



Overcoming Therapeutic Inertia as the Achilles' Heel for Improving Suboptimal Diabetes Care: An Integrative Review

Boon-How Chew^{1,2}, Barakatun-Nisak Mohd-Yusof³, Pauline Siew Mei Lai⁴, Kamlesh Khunti^{5,6}

¹Department of Family Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; ²Clinical Research Unit, Hospital Pengajar Universiti Putra Malaysia (HPUPM Teaching Hospital), Persiaran MARDI-UPM; ³Department of Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang; ⁴Department of Primary Care Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; ⁵National Institute for Health Research Applied Research Collaboration East Midlands, Leicester Diabetes Centre; ⁶Diabetes Research Centre, Leicester General Hospital, University of Leicester, Leicester, UK

The ultimate purpose of diabetes care is achieving the outcomes that patients regard as important throughout the life course. Despite advances in pharmaceuticals, nutraceuticals, psychoeducational programs, information technologies, and digital health, the levels of treatment target achievement in people with diabetes mellitus (DM) have remained suboptimal. This clinical care of people with DM is highly challenging, complex, costly, and confounded for patients, physicians, and healthcare systems. One key underlying problem is clinical inertia in general and therapeutic inertia (TI) in particular. TI refers to healthcare providers' failure to modify therapy appropriately when treatment goals are not met. TI therefore relates to the prescribing decisions made by healthcare professionals, such as doctors, nurses, and pharmacists. The known causes of TI include factors at the level of the physician (50%), patient (30%), and health system (20%). Although TI is often multifactorial, the literature suggests that 28% of strategies are targeted at multiple levels of causes, 38% at the patient level, 26% at the healthcare professional level, and only 8% at the healthcare system level. The most effective interventions against TI are shorter intervals until revisit appointments and empowering nurses, diabetes educators, and pharmacists to review treatments and modify prescriptions.

Keywords: Diabetes mellitus; Therapeutics; Medication adherence

INTRODUCTION

The incidence and prevalence of diabetes mellitus (DM) continue to rise worldwide [1], accompanied by physical and mental suffering for people living with DM and their caregivers, higher healthcare costs, and increasing quantities of drugs and research

on DM-related health conditions. Despite extensive advances in pharmaceuticals, nutraceuticals, medical programs, clinical care, information technologies, and digital health in diabetes care, the levels of treatment target achievement in people with DM remain quite high, defying and defeating all diabetes experts and centres. At best, 50% of patients achieve a hemoglobin

Received: 23 December 2022, **Revised:** 28 January 2023,
Accepted: 6 February 2023

Corresponding author: Boon-How Chew
Department of Family Medicine, Faculty of Medicine and Health Sciences,
Universiti Putra Malaysia, Serdang, Malaysia
Tel: +60-039769-9763, **E-mail:** chewboonhow@upm.edu.my

Copyright © 2023 Korean Endocrine Society

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

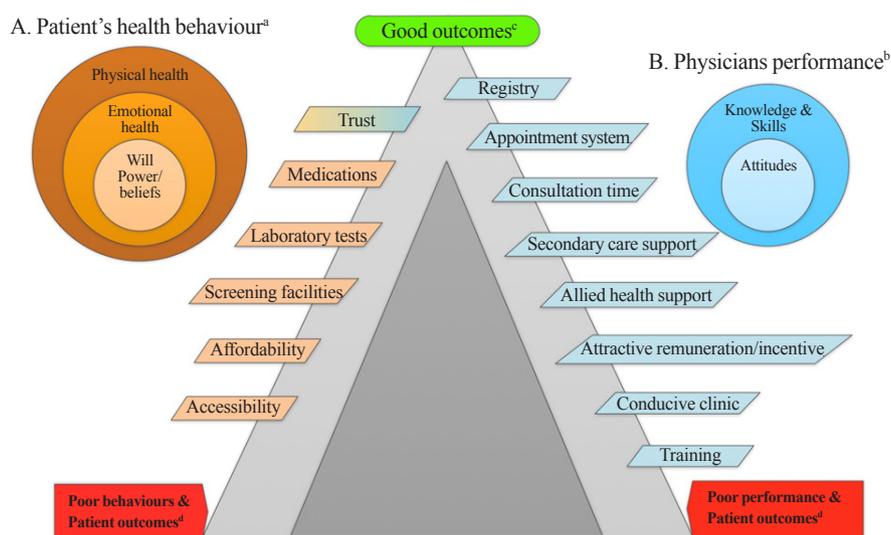
A1c (HbA1c) level <7.0% (<53 mmol/mol), 80% attain a blood pressure <140/90 mm Hg, and 60% reach the low-density lipoprotein (LDL) cholesterol target; in many developing countries, fewer than 5% of patients attain all these three targets [2], while this proportion could be higher than 20% in some developed countries [3].

