

How can the selection of patients with type 1 diabetes suitable for adjunctive treatment with SGLT inhibitors be optimized?

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What is the rationale for using SGLT inhibitors as an adjunct to insulin therapy in patients with type 1 diabetes?



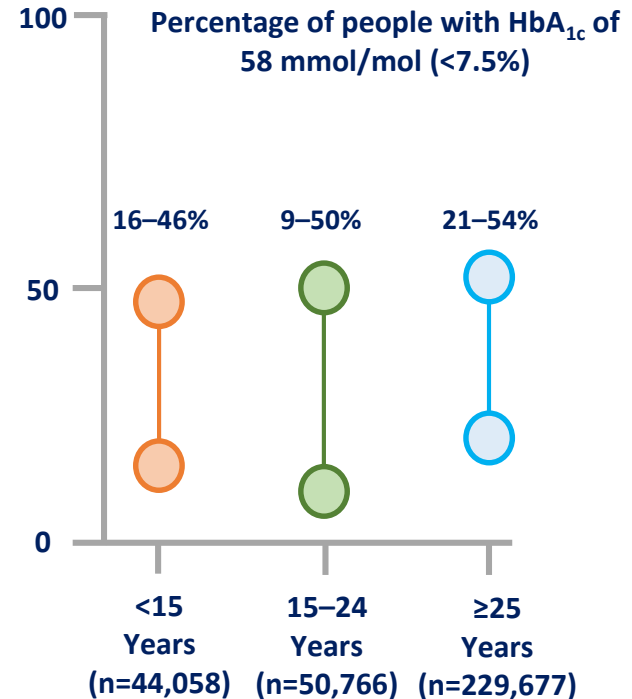
Dr Manon Khazrai

Dietitian and Counsellor
Endocrinology and Diabetes Clinic
Campus Bio-Medico University,
Rome, Italy

Many people with type 1 diabetes do not achieve good glycaemic control

- A comparison of glycaemic control among children* and/or adults with type 1 diabetes using data from regional or national registries showed that **many people do not achieve good glycaemic control**
- Data were obtained for 324,501 children and/or adults from:** Australia, Austria, Denmark, France, Germany, Greece, Ireland, Italy, Latvia, The Netherlands, New Zealand, Norway, Sweden, UK, Ukraine, USA

Chronic exposure to hyperglycaemia in type 1 diabetes carries an increased risk of microvascular and macrovascular disease²



*SGLT inhibitors are not approved for use in children; **Some data are national and some are regional; HbA_{1c}, glycated haemoglobin

1. McKnight JA, et al. *Diabet Med.* 2015;32:1036–1050; 2. McCrimmon RJ, et al. *Diabetologia* 2018;61:2126–2133.

Barriers to reaching glycaemic targets



Fear of hypoglycaemia¹



Fear of weight gain¹

Other factors may include:

- Limitations of current insulin delivery systems (peripheral drug delivery and lack of feedback inhibition)²
- Age at onset of diabetes³
- Genetic background⁴
- HbA_{1c} values before the intervention and C-peptide levels³
- Diabetes-related knowledge³
- Economic status⁴
- Psychological factors such as lack of motivation, emotional distress, depression and eating disorders⁴
- Lifestyle factors such as smoking³

HbA_{1c}, glycated haemoglobin

1. Danne T, et al. *Diabetes Care* 2019;42:1147–1154; 2. McCrimmon RJ, et al. *Diabetologia* 2018;61(10):2126–2133; 3. Bott U, et al. *Diabet Med.* 1994;11:362–371;

