Delivering joined-up care for people with type 2 diabetes: rationale, challenges and examples

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Abstract

Background: Approximately 3.8 million people in the UK have type 2 diabetes mellitus (T2DM) and are, as a consequence, at risk of developing cardiovascular (CV) or kidney disease. Intensive glucose control alone does not substantially reduce the risk of macrovascular events. However, new glucose-lowering medications (sodium–glucose co-transporter 2 inhibitors [SGLT2is] and glucagon-like peptide 1 receptor agonists) can significantly reduce the risk of major CV adverse events in people with T2DM; furthermore, SGLT2is have demonstrated significant reductions in the risk of hospitalization for heart failure and renal events. As a consequence, there has been a shift in the focus of care from glucose management to preservation of organ function.

Main text: The emergence of new treatments and the increasing pressure on secondary care systems have called into question the way in which care is provided to people with T2DM.

The ongoing COVID-19 pandemic has further highlighted the need for novel and improved approaches of integrated care between primary and secondary healthcare systems and multi-disciplinary working. Setting up such systems in the UK, however, is challenging.

Conclusion: When barriers are removed, successful integrated care systems can be established, which improve care for patients with T2DM and alleviate pressure on secondary care.

Keywords: Type 2 diabetes, Cardiovascular disease, Chronic kidney disease, Multidisciplinary care, General practice

Key messages

- The rapidly increasing number of patients with type 2 diabetes (T2DM) is placing a considerable burden on secondary care systems
- The focus of T2DM management is shifting from glucose control to cardiovascular and renal protection, which is particularly important in the context of COVID-19
- Integrated, multidisciplinary, community-based care offers the potential to improve outcomes for people with diabetes and reduce the pressure on secondary care systems
- Difficulties in sharing patient information, a lack of connectivity between secondary and primary care, and the complexities of National Health Service England internal market are barriers to setting up integrated community-based care systems
- When these barriers are overcome, however, successful integrated care systems can be established that offer benefits to patients and healthcare systems alike

Background

The evolutions of care for patients with type 2 diabetes

Diabetes is now seen as a modern pandemic. In 2017 there were estimated to be 58 million people in Europe with diabetes, a figure which is set to rise to 67 million within the next 25 years (1). Over 90% of adults with diabetes have type 2 diabetes mellitus (T2DM) (2-4), the prevalence of which is increasing as a consequence of an ageing population, changes in diet, increasing obesity and more sedentary lifestyles (5).

The close relationship between T2DM and both cardiovascular disease (CVD) (6) and chronic kidney disease (CKD) is well established (7, 8). Given that hyperglycaemia promotes CVD and CKD, there was a presumption that tight glucose control would slow the progression of these complications. This theory, however, was challenged by the United Kingdom Prospective Diabetes Study (UKPDS) in 1998, which suggested that glucose control did not have a major impact on largevessel disease (9). This led to a degree of nihilism among clinicians regarding glucose management, and a greater focus on managing hypertension and lipids.

The rationale for integrated care in type 2 diabetes mellitus

By the late 2000s, T2DM was being recognized as a vascular disease, but there was no meaningful collaboration between diabetologists and specialists who were managing vascular complications. Cardiologists would manage people with T2DM acutely following a cardiovascular (CV) event, then pass them back to primary care or a diabetologist for continued glucose management. In a similar manner, renal services would await the point at which patients with T2DM were approaching the need for dialysis before becoming involved in their care.

The therapeutic landscape began to change in 2015, catalysed by a meta-analysis of data on the thiazolidinedione, rosiglitazone, which suggested that it was associated with an increased risk of CVD in people with T2DM (10). Although this finding was largely repudiated several years later, it prompted the US Food and Drug Administration (FDA) to mandate that all new glucose-lowering therapies undergo trials to demonstrate CV safety (11). The first of the modern CV outcomes trials

(CVOTs) to show superiority of a glucose-lowering therapy over placebo assessed a sodium–glucose co-transporter 2 inhibitor (SGLT2i) and was presented in September 2015. The Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes (EMPA-REG) study reported not only CV safety but also a 14% reduction in the primary composite endpoint of CV death, non-fatal myocardial infarction and non-fatal stroke compared with placebo (the three-point major adverse CV event [MACE] endpoint). In addition, there were significant reductions in the relative risk of hospitalization for heart failure (HF), CV death and all-cause mortality (12). These surprising findings were supported subsequently by data from CVOTs assessing the other licenced SGLT2is, canagliflozin, dapagliflozin and ertugliflozin (13-15) (Table 1). Glucagon-like peptide 1 receptor agonists have also demonstrated CV benefits in patients with T2DM. Indeed, four of the seven members of the drug class significantly reduced the risk of MACE in their respective CVOT (16-19) (Table 1).

