NICE National Institute for Health and Care Excellence

Consultation report: CKD SGLT2i

Consultation period: 13 April – 15 May 2023

Date of Indicator Advisory Committee meeting: 6 June 2023

Commercial in-confidence information has been redacted.

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Chronic kidney disease: SGLT2 inhibitors

Three options were presented for consultation based on NICE guidance and assumptions about the use of SGLT2 inhibitors in practice:

IND2022-142: The percentage of patients on the CKD register and currently treated with an ARB or ACE inhibitor who are also currently treated with an SGLT2 inhibitor if they have either:

- a urine ACR of 22.6 mg/mmol or more
- type 2 diabetes and a urine ACR over 30 mg/mmol.

IND2022-135: The percentage of patients on the CKD register and currently treated with an ARB or an ACE inhibitor who are also currently treated with an SGLT2 inhibitor if they have either:

- a urine ACR of 22.6 mg/mmol or more
- type 2 diabetes and a urine ACR 3 mg/mmol or more.

IND2022-143: The percentage of patients on the CKD register and currently treated with an ARB or an ACE inhibitor who are also currently treated with an SGLT2 inhibitor if they have either:

- a urine ACR of 22.6 mg/mmol or more
- type 2 diabetes.

Rationale

Chronic kidney disease (CKD) is a long-term condition characterised by abnormal function or structure (or both) and is an important public health problem associated with significant morbidity, premature mortality and high health care costs. Management of CKD aims to prevent or delay disease progression and the development of complications. SGLT2 inhibitors can be used as an add on to standard care with ACE inhibitors and angiotensin receptor blockers (ARBs) for people with CKD as there is evidence for benefits in terms of CKD progression, cardiovascular events and mortality.

Summary of consultation comments

Stakeholders welcomed the inclusion of an indicator on SGLT2 inhibitors, commenting that it will have a positive impact on CKD progression, cardiovascular events and mortality.

Some concerns were highlighted:

- The numbers of patients eligible for treatment with an SGLT2 inhibitor who will be excluded from the denominator due to compromises made in the draft indicators. One stakeholder estimated this could be 50% of those eligible:
    - Patients with eGFR between 60 and 75 are excluded but are eligible for treatment according to NICE TA775.
    - Patients without an ACR test will not be included and the impact of the low rate of ACR testing in general practice may be great.
    - Poor coding of type 2 diabetes, diabetic kidney disease and CKD means that eligible patients may not be included in the indicator.
- There is potential for mismatch between the existing QOF indicator for ACE inhibitors in patients with diabetes, with some patients eligible for ACE inhibitors or ARBs but not SGLT2 inhibitors.
- Stakeholders suggested an indicator should use SNOMED cluster codes for microalbuminuria (MAL_COD) or proteinuria (PRT_COD) and ACR category (i.e., CKD G3 to 5 A3, part of CKD_COD). They also note there are limitations associated with this suggestion.
- The risk of diabetic ketoacidosis associated with use of SGLT2 inhibitors.
- The potential for burden of workload on general practice associated with indicators IND 2022-135 or IND 2022-143. Stakeholders suggest a stepwise approach with introduction of IND 2022-142 at first.
- Stakeholders suggested that the payment threshold could be adjusted to reflect the denominator rather than the CKD register size, to overcome some of the issues highlighted above.

Stakeholders also suggested a number of exclusions that should be applied to the indicator (patients with type 1 diabetes, diabetic ketoacidosis, secondary pancreatitis diabetes or Fournier's gangrene). They also suggested it should include a focus on underserved groups.

Stakeholders noted that use of SGLT2 inhibitors in CKD is a developing area with trial data available for an alternative SGLT2 inhibitor (empagliflozin) and a NICE technology appraisal in development. This may specify alternative thresholds for eGFR and urine ACR levels. One stakeholder suggested it may be preferable to pause the indicator development until publication of the NICE technology appraisal on empagliflozin for treating CKD, but another was concerned about a delay.

Specific questions included at consultation

7. The indicators are proposed for measurement at a general practice level. Are SGLT2 inhibitors prescribed in general practice for management of chronic kidney disease in adults without type 2 diabetes?

Stakeholders had a mixed view on whether SGLT2 inhibitors are prescribed by general practitioners. They noted that prescribing for type 2 diabetes is almost routine practice but less so for CKD. They also commented that some areas are advised that SGLT2 inhibitors are only suitable for GP prescribing following recommendation/initiation by a specialist. Stakeholders suggested a need for upskilling primary care and proposed multidisciplinary team approach for implementation of the indicator.

8. The indicators are based on recommendations in NICE's guideline on type 2 diabetes in adults and NICE's technology appraisal on dapagliflozin for treating CKD. The proposed indicators define the population according to presence of CKD, type 2 diabetes and urine albumin concentration. Of the three populations with CKD and type 2 diabetes included in the indicator options, who would be offered an SGLT2 inhibitor to manage their CKD according to your local practice and would be suitable for inclusion in the denominator for the indicator?