The elusive nature of disease control in diabetes care has been attributed to clinical inertia and treatment non-adherence [4,5], as well as the progressive nature of DM, especially type 2 diabetes (T2D), which leads to increasing insulin resistance and deficiency, microvascular and macrovascular complications, poor quality of life, and mortality [6]. The corresponding terms that refer more specifically to medication use are therapeutic inertia (TI) and medication non-adherence, respectively. TI has been recognised for over 30 years, and it has indeed received much attention through well-concerted efforts and organised

initiatives in Europe [7] and in the United States (<https://www.therapeuticinertia.diabetes.org/>) [8,9].

Clinical care for people with DM is quite challenging and has been described using terms such as challenging, complex, costly, and confounded [10]. It is a difficult task to organise quality diabetes care with effective therapies and efficient therapists, since a multidisciplinary team of members must share similar passion, vision and skills for patient-centred care, particularly in a dynamic health system where the health care setting and daily practice frequently change, and these challenges are further exacerbated by the requirement for treatment to be sustainable for the patient's lifetime. Equally challenging or even more uphill tasks are encouraging people with DM to participate actively and supporting them to care for themselves effectively and efficiently (Fig. 1).

People with DM present complexities due to the progressive



A. Patient's health behaviour

- Accessibility of health services including personal coaching, psycho-educational programs and emergency services
- Affordability of medical or surgical therapies
- Availability of all required screening facilities
- Timely and availability of the necessary laboratory tests
- Continuous availability of all types of medications
- Trust in the healthcare professionals and health systems^e
- Aligned health beliefs, knowledge, and motivation^f

B. Physician performance

- Training on the standards of diabetes care and prescribing habits
- Conducive clinic environment for physicians and patients
- Attractive remuneration, incentive and career development paths
- Presence of dedicated allied health team for patient support and risk factors management
- Supportive hospital specialists and secondary care services
- Appropriate length of consultation time is further protected by good appointment systems
- Registry that allows periodic and regular assessment of clinical performance

Fig. 1. The “double valleys” of challenges in diabetes care for good outcomes. ^aPatient's favourable outcomes depend on self-management and health behaviours such as that enhance physical health and emotional resilience stemming from will power and health beliefs; ^bPhysicians performance depends on knowledge in diabetes care and attitudes of the physician towards patients under their care; ^cGood outcomes are defined as achievement of treatment targets, healthy lifestyles, and good quality of life; ^dPoor outcomes are defined as the opposite of the good outcomes; ^eThis attitude is affected by the attitudes of the treating physicians and delivery of the healthcare services; ^fPatient's health behaviours are formed from health beliefs, own health knowledge (literacy) and that of their physicians that may affect patient's motivation.

nature of the disease, its associated comorbidities, required adherence to the prescribed treatments, lifestyle modifications needed, and screening follow-ups, all of which must be managed while dealing with the emotional distress and worry of physical and psychological complications [11-13]. The management of DM is increasingly costly, with the aim of achieving early target treatment control with multiple (and sometimes novel and expensive) pharmacological and non-pharmacological modalities. The metabolic legacy effect and vascular memory [14] exert prolonged beneficial effects of earlier control of glycemia, blood pressure, and lipid levels on later diabetes-related complications [15,16]. Maintaining and personalising these control indicators according to patients' risk profiles with safe medications requires well-trained physicians and vigilant screening procedures [17]. Moreover, validated tools and well-equipped facilities are needed for the earlier detection of diabetes-related complications. Treating multiple risk factors to the recommended targets and managing comorbidities related to or in the presence of DM, while simultaneously coordinating the treatment of complications among different specialties and providing psychosocial support for the patient's well-being throughout the different stages of the life cycle, demands a coherent clinical care team and delivery system. Facing these tasks, almost all healthcare professionals and established healthcare systems are often confounded and have to navigate conflicting demands due to the characteristics of patients and healthcare professionals, as well as differences in levels of healthcare systems (primary, secondary, or tertiary), models of care (public or private, standard usual clinical practice or specialized such as chronic care model, conventional, or digitalised), and cultural backgrounds to provide evidence-based diabetes care [18-20].

The above explanation indicates why little improvement has been achieved in glycemic control since 2004, when the Global Partnership for Effective Diabetes Management, a multidisciplinary group of leading institutions and diabetes organizations worldwide, provided practical guidance to facilitate improved treatment outcomes for people with T2D [21,22]. Hence, the challenges and unmet needs of complex patients with DM warrant revisiting TI and medication non-adherence as challenges that lead to ineffective diabetes care and could be the Achilles' heel for improving suboptimal diabetes care.