Positive results from landmark trials that evaluated the effect of SGLT2 is on renal outcomes and HF confirmed that the benefit of SGLT2i therapy extended beyond MACE (20-23) (Table 2). Indeed, the findings from the CREDENCE (Canagliflozin Evaluation of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Participants with Diabetic Nephropathy) trial have brought about a change in the canagliflozin summary of product characteristics. Canagliflozin can be initiated in patients with T2DM and an estimated glomerular filtration rate as low as 30 mL/min/1.73 m² in the presence of macroalbuminuria (urine albumin: creatinine ratio > 30 mg/mmol), and patients with macroalbuminuria who are already taking canagliflozin can continue until dialysis or transplant (24). Currently, the other SGLT2is cannot be initiated in patients with an eGFR below 60 mL/min/1.73 m² for the treatment of hyperglycaemia and should be discontinued when the eGFR drops below 45 mL/min/1.73 m² (25-27). Dapagliflozin (10 mg) has been approved for the treatment of heart failure with reduced ejection fraction (HFrEF) in patients with or without T2DM regardless of renal function; however, additional glucose-lowering medications should be considered in patients with HFrEF and T2DM if their eGFR falls persistently below 45 mL/min/1.73 m² (25).

Now, more than ever, there is a compelling reason for diabetologists to work more closely with cardiology and renal colleagues to identify patients who will benefit most from new glucose-lowering therapies. The urgent need for integrated care for people with diabetes has been intensified by the COVID-19 pandemic. Data from English hospitals demonstrated that a third of COVID-19-related deaths occurred in people with diabetes. Furthermore, CV or renal complications were independent risk factors for COVID-19-related death in this cohort(28). In the Covid-19 era, it has become even more important that all modifiable CV-renal risk factors are minimized in patients with diabetes to limit the risk of hospitalization.

Barriers to integrated care for people with type 2 diabetes mellitus

Despite the growing evidence base supporting a multidisciplinary approach to diabetes management, this is not commonplace in the UK. Setting up integrated care systems within the UK National Health Service (NHS) framework can be challenging. Sharing patient information among practitioners in different settings is a critical aspect of any putative integrated care system but difficulties with IT connectivity within the NHS represent a considerable hurdle to establishing effective multidisciplinary care teams (MDTs).

Integrated care systems also require close ties between primary and secondary care, and the commitment of the participating healthcare professionals (HCPs). Unfortunately, such close ties are not universal, the NHS internal market system can hinder the development of links between tiers of care and not all HCPs are convinced of the value and efficiency of multidisciplinary care.

Despite these challenges, integrated care systems have been set up successfully around the UK. Here we describe two case studies from very different healthcare environments.

Integrated care case study 1: the south London experience

Geography and patient population

Lambeth, South London, is among the most densely populated boroughs in England and Wales (29). The population is characterized by significant ethnic diversity, young age and difficult socioeconomic circumstances (30).

A typical primary care practice in London will have 500–1000 patients with T2DM, of whom between 200 and 400 may have CV risk factors and/or early evidence of CKD (31). On average, people in Lambeth develop T2DM at a younger age than those in other parts of the UK, and are predisposed to developing CV–renal complications (31). The primary aim of the service was to address the high burden of CV–renal risk by facilitating the early identification of high-risk patients, and rapid referral to secondary care.

Team structure

Delivery of the integrated care service required a MDT of HCPs with expertise in caring for people with T2DM and CV–renal complications. The team comprises a specialist diabetes nurse, a dietician, a clinical consultant pharmacist, a primary care physician (PCP) and a diabetologist. A dedicated administrator was also recruited to manage the logistical aspects of the integrated care system.

