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著者	MAEGAWA Hiroshi, ISHIGAKI Yasushi, LANGER Jakob, Saotome-Nakamura Ai, ANDERSEN Marc, Japan Diabetes Clinical Data Management (JDDM) Study Group
journal or publication title	Journal of diabetes investigation
year	2020-07-08
URL	http://hdl.handle.net/10422/00012788

doi: 10.1111/jdi.13352(https://doi.org/10.1111/jdi.13352)

JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes
ORIGINAL ARTICLE

Clinical inertia in patients with type 2 diabetes treated with oral antidiabetic drugs: Results from a Japanese cohort study (JDDM53)

Hiroshi Maegawa[1]*, Yasushi Ishigaki[2], Jakob Langer[3], Ai Saotome-Nakamura[3], Marc Andersen[4], on behalf of the Japan Diabetes Clinical Data Management (JDDM) Study Group

[1]Department of Medicine, Shiga University of Medical Science, Otsu, Japan, [2]Department of Internal Medicine, Iwate Medical University, Morioka, Japan, [3]Novo Nordisk Pharma Ltd, Tokyo, Japan, and [4]StatGroup ApS, Copenhagen, Denmark

Keywords
Antidiabetic drugs, Diabetes mellitus type 2, Japanese adults

***Correspondence**
Hiroshi Maegawa
Tel.: +81-77-548-2222
Fax: +81-77-543-3858
E-mail address:
maegawa@belle.shiga-med.ac.jp

J Diabetes Investig 2020

doi: 10.1111/jdi.13352

ABSTRACT

Aims/Introduction: Treatment intensification is commonly delayed in people with type 2 diabetes, resulting in poor glycemic control for an unacceptable length of time and increased risk of complications.

Materials and Methods: This retrospective study investigated clinical inertia in 33,320 Japanese adults with type 2 diabetes treated with oral antidiabetic drugs (OADs) between 2009 and 2018, using data from the Computerized Diabetes Care (CoDiC®) database.

Results: The median time from first reported glycated hemoglobin (HbA1c) ≥7.0% (≥53 mmol/mol) to treatment intensification was considerably longer and HbA1c levels were higher the more OADs the patient was exposed to. For patients receiving three OADs, the median times from HbA1c ≥7.0% (53 mmol/mol) to intensification with OAD, glucagon-like peptide-1 receptor agonist or insulin were 8.1, 9.1 and 6.7 months, with a mean HbA1c level at the time of intensification of 8.4%, 8.9% and 9.3%, respectively. The cumulative incidence for time since the first reported HbA1c ≥7.0% (≥53 mmol/mol) to intensification confirmed the existence of clinical inertia, identifying patients whose treatment was not intensified despite poor glycemic control. HbA1c levels ≥7.0% (≥53 mmol/mol) after ≥6 months on one, two or three OADs were observed in 42%, 51% and 58% of patients, respectively, showing that approximately 50% of patients are above HbA1c target regardless of how many OADs they take.

Conclusions: Real-world data here show clinical inertia in Japanese adults with type 2 diabetes from early diabetes stages when they are receiving OADs, and illustrate a need for earlier, more effective OADs or injectable treatment intensification and better communication around the existence of clinical inertia.

INTRODUCTION

It is estimated that approximately 10 million people in Japan have "strongly suspected diabetes"[1]. Tight glycemic control in people with type 2 diabetes is required to minimize the risk of later complications[2–5]. Data from the Japan Diabetes Complications Study and the Japanese Elderly Diabetes Intervention Trial[6] showed that a 1%-point increase in the glycated hemoglobin (HbA1c) level resulted in a significantly increased relative risk of micro- and macrovascular complications, with hazard ratios of 1.22 ($P = 0.03$) and 1.23 ($P = 0.02$) for coronary heart disease and stroke, respectively[6].