- patients with type 2 diabetes and urine ACR over 30 mg/mmol only
- patients with type 2 diabetes and urine ACR 3 mg/mmol or more only
- patients with type 2 diabetes, regardless of urine ACR result.

Stakeholders supported the third option as this does not rely on an ACR result for patients with type 2 diabetes and aligns with the NICE technology appraisal for dapagliflozin (TA775). They noted that the options may cause confusion. This is currently the only SGLT2 inhibitor recommended by NICE for treatment of CKD. They noted that using option 1 would restrict use of SGLT2 inhibitor in patients with type 2 diabetes when compared with those without. They also noted that many patients with CKD and type 2 diabetes should have an SGLT2 inhibitor based on an increased risk of cardiovascular disease (QRISK score).

9. The indicators use the last recorded urine ACR for inclusion in the denominator and so patients with an ACR that has improved from baseline will not be included if the last ACR is below the inclusion threshold. Is this approach acceptable?

Stakeholders mostly agreed that using the last recorded ACR is not acceptable, with one stakeholder agreeing that the specified approach is appropriate. Comments suggested using ACR results would exclude a number of eligible patients due to low ACR testing rates. They also noted potential for differential impact as ACR testing rates differ between primary care practices.

Stakeholders commented that SGLT2 inhibitor treatment is intended for use in patients with persistently raised ACR and the last ACR result is not a good indicator of this. Some patients may have a raised ACR due to UTI, a one-off raised ACR and people who do have proteinuric kidney disease but are effectively treated. Stakeholders also noted outcomes from the EPMA kidney study that demonstrate benefits to patients with low levels of albuminuria.

Considerations for the advisory committee

The committee is asked to consider:

- whether the variation in general practice prescribing of SGLT2 inhibitors will limit implementation and acceptability of an indicator
- if the compromises made, such as using the QOF CKD register and last ACR result, are acceptable
- which of the indicators are suitable for progression, considering the stakeholder comments on ACR measurement and the NICE recommendations underpinning the indicators
- what conditions should be excluded from the indicator specification
- whether to progress an indicator at this time or wait until there are NICE recommendations on other SGLT2 inhibitors (empagliflozin)[1].

[1] NICE are appraising the clinical and cost effectiveness of empagliflozin within its marketing authorisation for treating chronic kidney disease, final guidance is expected in February 2024

Appendix A: Consultation comments

ID	Proforma question no.	Stakeholder organisation	Comment	NICE responses
1	General	BMA	In the opinion of BMA's General Practitioners Committee (England), QOF needs a wholesale review, and introducing new indicators and tinkering with old ones does not fit with the agreement to carry out a wholesale review made by NHSE and DHSC. In addition, when patients have multiple co-morbidities, single disease measures can be challenging. It would be helpful if NICE could advise whether there are conditions or medications for other conditions, that commonly occur with the single disease, that will result in a caution flag when co-prescribing, and if there are, provide guidance on whether to prescribe.	Thank you for your comment. NICE indicators are supported by evidence-based recommendations and measure outcomes that reflect quality of care; they are not advisory products. Users should follow clinical guidance when prescribing. Personalised care adjustments could be used when prescribing an SGLT2 inhibitor is inappropriate.
2	General	Diabetes UK	We welcome an incentive which has an impact on the treatment options available to people living with Diabetes and chronic kidney disease. This incentive would improve outcomes as research has shown that in people with type 2 diabetes and kidney disease SGLT2 inhibition can slow the progression of chronic kidney disease and reduce cardiovascular problems.	Thank you for your comment.

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3	General	Diabetes UK	We are concerned that poor clinical coding of diabetic kidney disease could be a barrier to implementation of this QOF.	Thank you for your comment. The NICE indicator advisory committee discussed coding issues and agreed that this could impact on patient inclusion in the denominator, however, they suggested the indicator had the potential to improve coding by increasing recognition of chronic kidney disease.
4	General	Diabetes UK	It is important that individuals with type 2 diabetes that are prescribed SGLT2 inhibitors have close monitoring and education from their diabetes team due to the risk of Diabetic Ketoacidosis.	Thank you for your comment. We agree that clinical guidance should be followed when prescribing SGLT2 inhibitors. Personalised care adjustments could be used when prescribing an SGLT2 inhibitor is inappropriate.
5	General	NHS England	IND2022-143: The percentage of patients on the CKD register and currently treated with an ARB or an ACE inhibitor who are also currently treated with an SGLT2 inhibitor if they have either: • a urine ACR of 22.6 mg/mmol or more • type 2 diabetes.	Thank you for your comment. The NICE indicator advisory committee progressed IND2022-135 as it is based on recommendations in NG28 on type 2 diabetes in adults. They agreed that implementation of the indicator should be accompanied