Methods

This focused integrative review attempts to update and delineate practical recommendations to overcome TI to achieve efficient and effective diabetes care in clinical settings based on the liter-

ature. It strives to offer best suggestions that are immediately useful in making important decisions to improvise existing diabetes care from the perspective of TI.

Therapeutic inertia

TI is defined as "providers' failure to increase therapy when treatment goals are not met" [23]. TI therefore relates to the prescribing decisions made by healthcare professionals, including doctors, nurses, and pharmacists. This comes in the form of inaction on the prescribers' behalf when reviewing treatment outcomes that are not at the recommended targets. This delay has been reported to be as long as a median of 7.0 years [4], which varies according to an individual's disease trajectory, with TI being shorter when diet and exercise are the treatment modality and the longest delay when initiating insulin [24]. An increased glycemic burden (the length of time with HbA1c levels above target) predisposes patients to more detrimental health effects of hyperglycemia [25]. The term "clinical inertia" is related to TI, but in a broader sense, since it encompasses the failure to advance any therapy, not restricted to medications, when it is appropriate to do so [26]. Several other related terms include "therapeutic momentum," "therapeutic inertia," "physician inertia," "non-adherence," and "failure to act."

TI also includes appropriate withholding or deintensifying of therapy [26]. Some coined the term "reverse clinical inertia" to refer to situations where deintensification would be appropriate when the clinical conditions require it to avoid over-treatment and adverse drug reactions. A preceding step to this could be "appropriate inaction" when complex or high-risk patients (such as the elderly, in whom polypharmacy is an issue, or individuals with frequent hypoglycemia, comorbidities, or short life expectancy) who have personalised treatment targets higher than that recommended. "Appropriate inaction" should be understood in contrast to "inappropriate inertia," which is considered to be true TI [27].

The consequences of TI are known and expected [25]. At one end are the persistent suboptimal control of diseases and risk factors, missed opportunities to improve the legacy effect of early glycemic control [28,29] leading to more hospitalization, diabetes-related complications, mortality, higher healthcare costs [30], and poorer mental health and quality of life [31]. At another end are the short-term adverse events from over-medicalization, such as hypoglycemia, hypotension, and drug-related effects [32]. The scale and scope of TI should be viewed based on the level of disease control among people with DM, with the exclusion of cases of appropriate inaction [33,34]. On this basis,

Table 1. Causes and Possible Interventions for Therapeutic Inertia

No.	Causes	Interventions
1	Healthcare system level factors, such as costs of new medications, formulary limitations, and health delivery or a working system that facilitates and supports proper use of treatment/medication	Improve medication availability, accessibility, and affordability. Implement care management interventions that involve virtual coaching of patients by healthcare professionals, including use of mobile applications, telemonitoring, point-of-care testing, and use of alerts, shared decision-making tools, or embedded practice advisories in the electronic health record or other practice quality improvement programmes. Empower nurses, diabetes educators, and pharmacists in medication review and modification within acceptable and evidence-based scopes. Pay due attention to the organizational culture and working system in order to encourage intrinsic ability of healthcare professionals and elicit their best clinical performance.
2	Physician/health professional level factors, such as competing priorities and lack of time, overconfidence in the quality of care and adherence to guidelines, lack of awareness of therapeutic inertia, delays in adopting new guidelines, discomfort or lack of familiarity with prescribing new medications, and perceptions that patients will not be amenable or adherent to medication changes	Deliver programmes to physicians and other healthcare professionals such as diabetes educators, nurses, and pharmacists that are designed to influence their behaviour such as educational programmes, feedback or reminders, medication knowledge and management, medical audits of health records to improve prescribing habits, and training on patient-centred communication skills. Regularly update nurses, diabetes educators, and pharmacists on medication and treatment guidelines to provide professional support to patients using medications.
3	Patient level factors, such as misperceptions about medication use, fear of unwanted side effects, and the impact of social determinants of health. This is close to the concept of medication (non-)adherence but different because it deals with medication initiated but irregularly used compared to therapeutic inertia, in which a medication is not even initiated.	Implement patient education or structured patient education programmes, family or peer support programmes, psychoeducation, or psychological interventions to improve health literacy, self-efficacy, and practical self-care activities. These require a holistic approach including the use of digital health technologies, and nonmedical interventions on the social determinants of health.

TI is estimated to affect 30% to 60% of patients, with the potential for improvement being greater in less-resourced countries than in more developed countries [1].