As type 2 diabetes is progressive, maintenance of good glycemic control necessitates that treatment is titrated or intensified as time goes on[7]. Guidelines from the American Diabetes Association recommend initial treatment with the oral antidiabetic drug (OAD), metformin, in combination with lifestyle modifications[8]. If an individualized HbA1c target is not achieved within 3 months of treatment, and in the absence of atherosclerotic cardiovascular disease or chronic kidney disease, treatment should be intensified by the addition of further OADs (sulfonylurea [SU], thiazolidinedione, dipeptidyl peptidase-4 inhibitor

Received 25 March 2020; revised 30 June 2020; accepted 5 July 2020

[DPP-4i] or sodium–glucose cotransporter 2 inhibitor), glucagon-like peptide-1 receptor agonists [GLP-1RAs] or basal insulin[8]. Japanese Clinical Practice Guidelines are in agreement, recommending that OADs and/or GLP-1RAs are given to non-insulin-dependent patients in whom glycemic control is not achievable with lifestyle modifications after 2–3 months, and that insulin therapy should be started when glycemic goals are no longer achievable with these[9].

The American Diabetes Association, International Diabetes Federation and Japanese Clinical Practice Guidelines recommend setting an HbA1c goal of <7.0% (<53 mmol/mol) in the majority of (non-pregnant) adults with type 2 diabetes[8–10]. The American Association of Clinical Endocrinologists supports a slightly more stringent HbA1c goal of ≤6.5% (≤48 mmol/mol) for most patients[11]. The American Diabetes Association and Japanese Clinical Practice Guidelines recommend more stringent goals (<6.5% [<48 mmol/mol] and <6.0% [<42 mmol/mol], respectively) for selected individuals if achievable without significant hypoglycemia or other adverse effects[8,9], but a less stringent goal of <8.0% (<64 mmol/mol) in elderly patients or those with, for example, a history of severe hypoglycemia, advanced vascular complications or extensive comorbidities[9,12].

Multiple studies have shown evidence of clinical inertia (inappropriately delayed treatment intensification) in people with type 2 diabetes, resulting in poor glycemic control for an unacceptable length of time[13,14]. A large retrospective cohort study of 81,573 people with type 2 diabetes in the UK treated with one, two or three OADs showed that in people with HbA1c ≥7.0% (≥53 mmol/mol), ≥7.5% (≥58 mmol/mol) or ≥8.0% (≥64 mmol/mol), the median time from above HbA1c cut-off to intensification with an additional OAD was 2.9, 1.9 or 1.6 years, respectively, for those taking one OAD, and >7.2, >7.2 and >6.9 years for those taking two OADs[15]. Data show that people with type 2 diabetes are receiving treatment with multiple OADs for long periods of time before their treatment is intensified, despite poor glycemic control. Several studies have also shown that clinical inertia exists in people with type 2 diabetes treated with OADs who are starting insulin therapy[15–18].

The Computerized Diabetes Care (CoDiC®) database was developed by the Japan Diabetes Clinical Data Management Study Group (JDDM) to promote clinical research on diabetes. This large, anonymized, longitudinal, validated database, which is updated annually, contains patient-level clinical information for approximately 60,000 patients treated by diabetes specialists in 61 JDDM participating diabetes institutions across Japan, including diagnosis, mortality, laboratory results and prescription data.[19] A cross-sectional study using data from the CoDiC® database investigated changes in OAD prescriptions and improved glycemic control from 2002 to 2011 in Japan.[20] The results showed a move toward polypharmacy, particularly including biguanides and DPP-4is, accompanied by an improvement in HbA1c levels[20]. Another recent, retrospective cohort study using data from the CoDiC® database showed that clinical inertia existed in Japanese clinical practice among people with type 2 diabetes treated with basal insulin[21].

Clinical inertia is a global problem, the extent of which has been shown to vary between countries[22–25]. The aim of the present retrospective study was to investigate clinical inertia in Japanese adults with type 2 diabetes treated with OADs, using prescription data from the CoDiC® database, including how and when they received treatment intensification.

