

THERAPEUTIC INERTIA IN CLINICAL CARE: A PRISMA-GUIDED META-ANALYTIC REVIEW**Bishouno Bhowmick¹, Pushpendra D. Pratap², Salma Khan³, Shaista Tabassum Rizvi⁴, Nida Akhlaq⁵, Sharique Ahmad⁶**

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ABSTRACT

The concept of therapeutic inertia (TI) is used to describe the inability to initiate, escalate, or de-escalate medical treatment based on evidence-based recommendations in the case of failure to achieve the treatment objectives. Regardless of significant progress in diagnostics, pharmacotherapy, and clinical decision support systems, TI continues to be a widespread obstacle to the optimal disease management in a wide range of chronic medical conditions. This is a review that summarizes recent systematic reviews, meta-analyses, and big observational studies to assess the prevalence of TI, multidimensional determinants of TI, and its clinical and economic outcomes. Specific attention is given to diabetes mellitus, hypertension, cardiovascular disease, and some of the neurological disorders to which TI has been studied the most. There is meta-analytic support that TI significantly postpones goal achievement and leads to undue morbidity, mortality and health spending. Multiplex interventions, particularly task-shifting and structured treatment algorithms, and digital decision support, are moderately and strongly effective in preventing TI. Therapeutic inertia needs to be addressed as one of the key quality-of-care issues in contemporary clinical practice.

INTRODUCTION

There is a growing tendency of managing chronic medical illnesses with a high focus on early diagnosis, personalized therapeutic goals, and prompt intensification of the treatment. Although there are strong, evidence-based clinical guidelines, there is still an existing gap between the recommended practice and clinical practice. Another key cause of this discrepancy is clinical inertia which is currently better described as the therapeutic inertia (TI) when not starting or failing to escalate therapy in the face of not attaining the treatment goals.^[1] TI was first reported in patients with hypertension, and has since been widely reported in a wide range of chronic diseases, such as diabetes mellitus, dyslipidemia, cardiovascular disease, chronic kidney disease, asthma, and osteoporosis and in a variety of neurological disorders.^[2] It is also important to note

that TI cannot be considered as a mere delay or care oversight. Instead, it is a multifaceted interaction of cognitive, behavioral and systemic mechanisms, which play in clinical decision-making. These could be exaggeration of care administered, underestimation of the risk of patient, apprehension over side effects, insufficient consultation period, fragmented healthcare services and insufficient resource or expert help.

Since chronic diseases constitute the largest part of the worldwide morbidity and mortality, the effects of TI on patient outcomes and healthcare costs are significant. Continuous inability to optimize therapy may lead to the development of the disease, its avoidable complications, and poor quality of life. Therefore, treatment and prevention of TI has become a pressing issue of concern among health care systems all over the world.^[4] The gaps in bridging the gap between guidelines and practice and

enhancing long-term outcomes in chronic disease management are becoming increasingly explored using strategies, including; clinician education, decision-support tools, patient engagement, performance feedback, and system-level interventions.

Conceptual Framework and Definition

Therapeutic inertia (TI) is also called failure or inability to make the proper change in treatment, i.e., an initiation, intensification, switching, or de-escalation of treatment in response to a clinical evidence that the existing management is insufficient or improper.^[5] Notably, the context of therapeutic non-intensification in TI excludes instances where non-intensification is clinically warranted, i.e. when the patients refuse treatment, have contraindications on record, or when the patients present with conflicting comorbidities that require the guideline-based approach to be deviated. Such situations are reflective of proper clinical judgment as opposed to inertia and should be distinctly defined to prevent a possibility of misclassification.

Modern conceptual frameworks refer to TI as a multifactorial and dynamic process, and not a failure in a single clinical condition. In essence, TI is a multifaceted result of clinician-, patient- and system-level factors that interrelate to affect the treatment decision in the long run. Cognition and behaviour among clinicians are central and could be risk aversion, confusion about the applicability of the guidelines, therapeutic pessimism, or overconfidence in the current disease control. Simultaneously, patient preferences and perceptions, such as fear of adverse effects, low health literacy, low adherence, and low involvement in shared decision-making can play an important role in influencing therapeutic adjustments.