Systems and processes: pre COVID-19

Local pathways were established to promote the early identification and referral of patients at high risk of CKD (5). In brief, people with a confirmed eGFR below 30 mL/min/1.73 m² or non-diabetic kidney disease are referred to secondary care immediately; patients with an eGFR higher than 30 mL/min/1.73 m² are referred to the MDT if they have an urine albumin : creatinine ratio (UACR) greater than 30 mg/mmol despite adequate renin–angiotensin–aldosterone system blockade, or if an annual fall in eGFR of greater than 5 mL/min/1.73 m² is observed. Patients are referred to the MDT for guidance on optimizing treatment in the context of CKD or CVD. Patients with acute or advanced CKD and/or CVD and those who require more

detailed investigation are referred to the relevant clinical service at Guy's and St Thomas' Hospital.

Multidisciplinary clinics are held weekly in four locations across Lambeth. During visits, serum creatinine, glycated haemoglobin (HbA_{1c}), plasma glucose and eGFR are measured at the point of care (POC) to enable prompt decision-making and triage. Joint decision-making is a key focus of the MDT. Shared plans are developed with patients which cover lifestyle, diet, self-care and management of medications, with an emphasis on sick day rules.

The MDT clinics use a dedicated electronic patient record platform, which gives clinicians access to local healthcare records from both primary and secondary care. This system facilitates sharing of key information and reduces duplication of care processes. The IT platform also enables virtual clinics, during which records from patients referred from local general practitioners are reviewed by the MDT, and advice and management plans are sent back to the referring clinicians.

Following an initial pilot period, the integrated-care service was funded by the local clinical commissioning group, which appreciated the importance of early identification of high-risk individuals, prompt triaging and the focus on delivery of an integrated hospital- and community-based service (Fig. 1).

Post-COVID-19 adaptations

At the beginning of the pandemic the MDT processes were restructured to meet social distancing requirements, meetings were held virtually and face-to face appointments with patients were kept to a minimum. However, patients with acute clinical needs such as rapid decline in renal function or inadequate glycaemic control that necessitated immediate administration of insulin were prioritized for face-to-face appointments. In addition, patients with mental health problems or communication difficulties were also seen in person.

A reduced-contact service was established to run alongside the face-to-face clinics. Patients were invited to a healthcare assistant-led screening clinic during which HbA_{1c},

blood pressure, cholesterol, serum creatinine, urine albumin, body mass index, foot health and smoking habits were measured and recorded electronically at POC. In addition, patients were able to add their own blood glucose readings to their records using the DIASEND platform. The complete electronic records and results were reviewed by the MDT and patients were contacted by phone a week later to discuss results and treatment plans.

Community renal diabetes clinics are held weekly. Eight face-to-face appointment and 18 telephone/virtual consultations are available, the latter being appropriate for patients for whom the key information described above is already available. In addition, twelve injectable medication starter sessions are provided weekly by specialist nurses.

Integrated care case study 2: the Western Health and Social Care Trust experience

Geography and patient population

The Western Trust serves a population of approximately 300,000 people in Northern Ireland and covers an area of 4842 km², which encompasses the counties of Derry/Londonderry, Tyrone and Fermanagh. In contrast to the population of Lambeth, more than half of the people served by the Western Trust reside outside the three main population centres. There are 49 general practices within the Western Trust that care for approximately 14,500 patients with diabetes; acute complications of diabetes are managed at two hospitals that lie 45 miles apart.

An acute shortage of consultants in 2012 led to a reassessment of diabetes services in the Western Trust. The essential service review revealed long waiting lists for, and waiting times at, consultant-led clinics, failings in shared-care arrangements with primary care, and duplication of services, all highlighting the need for a service redesign

Team structure

To relieve the pressure on secondary care, a community-based Diabetes Specialist Team (DST) was set up, comprising diabetologists, nurses, dieticians, podiatrists, podiatry assistants, pharmacists, psychologists, exercise professionals and clerical staff. Funding from 'Transforming Your Care for Integrated Care Partnerships' (*should this be referenced?*) allowed additional staff to be recruited to the DST.

