What are the HbA1c thresholds for initiating insulin therapy in people with type 2 diabetes in UK primary care?

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Background

For people with type 2 diabetes mellitus (T2DM), insulin therapy is often eventually required to maintain optimal glycaemic control.

Concerns of both physicians and patients surrounding the use of insulin creates barriers to initiating insulin therapy, increasing the likelihood that effective treatment may be delayed and that the risk for complications may be increased[1]. Despite consensus guidelines, studies highlight that initiation of insulin is often delayed[2]. This is likely to be due to physicians adopting a patient-centred approach to initiating insulin therapy[3].

Aim

We characterise the level of glycaemic control at which insulin was initiated in a large primary care cohort of people with T2DM in the UK. We compared the threshold for initiation of insulin therapy with recommended thresholds (Table 1).

Methods

We performed a **retrospective cohort analysis** using a primary care sentinel network (Royal College of General Practitioners Research and Surveillance Centre).

We identified the first insulin prescription in a cohort of people with T2DM between 1st January 2005 and 31st July 2015. We excluded people who had their first insulin prescription within 12 months of joining their registered practice to ensure only people receiving their first insulin prescriptions were captured.

We compared the HbA1c value at which insulin was initiated against a number of potential influencing factors, using linear regression. Potential influencing factors explored included patient age, gender, ethnicity, socioeconomic status, smoking status, alcohol use, duration of diabetes, body mass index (BMI), comorbidities, and number of concomitant and previous diabetes medications. Socioeconomic status was measured using index of multiple deprivation (IMD) score, with higher scores in people with higher levels of deprivation.

The analysis was performed using R version 3.2.3.

Results

From 58,717 people with T2DM we identified 4,527 (7.7%) people with a first insulin prescription and an HbA1c measurement preceding the initiation of treatment. The mean insulin initiation threshold was at HbA1c of 83.9 (SD 22.1) mmol/mol.

There was no association between the threshold for insulin initiation and age (Figure 1), gender, alcohol consumption, or number of concurrent therapies. Factors associated with insulin association are shown in Table 2.

	HbA1c thresholds for insulin initiation
NICE[4]	Individual thresholds, particularly if ≥75mmol/mol†
ADA[5]	≥ 53mmol/mol
IDF[6]	≥ 65 mmol/mol*

† To be added with metformin

* On dose-optimized oral hypoglycemic therapy

Table 1. Recommended HbA1c thresholds for the initiation of insulin therapy. Note: these thresholds vary according to a number of factors including (but not limited to) cardiovascular risk profile, hypoglycaemia risk, life expectancy, and patient perception/numeracy[5].

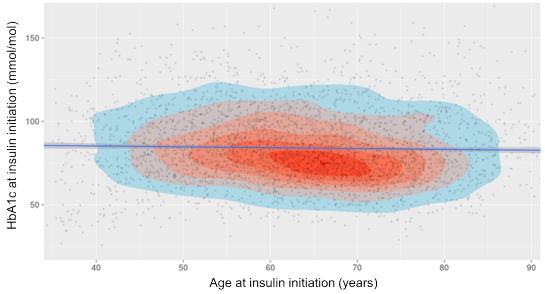

Figure 1. A scatterplot of HbA1c value (mmol/mol) at insulin initiation against age at initiation of insulin. Each person is shown by a single data point. Areas of greatest person density are shown in red.

Characteristic	ß-coefficient (95% CI)	P value
IMD score	0.09 (0.05 to 0.14)	<0.001
Ethnicity		
White	1.00 [reference]	
Asian	-2.99 (-5.78 to -0.19)	0.036
Black	2.05 (-1.93 to 6.03)	0.313
Mixed	-1.37 (-9.78 to 7.03)	0.749
Other	-7.43 (-16.93 to 2.08)	0.126
Smoking status		
Never smoked	1.00 [reference]	
Active	3.79 (1.30 to 6.28)	0.003
Ex-smoker	0.57 (-1.08 to 2.21)	0.500
Duration of diabetes (years)	0.37 (-5.07 to 0.63)	0.006
Complications	0.21 (-6.87 to 0.32)	<0.001
Retinopathy	2.11 (0.59 to 3.63)	0.007
Comorbidities		
CKD	-4.92 (-10.15 to 0.31)	0.065
CHD	-3.28 (-5.23 to -1.33)	<0.001
Hypertension	-1.59 (-3.15 to -0.03)	0.046
Previous medications		
None	1.00 [reference]	
One	0.14 (-2.04 to 2.32)	0.898
Two	2.51 (0.25 to 4.78)	0.029
Three	2.87 (0.27 to 5.47)	0.031
Four	4.34 (0.88 to 7.79)	0.014
Three or more	1.40 (-3.52 to 6.32)	0.578

Table 2. Associations of clinical characteristics with the threshold at which insulin is initiated (HbA1c in mmol/mol) in 4,527 people with T2DM estimated from linear regression.

Conclusion

The threshold for insulin initiation in the UK is high compared to recommended targets and is likely to be contributing to poor glycaemic control. The high HbA1c threshold for insulin initiation equates to a mean capillary glucose of 12.7 mmol/L, which is just above the renal threshold for glucose[7], and therefore likely to lead to symptoms.

Clinicians do not appear to substantially tailor insulin initiation thresholds by patient factors. Good glycaemic control is vital for prevention of macrovascular and microvascular complications and therefore approaches to improve current treatment practices are urgently needed.

Key findings

- The mean HbA1c at insulin initiation was high.
- No association was found between the threshold for insulin initiation and age, gender, alcohol consumption, or number of concurrent therapies.
- Approaches to improve current treatment practices are urgently needed to prevent macrovascular and microvascular complications.

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