Health system structures and limitations, including inadequate consultation time, poor clinical decision-support tools, discontinuous care pathways and insufficient access to medications or specialist services are also crucial factors. According to recent conceptual models, TI can be described as a dynamic process whose interactions are affected by interactions between:

- **Clinician cognition and behaviour**
- **Patient preferences and perceptions**
- **Health system structures and constraints.**

This framework was confirmed in several chronic disease contexts and currently forms the basis of the proposed targeted, multidimensional interventions to minimize TI and enhance clinical outcomes in the long-term.^[6]

MATERIALS AND METHODS

PRISMA-Guided Evidence Synthesis

1. Search Strategy

A systematic literature review was performed in PubMed, Embase, Scopus, and Cochrane Library to find articles published since January 2000 to

December 2024. Search terms included combinations of "therapeutic inertia", "clinical inertia", "treatment intensification", "diabetes", "hypertension", "chronic disease", and "meta-analysis".

2. Eligibility Criteria

Inclusion Criteria

- Systematic reviews or meta-analyses
- Large observational cohort studies (>1,000 participants)
- Randomized controlled trials evaluating interventions to reduce therapeutic inertia
- Adult populations (≥18 years)

Exclusion Criteria

- Case reports or small case series
- Pediatric -only populations
- Non-English language publications

3. PRISMA-Style Flow Diagram (Textual Schematic)

Identification

Records identified through database searching (n = 2,146)

Screening

Records after duplicates removed (n = 1,782)

Records screened by title and abstract (n = 1,782)

Records excluded (n = 1,504)

Eligibility

Full-text articles assessed for eligibility (n = 278)

Full-text articles excluded with reasons (n = 213):

- Inadequate outcome reporting (n = 94)
- No explicit assessment of therapeutic inertia (n = 76)
- Methodological limitations (n = 43)

Included

Studies included in qualitative synthesis (n = 65)

Studies contributing to quantitative/meta-analytic synthesis (n = 32)

Epidemiology and Prevalence of Therapeutic Inertia

1. Diabetes Mellitus

Therapeutic inertia is most comprehensively studied in type 2 diabetes mellitus (T2DM). Large cohort studies indicate that treatment intensification is often delayed by several years despite persistent hyperglycemia.^[7] The meta-analytic data indicate that 30-60 percent of patients with HbA1c levels exceeding the guideline levels fail to receive prompt treatment escalation.^[8]

A meta-analysis of observational studies showed that the median delay time was 1.52-2.52 years before intensification following loss of glycemic control, which was significantly greater than the cumulative glycemic burden.^[9] This is a prolonged delay that has been reported throughout the primary care, specialized clinics and various healthcare systems.^[10]

2. Hypertension

Hypertension is another archetypal disease with high incidences of TI. Research documents indicate that therapeutic modifications are not observed in up to 70-80 percent of clinical interactions where blood pressure is above recommended levels.^[11] Population based cohort meta-analysis indicates that TI is among

the best predictors of uncontrolled hypertension regardless of adherence to medication.^[12] Importantly, TI is more common when the values of blood pressure are slightly above the goals, which shows the importance of a phenomenon known as threshold hesitation in clinicians.^[13]

3. Cardiovascular and Metabolic Disorders

TI is increasingly recognized in dyslipidemia and secondary cardiovascular prevention. Failure to intensify statin therapy or add non-statin lipid-lowering agents despite elevated LDL-cholesterol levels is widely reported.^[14] Similar patterns are

observed in heart failure, where under-utilization and under-titration of guideline-directed medical therapy remain common.^[15]

4. Neurological and Other Chronic Conditions

Emerging evidence indicates significant TI in neurological disorders such as multiple sclerosis and Parkinson's disease, where delayed initiation or escalation of disease-modifying therapies adversely affects long-term outcomes.^[16] TI has also been described in asthma, chronic obstructive pulmonary disease, osteoporosis, and chronic kidney disease, though systematic data remain limited.^[17]

Table 1: Summary of Key Meta-Analyses and Systematic Reviews on Therapeutic Inertia

