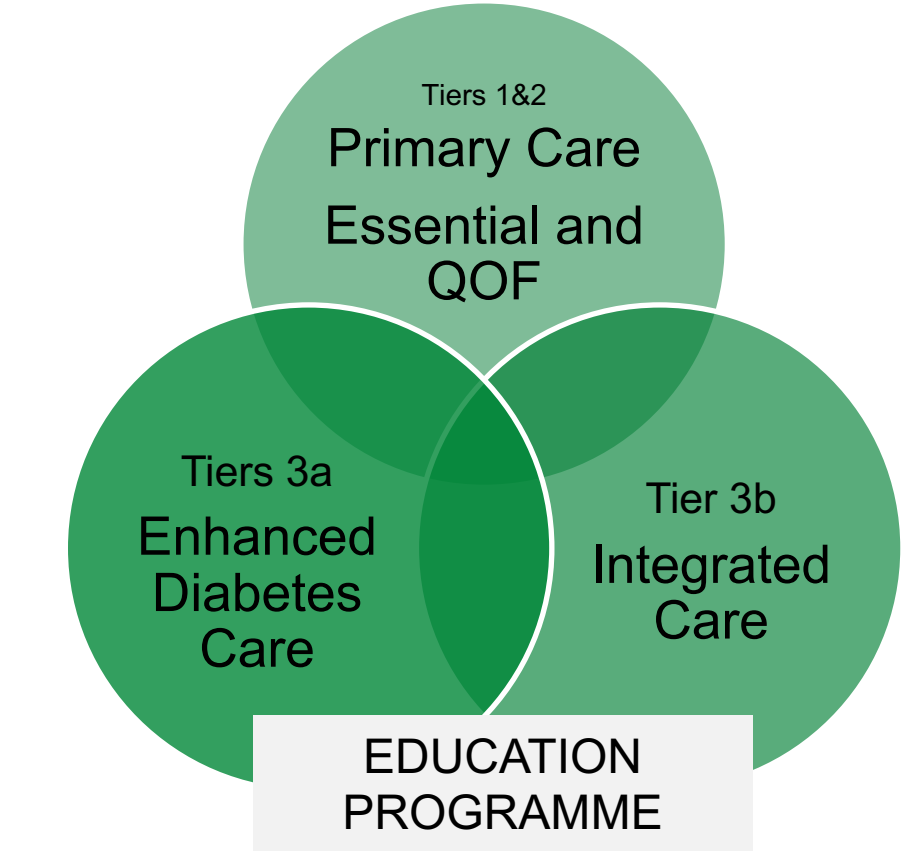
Delivery of primary care 2023

Primary Care (95%)

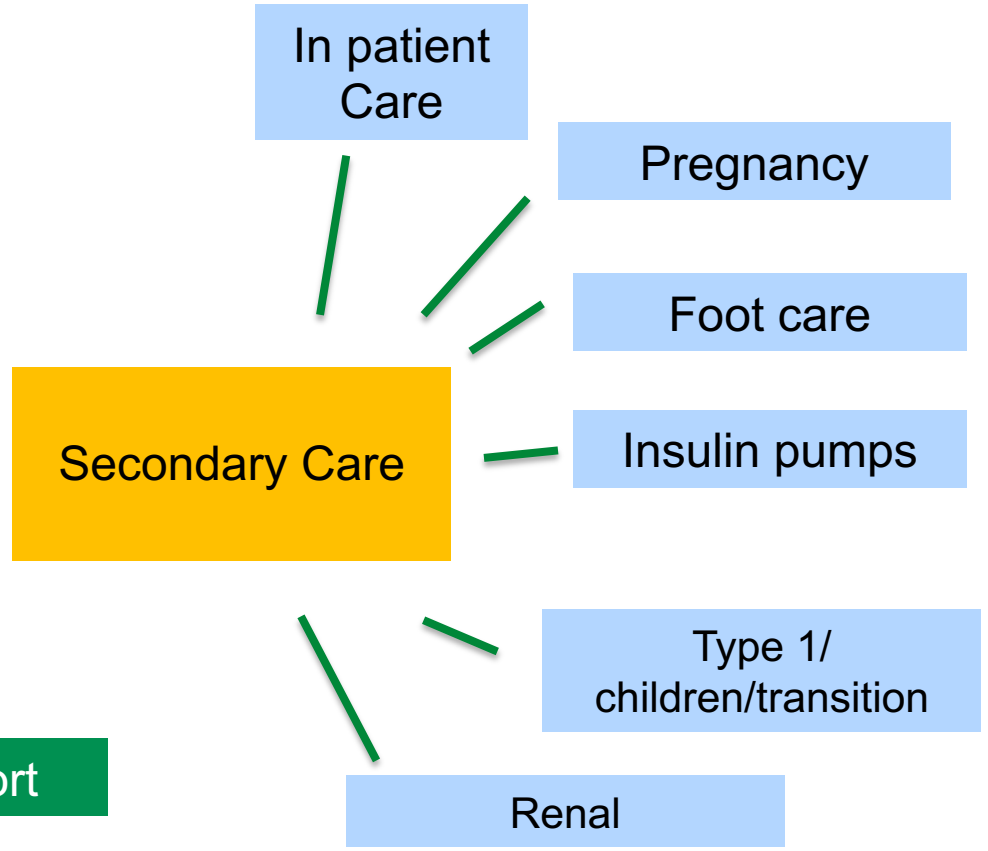
Secondary Care (5%)

