a:care

Cracking the code of medication non-adherence

and shifting paradigm from ‘treating diseases’ to ‘treating patients’

Olivier Gryson, Oana Butu

Abbott

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Cracking the code of medication non-adherence

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Supporting medication adherence: A call to healthcare professionals

Medicines keep you healthy only if you take them. That's a simple truth. Still, the reality is that many people don't. Nearly one-half of patients don't take their medicines as prescribed, and one-third never fill their prescriptions. Globally, this is a massive medical challenge that keeps people from living their healthiest lives.

In creating a:care, Abbott worked with the brightest brains in behavioral science, and using the power of digital health, we have developed a pioneering program that focuses on education, insights, and coaching to support healthcare professionals (HCPs) and help people better stick to their treatment so that they can live healthier lives.

Since 2021, the a:care Congress has established itself as one of the largest educational events on adherence and behavioral science, and the last edition welcomed around 20,000 participants from countries across the globe. With an endorsement by over 65 leading medical societies, through a:care, we bring science and innovation in digital health to emerging countries.

This a:care book is designed to enhance medication adherence through the integration of behavioral science and technology. It distils years of expert insights from the Abbott a:care program into practical, accessible strategies to help HCPs improve patient adherence.

Abbott's a:care program is non-commercial and does not promote any Abbott product. Launched by Abbott based on long-standing science and the expertise of leading professionals in behavioral science and other fields, this book, and indeed the Abbott a:care program, is intended for HCPs struggling with patient adherence; medical and pharmacy students looking to enhance their communication skills with patients; and policymakers seeking to understand non-adherence and its impact on healthcare systems.

This book represents Abbott's perspective, and we encourage readers to explore the information presented here and complement it with additional knowledge and resources available online.

Foreword
Prof. John Weinman

Medication adherence is a massive public health problem, which has not been taken seriously enough by policymakers or HCPs in healthcare sectors around the world. What makes this even more concerning is that there is now so much evidence showing that medication adherence is sub-optimal across all treatments, which has huge impacts on morbidity, mortality, and healthcare costs.

I taught medical students for over 30 years in a prestigious medical school, where only one hour in the whole five year curriculum was dedicated to the topic of medication adherence. As we had a problem-based curriculum, this session was embedded in a scenario about a patient with asthma, which had the unfortunate effect of making many students believe that non-adherence was something which only occurred with the use of preventer inhalers in people with asthma!

In an era of evidence-based medicine, it is really difficult to understand why the adherence issue has not been taken more seriously by health policymakers or HCPs. Even though influential organisations such as the World Health Organization (WHO) and Organisation for Economic Co-operation and Development (OECD) have emphasized the global extent and impact of poor adherence, there is very little evidence that the situation is improving in daily healthcare practice.

As a behavioral scientist, who has worked as a researcher and educator in healthcare for many years, I have witnessed the limited understanding of the nature and causes of non-adherence alongside the unwillingness of many healthcare staff to commit time and effort to engage in effective adherence support of their patients. This is despite the fact that many years of behavioral science research has provided us with very detailed evidence and insights into the reasons for and impact of low adherence, not only to medication but also to other key health advice such as dietary and exercise recommendations. Quantitative and qualitative research involving people across the full spectrum of major health conditions has shown that a wide range of cognitive, motivational, and contextual factors influence why individuals do not follow medical treatment or advice, at every phase of adherence, from initiation to long-term persistence.

While it is crucial to understand an individual's reasons for their reluctance or unwillingness to take their medicines in order to provide targeted support, the key role of the HCP has not been sufficiently emphasized. As a number of authors in this book have described, HCPs are very often unaware of the full extent of non-adherence, particularly in their own patients. One unfortunate finding from a recent study of HCPs' views of non-adherence was that they perceived that the largest barrier to adequate medication-adherence management was lack of patient awareness rather than any shortcoming in their own practice, such as the ability to ask about adherence as part of their routine consultations (Hafez et al, 2024[1]). However, almost all the respondents in that survey did recognize their own limitations and the need for educational training on medication-adherence management. This reflects the fact that very little training is provided in current undergraduate healthcare education and, where it is, it is usually insufficient to enable clinicians to discuss and support adherence challenges in an effective way. Part of this is due to rushed and poor communication combined with a lack of understanding and skill in the use of behavioral diagnosis and behavior change techniques. The science of behavior change has grown massively in the past decade, but the learnings from this have not really filtered through to healthcare training and clinical practice.