METHODS

Study design and participants

This retrospective analysis was carried out using data extracted from the CoDiC® database[19] by the JDDM Study Group. Retrieved data included prescriptions of antidiabetic medication (including drug name, dose and frequency), prescriptions of selected other medications and drug category, patient visit and examination results, and patient characteristics including date of birth, sex, diagnosis date of type 2 diabetes, and date for the first contact recorded in the CoDiC®. Patients were included in the overall study population if they had a diagnosis of type 2 diabetes, were aged ≥18 years, and had at least one OAD prescription in the period between 1 January 2009 and 31 December 2011. Only individuals with an available first visit date were included. In cases where the first visit date was after the first prescription, the individual was excluded. Follow up started from the first OAD prescription between 2009 and 2011, and was until 12 March 2018. Only OAD regimens that started >91 days after the start of the observation period were included to ensure that they were not ongoing regimens. The JDDM ethics committee approved the study protocol. Written informed consent was not required from patients because of the retrospective nature of this study. The option to "opt out" and how to do it were made clear through a poster in each clinic describing the study (available here [Japanese]: http://jddm.jp/).

End-points

The protocol-specified primary end-point was time from the start of an OAD regimen (limited to one, two or three OADs) to a treatment change. Treatment change comprised the addition of one or more OADs, insulin, GLP-1RA or GLP-1RA plus insulin (representing treatment intensification), change in OADs not consisting of OAD addition, discontinuation of OAD (none of which qualified as treatment intensification), or no further prescription information being available.

The main secondary end-point, a subset of the primary end-point dataset providing a measure of clinical inertia, was time to treatment change (as described above), or HbA1c <7.0%, from the first HbA1c above target (HbA1c ≥7.0% [≥53 mmol/mol]) after ≥6 months of taking OADs. Additional end-points included HbA1c level at time of intensification, and the proportion of patients with an HbA1c level above target (using HbA1c ≥7.0% [≥53 mmol/mol], ≥7.5% [≥58 mmol/mol] or ≥8.0% [≥64 mmol/mol] as the cut-off) after ≥6 months of taking OADs.

Additional analyses investigated the proportion of patients with HbA1c ≥7.0% (53 mmol/mol) after ≥6 months of taking OADs, stratified by the most frequent types of OAD received (i.e., metformin, SU or DPP-4i for one OAD; metformin + SU, SU + DPP-4i or metformin + DPP-4i for two OADs; SU + metformin + DPP-4i, SU + metformin + alpha-glucosidase or SU + metformin + thiazolidinedione for three OADs). Additional analyses were also carried out on differences in outcomes between OAD regimens containing DPP-4is and those without, given their frequent use in Japan.

Statistical analysis

Data were analyzed for each of the OAD regimens (comprising of one, two or three OADs). Only the first instance of repeated OAD regimens was used in the analysis. No adjustment for multiplicity was carried out. All outcomes, exposure and confounding variables were reported using descriptive statistics.

Time from the start of an OAD regimen to treatment change, and time to treatment change or HbA1c <7.0% from the first HbA1c ≥7.0% (≥53 mmol/mol), after ≥6 months of taking OADs, were analyzed as time-to-event data with competing risks for estimation of the cumulative incidence function. The causes were derived from the status at the end of the OAD regimen, with the exception of using censoring for no further information when the end date was on or after 1 January 2018. The estimated cumulative incidence function was presented graphically for all causes, and in tabular format for treatment intensification causes and selected timepoints. The HbA1c level at time of treatment intensification was reported using the mean and standard deviation.

RESULTS

Over the course of the study, 10,217, 13,061 and 10,042 participants (with at least one OAD prescription between 1 January 2009 and 31 December 2011) were exposed to regimens with one, two or three OADs, respectively. The most frequently reported OADs were biguanides, SUs or DPP-4is for regimens containing one OAD (~25% for each); SUs + biguanides (23%) for regimens containing two OADs; and SUs + biguanides + DPP-4i (38%) for regimens containing three OADs (Table S1).