CAUSES OF THERAPEUTIC INERTIA

The three broad causal categories of TI are those at the physician, patient, and healthcare system levels (Table 1). The proportions of TI due to these reasons have been estimated to be about 50%, 30%, and 20%, respectively [25,35]. The main causes in the literature have been identified as physicians' overestimation and misperception of care provided, the use of soft reasons to delay or avoid treatment intensification, a lack of training and education on drugs and effective prescribing, and practice organization without an emphasis on achieving therapeutic goals [36]. The soft reasons may include a lack of consultation time, with busy clinics or "busy" patients, or feeling (without asking) that the patient would resist any form of treatment intensification. In contrast, hard reasons are those with objective measures for their existence such as not filling prescriptions, experiencing adverse effects of medications, and clinic non-attendance.

It is often believed that healthcare providers are the main cause of TI. However, this conclusion must be made with caution because the clinical performance of healthcare providers is multifactorial and the causes of TI vary according to differences in health settings (primary, secondary, or tertiary care settings), the backgrounds of healthcare professionals (physicians with or without specialization or further training in diabetes care, different categories of non-physician healthcare professionals), and the complexities of people living with DM (personal values and belief systems, as well as the different life demands faced in different stages of the life cycle). Sadly, a literature review reported that only 28% of interventions targeted multiple levels of causes [36]. Patient level TI is very similar to medication/treatment non-adherence, except that the former concept relates to the non-initiation and non-intensification of medication/treatment, while the latter deals with missing doses or altered dosages of the prescribed medications/treatments [37-39]. Patient level causes include misperceptions about diabetes, fear of medications' side effects, affordability, and therapeutic relationship or professional rapport with their healthcare providers [25,36]. The TI causes at the healthcare system level include care disorganization, which leads to poor working systems and environments

for healthcare professionals to work collaboratively and effectively [40,41], and insufficient availability and accessibility of medications and related services [42].

INTERVENTIONS TO OVERCOME THERAPEUTIC INERTIA

Many publications have investigated the possible causes of TI and potential interventions to overcome them. Table 1 lists some examples from the literature. When facing a multifactorial condition such as TI, it is logical to intervene as a multidisciplinary team of healthcare professionals with a working system [43] that is dynamic and provides the flexibility to overcome the causes of TI [44]. One systematic review [44] identified studies published up to January 2022 that were conducted in the United States and included adults at risk for or with T2D. The outcomes included HbA1c levels, blood pressure, lipid levels, self-care, and quality of life. The findings indicated that multicomponent interventions that combined both medical and nonmedical approaches improved clinical outcomes for people with T2D (HbA1c 1.1% lower at a 3-month follow-up). HbA1c levels improved significantly (0.15% to 1.74% lower) with the use of food supplementation with referral and diabetes support, financial incentives with education and skills training, the use of housing relocation with counselling support (4.3% lower DM prevalence after 10 to 15 years of follow-up), and the integration of nonmedical interventions into medical care using the electronic medical record [44]. Multifaceted versus single-faceted interventions in other studies also led to statistically significant improvements in the odds of medication adherence in diabetes care (subgroup analysis: odds ratio, 2.05; 95% confidence interval, 1.62 to 2.60; $P=0.010$) [45]. Efficient and effective care management, and patient education interventions require multidisciplinary approaches and coordination [23]. Patient education may include virtual coaching, supported by telemonitoring, point-of-care testing through electronic portals, and shared decision-making tools, and these interventions may be facilitated by embedded alerts and practice advisories in the electronic health record [23]. A community-based approach including lectures and discussions on diet plans and self-management activities addressing relevance, individualization, feedback, reinforcement, and facilitation in healthy living may also be effective in attaining lower weight, glycemic control, and blood pressure targets [46].

The individual component of multicomponent interventions for TI consists of those at the healthcare system, physician, and

patient levels, as further elaborated below.

Healthcare system level

To overcome TI at the healthcare system level will require policy decisions such as ensuring the availability of all types of antidiabetic medications [40]. This includes having these medications accessible for prescription by different levels of physicians and healthcare professionals, while not being hindered by over-restrictive procedures for newer and more costly medications that have fewer side effects, especially in a healthcare system that subsidises the cost of medications [41]. In addition, this will require empowered nurses, diabetes educators, and pharmacists who could provide timely professional support for medication use [23]. This would require delegated permission to review and modify the prescribed medications within a certain scope, as well as efficient referral from these healthcare professionals to physicians when a need arises to intensify the therapeutic regimen. In some countries, nurses (e.g., in the United Kingdom, Netherlands, and the United States) and pharmacists (e.g., in the United States, Australia, and Spain) who are more accessible than doctors have been trained and empowered to prescribe medications and adjust the dosage of medications [47,48]. This decreases the workload of physicians and could provide timely professional support for medication use.