Condition	Study (Year)	Study Type	Population	Key Findings Related to Therapeutic Inertia
Type 2 Diabetes Mellitus	Tricco et al. (2012)	Systematic review & meta-analysis	Adults with T2DM	Interventions addressing therapeutic inertia reduced HbA1c by a pooled mean of 0.5%; nurse- and pharmacist-led models were most effective
Type 2 Diabetes Mellitus	Khunti et al. (2018)	Narrative synthesis of cohort studies	Primary care & specialist settings	Median delay of treatment intensification exceeded 18 months after HbA1c target failure
Hypertension	Okonofua et al. (2006)	Observational cohort	Primary care patients	Therapeutic inertia observed in >70% of visits with uncontrolled blood pressure
Hypertension	Redon et al. (2016)	Systematic review	European cohorts	TI strongly associated with near-threshold BP values and clinician risk aversion
Cardiovascular Disease	Greene et al. (2018)	Meta-analysis of RCTs	Heart failure patients	Under-titration of guideline-directed therapy contributed to excess hospitalization and mortality
Multimorbidity	Lebeau et al. (2014)	Systematic review	Chronic disease populations	TI driven by interaction of clinician cognition, patient preference, and system barriers

Determinants of Therapeutic Inertia

1. Clinician-Related Factors

Clinician-related determinants represent the most frequently cited contributors to TI. These include:

- Overestimation of care quality
- Risk aversion related to adverse drug effects
- Limited familiarity with evolving guidelines
- Competing clinical priorities during brief consultations.^[18]

Cognitive biases, such as status quo bias and therapeutic nihilism, further reinforce inertia, particularly in older patients or those with multiple comorbidities.^[19]

2. Patient-Related Factors

Patient preferences, beliefs, and behaviours significantly influence therapeutic decisions. Fear of side effects, injection aversion, pill burden, and low perceived disease severity can discourage treatment escalation.^[20] In shared decision-making contexts, clinicians may defer intensification in response to patient hesitation, even when clinical indicators strongly favor escalation.^[21]

3. Health System and Structural Barriers

At the system level, there are fragmented care, limited access to diagnostics, insufficient follow-up systems and no integrated clinical decision support systems.^[22] TI is also worsened by medication availability and cost limitation in low- and middle-income nations.^[23]

Table 2: Determinants of Therapeutic Inertia Across Medical Conditions

Domain	Determinant	Description
Clinician-related	Risk aversion	Fear of adverse effects such as hypoglycemia, hypotension, or polypharmacy
	Knowledge gaps	Limited familiarity with updated clinical guidelines
	Cognitive bias	Status quo bias, therapeutic nihilism, and overestimation of care quality
Patient-related	Treatment resistance	Fear of injections, side effects, or medication burden
	Low disease perception	Underestimation of long-term risks associated with poor control
	Socioeconomic factors	Limited health literacy, financial constraints
System-related	Fragmented care	Poor coordination between primary and specialist services
	Limited decision support	Absence of EHR-embedded alerts or treatment algorithms
	Resource constraints	Medication availability, diagnostic access, reimbursement barriers

Clinical and Economic Consequences

1. Impact on Disease Outcomes

There is meta-analytic support always that associates TI with worse clinical outcomes. Delayed intensification is linked to increased microvascular

and macrovascular complications in diabetes such as nephropathy, retinopathy, myocardial infarction and stroke.^[24]

TI in hypertension leads to a long-term exposure to high blood pressure, which significantly raises the risk of cardiovascular disease and general death.^[25]

2. Healthcare Utilization and Costs

TI enhances the use of health care by raising the rates of hospitalization, emergency care, and the management of long-term complications. Analysis of the economy estimates that the failure to make T2DM therapy more intensive alone costs billions of preventable healthcare spending every year.^[26]

Meta-Analytic Evidence on Interventions to Reduce Therapeutic Inertia

1. Provider-Focused Interventions

Systematic reviews show that isolated educational interventions for clinicians yield modest reductions in TI, particularly when not reinforced by system-level changes.^[27] However, when combined with audit-and-feedback mechanisms, guideline adherence improves significantly.^[28]

2. Task-Shifting and Multidisciplinary Care

Meta-analyses have shown that nurse and pharmacist-led interventions are effective in controlling diseases better than usual care. The evidence of this can be seen in the pooled data demonstrating a decrease in HbA1c of 0.4-0.8% in diabetes when the non-physician providers are enabled to modify the therapy through protocols.^[29]