4. Devries JH, et al. *Diabet Med.* 2004;21(12):1263–1268.

The goals of adjunct therapy in type 1 diabetes



Reduction of HbA_{1c} without increasing hypoglycaemia and weight gain¹



Reduction of glucose variability²



Reduction of complications through improved glycaemic control^{3,4}

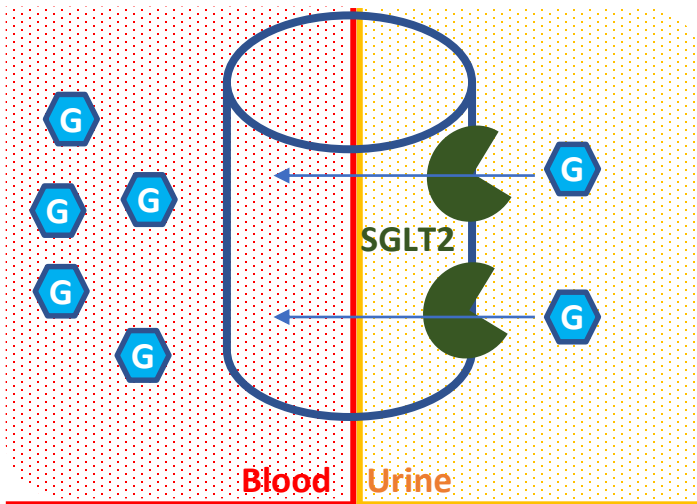


Adjunct therapy does not replace insulin^{1,3,4}

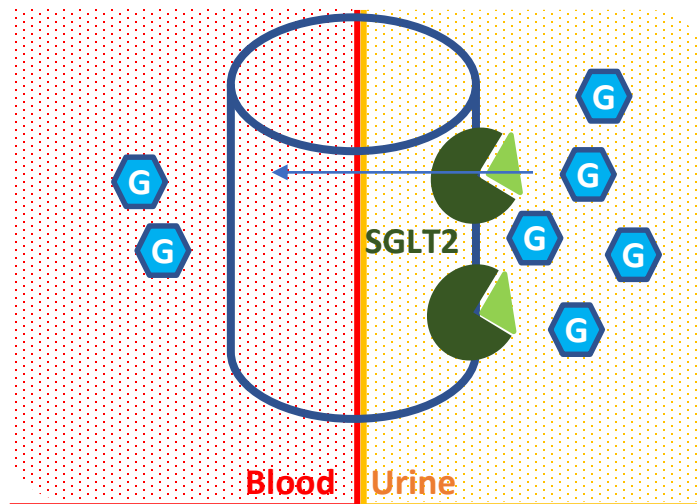
HbA_{1c}, glycated haemoglobin

1. Danne T, et al. *Diabetes Care* 2019;42:1147–1154; 2. Pettus JH, et al. *Diabetes Technol Ther.* 2019;21:336–343; 3. Tosur M, et al. *Curr Diab Rep.* 2018;18:79; 4. DCCT/EDIC Writing Team *JAMA.* 2002;287:2563–2569.

SGLT inhibitors: an insulin-independent approach that removes excess glucose by reducing the renal threshold^{1,2}



SGLT2 mediates the reabsorption of ~90% of filtered glucose in the S1 segment of the renal proximal tubule³



▲ SGLT2 inhibitors block SGLT2, thereby increasing the glucose excreted in the urine and decreasing plasma glucose³

Dual SGLT1 and 2 inhibitors also reduce glucose reabsorption in the gastrointestinal tract.⁴

SGLT, sodium-glucose co-transporter

1. Marsenic O. *Am J Kidney Dis.* 2009;53:875–885; 2. Mudaliar S, et al. *Diabetes Care* 2016;39:1115–1122; 3. Gomez-Peralta F, et al. *Diabetes Ther.* 2017;8:953–962;

4. Sands AT, et al. *Diabetes Care* 2015;38:1181–1188.

SGLT inhibitors* can be prescribed to adults for the treatment of type 1 diabetes^{1,2}



