Table 1: Characteristics of those patients who progressed insulin therapy during the study

Baseline Characteristic*	End of Study HbA_{1c} ≤53mmol/mol (n=255)	End of Study HbA_{1c} >53mmol/mol (n=669)	P value**
Age, years	62.7±10.6	59.9±10.5	0.01
Male	135(53)	333(50)	0.45
HbA_{1c}, mmol/mol, (SD)	57.4± (8.5)	69.4±(8.5)	<0.01
Family history of diabetes	144(56)	408(61)	<0.01
Other Diabetes Medication			
Basal insulin	122(48)	330(49)	0.76
Short-acting insulin	27(10)	64(10)	0.75
Mixed insulin	65(25)	179(27)	0.72
Metformin	114(45)	374(56)	<0.01
Sulfonylurea	62(24)	199(30)	0.14
Dipeptidylpeptidase-4 inhibitor	28(11)	77(11)	0.79
Glucagon-like peptide-1 agonist	11(4)	25(4)	0.66
Thiazolidinedione	9(4)	40(6)	0.20
Region			
Asia	87(34)	248(37)	0.45
Europe	72(28)	124(19)	<0.01
Middle East	42(17)	123(18)	0.61
North America	31(12)	91(14)	0.64
Latin America	23(9)	83(12)	0.30

* Mean ± SD for continuous and Number (%) for categorical variables
** Univariate linear or logistic regression

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A cloud-based electronic health records study of treatment intensification patterns in type 2 diabetes patients uncontrolled on ≥2 oral anti-diabetes drugs

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Background and aims: Clinical inertia is an ongoing barrier in diabetes care. To further understand the extent of clinical inertia, this study assessed treatment intensification patterns and their associated demographic and clinical characteristics in patients (pts) with uncontrolled type 2 diabetes (T2D) using data from a US cloud-based electronic health records (EHR) platform.
Materials and methods: Insulin-naive adult pts with T2D prescribed ≥ 2 different types of oral antidiabetes drug (OAD), with the most recent prescription in the 6 months prior to an uncontrolled HbA_{1c} level (i.e., HbA_{1c} > 7.0%), were identified from Jan. 2011 to Dec. 2015 in the Practice Fusion EHR database with > 30 million pts across the US. The most recent uncontrolled HbA_{1c} date following the prescription of a 2nd OAD marked the index date. The baseline period was defined as the 6 months prior to the index date; the observation period was defined as the 6 months post index date. Treatment intensification patterns during the observation period were assessed and used to classify pts into 4 cohorts: a) no intensification, and intensification with b) an additional OAD, c) a basal insulin, and d) a glucagon-like peptide-1 receptor agonist (GLP-1 RA). Baseline demographics and clinical characteristics including age, gender, mean HbA_{1c}, and mean BMI of pts across the cohorts were compared using chi-square tests or ANOVA.
Results: Of the 25,365 eligible pts, the majority did not intensify their treatment regimens (71.7%; n = 18,197); 19.9% (n = 5,047) of pts received an additional OAD; 6.7% (n = 1,690) added a basal insulin; and 1.7% (n = 431) added a GLP-1 RA. Baseline age, gender, mean HbA_{1c}, and mean BMI were significantly different across the 4 cohorts (all P values ≤ 0.001). In particular, and compared to pts who intensified with an additional OAD, basal insulin, or GLP-1 RA, pts with no intensifications were older and had a lower mean HbA_{1c}. Compared to pts who intensified with a basal insulin or GLP-1 RA, pts with no intensifications were also less likely to be female. While all pts had obesity (mean BMI > 30 kg/m2), pts who intensified with a GLP-1 RA had the highest BMI (mean: 37.0 kg/m2; standard deviation: 7.5). Table 1 presents the distribution of the demographic and clinical characteristics across the cohorts.
Conclusion: Clinical inertia is common among adult pts with uncontrolled T2D. In this EHR database covering a broad range of US practices, the majority of pts on ≥ 2 OADs with uncontrolled HbA_{1c} levels had no change in therapy. This was especially true in older pts and those with lower levels of uncontrolled HbA_{1c}. When pts intensified therapy, most added an additional OAD. Intensification to injectable forms of therapy was infrequent, occurring less than 10% of the patients.

Table 1. Distribution of demographic and clinical characteristics across treatment intensification

Characteristic	No intensification (n = 18,197)	Additional OAD (n = 5,047)	Basal insulin (n = 1,690)	GLP-1 RA (n = 431)	*P* value
Age, years, mean (SD)	62.4 (12.3)	61.5 (12.0)	60.8 (12.5)	57.6 (11.1)	< 0.001
Female, n (%)	8,759 (48.2)	2,375 (47.1)	873 (51.7)	232 (53.8)	0.001
HbA_{1c}, %, mean (SD)	8.2 (1.3)	8.6 (1.4)	9.5 (1.8)	8.7 (1.4)	< 0.001
BMI, kg/m^2, mean (SD)	32.3 (6.8)	32.4 (6.9)	32.9 (7.1)	37.0 (7.5)	< 0.001

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What are the HbA_{1c} thresholds for initiating insulin therapy in people with type 2 diabetes in UK primary care?