Seidu S et al. Diabet. Med. 2017; 34: 748–750
Boels AM, Primary Care Diabetes 2017; 11: 71–77.

Leicester Commissioning Pathway: Super Six and Necessary Nine!



DSN and Medicine management Support



Seidu S et al. Diabet. Med. 2017; 34: 748–750

Model of care is safe and cost-effective

Clinical outcomes from the RCT. [7]

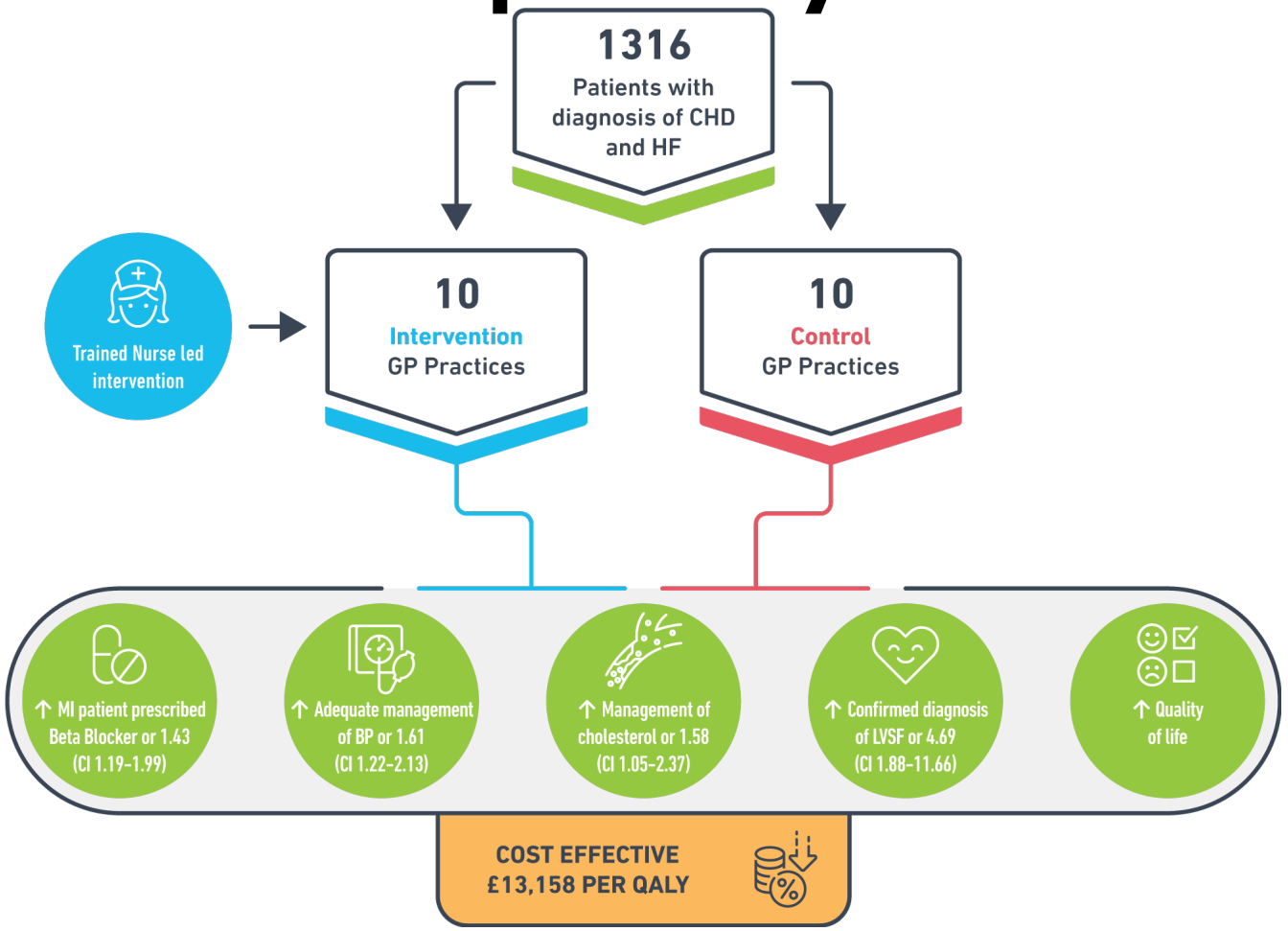
Outcome	Mean difference (95% CI)	p-value
Non-elective bed days		
Diabetes as a primary diagnosis	2.20 (-0.92, 5.32)	0.14
Diabetes as a primary or secondary diagnosis	2.78 (-2.71, 8.27)	0.27
First outpatient attendance	0.02 (-0.47,0.52)	0.92
Admissions with type 2 diabetes complications	0.30 (-0.85, 1.45)	0.55