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			Of the three options presented for consultation I would suggest this is the most appropriate for the following reasons: 1. The completion of the urine ACR care process is generally poor and the other two options would lead to people with type 2 diabetes at high risk of progression of CKD and CV events missing out inappropriately if their urine ACR is not routinely checked 2. Most middle aged and older people with type 2 diabetes and CKD, will have a QRISK score higher than 10% and should have an SGLT2 inhibitor anyway (as per NG28) On a more general note, the reintroduction of QOF indicators for annual urine ACR measurements for people with diabetes and/or CKD should be considered for next year in order to improve care and coding for people with diabetes and/or CKD.	by NM109 on annual ACR measurement.
6	General	NHS England – Learning Disability and Autism Programme	• If urinary ACR continues to be a requisite in diagnostic process then this should also be part of the SGLT2 pathway, however for simplicity in primary care and what I am aware of from the evidence this should probably be for all T2DM…It will save complication in process on reviewing should a patient tip into an ACR criteria. • There will be a need for upskilling primary care and proposed MDT approach for working this indicator through.	Thank you for your comment. The NICE indicator advisory committee agreed that implementation of the indicator should be accompanied by NM109 on annual ACR measurement. The NICE indicator advisory committee progressed IND2022-135 as it is

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			Can part of this indicator also being identification of which underserved groups are most likely to be impacted so can be targeted in primary care.	based on recommendations in NG28 on type 2 diabetes in adults.
7	General	NHS England – Primary Care Team	• SLGT2 are prescribed for diabetes – almost routinely by GPs – less so for CKD. • In some areas the medicines management advice is 'Suitable for GP prescribing following recommendation/initiation by specialist'. This may mean that where there are long waits for access to specialist clinics (typically more deprived areas where disease will likely be more prevalent) patients may wait to get initiated as a consequence of delayed access to secondary care. Perhaps adding an exclusion – i.e., referred to specialist for advice?	Thank you for your comment. The NICE indicator advisory committee discussed prescribing of SGLT2 inhibitors and agreed that this is likely to increase in general practice and noted local support from secondary care may be available to support prescribing.
8	General	NHS England – Renal Services Transformation Programme	1) All 3 proposed indicators are reasonable. 2) The EMPA-Kidney data provides a rationale for SGLT2i in patients with CKD with eGFR > 20mls/min. https://www.nejm.org/doi/full/10.1056/NEJMoa2204233 This threshold is lower than that seen in the DAPA-CKD study. The NICE TA for empagliflozin is awaited The EMPA-Kidney study also included patients that did not have albuminuria. Pre-specified analysis of the subgroup without proteinuria did not meet the primary endpoint,	Thank you for your comment. We are aware of the NICE technology appraisal for empagliflozin for treating chronic kidney disease in development. The published indicator will be reviewed with any change in published recommendations. The NICE indicator advisory committee agreed that implementation of the indicator should be accompanied by NM109 on annual ACR measurement. The NICE

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			however event rates would have been expected to be lower. Figure S4 supplementary data. This also supports the importance of albuminuria in predicting events. Patients in EMPA-Kidney without albuminuria had an improvement in the mean annual rate of change in estimated GFR (eGFR slope). The UKKA are currently consulting on an update to the UKKA SGLT2i guidelines published in 2021 (https://ukkidney.org/health-professionals/guidelines/guidelines-commentaries). The changes include removing the requirement for urine ACR in patients with eGFR 20 to 45 and 'suggest' hat SGLT2i can be used in this cohort if they have progressive CKD. The NICE TA will provide clarity on whether this is a reasonable position nationally. Recommendation: it may be preferable to wait for the empagliflozin TA as this may negate the need for urine ACR, thereby creating a simpler indicator which may be more feasible. The risk of removing uACR is that this may discourage uACR collection leading to the continued delayed diagnosis that we experience at the moment. The community may wish to focus on improving uACR uptake in primary care. 3) The opportunity to treat patients with albuminuria with an eGFR up to 75mls/min is still important for early prevention of	indicator development programme currently do not plan to develop an indicator on a register for people with CKD stages 1 and 2. The indicator advisory committee in June 2022 discussed the potential for large workloads associated with stage 1 and 2 CKD. The Quality and Outcomes Framework guidance also notes that people with GFR less than 60 ml/min/1.73m^2 are more likely to have hypertension, diabetes and CVD compared to people with GFR more than 60 ml/min/1.73m^2.

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			progression particularly as uACR is the strongest predictor of outcomes as reflected in the KFRE. Recommendation: develop register for CKD 1- 5 with or without proteinuria	
9	General	Royal College of General Practitioners	The RCGP is calling for an immediate suspension of QOF during the current crisis with the need of a review to identify 5-10 indicators that have the greatest evidence of impact on patient outcomes that could be retained once QOF is re-introduced. Over the years, QOF has become painfully detailed in terms of reporting, both clinically and administratively, causing increasing frustration for GPs. This can divert the attention of GPs away from the patients sitting in front of them in consultations. It is also likely to be driving an increase in the number of unnecessary appointments, which may be more about ticking a box to reach a target rather than looking at what is needed by the individual patient.	Thank you for your comment.
10	General	UK Kidney Association – endorsed by Royal College of Physicians	The UK Kidney Association (UKKA) welcomes the consideration of an indicator related to the use of SGLT2 inhibitors in people with CKD. We highlight that the data from all the cardiovascular prevention studies and all the kidney specific studies utilising SGLT2 inhibitors suggest a benefit of between 30 to 40% in relation to hard renal endpoints. This is seen when these agents are used in addition to inhibitors of the renin-angiotensin-aldosterone system (RAASi) and need to be seen in the context that RAASi are standard of care for	Thank you for your comment.