Looking ahead, there is an enthusiastic but rather naïve belief that developments in artificial intelligence (AI), interactive digital technology and precision medicine will solve the adherence problem and, in doing so, obviate the need for HCPs to embrace the adherence challenge. Ultimately these developments may well provide important ways of ensuring that medicines are taken more systematically and effectively, but current evidence indicates that they are not instant solutions. For example, a very recent review of the use of AI tools in adherence interventions concluded that the evidence is still both limited and weak (Reis et al, 2025[2]). Similarly, although studies of digital adherence interventions have shown some promise, patients still value the presence of an attentive and skilled practitioner (Crawshaw & McLeary, 2025[3]). Even though advances in precision medicine, particularly in pharmacogenomic prescribing, will ensure that patients will receive more effective medicines with less side effects, it is very unlikely that this will make the adherence problem magically disappear. Indeed, evidence from a review of studies examining the behavioral impacts of pharmacogenomic prescribing indicates that they have little or no effects on treatment adherence (Galloway et al, in press[4]).

Where does this leave us in making progress with the adherence challenge? It is obvious that there is an urgent need for all those involved in healthcare training and practice to take this challenge much more seriously. This is why such initiatives as the a:care program are to be so strongly welcomed. This book not only provides a really excellent overview of the progress which has been made but also some really helpful resources for clinicians seeking to improve

their practice in adherence support. This is why I am so pleased to provide a foreward to this ground-breaking book. Over the past few years Abbott has shown that they take the problem of medication adherence very seriously and have created a range of important initiatives, which are presented in this book.

Prof. John Weinman

Professor of Psychology as applied to Medicines in the School of Cancer & Pharmaceutical Sciences. Emeritus Professor at the Institute of Psychiatry, Psychology & Neuroscience in King's College London. UK Co-Director of KCL/KHP Centre for Adherence Research and Education.

1. Hafez, G., Aarnio, E., Mucherino, S., Kamusheva, M., Qvarnström, M., Potočnjak, I., et al. (2024). Barriers and unmet educational needs regarding implementation of medication adherence management across europe: Insights from COST Action ENABLE. J Gen Med. 530 doi: 10.1007/s11606-024-08851-2.
2. Reis ZSN, Pereira GMV, Dias CdS, Lage EM, de Oliveira IJR and Pagano AS (2025) Artificial intelligence-based tools for patient support to enhance medication adherence: a focused review. Front. Digit. Health 7:1523070. doi: 10.3389/fdgth.2025.1523070.
3. Crawshaw, J. & McLeary, N, (2025) Healthcare provider interventions to support medication adherence: state-of-the-science overview. Front. Pharmacol., Volume 16, https://doi.org/10.3389/fphar.2025.1567967.
4. Galloway, L., Weinman, J. & Wright, A. The impact of pharmacogenetic testing on medication adherence and psychological factors associated with adherence : A narrative review, in preparation.

Foreword
Dr. Sheri D. Pruitt

Medication adherence is a crucial yet often ignored challenge in healthcare. Despite decades of innovation in medication development, patients worldwide still struggle to take medications as their HCPs recommend. It is well-documented that medication non-adherence results in poorer health outcomes, preventable hospitalizations, and unnecessary healthcare costs. As former U.S. Surgeon General C. Everett Koop plainly stated: “Drugs don’t work in patients who don’t take them.”