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% CrI -148,-28)**

Savings if rolled out in UK **-£276,200,000 (95% CI -495,400,000, -94,480,000).**

Seidu S et al. 2021;15:601-606

Disease management program of heart failure in primary care



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 to end. She also

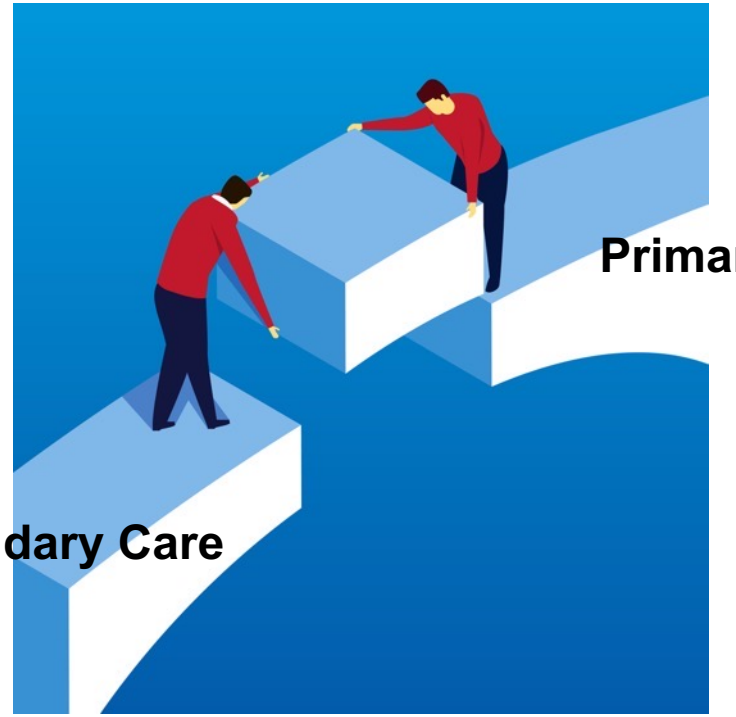
entrance, will become a thing of the past," she said. "In future, we will be working together in one integrated system of care."

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 argued, allow real integration across services.