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			kidney disease even though the original studies with RAASi demonstrated that they have lower benefit in relation to hard renal endpoints than seen with SGLT2 inhibitors. Wider use of SGLT2 inhibitors is therefore likely to make a significant difference in progression of chronic kidney disease and subsequent need for end-stage kidney failure treatment.	
11	General	UK Kidney Association – endorsed by Royal College of Physicians	The demonstration of the benefit of SGLT2 inhibitors in relation to CKD progression was originally seen in the first major cardiovascular outcome trial for empagliflozin in 2014. Subsequently there have now been 3 renal specific studies the first of which was published in April 2019. The percentage of patients who are now on appropriate therapy for prevention of CKD progression is disappointingly low 4 years after this study was published. The UKKA would be concerned if the development of this indicator is delayed because there is only one current SGLT2 inhibitor licensed for use in CKD.	Thank you for your comment. The indicatory advisory committee approved publication of IND2022-135.
12	General	UK Kidney Association – endorsed by Royal College of Physicians	Of the 3 indicators proposed the UKKA would strongly recommend indicator IND2022-143 although indicator 135 would be acceptable for the present. Indicator 142 would be perverse in that it restricts provision of SGLT2i in people with type 2 diabetes more tightly than those without type 2 diabetes.	Thank you for your comment. The indicatory advisory committee approved publication of IND2022-135.
13	General	UK Kidney Association – endorsed by Royal College of Physicians	It is highlighted that the outcome from the EMPA kidney study and previous studies demonstrate the benefits to people with type 2 diabetes with very low/normal levels of albuminuria. It is likely therefore that if a person with type 2	Thank you for your comment.

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			diabetes is already on the CKD register with impaired kidney function, they would benefit from an SGLT2 inhibitor irrespective of the presence of albuminuria and this is consistent with other NICE recommendations.	
14	General	UK Kidney Association – endorsed by Royal College of Physicians	The implementation of this indicator will improve outcomes for people with CKD, however it is very important to highlight that if any indicator is reliant on the measurement of urine albumin creatinine ratio it would be perverse not to have a QOF indicator relating to increasing the utilisation of urine albumin creatinine ratio in people at risk of CKD or with CKD	Thank you for your comment. The NICE indicator advisory committee agreed that implementation of the indicator should be accompanied by NM109 on annual ACR measurement.
15	General IND 2022-135	Clinical Digital Resources Collaborative	Your proposals for the CKD indicators will cause very significant problems and risk of clinical harm. IND2022-135 aligns most closely to the NICE guidance for SGLT2 use - although it excludes patients with • CKD and ACR>=22.6 and eGFR 60-75. • T2DM and persistent ACR>=3 with eGFR >=60 But there are major problems with the way you have structured it. 1. SGLT2 treatment is intended for use for people who have persistently raised ACR, not based on the last reading. The last ACR reading will often not be a useful indicator e.g., patients with a UTI, patients with	Thank you for your comment. The indicator advisory committee discussed whether the last ACR reading would be appropriate. Personalised care adjustments could be used if a patient is not suitable for inclusion in the indicator. The indicator advisory committee discussed coding issues and agreed that this could impact on patient inclusion in the denominator, however, they suggested the indicator had the potential to improve coding by increasing recognition of chronic kidney disease. NHS England

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			a one-off raised ACR, patients who do have proteinuric kidney disease but who are effectively treated (RAS blockade, SGLT2i) leading to a reduction in renal protein loss. In the same way that you don't use last eGFR to define CKD G stage in this indicator, you shouldn't use last ACR to define CKD A stage. 2. The number of people with diabetic kidney disease whose proteinuria/microalbuminuria is 'in remission' is high. In a sample of ~500K patients in County Durham there are 6172 diabetic patients with coding suggesting diabetic renal disease in line with IND2022-135 (i.e., CKD A2/A3 codes or codes in the MAL/PRT QoF clusters). This is 16% of all diabetics. However, 1962 (31.8%) of these patients did not have a last ACR result <3. i.e., they would be inappropriately removed from the denominator. 3. Your denominator does not include diabetic patients with a persistent ACR >=3 who don't have CKD3-5, despite NICE recommending these patients for SGLTi therapy. In a sample of ~500K patients in County Durham 3809 (10.2%) diabetic patients have coded evidence of persistent microalbuminuria/albuminuria but do not have a code for CKD G3-5. This number reduces to 3310 if you exclude people with coded CKD G3-5 OR the last eGFR suggests possible CKD G3-5 – but this is still 8.8% of diabetics.	have drafted business rules that suggest this indicator is feasible. The accompanying report suggests some SNOMED code clusters that could be used to extract patient data. We have also included the codes suggested in your comments in the validity assessment for this indicator.