The baseline characteristics of participants exposed to one, two or three OADs are presented in Table S2. Two-thirds of the participants in each group were men, the mean age at OAD regimen start ranged 62–63 years across the groups and 42–45% of the participants were aged ≥65 years (Table S2). The mean time from documented diabetes onset to starting an OAD regimen ranged 8.9–12.1 years, with a mean HbA1c level before starting an OAD regimen ranging 7.7–8.0% (Table S2).

The median time to treatment intensification from the first reported HbA1c value ≥7.0% (53 mmol/mol) and mean HbA1c at time of intensification are shown in Table 1. Time to intensification with any treatment was considerably longer and HbA1c levels were higher the more OADs the patient was exposed to, and intensification with insulin was generally carried out earlier compared with other intensification options. For participants taking one OAD, the median times from the first reported HbA1c value ≥7.0% (53 mmol/mol) to intensification with OAD, GLP-1RA or insulin alone were 3.7, 5.6 and 3.3 months, with a mean HbA1c level at the time of intensification of 8.1%, 7.8% and 9.3%, respectively. For participants taking three OADs, the median times from HbA1c ≥7.0% (53 mmol/mol) to intensification were 8.1, 9.1 and 6.7 months, respectively, with a mean HbA1c level at the time of intensification of 8.4%, 8.9% and 9.3%.

The cumulative incidence for time since the first reported HbA1c value ≥7.0% (53 mmol/mol) to treatment intensification in patients taking one, two or three OADs is shown in Figure 1. The grey area shows patients whose treatment was not intensified, despite having an HbA1c ≥7.0% (53 mmol/mol), giving a clear measure of the extent of clinical inertia

Table 1 | Median time to treatment intensification* from the first glycated hemoglobin ≥7.0% (≥53 mmol/mol) after 6 months of treatment, and mean glycated hemoglobin at the time of intensification

	1 OAD (*n* = 3,960)	2 OADs (*n* = 6,278)	3 OADs (*n* = 5,615)
Median time in months (range) from the first HbA1c ≥7.0% (≥53 mmol/mol) to treatment intensification with:			
OAD add-on	3.7 (0.1–76.3) (*n* = 1,257)	5.7 (0.1–81.3) (*n* = 1,538)	8.1 (0.1–82.7) (*n* = 626)
GLP-1RA	5.6 (0.9–28.8) (*n* = 18)	5.8 (0.1–36.2) (*n* = 32)	9.1 (0.1–74.3) (*n* = 76)
Insulin	3.3 (0.1–35.2) (*n* = 37)	4.3 (0.1–61.0) (*n* = 78)	6.7 (0.1–66.3) (*n* = 151)
	1 OAD (*n* = 3,762)	2 OADs (*n* = 5,997)	3 OADs (*n* = 5,348)
Mean HbA1c % (SD) at the time of intensification (after HbA1c ≥7.0% [≥53 mmol/mol]) with:			
OAD add-on	8.1 (1.0) (*n* = 1,257)	8.3 (1.0) (*n* = 1,538)	8.4 (1.0) (*n* = 626)
GLP-1RA	7.8 (0.6) (*n* = 18)	9.2 (1.3) (*n* = 32)	8.9 (1.3) (*n* = 76)
Insulin	9.3 (2.0) (*n* = 35)	9.4 (1.9) (*n* = 78)	9.3 (1.4) (*n* = 151)

*The main secondary end-point was time to treatment change (comprising the addition of one or more oral antidiabetic drug [OADs], insulin, glucagon-like peptide-1 receptor agonist [GLP-1RA] or GLP-1RA plus insulin [representing treatment intensification, as reported here], change in OAD dose or brand, discontinuation of OAD, no further prescription information being available, censoring or glycated hemoglobin [HbA1c] <7.0%) from the first HbA1c ≥7.0% (≥53 mmol/mol) after ≥ 6 months of taking OADs. SD, standard deviation.