Systems and processes

Several types of clinic are now run across the Western Trust to meet the different needs of patients with diabetes. On a weekly basis: nine consultant-led clinics are held at the three main hospital sites; 15 joint clinics involving diabetes specialist nurses and dieticians are held at local primary care-centres and the three hospital sites; four clinics, specifically for patients newly diagnosed with diabetes, are held at local centres; and an additional 10 clinics led by diabetes specialist nurses are held in local primary care centres.

The Western Trust was an early adopter of the Northern Ireland Electronic Care Record system. This allowed the creation of a Trust-wide central electronic portal for triaged referral from primary care to any of the DST clinics described above, and the standardization of treatment strategies and referral pathways across the Trust. PCPs can upload information including notification of a new diagnosis, HbA_{1c}, eGFR and presence of CV risk factors or complex complications, and request advice on the most appropriate treatments. This information can be reviewed to ensure that patients are referred to the most suitable clinic and medication advice can be sent directly to the referring PCP.

Setting up the DST was not without obstacles. Joint clinic codes and reporting methods proved difficult to align, owing to an ageing patient administration system; recruitment difficulties due to temporary funding arrangements with integrated care providers and overcoming resistance to change among some staff members were, and remain, challenging issues.

Patients have benefited in several ways: offering joint clinics in a planned pathway reduced the number of appointments; the electronic triage system allowed Trustwide referrals to be processed more quickly and updated treatment regimens to be planned and circulated more efficiently; and sharing treatment plans and discussions of next treatment steps has had a beneficial educational bonus. In addition, risk stratification has improved waiting times with new referral and recall dates now on target in some areas and reduced to a delay of 2–6 months in others (Fig.2).

Discussion

New glucose-lowering drug classes with proven CV and renal benefits are shifting the paradigm of diabetes care from management of glycaemia to protection of organ function. At the same time, the rising prevalence of T2DM is placing considerable pressures on healthcare systems and the COVID-19 pandemic has further highlighted the importance of reducing the CV and renal complications in people with diabetes. This combination of factors makes the care of people with T2DM in the primary care setting more complex than ever before. The often siloed system of primary care and secondary care is not suited to the management of this rapidly growing population whose needs span the two care settings.

Despite the obstacles, the two case studies above show how innovative integrated systems can bring multidisciplinary diabetes care to the community, resulting in shorter waiting times, less duplication of procedures, less pressure on secondary care and better outcomes for patients.

The different approaches taken by the teams in Lambeth and the Western Trust reflect the different needs of the populations they serve and suggest that a 'one size fits all' approach is not appropriate. However, there are several factors that appear to be pivotal to the success of such systems: IT platforms that allow information to be shared among HCPs; flexible referral processes that allow easy movement of patients to the most appropriate clinic; and perhaps most importantly, the availability of dedicated, specially trained HCPs.

The combination of increasing numbers of patients with diabetes and a rapidly evolving treatment landscape has placed unprecedented pressure on healthcare systems and exposed the limitations of established care models. However, innovative integrated community-based care programmes can relieve the pressure on healthcare systems, maximize the benefits offered by new treatments and improve outcomes for patients with diabetes.

Abbreviations

ACR: albumin : creatinine ratio; CANVAS: Canagliflozin Cardiovascular Assessment Study; CI: confidence interval; CKD: chronic kidney disease; CREDENCE: Evaluation of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Participants with Diabetic Nephropathy; CV: cardiovascular; CVD: cardiovascular disease; CVOT: cardiovascular outcomes trial; DAPA-HF: Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure; DECLARE-TIMI 58: Dapagliflozin Effect on Cardiovascular Events—Thrombolysis in Myocardial Infarction; DSN: diabetes specialist nurse; DST: Diabetes Specialist Team; eGFR: estimated glomerular filtration rate; EMPA-REG: Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes; GLP1RA: glucagon-like peptide 1 receptor agonist; Harmony Outcomes: Albiglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Cardiovascular Disease; HbA1c: glycated haemoglobin; HCP: healthcare professional; HHF: hospitalization for heart failure; HR: hazard ratio; IT: information technology; LEADER: Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results; MACE: major adverse cardiovascular event; MDT: multidisciplinary care team; MI: myocardial infarction; NA: not available; NHS: National Health Service; POC: point of care; REWIND: Dulaglutide and Cardiovascular Outcomes in Type 2 Diabetes; SGLT2i: sodiumglucose co-transporter 2 inhibitor; T2DM: type 2 diabetes mellitus; SUSTAIN-6: Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes; UKPDS: United Kingdom Prospective Diabetes Study.

