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Therapeutic inertia among individuals with uncontrolled type 2 diabetes: a UK population-based retrospective analysis

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Aim

To examine patterns of treatment intensification and modification in adults with uncontrolled type 2 diabetes (T2D) receiving treatment with non-insulin glucose-lowering agents in the UK.

Introduction

- In individuals with T2D, early glycaemic control leads to better clinical outcomes and reduces the risk of developing macrovascular and microvascular complications.[1]
- Therapeutic inertia, defined as the failure to intensify or reduce therapy when clinically indicated, can negatively affect glycaemic control.[1,2]
- Despite the availability of effective treatment options, therapeutic inertia is present in all stages of treatment intensification (from the first non-insulin treatment to insulin initiation and intensification), affecting approximately 30–50% of individuals with T2D in real-world clinical practice, highlighting the need for further investigation.[2,3]

Methods

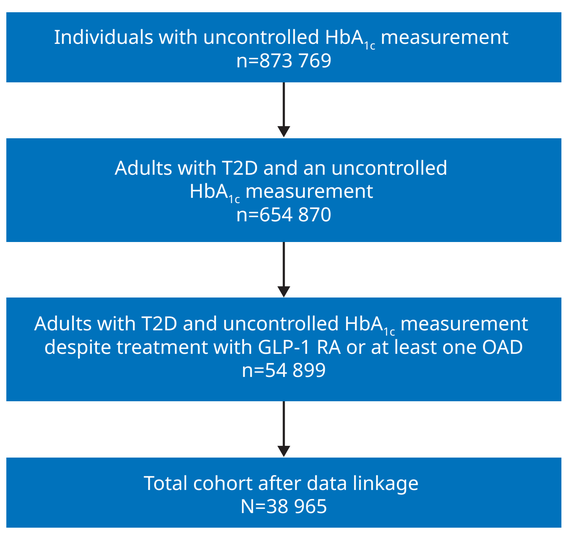
- This retrospective cohort analysis used data extracted from the UK Clinical Practice Research Datalink (protocol number 23_002753), a primary care database containing anonymised, linked and longitudinal medical records for approximately 11 million individuals registered with general practitioners in the UK.[4] Data from the period 1 January 2012 to 31 March 2020 were analysed.
- Eligible participants were insulin-naive adults (aged ≥18 years) with T2D who had an uncontrolled glycated haemoglobin (HbA_{1c}) measurement of ≥7.5% by March 2019 (index event) and were treated with non-insulin glucose-lowering agents – either an injectable or oral glucagon-like peptide-1 receptor agonist (GLP-1 RA) or at least one oral antidiabetic drug (OAD) – before and at the time of the index event.
- Treatment modifications, including treatment intensification and treatment optimisation, were assessed during the 12 months following the index event.
  - **Timely treatment intensification** was defined as the initiation of GLP-1 RA (if not already prescribed), insulin or an increase in the number of OADs in the 12 months after index. Delayed treatment intensification was defined as the absence of these changes in the 12 months after index.
  - **Timely treatment optimisation** was defined similarly to intensification, but considered both increases and reductions in the number of OADs in the 12 months after index. Delayed treatment optimisation was defined as the absence of these changes in the 12 months after index.
- Descriptive statistics were used to summarise baseline characteristics and the patterns of treatment intensification and treatment optimisation.

Results

Population

- In total, 38 965 eligible individuals were included in the analysis (**Figure 1**).
- Individuals' characteristics at index are presented in **Table 1**.
  - In the total cohort (N=38 965), the mean (standard deviation) HbA_{1c}, age, diabetes duration and body mass index at index were 8.4% (1.2%), 66.4 (11.9) years, 10.5 (4.8) years and 31.5 (6.5) kg/m², respectively.
  - The most common pre-existing comorbidities at index were retinopathy, neuropathy, a history of hypoglycaemia and cerebrovascular diseases (**Table 1**).

Figure 1. Cohort selection



Individuals were excluded if they had received previous insulin treatment, were pregnant in the 12 months before index or 3 years after index, had no general practitioner activity for more than 5 years, had a diagnosis of type 1 diabetes or died in the 12 months after index. Uncontrolled HbA_{1c} was defined as an HbA_{1c} measurement of ≥7.5% at index. The data used in this study are representative of individuals registered with general practitioners in England rather than the entire UK owing to the data linkages required for the study endpoints.
GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated haemoglobin; n, number of individuals; OAD, oral antidiabetic drug; T2D, type 2 diabetes.