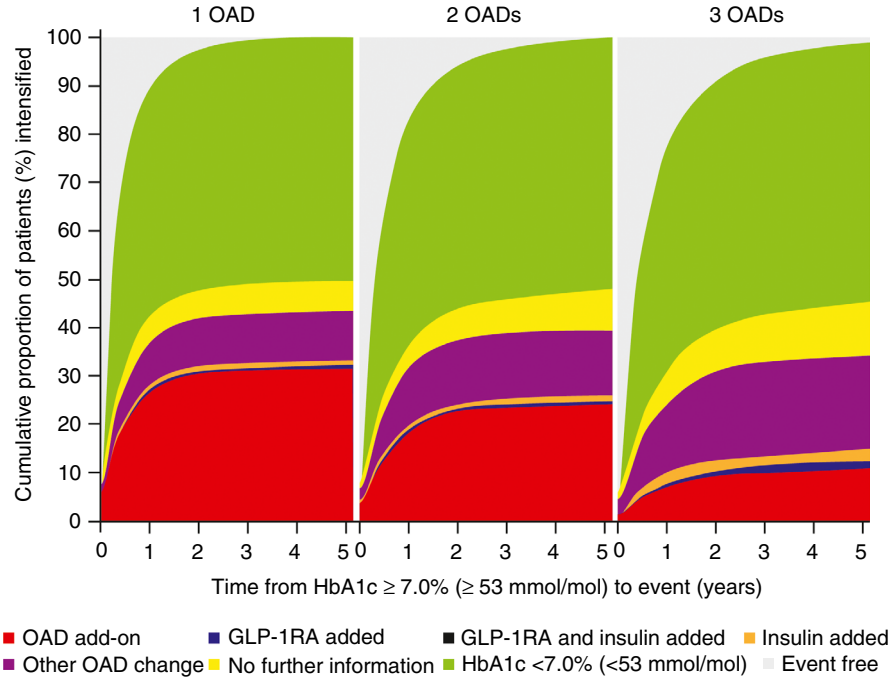

Figure 1 | Cumulative incidence for time since the first reported glycated hemoglobin (HbA1c) value ≥7.0% (≥53 mmol/mol) to first event in patients taking one, two or three OADs. GLP-1RA, glucagon-like peptide-1 receptor agonist; OAD, oral antidiabetic drug.

(Figure 1). As expected, the level of clinical inertia increased the more OADs the patient was exposed to.

The median time from the start of an OAD regimen to treatment intensification and mean HbA1c values at that time are shown in Table 2. The time from the start of an OAD regimen to intensification with any OAD treatment was again considerably longer the more OADs the patient was exposed to. The cumulative incidence function for time since regimen start to intensification is shown in Table S3 for causes related to treatment intensification and selected timepoints.

The proportion of patients with an HbA1c value ≥7.0% (≥53 mmol/mol), ≥7.5% (≥58 mmol/mol) or ≥8.0% (≥64 mmol/mol) after ≥6 months on an OAD regimen is shown in Table 3. An HbA1c value ≥7.0% (≥53 mmol/mol) after ≥6 months of taking OADs was reported in 42%, 51% and 58% of patients taking one, two and three OADs, respectively, indicating that there was still a large proportion of uncontrolled patients taking multiple OADs. Stratification of these data by the most frequent type of OAD used showed similar proportions of patients with uncontrolled disease (Table S4). In patients taking one OAD, HbA1c ≥7.0% (≥53 mmol/mol) was reported for 46%, 44% and 45% of patients intensified with metformin, SU and DPP4-i, respectively. The proportion of patients with HbA1c ≥7.0% (≥53 mmol/mol) was generally lower in older people (37%, 46% and 52%, respectively, in patients aged ≥ 75 years taking one, two or three OADs; Table 3). An HbA1c level ≥7.5% (≥58 mmol/mol) after ≥6 months of taking OAD was observed in 27%, 36% and 44% of patients, and an HbA1c ≥8.0% (≥64 mmol/mol) in 15%, 21% and 29% of patients taking one, two or three OADs, respectively (Table 3).

The median time from the first HbA1c ≥7.0% (≥53 mmol/mol) to treatment intensification was longer for patients on regimens containing three OADs that included DPP-4is (Table S5).