Declarations

- Ethics approval and consent to participate: not applicable
- Consent for publication
- Competing interests
 - SCB
 - Senior clinical academic since 1993, since that time reports having received honoraria, teaching and research sponsorship/grants from the following:

Abbott, Astra-Zeneca, Boehringer Ingelheim, Bristol Myers Squibb, Cellnovo, Diartis, Eli Lilly, GlaxoSmithKline, Merck Sharp and Dohme, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Schering-Plough, Servier and Takeda

- Received funding for the development of educational programmes from Cardiff University, Doctors.net, Elsevier, Onmedica, Omnia-Med and Medscape
- Owns a share of Glycosmedia which carries sponsorship declared on site.
- JK
 - Attended scientific advisory boards for and received honoraria or consulting fees from Eli Lilly, Novo Nordisk, Sanofi, Napp, AstraZeneca, and Boehringer Ingelheim
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References

1. International Diabetes Federation. IDF diabetes atlas 2017 [cited 2019 November]. Available from: https://www.diabetesatlas.org/en/resources/.

2. Evans JM, Newton RW, Ruta DA, et al. Socio-economic status, obesity and prevalence of type 1 and type 2 diabetes mellitus. Diabet Med. 2000;17(6):478–80.

3. Bruno G, Runzo C, Cavallo-Perin P, et al. Incidence of type 1 and type 2 diabetes in adults aged 30-49 years: the population-based registry in the province of Turin, Italy. Diabetes Care. 2005;28(11):2613 –19. 10.2337/diacare.28.11.2613

4. Holman N, Young B, Gadsby R. Current prevalence of type 1 and type 2 diabetes in adults and children in the UK. Diabet Med. 2015;32(9):1119–20. 10.1111/dme.12791

5. Saito I, Kokubo Y, Yamagishi K, et al. Diabetes and the risk of coronary heart disease in the general japanese population: The Japan public health center-based prospective (JPHC) study. Atherosclerosis. 2011;216(1):187–91. 10.1016/j.atherosclerosis.2011.01.021

International Diabetes Federation. Diabetes and cardiovascular disease 2016 [cited
 2019 January]. Available from: <u>www.idf.org/cvd</u>.

Dean J. Organising care for people with diabetes and renal disease. J Ren Care.
 2012;38 Suppl 1:23 –9. 10.1111/j.1755-6686.2012.00272.x

King P, Peacock I, Donnelly R. The UK prospective diabetes study (UKPDS): clinical and therapeutic implications for type 2 diabetes. Br J Clin Pharmacol. 1999;48(5):643–8.
 10.1046/j.1365-2125.1999.00092.x

9. UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998;352(9131):837–53.

10. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. N Engl J Med. 2007;356(24):2457–71.

10.1056/NEJMoa072761

11. United States Food and Drug Administration. Diabetes mellitus -evaluating cardiovascular risk in new antidiabetic therapies to treat type 2 diabetes 2008 [cited 2019 November]. Available from: <u>https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diabetes-mellitus-evaluating-cardiovascular-risk-new-antidiabetic-therapies-treat-type-2-diabetes</u>.

12. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med. 2015;373(22):2117–28.

10.1056/NEJMoa1504720

13. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med. 2017;377(7):644–57. 10.1056/NEJMoa1611925

14. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2019;380(4):347–57. 10.1056/NEJMoa1812389

15. Cannon CP, Pratley R, Dagogo-Jack S, et al. Cardiovascular Outcomes with Ertugliflozin in Type 2 Diabetes. N Engl J Med. 2020;383(15):1425-35.

10.1056/NEJMoa2004967

 Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. Lancet. 2019;394(10193):121–30. 10.1016/S0140-6736(19)31149-3

Hernandez AF, Green JB, Janmohamed S, et al. Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial. Lancet. 2018;392(10157):1519–29.
10.1016/S0140-6736(18)32261-X

18. Marso SP, Bain SC, Consoli A, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2016;375(19):1834–44.

10.1056/NEJMoa1607141

19. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2016;375(4):311–22. 10.1056/NEJMoa1603827

20. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med. 2019;381:1995–2008.