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			4. The number of people with non-diabetic proteinuric CKD3-5 whose proteinuria is 'in remission' is high. In a sample of ~500K patients in County Durham there are 581 (0.1% of the population) patients with coded CKD G3-5 A3 (i.e. ACR persistently >30) who don't also have diabetes. Of these 368 (63.3) do not have their last ACR reading >=22.6 Other less significant points: 5. There is significant problem with under-coding of CKD which you are well aware of. 6. There is a problem with coding diabetes subtype. In a 500K County Durham sample (where there has been considerable effort to improve this), 1.3% of diabetic patients do not have a subtype and 2.3% have multiple subtypes. 7. It will be important to include the follow criteria as exclusions to remove people from the denominator. Type 1 diabetes Diabetic ketoacidosis Fournier's gangrene If you don't do this, there is a risk patients will be included in work to do lists and inappropriately and dangerously given SGLT2i therapy.	

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			In summary, the proposed indicator will cause many problems because the denominator will be wildly inaccurate: 1. Many patients whose proteinuria is in remission will be inappropriately excluded. 2. Many patients with diabetic kidney disease in the CKD G1 and G2 categories will be inappropriately excluded. 3. Some patients with one-off or spurious raised ACR (e.g. due to UTI) will be inappropriately included. 4. Some patients may be included who should definitely not be given SGLT2i therapy. 5. There will be a confusing mismatch between the existing DM QoF indicator for ACEI/A2RB therapy e.g., many patients will be flagged as eligible for ACEi/A2RB but not for SGLT2i, despite the latter being indicated. In total I estimate that 50% of people who should be in the denominator will be inappropriately excluded by your current plans if you use IND2022-135 My recommendation to deal with these issues: 1. The denominator should be: The number of patients on the CKD register with ARB or an ACE inhibitor prescribed in the last 6 months and either:	

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			• No diabetes and current CKD G3-5 A3 code • Type 2 diabetes and a code in the MAL* or PRT cluster Both the groups above should then exclude patients with type 1 diabetes, secondary pancreatic diabetes, diabetic ketoacidosis, Fournier's gangrene. • *It is important that the MAL cluster should be updated to include CKD Gx A2 codes which it currently doesn't include (despite the PRT cluster including CKD Gx A3 codes). If this isn't done, then these codes should be added i.e. second criteria should be Type 2 diabetes and a code in the MAL* or PRT cluster 2. To get around the problem of poor coding, the payment should be adjusted for the size of the denominator of this indicator and not the total CKD3-5 register. This will promote the uptake of eGFR, ACR testing and appropriate coding of diabetes and CKD. (This should also be done for the current QoF indicator for ACEi/A2RB used for diabetes with ACR>=3). This is critical to prevent gaming of the system. 3. This solution does leave a small gap i.e., patients without diabetes, with CKD G3-5 and ACR persistently in the 22.6- 30 range. The numbers of patients affected is tiny. In a sample of 500K patients in County Durham: the number of patients with:	

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			• CKD G3-5 (either based on coded information or last eGFR) AND • Last ACR >=22.6 • No diabetes AND • Not coded with CKD Gx A3- AND • Last ACR is not >30 (i.e., should be coded as A3, if persistent) ……is 119 and some of these patients will be excluded once repeated eGFR or ACR measurements are conducted. In my own practice (6060 patients) where the prevalence of diabetes, CKD3-5 and hypertension is very high (7.3%, 4.5%, 21.7% resp) and the ACR testing coverage is high (70% of people with CKD1-5, hypertension, ASCVD, DM and heart failure have had an ACR in the last 12 months), the number is 1. There is also a very small group of people with non-diabetic CKD G2 (eGFR 60-75) and persistently raised ACR >=22.6 who are also not covered, but these have never been covered by your proposals anyway.	
16	General ID 2022-142	Royal College of General Practitioners	The RCGP would recommend 142 as the preferred choice. If either of the other 2 options were chosen the burden of workload on primary care would be significant. We would recommend a stepwise approach to introducing this into QOF to ensure that those who will benefit most will be treated first. i.e ACR>30 and DM2.	Thank you for your comment. The indicator advisory committee approved IND2022-135 for publication. Data from CPRD Aurum suggests less than 20 patients per 10,000 practice would be included in the