3. Clinical Decision Support Systems

TI can be greatly minimized through the use of digital decision support tools located in electronic health records because they initiate timely adjustment in treatment. According to meta-analytic results, enhanced target achievement is seen across various chronic conditions but implementation fidelity is an issue.^[30]

4. Patient-Centered and Behavioural Strategies

Interventions promoting shared decision-making, structured goal setting, and patient education demonstrate additive benefits when integrated into broader care models.^[31]

Table 3: Evidence-Based Interventions to Reduce Therapeutic Inertia

Intervention Type	Strategy	Evidence Strength
Educational	Academic detailing, guideline workshops	Low-moderate (effective only when combined with system changes)
Multidisciplinary care	Nurse-led or pharmacist-led treatment adjustment	High (consistent HbA1c and BP improvements in meta-analyses)
Decision support systems	EHR alerts, algorithm-based prompts	Moderate-high (improves guideline adherence)
Audit and feedback	Performance benchmarking with peer comparison	Moderate
Patient-centered care	Shared decision-making, goal-setting	Moderate (enhances acceptance of intensification)
Policy/system redesign	Protocol-driven care pathways	Emerging but promising

Special Consideration: De-intensification Inertia

While most literature focuses on under-treatment, failure to de-intensify therapy in patients at risk of harm (e.g., frail elderly individuals) represents an equally important but under-recognized form of TI. Studies indicate that overtreatment contributes to hypoglycemia, hypotension, falls, and reduced quality of life.^[32] Balanced, patient-centered approaches are therefore essential.

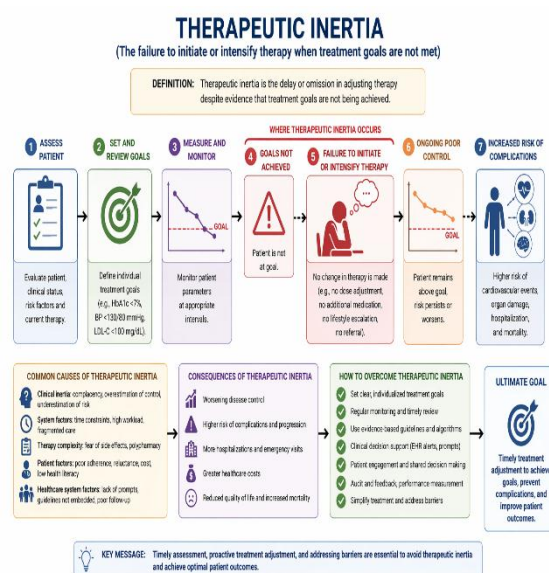


Figure 1: This schematic depicts *therapeutic inertia*, defined as the failure to initiate or intensify treatment despite unmet clinical goals. The workflow progresses from patient assessment, goal setting, and monitoring to identification of uncontrolled disease. The critical step is the lack of therapeutic adjustment despite suboptimal outcomes, leading to persistent

poor control and increased risk of complications such as cardiovascular events and organ damage.

The lower panel summarizes key contributors, including clinician-related, patient-related, therapy-related, and health system barriers, along with major consequences like disease progression and increased healthcare burden. It also highlights corrective strategies—regular monitoring, adherence to guidelines, decision-support tools, and patient engagement.

Overall, the figure emphasizes that timely treatment modification is essential to achieve targets and improve patient outcomes.

Future Directions and Research Gaps

Despite growing recognition, several gaps remain:

- Limited disease-specific meta-analyses beyond diabetes and hypertension
- Underrepresentation of low-resource settings
- Lack of standardized metrics to quantify TI
- Insufficient integration of behavioural science into intervention design.^[33]

Future research should focus on pragmatic trials, implementation science, and policy-level interventions.

CONCLUSION

Therapeutic inertia is a prevalent multifactorial phenomenon that compromises the efficacy of contemporary medical services. There is solid evidence to prove that TI has a significant impact of delaying the control of the disease, causing more complications, and has a great economic cost. The effectiveness of multifaceted interventions including task-shifting, decision support system and team-based care is supported by the findings of meta-analyses. The problem of therapeutic inertia needs to be brought to the forefront as one of the key issues in quality improvement and guideline implementation in any medical field.

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