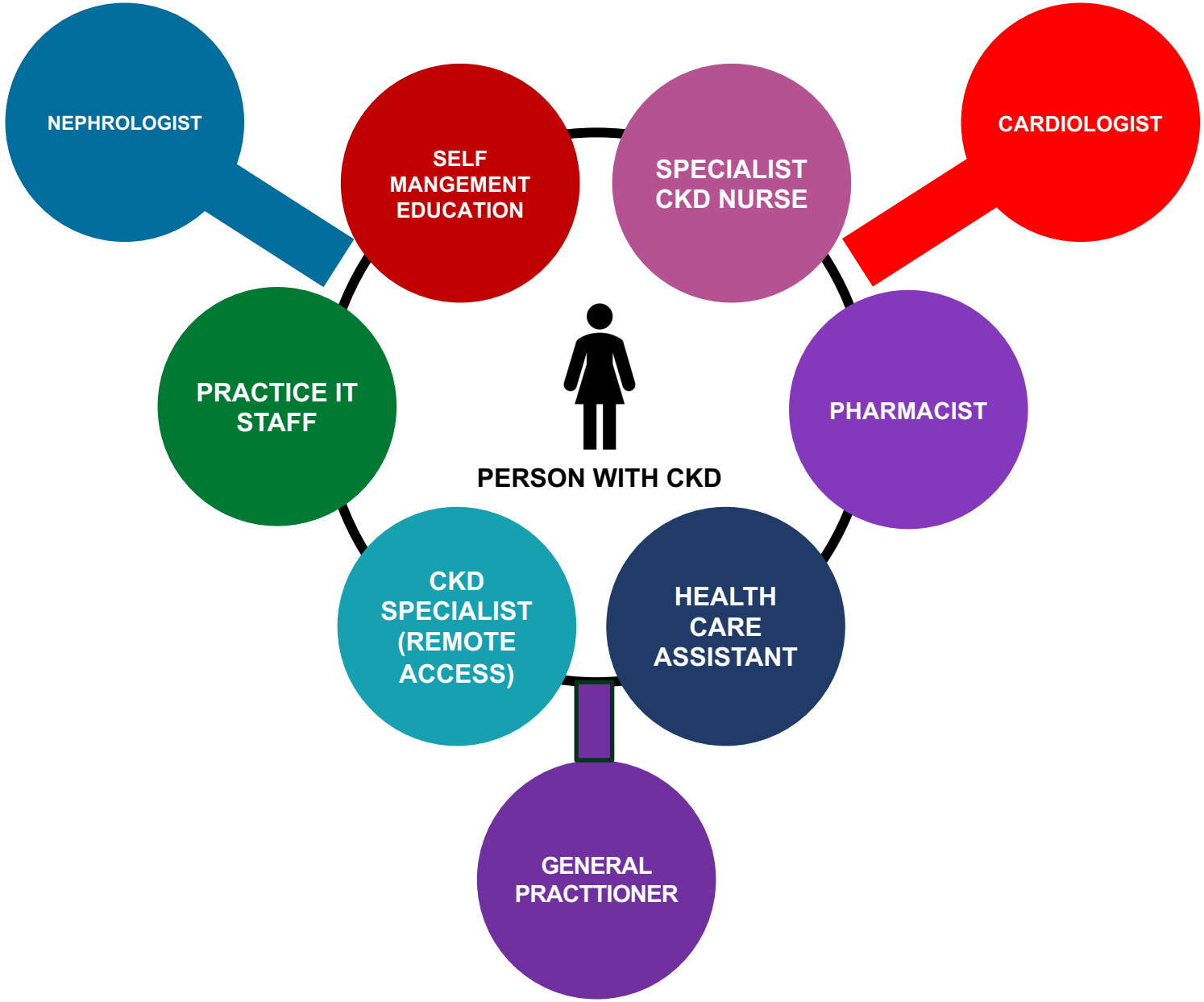
One of the things that must change is our relationship with our specialist colleagues

about pilot schemes to extend general practices' opening hours.

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



Integrated multidisciplinary model of care for CKD



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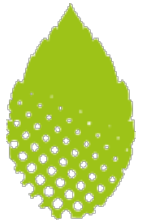
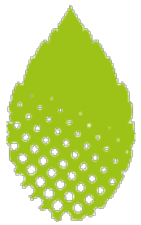
Integrated care: the key to management of CKD

- 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

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