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				denominator and so the indicator is not suitable for inclusion in QOF.
17	General IND 2022-143	Primary Care Cardiovascular Society	Of the three options presented we would recommend this indicator (IND2022-143) - i.e. no ACR threshold for people with diabetes. This aligns to current guidance for dapagliflozin in CKD. This also applies to the prescribing of SGLT2i for heart failure patients (i.e., without the need for ACR/ no ACR threshold) We agree with the use of the last recorded urine ACR for inclusion in the denominator and so patients with an ACR that improved from baseline will not be included if the last ACR is below the inclusion threshold. SGLT2i in CKD should be prescribed in primary care as many of this cohort will not be under specialist services. Primary needs a contractual enabler to give SGLT2i in non-diabetics in CKD and in heart failure.	Thank you for your comment. The indicator advisory committee approved IND2022-135 for publication based on recommendations in NICE's guideline on type 2 diabetes in adults and NICE's technology appraisal of dapagliflozin for treating chronic kidney disease.
18	7	AstraZeneca	SGLT2 inhibitors are prescribed in general practice for the management of chronic kidney disease (CKD) in adults without type 2 diabetes (T2D). AstraZeneca's position is that the use of SGLT2 inhibitors in people with CKD is to be included into the general practice indicator suitable for use in the Quality and Outcomes Framework (QOF) as an SGLT2 inhibitor can be used as an add on to standard care with	Thank you for your comment.

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			angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) in this patient population. This is based on benefits in terms of CKD progression, cardiovascular events and mortality.[1] This would ensure that eligible patients are prescribed an SGLT2 inhibitor, thus, would benefit from optimised treatment outcomes, including benefits listed above (i.e., CKD progression, cardiovascular events and mortality). Currently, dapagliflozin is the only SGLT2 inhibitor licensed in adults for the treatment of CKD[2, 3] and recommended by NICE.[1] Dapagliflozin, is routinely commissioned across the primary and secondary care treatment settings for patients with CKD, as detailed above,[1] in addition to T2D,[4-6] and heart failure with reduced ejection fraction (HFrEF).[7] Thus, clinicians across care settings have considerable clinical experience with prescribing dapagliflozin. A 2023 UK Clinical Practice Research Datalink (CPRD) study, demonstrates that dapagliflozin is used in general practice for the management of CKD in [redacted] of patients without co-morbid T2D, in [redacted] of patients with co-morbid T2D, and in [redacted] of patients with co-morbid heart failure.[8] Therefore, aligning the QOF indicators with the current treatment pathway will lead to improvements in care and outcomes for patients. Alternatively to the general practice indicator suitable for use in the QOF and in the case where QOF would be removed, inclusion of the CKD SGLT2 inhibitor indictors into the Directed Enhanced Service (DES) is suitable, thus, would	

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			ensure eligible patients are prescribed an SGLT2 inhibitor to benefit from optimised treatment outcomes. 1. National Institute for Health and Care Excellence (NICE). Dapagliflozin for treating chronic kidney disease [TA775]. Available at: https://www.nice.org.uk/guidance/ta775 [accessed 02 May 2023]. 2022. 2. Electronic Medicines Compendium (EMC). Forxiga 10 mg film-coated tablets [SmPC]. Available at: https://www.medicines.org.uk/emc/product/7607/smpc [accessed 06 May 2023]. December 2022. 3. Electronic Medicines Compendium (EMC). Jardiance 10 mg film-coated tablets [SmPC]. Available at: https://www.medicines.org.uk/emc/product/5441/smpc [accessed 02 May 2023]. February 2023. 4. National Institute for Health and Care Excellence (NICE). Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes [TA390]. Available at: https://www.nice.org.uk/guidance/ta390 [accessed 01 June 2022]. 2016. 5. National Institute for Health and Care Excellence (NICE). Dapagliflozin in combination therapy for treating type 2 diabetes [TA288]. Available at: https://www.nice.org.uk/guidance/ta288 [accessed 01 June 2022]. 2016. 6. National Institute for Health and Care Excellence (NICE). Dapagliflozin in triple therapy for treating type	

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			2 diabetes [TA418]. Available at: https://www.nice.org.uk/guidance/ta418 [accessed 01 June 2022]. 2016. 7. National Institute for Health and Care Excellence (NICE). Dapagliflozin for treating chronic heart failure with reduced ejection fraction [TA679]. Available at: https://www.nice.org.uk/guidance/ta679 [accessed 28 April 2022]. 2021. 8. AstraZeneca UK Ltd. Data on File. ID: REF-188996 May 2023.	
19	7	BMA	7. We don't know whether practices across the country prescribe SGLT2 inhibitors without type 2 DM, so we cannot comment.	Thank you for your comment.
20	7	National Kidney Federation	The indicators are proposed for measurement at a general practice level. Are SGLT2 inhibitors prescribed in general practice for the management of chronic kidney disease in adults without type 2 diabetes? Not as we know.	Thank you for your comment.
21	7	NHS England	Yes, but not consistently. Note that coding of CKD is suboptimal though clinicians can usually ascertain CKD status from looking at results in the clinical system. It may be that an indicator helps improve coding.	Thank you for your comment.
22	7	Royal College of General Practitioners	SGLTi are increasing in the amount they are prescribed but most commonly for those with DM2 and are not commonly prescribed for CKD alone. This would therefore be a significant shift for primary care and require training and upskilling and investment in CPD for GPs and their teams.	Thank you for your comment. The NICE indicator advisory committee discussed prescribing of SGLT2 inhibitors and agreed that this is likely to increase in general practice and noted local