Table 1: Individuals' characteristics at index[a] by treatment intensification

	Total (N=38 965)	Timely treatment intensification (n=11 330)	Delayed treatment intensification (n=27 635)
Age, mean (SD), years	66.4 (11.9)	64.8 (11.8)	67.1 (11.8)
Age group, n (%)			
18–39 years	479 (1.2)	176 (36.7)	303 (63.3)
40–59 years	10 712 (27.5)	3620 (33.8)	7092 (66.2)
≥60 years	27 774 (71.3)	7534 (27.1)	20 240 (72.9)
Sex, female, n (%)	15 217 (39.1)	4656 (41.1)	10 561 (38.2)
Duration of T2D, mean (SD), years	10.5 (4.8)	10.3 (4.9)	10.6 (4.8)
HbA_{1c} level, mean (SD), %	8.4 (1.2)	8.8 (1.5)	8.3 (1.0)
Individuals with HbA_{1c} ≥8%, n (%)	20 335 (52.2)	7364 (36.2)	12 991 (63.8)
Individuals with HbA_{1c} ≥9%, n (%)	7654 (19.6)	3326 (43.5)	4328 (56.5)
Pre-index treatment category, n (%)			
GLP-1 RA	1845 (4.7)	581 (5.1)	1264 (4.6)
2 OADs	29 001 (74.4)	8838 (78.0)	20 163 (73.0)
>2 OADs	8119 (20.8)	1911 (16.9)	6208 (22.5)
Pre-index BMI			
Individuals with a recorded measurement, n (%)	27 491 (70.6)	8014 (70.7)	19 447 (70.4)
BMI, mean (SD), kg/m²	31.5 (6.5)	32.4 (6.9)	31.1 (6.3)
Pre-existing comorbidities, n (%)			
Retinopathy	9450 (24.3)	2715 (24.0)	6735 (24.4)
Neuropathy	3303 (8.5)	956 (8.4)	2347 (8.5)
History of hypoglycaemia	1911 (4.9)	539 (4.8)	1372 (5.0)
Cerebrovascular diseases	1216 (3.1)	350 (3.1)	866 (3.1)
End-stage renal disease	179 (0.5)	79 (0.7)	100 (0.4)

[a]Date of uncontrolled HbA_{1c} (≥7.5%) measurement.
BMI, body mass index; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated haemoglobin; n, number of individuals; OAD, oral antidiabetic drug; SD, standard deviation; T2D, type 2 diabetes.

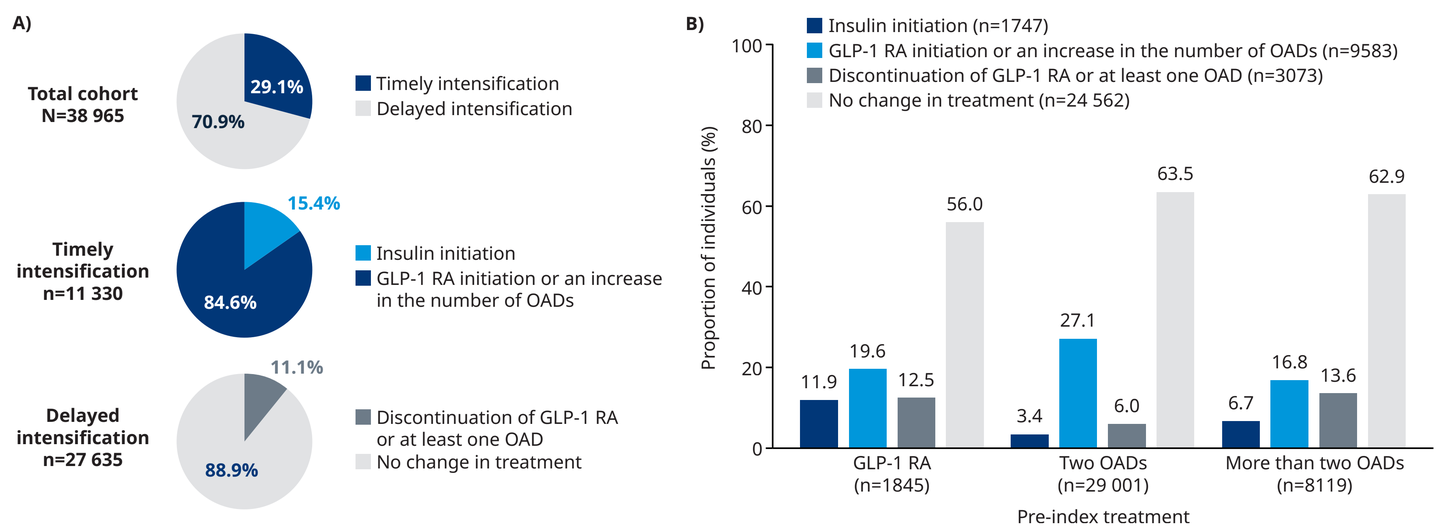
Treatment intensification patterns

- **Of the total cohort (N=38 965), 70.9% experienced a delay in treatment intensification.** Among these, 88.9% had no change in treatment and 11.1% discontinued GLP-1 RA or at least one OAD in the 12 months after index.
- In contrast, 29.1% of the total cohort received timely intensification, of which 15.4% initiated insulin and 84.6% either initiated a GLP-1 RA or increased their number of OADs compared with their pre-index treatment (**Figure 2A**).
  - Timely treatment intensifiers were slightly younger and had a higher mean HbA_{1c} at index than delayed intensifiers (**Table 1**).
- 11.9% of individuals receiving a GLP-1 RA initiated insulin versus 3.4% of individuals receiving two OADs before index (**Figure 2B**). Almost two-thirds of individuals receiving two OADs (63.5%) or more than two OADs (62.9%) before index did not experience any change to their treatment in the 12 months after index (**Figure 2B**).