Authors Dr. Olivier Gryson and Ms. Oana Butu recognized Koop’s wisdom and identified a significant gap in our current approach to medication adherence. While most healthcare efforts focus on discovering new medicines, advancing technology, and simplifying medication regimens, the human element—in both patients and HCPs—is often overlooked. “Cracking the Code of Medication Non-adherence” addresses that gap. It is a comprehensive, interdisciplinary, and practical guide that explores not only what adherence is but also why it happens and how to improve it. This book arrives at a pivotal moment in healthcare, as the focus begins to shift from treating diseases to delivering person-centered care.

The authors’ work is grounded in both scientific principles and practical experience, as well as a shared passion for helping patients. I’ve had the privilege of collaborating with them since the beginning of a:care, a program they lead that supports HCPs in improving patients’ adherence to treatment recommendations. Through the a:care initiative, we have trained thousands of clinicians worldwide through masterclasses and conferences. Time and again, I’ve seen Olivier’s and Oana’s boundless enthusiasm, innovation, and leadership in developing and implementing a global program that integrates behavioral science principles into educational and practical tools to help HCPs and patients achieve better health outcomes. This book is a culmination of their research, innovation, and implementation.

Having worked in behavioral medicine and behavioral science for over 30 years, and as a co-author of the WHO′s landmark 2003 report, "Adherence to Long-term Therapies," I can confidently say that nothing of this importance has been published since. The WHO report redefined adherence as a complex, multifaceted problem that extends beyond the patient to encompass the condition, the treatment, the social and economic context, and the healthcare system—informing us that adherence is far more than just patient education and reminders. "Cracking the Code of Medication Non-adherence" builds on the WHO′s insight, offering a practical, current, and generalizable approach for today's healthcare systems and HCPs.

Whether you are a clinician, researcher, educator, healthcare administrator, policy leader, or student, this book will challenge and empower you. Let it serve as a call to action by shifting the conversation from "Why don't patients adhere?" to "What can we do differently to improve adherence?" "Cracking the Code" offers solutions that are not only evidence-based but also practical, scalable, and grounded in the patient–provider relationship.

Dr. Sheri D. Pruitt
Former Director of Behavioral Science Integration, Kaiser Permanente USA.
Current Independent Behavioral Science Consultant and Clinical Psychologist.

Foreword
Dr. Olivier Gryson

The journey into the field of pharmacy often begins with a rigorous academic foundation. In many educational systems, the first year serves as a demanding selection process, emphasizing memorization, analytical thinking, and proficiency in subjects such as mathematics and physics. Success in these areas is often a prerequisite for advancing toward a Doctor of Pharmacy degree.

Pharmacy education is typically highly technical, focusing on the intricate interactions between molecules and biological systems. Students learn how the development of new compounds can lead to innovative treatments for a wide range of diseases. However, the scope of this training extends beyond chemistry and biology. Core values such as precision, humility in the face of uncertainty, and the ethical principle of *primum non nocere* (first, do no harm) are also deeply embedded in the curriculum.

Despite this comprehensive training, a critical insight has emerged within the healthcare community: a significant proportion of patients do not adhere to their prescribed treatments. This realization has prompted reflection on whether the traditional focus on disease mechanisms and pharmacological solutions has overshadowed the importance of understanding the patient experience.

In professional settings such as medical congresses and industry forums, discussions often center on clinical innovation and therapeutic advancements. Yet, there remains a noticeable gap in addressing patient psychology and the behavioral factors influencing treatment adherence.

This gap has inspired initiatives aimed at bridging the divide between medical science and psychological understanding. One such, Abbott's a:care initiative, seeks to reframe healthcare delivery by emphasizing the importance of treating patients, not just diseases. The a:care book was developed to share insights into patient behavior with HCPs, fostering a more holistic approach to care.

The contributions of experts in health psychology, such as Prof. Weinman, have been instrumental in highlighting the complexity of adherence. These insights underscore that reminders and

instructions alone are insufficient; a deeper understanding of patient motivations and barriers is essential.