**Adjunct to
insulin**



**In patients with
BMI ≥ 27 kg/m²**

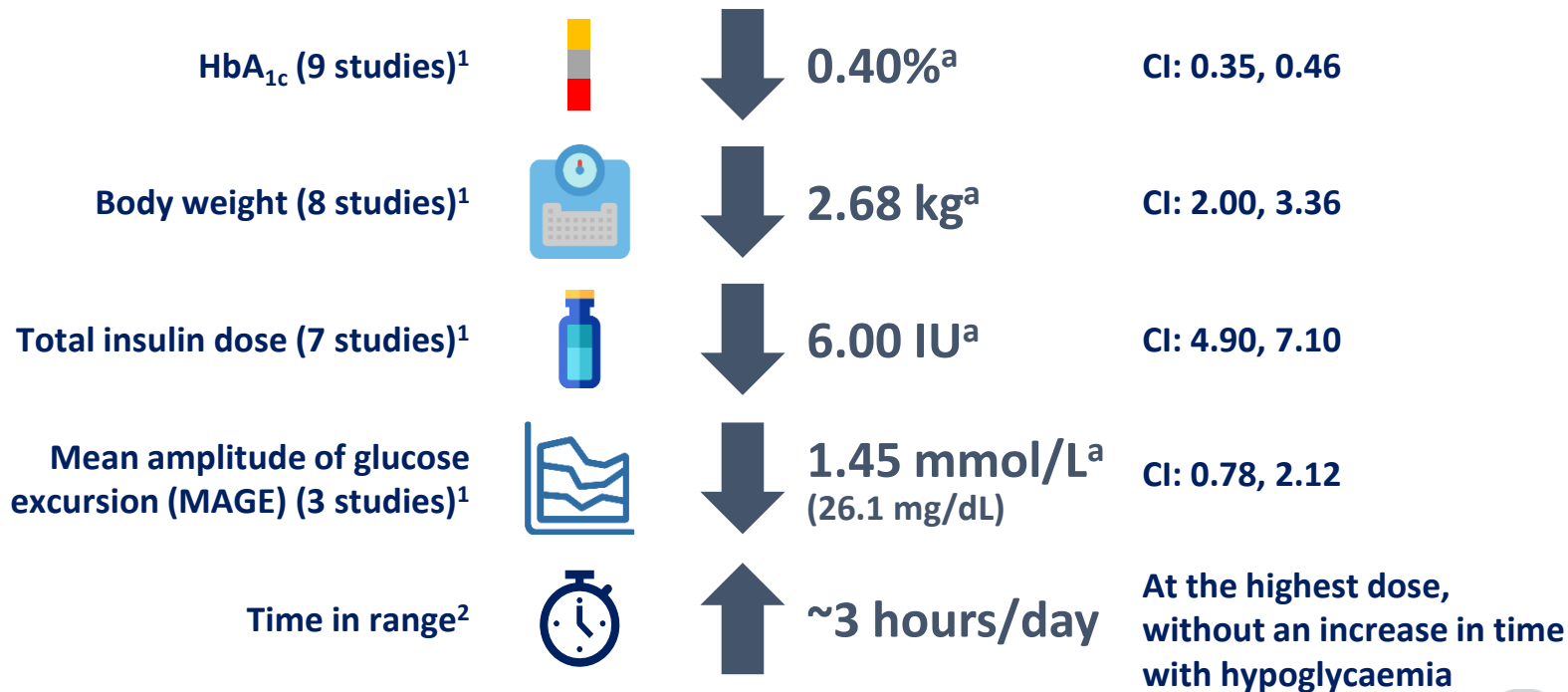


**Using approved doses
per medication^a**

*Only dapagliflozin (an SGLT2 inhibitor) and sotagliflozin (an SGLT1/2 inhibitor) are approved for use in patients with type 1 diabetes in Europe; ^aPlease check respective doses before prescription; BMI, body mass index; SGLT, sodium-glucose co-transporter

1. EMA press release. Dapagliflozin. [Cited July 2019] Available from: <https://www.ema.europa.eu/en/news/first-oral-add-treatment-insulin-treatment-certain-patients-type-1-diabetes>; 2. EMA press release. Sotagliflozin. [Cited July 2019] Available from: <https://www.ema.europa.eu/en/news/new-add-treatment-insulin-treatment-certain-patients-type-1-diabetes>.

Efficacy of SGLT inhibitor adjunct therapy in type 1 diabetes



^aWeighted mean difference

CI, confidence interval; HbA_{1c}, glycated haemoglobin; SGLT, sodium-glucose co-transporter

1. Yamada T, et al. *Diabetes Obes Metab*. 2018;20:1755–1761; 2. Danne T, et al. *Diabetes Care* 2019;42:1147–1154.