DISCUSSION

Both international and Japanese consensus guidelines for the management of type 2 diabetes recommend an individualized stepwise approach to intensifying treatment[8,9]. The guidelines stipulate that treatment should be re-evaluated every 3–6 months to avoid clinical inertia[8].

Using the CoDiC® database, the present study investigated clinical inertia and treatment intensification in Japanese people with type 2 diabetes treated with one, two or three OADs. The most frequent components of the studied OAD regimens were biguanides, such as metformin, SU and DPP-4i, in alignment with what is seen in routine clinical practice.

The time to intensification, with any treatment, from the first HbA1c value reported to be out of control (≥7.0% [≥53 mmol/mol]) was considerably longer the more OADs the patient was exposed to. Cumulative incidence data showing the proportion of patients whose treatment was not intensified despite having an HbA1c level ≥7.0% (≥53 mmol/mol), that is, omitting data for those patients whose disease is under control, confirmed

Table 2 | Median time from start of an oral antidiabetic drug regimen to treatment intensification* and mean glycated hemoglobin at the time of intensification

	1 OAD (n = 10,209)	2 OADs (n = 13,054)	3 OADs (n = 10,038)
Median time in months (range) from the start of OAD regimen to intensification with:			
OAD add-on	6.2 (0–95.2) (n = 4,773)	9.9 (0–95.4) (n = 4,122)	18.0 (0–92.0) (n = 1,407)
GLP-1RA	5.1 (0–67.6) (n = 86)	7.8 (0.2–45.3) (n = 83)	16.1 (0.1–90.8) (n = 138)
Insulin	2.0 (0–68.7) (n = 240)	4.2 (0–69.1) (n = 284)	9.5 (0.1–74.7) (n = 305)
	1 OAD (n = 8,081)	2 OADs (n = 11,104)	3 OADs (n = 8,653)
Mean HbA1c % (SD) at the time of intensification with:			
OAD add-on	7.9 (1.2) (n = 4,435)	8.0 (1.1) (n = 3,917)	8.1 (1.0) (n = 1,356)
GLP-1RA	7.9 (1.5) (n = 65)	8.6 (1.5) (n = 75)	8.6 (1.3) (n = 125)
Insulin	8.7 (2.0) (n = 167)	9.1 (1.9) (n = 230)	9.2 (1.6) (n = 277)

*The primary end-point was the time from the start of an oral antidiabetic drug (OAD) regimen to treatment change (comprising addition of one or more OADs, insulin, glucagon-like peptide-1 receptor agonist [GLP-1RA] or GLP-1RA plus insulin [representing treatment intensification, as reported here], change in OAD dose or brand, discontinuation of OAD, no further prescription information being available, or censoring). HbA1c, glycated hemoglobin; SD, standard deviation.

Table 3 | Proportion of patients with glycated hemoglobin ≥7.0% (≥53 mmol/mol), ≥7.5% (≥58 mmol/mol) or ≥8.0% (≥64 mmol/mol), after ≥6 months on an OAD regimen

	HbA1c ≥7.0% (≥53 mmol/mol)					HbA1c ≥7.5% (≥58 mmol/mol)		HbA1c ≥8.0% (≥64 mmol/mol)
	All patients	Age <45 years	Age 45 to <65 years	Age ≥65 years	Age ≥75 years	All patients	Age ≥65 years	All patients
1 OAD	41.7%	44.3%	43.7%	38.8%	36.7%	27.1%	23.4%	15.2%
2 OADs	50.5%	50.3%	52.2%	48.6%	46.0%	35.9%	32.8%	21.4%
3 OADs	58.0%	59.2%	60.6%	54.9%	52.0%	44.1%	39.3%	28.7%

HbA1c, glycated hemoglobin; OAD, oral antidiabetic drug.

the existence of clinical inertia in this population. As might be expected, a higher HbA1c was observed at the time of intensification in those patients on regimens comprising of three OADs, compared with those taking one or two OADs, indicative of the disease progression in those individuals. The median time from the start of an OAD regimen to treatment intensification with any OAD treatment was also considerably longer, and HbA1c levels were higher the more OADs the patient was exposed to.