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				support from secondary care may be available to support prescribing.
23	8	AstraZeneca	As outlined in the answer to question 7 above, dapagliflozin is currently the only SGLT2 inhibitor indicated and recommended by NICE for both T2D and CKD.[2, 3] Consequently, if a patient with CKD is also diagnosed with T2D and eligible for treatment with a SGLT2 inhibitor, dapagliflozin is the treatment of choice. This applies regardless of urine albumin to creatinine ratio (uACR) results as initiation of dapagliflozin in T2D is irrespective of uACR. It is important to note that not all patients with CKD are referred for uACR testing in order not to burden the NHS with over testing. In the National CKD Audit, it is reported that 53.9% of people with diabetes are annually referred for uACR tests by their general practitioner (GP) with a wide variation between practices in whether tests have been used in the last year.[9] As illustrated by the results of a 2021 analysis of the UK CPRD, [redacted] of patients with CKD and T2D had a recorded uACR.[10] Out of those with CKD, T2D and recorded uACR, [redacted] had a uACR of 3mg/mmol or more and [redacted] had a uACR of over 30mg/mmol.[10] When under testing is accounted for, the proportions of patients with CKD and T2D dropped to [redacted] of patients having an uACR of 3mg/mmol or more and [redacted] having an uACR of over 30mg/mmol.[10] Thus, defining the populations with CKD and T2D based on any uACR thresholds, may risk excluding a	Thank you for your comment. The indicator advisory committee approved IND2022-135 for publication.

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			substantial proportion of patients with both conditions eligible to dapagliflozin as uACR may not be available for all patients. Therefore, for the reasons outlined above, of the three populations with CKD and T2D included in the indicator options, the population number 3 “patients with T2D, regardless of uACR result” is the most suitable for inclusion in the denominator for the indicator while number 1 “patients with T2D and uACR over 30 mg/mmol only” is the least suitable excluding the greater proportion of eligible patients. The inclusion of population number 3 would ensure that no eligible patients are excluded from the denominator for the indicator and would reduce any barriers to implementing optimal care for patients. If NICE do perceive there to be a need to have an indicator with a uACR restriction, then AstraZeneca would support indicator number 2 which states that the denominator for the indicator should be in patients with T2D and uACR 3 mg/mmol or more only as this aligns with NG28 guidelines, and, therefore, clinical practice, which states that SGLT2 inhibitors should be: • Considered for adults with T2D and CKD who are taking an ARB or an ACE inhibitor if ACR is between 3 and 30 mg/mmolor; • Offered for adults with T2D and CKD who are taking an ARB or an ACE if ACR is over 30 mg/mmol and they meet the criteria in the marketing authorisation	

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			(including relevant estimated glomerular filtration rate [eGFR] thresholds. 1. National Institute for Health and Care Excellence (NICE). Dapagliflozin for treating chronic kidney disease [TA775]. Available at: https://www.nice.org.uk/guidance/ta775 [accessed 02 May 2023]. 2022. 2. Electronic Medicines Compendium (EMC). Forxiga 10 mg film-coated tablets [SmPC]. Available at: https://www.medicines.org.uk/emc/product/7607/smpc [accessed 06 May 2023]. December 2022. 3. Electronic Medicines Compendium (EMC). Jardiance 10 mg film-coated tablets [SmPC]. Available at: https://www.medicines.org.uk/emc/product/5441/smpc [accessed 02 May 2023]. February 2023. 4. National Institute for Health and Care Excellence (NICE). Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes [TA390]. Available at: https://www.nice.org.uk/guidance/ta390 [accessed 01 June 2022]. 2016. 5. National Institute for Health and Care Excellence (NICE). Dapagliflozin in combination therapy for treating type 2 diabetes [TA288]. Available at: https://www.nice.org.uk/guidance/ta288 [accessed 01 June 2022]. 2016. 6. National Institute for Health and Care Excellence (NICE). Dapagliflozin in triple therapy for treating type	

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			2 diabetes [TA418]. Available at: https://www.nice.org.uk/guidance/ta418 [accessed 01 June 2022]. 2016. 7. National Institute for Health and Care Excellence (NICE). Dapagliflozin for treating chronic heart failure with reduced ejection fraction [TA679]. Available at: https://www.nice.org.uk/guidance/ta679 [accessed 28 April 2022]. 2021. 8. AstraZeneca UK Ltd. Data on File. ID: REF-188996 May 2023. 9. Nitsch D, Caplin B, Hull SA, et al. National Chronic Kidney Disease Audit: National Report (Part 1) 2017. Healthcare Quality Improvement Partnership. 2017. 10. AstraZeneca Data on File 2021: REF-109687 (CPRD Analysis).	
24	8	BMA	8. The complexity and breadth of working in general practice makes it difficult to operate to these guidelines, which was only introduced last year and is one of hundreds of guidelines that GPs must have regard to – all of which frequently change. GPs tend to refer to a guideline when they are delivering the care, just in case it has recently changed. Guidelines need to be related to the condition so that appropriate guideline can be found during a highly pressured surgery. Releasing a NICE technology appraisal guidance on a medication and expecting it to be picked up and embedded	Thank you for your comment.