The performance of physicians and healthcare professionals in diabetes care is also influenced by a positive organizational culture beyond the working system [43]. This is because providing quality service to their patients is believed to be intrinsic to every physician [43]. Truly qualified physicians just require a “normal” environment that allows them to practice the best medicine. This includes an appropriate patient load per day, administrative duties and deadlines, requirements for research and publication, remuneration and recognition, and an always fully effective if not seamless interdisciplinary referral system that satisfies patients’ needs for other clinical or medical services. When these extrinsic and intrinsic factors are upheld well in any healthcare system, the working environment would cultivate a resilient healthcare workforce capable of assisting diabetes patients to overcome the many personal challenges of medication non-adherence and TI [49-51].

Healthcare professional level

At the healthcare professional level [23], interventions include educational programs that modify physician behaviour using in-person training, written educational materials, feedback and reminders, and in-person support from specialists and other clini-

cal staff. Academic profiling, comprising but not limited to benchmarking [52], medical audits, and feedback on prescribing habits, may improve the achievement of treatment targets (HbA1c, systolic blood pressure, and LDL cholesterol) and prescribing skills, respectively. For nurses and diabetes educators, interventions that are similar to those mentioned above could enable them to use evidence-based protocols to provide diabetes management, including treatment initiation or intensification, as these professionals have been observed to succeed better than physicians in bringing glucose, blood pressure, and lipid levels under control [23,53]. Pharmacists are another group of health-care professionals who could lead interventions to provide medication therapy management services, if they have sufficient autonomy to provide medication review and make guideline-based medication adjustments [23]. Non-physician healthcare professionals' roles in diabetes medication review and modification require a sufficient number of these staff at health facilities, physicians' supportive input and cooperation, upholding of medical ethics (confidentiality, non-maleficence, and autonomy) in patient care, and regular training and upskilling on the agreed-upon protocols. Therefore, an integrated team approach and an effective organizational culture involving regular medical audits to battle TI are indispensable [35].

Patient level

Most interventions to overcome TI have been reported at the patient level. In general, the principles of the biopsychosocial-spiritual concept of human needs and holistic care apply. Interventions ranging from knowledge provision about the disease and therapies (health literacy), practical skills training, cognitive behavioural therapy for alignment of one's personal belief system, emotional intelligence for better motivation and self-efficacy, psychoeducation to improve mental well-being [54] and nonmedical social interventions [44] could all contribute to therapeutic adherence or lower TI. These interventions are more effective when incorporating a multidimensional approach than when comprising a singular component. The elements to be included in these interventions include education, regular and shorter patient contact [45], as well as a focused agenda on treatment adherence [55], electronic health (eHealth), and telehealth [56] interventions that address diabetes self-management behaviours, have higher levels of health care provider engagement, and have greater effects on lowering HbA1c levels than usual care alone [57]. However, further research is needed on the effectiveness of mobile health interventions on patient adherence behaviour [56].

It is estimated that approximately 10% to 15% of patients will have a serious cardiometabolic phenotype and/or will refuse therapy interventions or have therapy phobia [58]. These individuals will not achieve treatment targets and may require more advanced treatment modalities that are simple, painless, lower-cost, or more automated.

CONCLUSIONS

A synthesis of the literature indicates that the causes of TI vary in terms of scale and scope in different settings in different countries. However, the causes are almost always multifactorial, multilevel, and complex, and they shift over time. Addressing TI involves hard knowledge and soft skills, infrastructure, personalization, and a focus on patients' biopsychosocial-spiritual domains. It goes without saying that before the right remedy can soothe an ailment, the right remedy for the actual ailment must be identified. In the context of TI, the cause is likely to be multifactorial. If these causal factors are clearly defined, successfully overcoming TI at that setting and facility is attainable. This will require collaborative and multidisciplinary approaches, involving stakeholders and patient-users, research to explore and confirm findings in an incremental manner, and conclusions drawn after high-quality clinical trials. However, common sense dictates that obvious problems are to be handled and solved unless the problems persist after a seemingly logical intervention, or an expensive intervention or investment is required to overcome a problem that causes TI. All individuals managing people with diabetes have a duty to overcome TI, be it medical or nonmedical [44]. Doing so is more likely to be successful when carried out in a consistent and personalised manner, according to patients' needs. The key general and powerful bullets against TI are giving shorter revisit appointments and empowering nurses, diabetic educators, and pharmacists to review treatments and modify prescriptions. The latter could be done safely and acceptably by having a clear clinical protocol that is based on the best evidence or national practice guidelines.