In patients taking three OADs, treatment was intensified after a median of 8.1 months with an OAD, 9.1 months with a GLP-1RA and 6.7 months with insulin. These findings highlight the issue of clinical inertia in this OAD polypharmacy population, particularly for those patients whose healthcare professionals might not want to consider initiating insulin or GLP-1RA therapy. Data show that people with type 2 diabetes can be treated ineffectively with OADs for a long time. More effective OADs and strategies are required to reduce clinical inertia and improve long-term glycemic control in these patients.

HbA1c levels ≥7.0% (≥53 mmol/mol) after ≥6 months on an OAD regimen comprising one, two or three OADs were observed in 42%, 51% and 58% of patients, respectively, showing that approximately 50% of patients are above HbA1c treatment target regardless of the number of OADs they take. The data presented here show persistently high HbA1c levels despite OAD treatment, and extensive delays in treatment intensification in patients taking one, two or three OADs. Additional analyses stratified by the most frequent type of OADs used did not show any differences in reaching glycemic targets, and the proportions of patients with uncontrolled disease were similar to the overall population.

Interestingly, the findings reported here show a lower degree of clinical inertia compared with those reported by Khunti *et al.*[15] from a large retrospective cohort study of people with type 2 diabetes in the UK treated with one, two or three OADs. Results from that study showed that in people with HbA1c ≥7.0% (≥53 mmol/mol), ≥7.5% (≥58 mmol/mol) or ≥8.0% (≥64 mmol/mol), the median time from above the HbA1c cut-off to intensification with an additional OAD was 2.9, 1.9 and 1.6 years, respectively, for those taking one OAD, and <7.2, <7.2 and <6.9 years, respectively, for those taking two OADs[15]. Differences in clinical inertia between the two studies could be explained by variation in healthcare systems and potential differences in population demographics. In the

latter study, a lower proportion of participants were men (51–57% across groups), compared with two-thirds of participants in the present study, and the mean baseline HbA1c levels before starting an OAD regimen were substantially higher (8.4%, 8.8% and 9.0% in people taking one, two or three OADs) compared with the present study (7.7%, 7.9% and 8.0%, respectively). A large-scale survey of Japanese type 2 diabetes patients in primary care, in which 53% had HbA1c levels <7.0% (<53 mmol/mol) and the mean HbA1c was 7.04%, also suggests comparatively good glycemic control in this population[26].

Japan is now facing a super-aged society, and the number of elderly patients with diabetes is rising steadily. Elderly patients might experience cognitive impairment or dementia, and have a tendency to suffer from severe hypoglycemia[27]. Guidelines from the Joint Committee of the Japan Diabetes Society and the Japan Geriatrics Society for Improvement in Treatment of Elderly Patients with Diabetes recommend that, if treatment intensification is difficult in an elderly patient, for example, due to moderate dementia, the target HbA1c should be set at <8.0% (<64 mmol/mol)[9].

The impact of setting different glycemic targets (HbA1c <7.5% and HbA1c <8.0%) on all end-points was analyzed, but it was beyond the scope of this article to present all the data here. However, the impact of varying the target definition across age subgroups is presented in Table 3, acknowledging that a uniform glycemic target might not be appropriate for all patients. Additional analyses according to age at the start of an OAD regimen (or after ≥6 months of treatment) were also beyond the scope and objectives of this study, but might be interesting for future research.

