A national audit of SGLT2 use in England We don't follow the NICE guidelines

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Aim

The use of sodium glucose co-transporter 2 (SGLT2) inhibitors in people with type 2 diabetes in the UK is growing rapidly. This newest class of oral therapy is substantially more costly than older therapies. The National Institute for Health and Clinical Excellence (NICE) therefore provides strict guidelines for the use of this class in the UK. We compare current use to the NICE guidelines in 128 GP practices in England.

Background

SGLT2 inhibitors have additional real world benefits beyond glycaemic control; weight loss, and blood pressure reduction.1 With empagliflozin, cardiovascular risk reduction has also been demonstrated in high risk populations and cardiovascular trials with other SGLT2 inhibitors are ongoing.^{2,3} These additional benefits make this class attractive, however the high costs should also be considered. NICE guidelines suggest restriction of the medication class to the following scenarios4:

Monotherapy:

Not recommended

First intensification:

In dual therapy with metformin:

Only when an SU is not indicated

When metformin use is CI or not tolerated: Not recommended

Second intensification:

In triple therapy with a metformin and pioglitazone:

Only when an SU is CI

Combination with insulin:

Can be used in combination with insulin therapy.

SU = sulphonylurea, CI = contraindicated

The NICE treatment algorithm is also shown in Figure 1. These guidelines contrast with those of the ADA and EASD which recommend SGLT2 monotherapy has parity with other therapies as second-line monotherapy after metformin, and parity with other therapies in dual therapy with metformin, and any triple therapy combination.5

ADULT WITH TYPE 2 DIABETES WHO CAN TAKE METFORMIN		METFORMIN CONTRAINDICATED OR NOT
If HbA1c rises to 48 mmol/mol (6.5%) on lifestyle Interventions: • Offer standard-release metformin • Support the person to aim for an HbA1c level of 48 mmol/ mol (6.5%)	If standard-release metformin is not tolerated, consider a trial of modified-release metformin	TOLERATED If HbA1c rises to 48 mmolimol (6.9%) on illestyle interventions: • Consider one of the following ⁶ : • a OPP-46, pioglizzone ⁶ or an SU
+		 Support the person to aim for an HbA1c
FIRST INTERSIFICATION HINAT crises to 58 mmol/mmol (7.5%): • Consider dual therapy with: • -methormin and a D1PT-44 - methormin and a D1PT-44 - methormin and an SU - methormin a	If triple therapy is not effective, not tolerated or contraindicated,	level of 48 mmol/mol (6.5%) for people on a DPP-4i or piogitazone or 53 mmol/mol (7.0%) for people on an SU
	consider combination therapy with metformin, an SU and a Gi R-1	↓ ↓
	mimetic" for adults with type 2 diabetes who: - have a DMI of 35 kg/m ²	FIRST INTENSIFICATION If HbA1c rises to 58 mmolimol (7.5%): • Consider dual therapy" with: • a DPP-4i and plogitazone" • a DPP-4i and an SU • plogitazone" and an SU
mal (7.0%)	or higher (adjust accordingly for people from black, Asian and other micrority ethnic proups)	
SECOND INTENSIFICATION I Makie can be dia manefund (7.5%): - oppoint and a state of the state of the state of the state - metformm, populacone' and an SU - ometformm, populacone' and an SU - ometform' an SU - o	and specific psychological or other rescaled produces there a DMI lower from DN spore, and for whom regular barray would for myorizations, or weight for myorizations, or weight for there is a specific product of the the	 Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)
		↓ ↓
		SECOND INTENSIFICATION If HbA1c rises to 58 mmol/mol (7.5%): • Consider insulin-based treatment
	would benefit other significant obesity-related comorbidities	 Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

Figure 1. NICE type 2 diabetes treatment algorithm.4

Methods

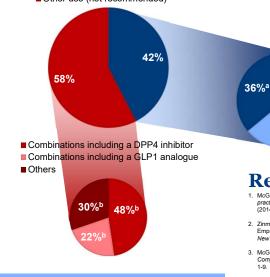
We identified a large cohort of people with type 2 diabetes from the University of Surrey-Lilly Real World Evidence database, using routinely collected primary care data from 128 practices. Within this cohort we identified everyone initiated on SGLT2 inhibitor therapy. We analysed GP prescribing records to identify concurrent therapies at the time of SGLT2 inhibitor initiation. We describe the proportion of people initiated on SGLT2 inhibitors as dual therapy with metformin, triple therapy including metformin, with insulin, and with other combinations which are not recommended by NICE.

Results

Of those with type 2 diabetes (N=60,327) we identified 1,642 people (2.7%) initiated on SGLT2 inhibitors. At initiation the mean age was 58.1 years (SD 10.5), body mass index 34.0 kg/m² (SD 6.4), and HbA1c 78.0 mmol/mol (SD 17.3).

SGLT2 was used as monotherapy in 40 people (2.4%), dual therapy with metformin in 180 people (11.0%), triple therapy including metformin in 266 people (16.2%), and with insulin in 477 people (29.0%). SGLT2 inhibitors were used in combinations not recommended by NICE in 945 people (57.5%), including combinations with DPP-4 inhibitors in 450 people (27.4%) and GLP-1 analogues 209 people (12.7%) (figure 2).

> NICE recommended combinations Other use (not recommended)



igure 2. The proportion of people initiated on SGLT2 inhibitors in NICE recommended combinations. Recommended combinations are

shown in blue and non-recommended combinations in red. a Percentage of those prescribed an SGLT2 inhibitor as part of a recommended combination, **b** Percentage of those prescribed an SGLT2 inhibitor as part of a non-recommended combination.

Conclusion

The majority current use of SGLT2 inhibitors in the UK does not adhere to the recommendations provided by NICE. Whilst and American guidelines European recommend a broader scope for the use of this class, cost is a major consideration within the NHS.

Of particular concern are the high levels of concurrent use with other costly therapies, namelv DPP-4 inhibitors, and GLP-1 analogues. These combinations have rarely been studied for efficacy and are not likely to represent cost effective treatment options.

Clinicians should be mindful of the costs and clinical uncertainties of prescribing in these combinations. Methods for restricting the use of these combinations of therapies may need to considered as the use of SGLT2 inhibitors continues to increase following the results of the EMPA-REG OUTCOMES trial.

Key points

- The majority (57.5%) of SGLT2 use is initiated in combinations which are not recommended by NICE.
- A large proportion of this use is in combination with other costly therapies (DPP-4 inhibitors 27.4% and GLP-1 analogues 12.7%).
- Combination of SGLT2 inhibitors with DPP-4 inhibitors or GLP-1 analogues may not represent a cost-effective treatment option and this usage requires further evaluation.

Dual therapy with metformin Triple therapy including metformin Recommended combination with insulin

References

38%^a

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