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Background and aims: 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 create barriers to initiating insulin therapy, increasing the likelihood that effective treatment is delayed and increasing the risk of developing complications. Despite consensus guidelines to the contrary, data from epidemiological and observational studies highlight that initiation is delayed in many cases until HbA1c has exceeded values of 75mmol/mol. We aimed to characterise the level of glycaemic control at which insulin was initiated in a large primary care cohort of people with T2DM in the UK.
Materials and 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 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. Factors 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 83.4 (SD 22.7) mmol/mol. There was no association between the threshold for insulin initiation and age, gender, alcohol consumption, BMI, or number of concurrent therapies. A lower glycaemic threshold (HbA1c in mmol/mol) for insulin initiation was associated with

Asian ethnicity (estimate -2.99; 95% CI -5.78 to -0.19; p=0.036), absence of retinopathy (-2.11; -3.63 to -0.59; p=0.007), coronary artery disease (-3.28; -5.23 to -1.33; p<0.001), and hypertension (-1.59; -3.15 to -0.03; p=0.046). A higher threshold was associated with higher IMD score (estimate 95% CI 0.09; 0.05 to 0.14; p<0.001), current smoking (3.79; 1.30 to 6.28; p=0.003), and a higher number of previous diabetes medications. Overall model performance was limited.
Conclusion: The threshold for insulin initiation in the UK is high and is likely to be contributing to poor glycaemic control. The high HbA1c threshold for insulin initiation equates to a mean capillary glucose of 13.0mmol/L, which is just above the renal threshold and therefore likely to lead to symptoms. Clinicians only moderately tailor insulin initiation thresholds by patient factors. Good glycaemic control is vital for prevention of complications and therefore approaches to improve this situation are urgently needed.
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Disclosure: W. Hinton: Grants; Eli Lilly.

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Defining insulin responders with a composite measure in an integrated real-world health system database compared to a clinical trials database

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Background and aims: Most insulin-treated patients with type 2 diabetes (T2D) do not meet the hemoglobin A_{1c} (HbA_{1c}) goal of <7% suggested by treatment guidelines. Previous analyses in an integrated insulin lispro clinical trial (CT) database described a composite HbA_{1c} measure which identified more patients with clinically relevant HbA_{1c} reductions than an HbA_{1c} target alone. The present analysis evaluated this composite HbA_{1c} measure in a real-world (RW) database and compared it with the results from a CT database.
Materials and methods: The US-based MedMining electronic medical records database has de-identified data on 30,040 individuals in the Geisinger integrated health system from 2004 to 2015. This analysis included 1134 patients with T2D ≥18 years of age who initiated any insulin regimen (with first use as the index date), and had HbA_{1c} values available at the baseline (BL) index date and the 6-month post-index endpoint, both within 90-day windows. Responders were defined as patients with an endpoint HbA_{1c} <7% and/or a ≥1% absolute decrease from BL in HbA_{1c}. BL demographics, percentage and characteristics of responders in this RW database were compared to those in a CT database.
Results: Patients in this RW cohort (N=1134) were 57.1 ± 30.5 years of age (mean ± SD), with BL HbA_{1c} of 9.1% ± 1.8%, similar to the CT cohort (N=4908; 57.9 ± 9.7 years and 8.8% ± 1.2%, respectively). The RW cohort had more female and Caucasian patients (53.5% and 96.7%, respectively) than in the CT cohort (48.4% and 66.0%, respectively). The body mass index (mean ± SD) in the US-based RW database (37.3 ± 8.8) was higher than in the international CT database (31.0 ± 5.7). Overall, the proportions of patients identified as responders were similar between the RW and CT cohorts (Table), with the composite measure identifying more responders than the HbA_{1c} <7% definition. In both the RW and CT cohorts, the composite measure identified increasingly greater proportions of responders across higher BL HbA_{1c} categories ≥9%, while the proportions of responders reaching HbA_{1c} <7% remained consistently low. Irrespective of the starting insulin regimen, the composite measure identified greater proportions of responders in both cohorts than the HbA_{1c} <7% definition.
Conclusion: In both the RW and CT cohorts, a composite HbA_{1c} measure (≥1% absolute decrease in HbA_{1c} from BL and/or HbA_{1c} <7%), identified more patients with clinically meaningful responses to insulin therapy than an HbA_{1c} target alone, particularly in patients with high baseline HbA_{1c}. This composite model of defining insulin therapy response may be useful in population management and quality measures.