Treatment optimisation patterns

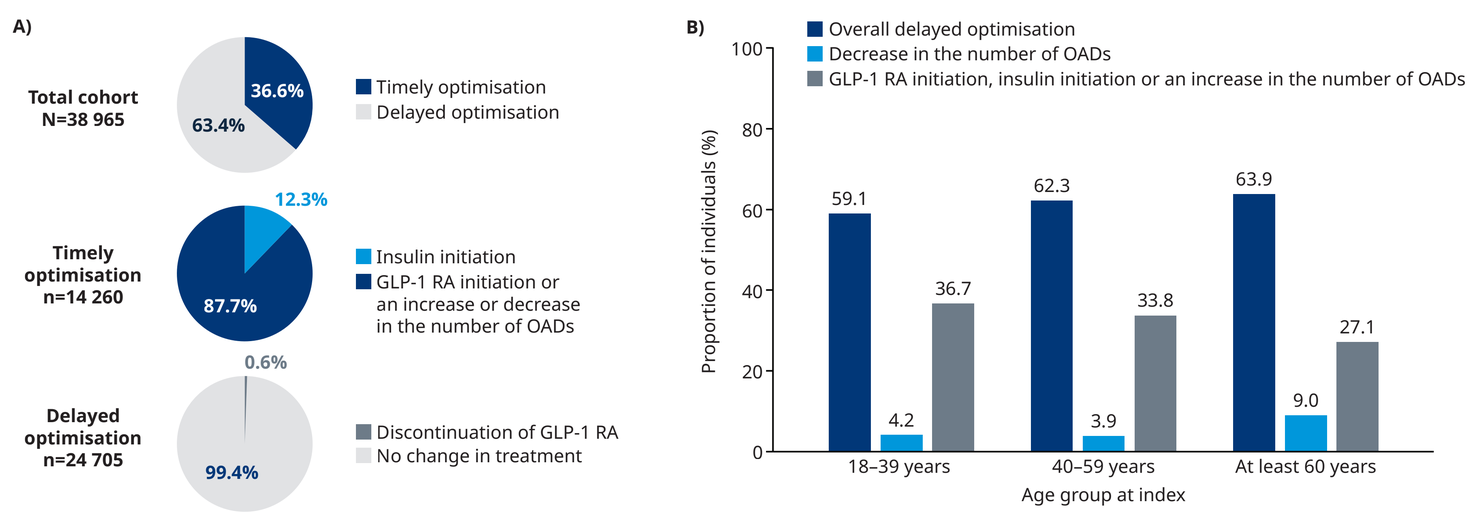
- **Of the total cohort (N=38 965), 63.4% experienced a delay in treatment optimisation, of which 99.4% had no treatment changes (Figure 3A).** Only 36.6% of the total cohort received timely optimisation, of which 12.3% initiated insulin and 87.7% either initiated a GLP-1 RA or had an increase or reduction in the number of OADs compared with before index (**Figure 3A**).
- A higher proportion of individuals aged at least 60 years than those in younger age groups had a reduction in the number of OADs. The highest proportion of individuals who initiated a GLP-1 RA, insulin or had an increase in the number of OADs was seen in individuals aged 18–39 years (36.7%), and the lowest proportion was seen in those aged at least 60 years (27.1%) (**Figure 3B**).
- Prior reports suggest that factors such as individual hesitancy, clinician-related barriers and broader healthcare system challenges may contribute to therapeutic inertia, delaying treatment intensification and optimisation.[1]

Figure 2. Treatment intensification patterns: overall (A) and by pre-index treatment (B)



Index: date of uncontrolled HbA_{1c} (≥7.5%) measurement. Timely treatment intensification: initiation of a GLP-1 RA, insulin or an increase in the number of OADs in the 12 months after index. Delayed treatment intensification: absence of intensification in the 12 months after index.
GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated haemoglobin; n, number of individuals; OAD, oral antidiabetic drug.

Figure 3. Treatment optimisation patterns: overall (A) and by age group at index (B)



Index: date of uncontrolled HbA_{1c} (≥7.5%) measurement. Timely treatment optimisation: initiation of a GLP-1 RA, insulin or an increase or decrease in the number of OADs in the 12 months after index. Delayed treatment optimisation: absence of optimisation in the 12 months after index.
GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated haemoglobin; n, number of individuals; OAD, oral antidiabetic drug.

Conclusion

- Based on this real-world analysis of UK clinical practice data, therapeutic inertia was common in the management of T2D, with nearly three-quarters of individuals not receiving treatment intensification and almost two-thirds not receiving treatment optimisation in the 12 months following an initial uncontrolled HbA_{1c} measurement.
- More individuals aged at least 60 years than younger individuals had a reduction in the number of OADs, while those aged 18–39 years had the highest percentages of individuals initiating GLP-1 RA or insulin, or increasing their number of OADs.

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