10.1056/NEJMoa1911303

21. Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2020. 10.1056/NEJMoa2024816

22. Packer M, Anker SD, Butler J, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med. 2020. 10.1056/NEJMoa2022190

23. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med. 2019;380(24):2295–306. 10.1056/NEJMoa1811744

24. Janssen-Cilag International NV. Invokana summary of product characteristics 2020 [cited 2020 01 October]. Available from: <u>https://www.ema.europa.eu/en/documents/product-</u> information/invokana-epar-product-information_en.pdf.

25. AstraZeneca AB. Foxiga summary of product characteristics 2020 [cited 2020 1 October]. Available from: <u>https://www.ema.europa.eu/en/documents/product-information/forxiga-epar-product-information_en.pdf</u>.

26. B.V. MSD. Steglatro summary of product characteristics 2020 [cited 2020 1 October]. Available from: <u>https://www.ema.europa.eu/en/documents/product-information/steglatro-</u> <u>epar-product-information_en.pdf</u>.

27. Boehringer Ingelheim International GmbH. Jardiance summary of product characteristics 2020 [cited 2020 1 October]. Available from:

https://www.ema.europa.eu/en/documents/product-information/jardiance-epar-productinformation_en.pdf.

28. Holman N, Knighton P, Kar P, et al. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. Lancet Diabetes Endocrinol. 2020;8(10):823-33. 10.1016/S2213-8587(20)30271-0

29. Office for National Sattistics. Population estimates for the UK 2019 [cited 2019December]. Available from:

https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/population estimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland.

30. Lambeth Council. Demography fact sheet 2017 [cited 2019 November]. Available from: https://www.lambeth.gov.uk/sites/default/files/ssh-demography-factsheet-2017.pdf.

31. Chamley M. Community diabetes in South London. Br J Diabetes. 2015;15(2):78–82.

Table 1. Trials demonstrating major adverse cardiovascular events or

hospitalization for heart failure benefit

Trial ^a	Glucose-lowering	CV risk status of	MACE HR	HHF HR
	agent	trial population	(95% CI)	(95% CI)
	SGLT2is			
EMPA-REG	Empagliflozin	≥ 99% with	0.86 (0.74–	0.65 (0.50–
(12)		CVD	0.99)	0.85)
CANVAS	Canagliflozin	66% with CVD	0.86 (0.75–	0.67 (0.52–
Program (13)			0.97)	0.87)
DECLARE-	Dapagliflozin	41% with CVD	0.93 (0.84–	0.73 (0.61–
TIMI 58 (14)			1.03)	0.88)
VERTIS CV	Ertugliflozin	100% with	0.97 (0.85–	0.70 (0.54–
(15)		ACVD	1.11) ^b	0.90)
	GLP1RAs			
REWIND (16)	Dulaglutide	31% with CVD	0.88 (0.79–	0.93 (0.77–
			0.99)	1.12)
Harmony	Albiglutide	99% with CVD	0.78 (0.68–	NA
Outcomes			0.90)	
(17)				
SUSTAIN-6	Semaglutide	83% with	0.74 (0.58–	1.11 (0.77–
(18)		CVD/CKD	0.95)	1.61)
LEADER (19)	Liraglutide	High CV risk	0.87 (0.78–	0.87 (0.73–
			0.97)	1.05)

^aBenefit in MACE or HHF as defined by a HR for which the upper CI did not pass

^b95.6% confidence interval

ACVD, atherosclerotic cardiovascular disease; CANVAS: Canagliflozin Cardiovascular Assessment Study; CI: confidence interval; CKD: chronic kidney disease; CV: cardiovascular; CVD: cardiovascular disease; DECLARE-TIMI 58: Dapagliflozin Effect on Cardiovascular Events—Thrombolysis in Myocardial Infarction; EMPA-REG: Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes; GLP1RA: glucagon-like peptide 1 receptor agonist; Harmony Outcomes: Albiglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Cardiovascular Disease; HHF: hospitalization for heart failure; HR: hazard ratio; LEADER: Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results; MACE: major adverse cardiovascular event; NA: not available; REWIND: Dulaglutide and Cardiovascular Outcomes in Type 2 Diabetes; SGLT2i: sodium–glucose co-transporter 2 inhibitor; SUSTAIN-6: Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes; VERTIS CV, Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular.