Baseline Variable and Subgroups	Responder Defined as HbA_{1c} <7% [n(%)]		Responder Defined as HbA_{1c} <7% and/or ≥1% Absolute Decrease in HbA_{1c} from BL [n(%)]	
	CT Cohort	RW Cohort	CT Cohort	RW Cohort
Overall	1991/4908 (40.6%)	420/1134 (37.0%)	3561/4908 (72.6%)	707/1134 (62.3%)
HbA1c ≥7% to <8%	677/1134 (59.7%)	187/374 (50.0%)	677/1134 (59.7%)	187/374 (50.0%)
HbA1c ≥8% to <9%	664/1638 (40.5%)	92/268 (34.3%)	1067/1638 (65.1%)	128/268 (47.8%)
HbA1c ≥9% to <10%	326/1135 (28.7%)	49/182 (26.9%)	915/1135 (80.6%)	129/182 (70.9%)
HbA1c ≥10% to <11%	153/572 (26.7%)	29/117 (24.8%)	525/572 (91.8%)	90/117 (76.9%)
HbA1c ≥11%	72/294 (24.5%)	63/193 (32.6%)	278/294 (94.6%)	173/193 (89.6%)
Basal Insulin Only	317/774 (41.0%)	191/568 (33.6%)	605/774 (78.2%)	352/568 (62.0%)
Bolus Insulin Only	123/348 (35.3%)	161/391 (41.2%)	227/348 (65.2%)	239/391 (61.1%)
Basal + Bolus Insulin	792/1806 (43.9%)	59/139 (42.4%)	1259/1806 (69.7%)	97/139 (69.8%)

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Exploring ideal time points for predicting glucose fluctuations in type 1 diabetics receiving insulin degludec: a continuous glucose monitoring study

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Background and aims: Insulin degludec (IDeg) is a novel ultra long acting basal insulin that allows once a daily dosage and a significantly lower the risk of hypoglycemia especially in Type 1 diabetes mellitus (T1DM) patients. Meanwhile, continuous glucose monitoring (CGM) alongside insulin use has become an ultimate tool to measure glycemic variability and prevent unwanted hypoglycemia. Unfortunately, the use of this device comes at a cost making it less practical for long-term use. In this study, we aimed to identify the optimal time-point for Plasma glucose (PG) measurement that best represents the treatment effect, especially glucose fluctuations, of IDeg users in T1DM by using CGM data.
Materials and methods: A total of 32 T1DM patients who were treated with IDeg at our university hospital were evaluated. Each patient had a CGM device placed on day 1 and was given 4 meals of standardized diabetic diet (1 meal on day 1 and 3 meals on day 2) in outpatient setting. The 24-hour CGM data acquired on day 2 was used for the current analysis. The 24-hour mean glucose value and daily glycemic variability [standard deviation (SD) of blood glucose and mean amplitude of glycemic excursions (MAGE)] was evaluated. The correlation between the parameters acquired from CGM and pre-prandial PG, 1 hour post-prandial PG, and 2 hour post-prandial PG was studied. Furthermore, regression models were constructed to best predict glucose fluctuations acquired by the CGM parameters.
Results: The patient characteristics were as follows [all values expressed as median (interquartile range)]: age, 47 (40-53); HbA1c, 7.9 (7.4-8.2) %; 24-hour mean glucose values, 151 (124-168) mg/dL; standard deviation (SD) of glucose, 67.1 (49.5-78.2); and MAGE, 115.3 (80.3-151.5). The 24-hour mean PG was significantly correlated with pre-breakfast PG (r = 0.41; p= 0.001), pre-lunch PG (r = 0.35; p=0.007), and pre-dinner PG (r = 0.41; p=0.001). The SD of glucose was correlated with the 1 hour post-breakfast PG (r = 0.23; p= 0.01), 1 hour post-lunch PG (r = 0.25; p= 0.05) and 1 hour post-dinner PG (r = 0.31; P = 0.001). MAGE was significantly correlated with 2 hour post-dinner PG (r = 0.28; P = 0.03) but not with 2 hour post-lunch or post-breakfast PG. Additionally, regression analysis suggested that the 24-hour mean PG, SD of glucose and MAGE could be predicted with the equation, (pre-dinner PG) x 0.29 + 115, (1 hour post-dinner PG) x 0.11 + 43.8, and (2 hour post-dinner PG) x 0.23 + 75.6, respectively.
Conclusion: Our current study found that 24-hour mean PG, SD of 24-hour glucose and MAGE in T1DM patients receiving IDeg can be