CONFLICTS OF INTEREST

Kamlesh Khunti chairs the American Diabetes Association Overcoming Therapeutic Inertia initiative. Kamlesh Khunti has acted as a consultant, speaker, or received grants for investigator-initiated studies from Astra Zeneca, Bayer, Novartis, Novo Nordisk, Sanofi-Aventis, Lilly and Merck Sharp & Dohme, Boehringer Ingelheim, Oramed Pharmaceuticals, and Applied

Therapeutics. No potential conflict of interest relevant to this article was reported by Boon-How Chew, Barakatun-Nisak Mohd-Yusof, and Pauline Siew Mei Lai.

ACKNOWLEDGMENTS

Boon-How Chew was given an honorarium to attend and speak at SICEM 2022 by the Korean Endocrine Society. Kamlesh Khunti is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM) and the NIHR Leicester Biomedical Research Centre (BRC).

ORCID

Boon-How Chew <https://orcid.org/0000-0002-8627-6248>

REFERENCES

- International Diabetes Federation. IDF Diabetes Atlas 2021. 10th ed. Brussels: IDF; 2021 [cited 2023 Feb 9]. Available from: https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf.
- Chan JC, Gagliardino JJ, Baik SH, Chantelot JM, Ferreira SR, Hancu N, et al. Multifaceted determinants for achieving glycaemic control: the International Diabetes Management Practice Study (IDMPS). *Diabetes Care* 2009;32:227-33.
- Goh CC, Koh KH, Goh S, Koh Y, Tan NC. Achieving triple treatment goals in multi-ethnic Asian patients with type 2 diabetes mellitus in primary care. *Malays Fam Physician* 2018; 13:10-8.
- Khunti K, Gomes MB, Pocock S, Shestakova MV, Pintat S, Fenici P, et al. Therapeutic inertia in the treatment of hyperglycaemia in patients with type 2 diabetes: a systematic review. *Diabetes Obes Metab* 2018;20:427-37.
- Edelman SV, Polonsky WH. Type 2 diabetes in the real world: the elusive nature of glycaemic control. *Diabetes Care* 2017;40:1425-32.
- Hussain S, Chowdhury TA. The impact of comorbidities on the pharmacological management of type 2 diabetes mellitus. *Drugs* 2019;79:231-42.
- Seidu S, Cos X, Brunton S, Harris SB, Jansson SP, Mata-Cases M, et al. 2022 Update to the position statement by Primary Care Diabetes Europe: a disease state approach to the pharmacological management of type 2 diabetes in primary care. *Prim Care Diabetes* 2022;16:223-44.
- Gabbay RA, Kendall D, Beebe C, Cuddeback J, Hobbs T, Khan ND, et al. Addressing therapeutic inertia in 2020 and beyond: a 3-year initiative of the American Diabetes Association. *Clin Diabetes* 2020;38:371-81.
- Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, et al. Management of hyperglycemia in type 2 diabetes, 2022: a consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2022;45:2753-86.
- Chew BH, Vos RC, Widyahening IS, Khunti K. Editorial: Achieving efficient diabetes care through understanding the risk factors, markers, and patient experiences. *Front Endocrinol (Lausanne)* 2022;13:854167.
- Bailey CJ, Kodack M. Patient adherence to medication requirements for therapy of type 2 diabetes. *Int J Clin Pract* 2011;65:314-22.
- Chan JC, So W, Ma RC, Tong PC, Wong R, Yang X. The complexity of vascular and non-vascular complications of diabetes: the Hong Kong Diabetes Registry. *Curr Cardiovasc Risk Rep* 2011;5:230-9.
- Chew BH, Shariff-Ghazali S, Fernandez A. Psychological aspects of diabetes care: effecting behavioral change in patients. *World J Diabetes* 2014;5:796-808.
- Khunti K, Kosiborod M, Ray KK. Legacy benefits of blood glucose, blood pressure and lipid control in individuals with diabetes and cardiovascular disease: time to overcome multifactorial therapeutic inertia? *Diabetes Obes Metab* 2018;20: 1337-41.
- Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-Year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 2008;359:1577-89.
- Jermendy G. Vascular memory: can we broaden the concept of the metabolic memory? *Cardiovasc Diabetol* 2012;11:44.
- American Diabetes Association. Standards of care in diabetes-2023. *Diabetes Care* 2023;46(Suppl 1):S1-291.
- Lee YK, Low WY, Ng CJ. Exploring patient values in medical decision making: a qualitative study. *PLoS One* 2013;8: e80051.
- Reach G. Clinical inertia, uncertainty and individualized guidelines. *Diabetes Metab* 2014;40:241-5.
- Chang S, Lee TH. Beyond evidence-based medicine. *N Engl J Med* 2018;379:1983-5.
- Del Prato S, Felton AM, Munro N, Nesto R, Zimmet P, Zinman B, et al. Improving glucose management: ten steps to get more patients with type 2 diabetes to glycaemic goal. *Int J Clin Pract* 2005;59:1345-55.