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			underestimates the challenges faced in general practice. GPs cannot attend update courses on a very frequent basis – they are time and resource heavy. Long Term Condition care is increasingly complex and yet GPs are not resourced to accommodate this and be able to deliver high quality care, nor to invest the time required to be able to adapt to every guideline introduction and embed change in a timely way. Regarding the 3 options, this requires a cost and risk:benefit analysis, including the GP service delivery costs, before considering the delivery implications (we are not referring to the costs to the commissioner).	
25	8	National Kidney Federation	The indicators are based on recommendations in NICE's guideline on type 2 diabetes in adults and NICE's technology appraisal on dapagliflozin for treating chronic kidney disease. The proposed indicators define the population according to the presence of CKD, type 2 diabetes, and urine albumin concentration. Of the three populations with CKD and type 2 diabetes included in the indicator options, who would be offered an SGLT2 inhibitor to manage their CKD according to your local practice and would be suitable for inclusion in the denominator for the indicator? · Patients with type 2 diabetes and urine ACR over 30 mg/mmol only	Thank you for your comment. The indicator advisory committee approved IND2022-135 for publication. The NICE indicator advisory committee agreed that implementation of the indicator should be accompanied by NM109 on annual ACR measurement.

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			· Patients with type 2 diabetes and urine ACR 3 mg/mmol or more only · Patients with type 2 diabetes, regardless of urine ACR result. Unfortunately, ACR testing is not widely used in general practice at the moment and therefore this may miss lots of kidney patients, we would like to see patients with type 2 diabetes, regardless of ACR results or not, offered SGLT2 inhibitors.	
26	8	NHS England	The question here relates to where to set the threshold re: ACR - in line with the 'offer rec' in NG28, the 'consider rec' in NG28, or the recs in the TA for dapagliflozin in CKD. Given there is a TA for SGLT2i use in CKD and T2DM without a minimum ACR, setting a minimum ACR level for people with T2DM within the proposed indicator may cause further confusion to clinicians in an already-confusing domain and may lead to the impression for clinicians that people with T2DM and ACR < 3 mg/mmol are not eligible for SGLT2i therapy. Therefore, the option of 'regardless of urine ACR result' is likely preferable. In any case, there is likely to be considerable overlap between people with T2DM and CKD and those with T2DM and elevated QRISK such that NG28 would recommend consideration of SGLT2i therapy anyway.	Thank you for your comment. The NICE indicator advisory committee progressed IND2022-135 as it is based on recommendations in NG28 on type 2 diabetes in adults
27	9	AstraZeneca	Assuming that the indicators will use the last recorded urine ACR for inclusion in the denominator and so patients with an ACR that has improved from baseline will not be included if	Thank you for your comment. The NICE indicator advisory committee agreed that

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			the last ACR is below the inclusion threshold is not an acceptable approach. The variation of uACR testing, discussed in question 8 above, between primary care practices creates inequality of care where not all patients across the UK are able to benefit from testing. Defining the populations with CKD and T2D based on any uACR thresholds, may risk excluding a substantial proportion of patients with both conditions eligible to dapagliflozin as uACR may not be available for all patients with CKD. With the exception of proposed indicator number 3, the other indicators could lead to potential for differential impact as uACR testing vary notably across England and Wales. Therefore, using the last recorded uACR or any other uACR threshold for inclusion in the denominator is not appropriate.	implementation of the indicator should be accompanied by NM109 on annual ACR measurement.
28	9	BMA	9. As we don't know the cost/risk: benefit of SGLT2 inhibitors with an ACR above baseline, or for a transient rise above baseline, so we cannot comment.	Thank you for your comment.
29	9	National Kidney Federation	The indicators use the last recorded urine ACR for inclusion in the denominator and so patients with an ACR that has improved from baseline will not be included if the last ACR is below the inclusion threshold. Is this approach acceptable? As indicated in question 8, ACR testing is not that common in general practice, so this method is not acceptable. It is important to delay the progression of chronic kidney disease leading to a patient going onto dialysis or having a transplant, therefore SGLT2 inhibitors look to help save money on dialysis and transplantation and most importantly as I said in	Thank you for your comment. The NICE indicator advisory committee agreed that implementation of the indicator should be accompanied by NM109 on annual ACR measurement.

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			my opening line, kidney patients live a long fulfilled life with the delay of the dreaded dialysis machine.	
30	9	NHS England	If no ACR threshold is used in people T2DM then this question is not relevant for that group. There may be problems with acceptability for an indicator which no longer keeps in the denominator those who have had an intended outcome in response to an intervention (here an improvement in ACR following SGLT2i use) - meaning that practices would not be consistently recognised for prior work.	Thank you for your comment.
31	9	Royal College of General Practitioners	The RCGP feel it is appropriate to use the last recorded ACR for the denominator.	Thank you for your comment.