The limitations of the present study were that only descriptive data were reported, with no statistical significance testing, and the results were retrospective and limited to Japan. Generalized conclusions made from this study to other populations or countries should be done with caution. In addition, treatment intensification and HbA1c values were not analyzed as a function of patient comorbidities/diabetic complications, which allow for a less stringent HbA1c goal. Finally, some of the DDP-4is used only became available part-way through the study, and therefore might have been misrepresented. The median time from the start of an OAD regimen to treatment intensification was longer for patients on regimens containing DPP-4is than for those not receiving DPP-4is. The median time from the first HbA1c ≥7.0% to treatment intensification was also longer for patients on regimens containing three OADs that included DPP-4is. It would be useful to carry out further, larger analyses of the impact of availability of DPP-4is on clinical inertia. The study period also resulted in sodium–glucose cotransporter 2 inhibitors not being reflected to an extent that matches their current magnitude of use. The changing treatment landscape for diabetes, including the expected launch of oral GLP-1RA and combination treatments, might have a significant effect on clinical inertia in the future. Finally, it was beyond the scope of this study to assess treatment adherence. The level of adherence to diabetes treatment might have influenced subsequent intensification and, thus, the extent of clinical inertia[28].

Increasing awareness might be key to minimizing clinical inertia in the treatment of type 2 diabetes. The Time2DoMore study, an online survey of 652 adults with diabetes and 337 treating physicians in six countries, concluded that impairment in communication is at the heart of clinical inertia[29]. It is important to assess the extent of clinical inertia in clinical practice in different regions, so that strategies to improve clinical care and outcomes can be implemented[30]. As the majority of patients in Japan are treated in a clinic rather than a hospital setting, the CoDiC® database is considered representative of the diabetes population in Japan. Furthermore, the CoDiC® database has previously been used to study clinical inertia in Japanese adults with type 2 diabetes treated with basal insulin[20,21].

Real-world data presented here show that clinical inertia exists in Japanese adults with type 2 diabetes from early stages of the disease when they are receiving treatment with OADs, and illustrate a need for earlier, more effective OAD or injectable treatment intensification, setting of individual treatment goals and better communication around the existence of clinical inertia. Strategies are needed to increase the number of patients undergoing effective therapy intensification and to reduce the delay in treatment intensification in Japan.

ACKNOWLEDGMENTS

The authors are grateful to the patients whose data contributed to this study, and to Jane Blackburn and Erin Slobodian, of Watermeadow Medical, an Ashfield company, part of UDG Healthcare plc (funded by Novo Nordisk A/S), for medical writing and editing assistance.

DISCLOSURE

This study was sponsored by Novo Nordisk A/S. HM has received research support unrelated to this study from Astellas Pharma Inc., AstraZeneca K.K., Ono Pharmaceutical, Nippon Boehringer Ingelheim, Takeda Pharmaceutical, Daiichi Sankyo, Mitsubishi Tanabe Pharma and Sanofi, and lecture fees from Astellas Pharma, Taisho Toyama Pharmaceutical, Ono Pharmaceutical, Novo Nordisk Pharma, Eli Lilly Japan, MSD, Daiichi Sankyo, Nippon Boehringer Ingelheim, Mitsubishi Tanabe Pharma, Sanofi, Kowa Pharmaceutical and Takeda Pharmaceutical. YI has received research support unrelated to this study from MSD, Ono Pharmaceutical, Tanabe Mitsubishi Pharma, Daiichi Sankyo and Novo Nordisk Pharma, and lecture fees from MSD, Ono Pharmaceutical, Tanabe Mitsubishi Pharma, Nippon Boehringer Ingelheim, Bayer Yakuhin, Novartis Pharma, Sanofi, Kowa Pharmaceutical and Takeda Pharmaceutical. MA has received consulting fees from Novo Nordisk. JL and AS-N are employees of Novo Nordisk.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 | Most frequently reported oral antidiabetic drug regimens.

Table S2 | Baseline characteristics of participants exposed to one, two or three oral antidiabetic drugs.

Table S3 | Cumulative incidence function for time since the start of an oral antidiabetic drug regimen to treatment intensification.

Table S4 | Proportion of patients with glycated hemoglobin ≥7.0% (≥53 mmol/mol), stratified by the type of oral antidiabetic drug used.

Table S5 | Time to treatment intensification from the first glycated hemoglobin ≥7.0% (≥53 mmol/mol) after 6 months of treatment, and the mean glycated hemoglobin at the time of intensification, for oral antidiabetic drug regimens with or without dipeptidyl peptidase-4 inhibitors.