22. McGill M, Felton AM; Global Partnership for Effective Diabetes Management. New global recommendations: a multi-disciplinary approach to improving outcomes in diabetes. *Prim Care Diabetes* 2007;1:49-55.
23. Powell RE, Zaccardi F, Beebe C, Chen XM, Crawford A, Cuddeback J, et al. Strategies for overcoming therapeutic inertia in type 2 diabetes: a systematic review and meta-analysis. *Diabetes Obes Metab* 2021;23:2137-54.
24. Mata-Cases M, Franch-Nadal J, Gratacos M, Mauricio D. Therapeutic inertia: still a long way to go that cannot be postponed. *Diabetes Spectr* 2020;33:50-7.
25. Khunti S, Khunti K, Seidu S. Therapeutic inertia in type 2 diabetes: prevalence, causes, consequences and methods to overcome inertia. *Ther Adv Endocrinol Metab* 2019;10:204-2018819844694.
26. Khunti K, Davies MJ. Clinical inertia: time to reappraise the terminology? *Prim Care Diabetes* 2017;11:105-6.
27. Safford MM, Shewchuk R, Qu H, Williams JH, Estrada CA, Ovalle F, et al. Reasons for not intensifying medications: differentiating “clinical inertia” from appropriate care. *J Gen Intern Med* 2007;22:1648-55.
28. Laiteerapong N, Ham SA, Gao Y, Moffet HH, Liu JY, Huang ES, et al. The legacy effect in type 2 diabetes: impact of early glycemic control on future complications (The Diabetes & Aging Study). *Diabetes Care* 2019;42:416-26.
29. Control Group; Turnbull FM, Abraira C, Anderson RJ, Byington RP, Chalmers JP, et al. Intensive glucose control and macrovascular outcomes in type 2 diabetes. *Diabetologia* 2009;52:2288-98.
30. Ali SN, Dang-Tan T, Valentine WJ, Hansen BB. Evaluation of the clinical and economic burden of poor glycemic control associated with therapeutic inertia in patients with type 2 diabetes in the United States. *Adv Ther* 2020;37:869-82.
31. Karam SL, Dendy J, Polu S, Blonde L. Overview of therapeutic inertia in diabetes: prevalence, causes, and consequences. *Diabetes Spectr* 2020;33:8-15.
32. Seidu S, Kunutsor SK, Topsever P, Hambling CE, Cos FX, Khunti K. Deintensification in older patients with type 2 diabetes: a systematic review of approaches, rates and outcomes. *Diabetes Obes Metab* 2019;21:1668-79.
33. Shivashankar R, Kirk K, Kim WC, Rouse C, Tandon N, Narayan KM, et al. Quality of diabetes care in low- and middle-income Asian and Middle Eastern countries (1993-2012): 20-year systematic review. *Diabetes Res Clin Pract* 2015;107:203-23.
34. Evans M, Engberg S, Faurby M, Fernandes JD, Hudson P, Polonsky W. Adherence to and persistence with antidiabetic medications and associations with clinical and economic outcomes in people with type 2 diabetes mellitus: a systematic literature review. *Diabetes Obes Metab* 2022;24:377-90.
35. Henriksen K, Battles JB, Marks ES, Lewin DI. *Advances in patient safety: from research to implementation (Volume 2: concepts and methodology)*. Rockville: Agency for Healthcare Research and Quality (US); 2005. Chapter, Clinical inertia and outpatient medical errors [cited 2023 Feb 10]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK20513>.
36. Wrzal PK, Bunko A, Myageri V, Kukaswadia A, Neish CS, Ivers NM. Strategies to overcome therapeutic inertia in type 2 diabetes mellitus: a scoping review. *Can J Diabetes* 2021;45:273-81.
37. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppert T, et al. A new taxonomy for describing and defining adherence to medications. *Br J Clin Pharmacol* 2012;73:691-705.
38. Vermeire E, Wens J, Van Royen P, Biot Y, Hearnshaw H, Lindenmeyer A. Interventions for improving adherence to treatment recommendations in people with type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2005;2005:CD003638.
39. Low LL, Tong SF, Low WY. Selection of treatment strategies among patients with type 2 diabetes mellitus in Malaysia: a grounded theory approach. *PLoS One* 2016;11:e0147127.
40. Kanumilli N, Brunton S, Cos X, Deed G, Kushner P, Lin P, et al. Global survey investigating causes of treatment inertia in type 2 diabetes cardiorenal risk management. *J Diabetes Complications* 2021;35:107813.
41. Chew BH, Hussain H, Supian ZA. Is therapeutic inertia present in hyperglycaemia, hypertension and hypercholesterolaemia management among adults with type 2 diabetes in three health clinics in Malaysia?: a retrospective cohort study. *BMC Fam Pract* 2021;22:111.
42. Ong SE, Koh JJ, Toh SE, Chia KS, Balabanova D, McKee M, et al. Assessing the influence of health systems on type 2 diabetes mellitus awareness, treatment, adherence, and control: a systematic review. *PLoS One* 2018;13:e0195086.
43. Rosenbaum L. Peers, professionalism, and improvement: reframing the quality question. *N Engl J Med* 2022;386:1850-4.
44. Egede LE, Walker RJ, Linde S, Campbell JA, Dawson AZ, Williams JS, et al. Nonmedical interventions for type 2 diabetes: evidence, actionable strategies, and policy opportunities. *Health Aff (Millwood)* 2022;41:963-70.
45. Fitzpatrick C, Gillies C, Seidu S, Kar D, Ioannidou E, Davies MJ, et al. Effect of pragmatic versus explanatory interven-