Table 2. Findings of dedicated renal or heart failure outcomes trials involvingSGLT2is

Trial	Glucose- lowering	Key baseline	Primary endpoint	HR (95% CI)				
	agent	characteris		(0070 01)				
	-	tics						
Dedicated renal outcomes trials								
CREDENCE	Canagliflozin	Mean eGFR	Composite of: doubling of	0.70				
(23)		56.2	serum creatinine, ESRD,	(0.59–				
		mL/min/1.73	or CV or renal death	0.82)				
		m ²		<i>p</i> =				
				0.00001				
Dapa-	Dapagliflozin	Mean eGFR	Composite of: sustained	0.61				
CKD (21) ^a		43.1	50% decrease in eGFR,	(0.51–				
		mL/min/1.73	ESRD, or CV or renal	0.72)				
		m²	death	<i>p</i> < 0.001				
Dedicated heart failure outcomes trials								
Dapa-	Dapagliflozin	Mean LVEF	Composite of: worsening	0.74				
HF(20) ^a		31.1 %	heart failure or CV death	(0.65–				
				0.85)				
				<i>p</i> < 0.001				

EMPEROR	Empagliflozin	Mean LVEF	Composite of:	0.75
reduced		27.4%	hospitalization for heart	(0.65–
(22) ^a			failure or CV death	0.86)
				<i>p</i> < 0.001

^aTrial populations included patients who did not have type 2 diabetes CI, confidence interval; CREDENCE, Evaluation of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Participants with Diabetic Nephropathy; CV, cardiovascular; Dapa-CKD; A study to evaluate the effect of dapagliflozin on renal outcomes and Cardiovascular mortality in patients with chronic kidney disease; DAPA-HF, Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure; eGFR, estimated glomerular filtration rate; EMPEROR; Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction; ESRD, endstage renal disease; HR, hazard ratio; LVEF, left ventricular ejection fraction

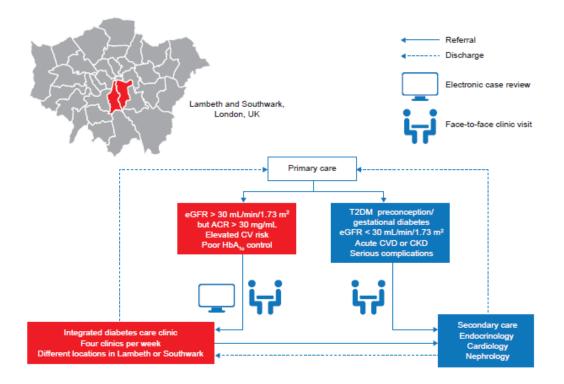


Fig. 1 Patient flow through the Lambeth integrated diabetes care pathway for renal disease

ACR: albumin: creatinine ratio; CKD: chronic kidney disease; CV: cardiovascular; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; HbA_{1c}: glycated haemoglobin; T2DM: type 2 diabetes mellitus

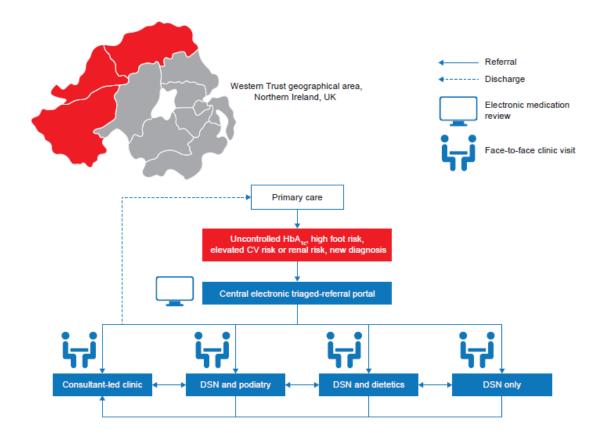


Fig. 2 Patient flow through the Western Trust integrated diabetes care programme CV: cardiovascular; DSN: diabetes specialist nurse; HbA_{1c}: glycated haemoglobin