- tions on medication adherence in people with cardiometabolic conditions: a systematic review and meta-analysis. *BMJ Open* 2020;10:e036575.
46. Wei X, Barnsley J, Zakus D, Cockerill R, Glazier R, Sun X. Evaluation of a diabetes management program in China demonstrated association of improved continuity of care with clinical outcomes. *J Clin Epidemiol* 2008;61:932-9.
 47. Laurant M, van der Biezen M, Wijers N, Watananirun K, Kontopantelis E, van Vught AJ. Nurses as substitutes for doctors in primary care. *Cochrane Database Syst Rev* 2018;7:CD001271.
 48. Hughes JD, Wibowo Y, Sunderland B, Hoti K. The role of the pharmacist in the management of type 2 diabetes: current insights and future directions. *Integr Pharm Res Pract* 2017;6:15-27.
 49. Bosch M, Dijkstra R, Wensing M, van der Weijden T, Grol R. Organizational culture, team climate and diabetes care in small office-based practices. *BMC Health Serv Res* 2008;8:180.
 50. Benzer JK, Mohr DC, Evans L, Young G, Meterko MM, Moore SC, et al. Team process variation across diabetes quality of care trajectories. *Med Care Res Rev* 2016;73:565-89.
 51. Warde CM, Linzer M, Schorling JB, Moore EM, Poplau S. Balancing unbalanced lives: a practical framework for personal and organizational change. *Mayo Clin Proc Innov Qual Outcomes* 2019;3:97-100.
 52. Hermans MP, Elisaf M, Michel G, Muls E, Nobels F, Vandenberghe H, et al. Benchmarking is associated with improved quality of care in type 2 diabetes: the OPTIMISE randomized, controlled trial. *Diabetes Care* 2013;36:3388-95.
 53. Cho MK, Kim MY. Self-management nursing intervention for controlling glucose among diabetes: a systematic review and meta-analysis. *Int J Environ Res Public Health* 2021;18:12750.
 54. Katon W, Russo J, Lin EH, Heckbert SR, Karter AJ, Williams LH, et al. Diabetes and poor disease control: is comorbid depression associated with poor medication adherence or lack of treatment intensification? *Psychosom Med* 2009;71:965-72.
 55. Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2014;2014:CD000011.
 56. Bingham JM, Black M, Anderson EJ, Li Y, Toselli N, Fox S, et al. Impact of telehealth interventions on medication adherence for patients with type 2 diabetes, hypertension, and/or dyslipidemia: a systematic review. *Ann Pharmacother* 2021;55:637-49.
 57. Robson N, Hosseinzadeh H. Impact of telehealth care among adults living with type 2 diabetes in primary care: a systematic review and meta-analysis of randomised controlled trials. *Int J Environ Res Public Health* 2021;18:12171.
 58. Camara S, Bouenizabila E, Hermans MP, Ahn SA, Rousseau MF. Novel determinants preventing achievement of major cardiovascular targets in type 2 diabetes. *Diabetes Metab Syndr* 2014;8:145-51.