The success of such initiatives also depends on dedicated leadership and organizational support. Collaborative efforts within the healthcare industry are paving the way for a more patient-centered model—one that prioritizes the well-being of individuals and acknowledges the psychological dimensions of health.

Dr. Olivier Gryson
Doctor of Pharmacy.
Global Head Digital Healthcare, Abbott.

Foreword
Ms. Oana Butu

> *"You have cancer"*

These words are among the most life-altering a person can hear. In that moment, the world shifts. While the healthcare professional may continue with clinical explanations and treatment plans, the patient often becomes overwhelmed, grappling with fear, confusion, and uncertainty. This moment marks the beginning of a complex emotional and medical journey, and it often reveals a critical gap in communication between patients and HCPs.

In oncology and other serious health conditions, the patient pathway is intricate and emotionally charged. Medical information, though essential, can be difficult to absorb in the wake of a diagnosis. This disconnect can lead to hesitation, fear-driven decisions, or even non-adherence to treatment plans. A growing body of evidence suggests that improving communication at these pivotal moments is essential to improving outcomes.

Efforts to address this challenge have increasingly focused on empowering patients with knowledge, tools, and support systems. However, a singular focus on the patient is not enough. HCPs also need resources and training to communicate effectively—especially during moments that define the patient experience. Enhancing adherence and engagement requires a dual approach: supporting both patients and the professionals who care for them.

Programs like a:care have emerged to bridge this gap. Designed to integrate behavioral science into clinical practice, a:care equips HCPs with tools to foster trust, empathy, and long-term engagement. The initiative emphasizes that effective communication is not a one-time event but an ongoing dialogue that evolves throughout the patient journey.

Developing such programs requires global collaboration and cultural sensitivity. Patient adherence is influenced by a wide range of factors, including local healthcare systems, societal beliefs, and communication norms. Tailoring solutions to these diverse contexts is essential for meaningful impact.

A key milestone in this movement was the creation of the a:care Congress, a global forum that brought together experts in behavioral science, digital health, and clinical care. More than just a conference, it represented a shift in mindset—recognizing that improving healthcare outcomes begins with improving how we connect with patients.

Technology has played a transformative role in this evolution, from AI-driven tools to digital adherence platforms. Yet, the most profound changes often occur in the human moments: when a diagnosis is delivered with compassion, when a patient feels truly heard, and when fear gives way to empowerment.

The future of healthcare lies in this integration of science, technology, and empathy. By equipping HCPs to guide patients not only through treatment but through the emotional landscape of illness, the healthcare system becomes more responsive, humane, and effective.

As the story of a:care continues to unfold, it serves as a call to action: to rethink patient engagement, to prioritize communication, and to recognize that healing begins not just with medicine, but with understanding.

Ms. Oana Butu
Global eHealth Lead.
a:care Lead, Abbott.

Genesis of a new approach to address non-adherence

> *"All patients lie"*
>
> *(Dr. Gregory House)*

On television, the "world's greatest doctor," Dr. House, employs a unique approach to patient care. He generally avoids direct encounters with patients, reducing them to a series of symptoms listed on a flipchart.

Dr. House formulates his diagnoses based on these symptoms, coupled with the information he acquires through unauthorized searches of the patients' homes. He operates under the belief that questioning patients is futile since "they all lie."

After establishing a diagnosis, Dr. House prescribes the appropriate treatment, leading to the patient's recovery by the episode's conclusion.

But how closely does this fictional portrayal align with reality? Is there truth to the notion that patients "lie"? If so, why might this be the case? Could it be that HCPs are not posing the correct inquiries? Or perhaps they are not adequately attending to th patients' answers?

While doctors are usually more empathetic than Dr. House, it must be acknowledged that medical training often emphasizes maintaining a professional detachment from patients, prioritizing symptoms and biological factors over the individuals themselves. This approach is deemed necessary for precise diagnostic processes.

Nonetheless, it is essential to confront the reality that medical and pharmaceutical education does not sufficiently emphasize the importance of understanding patients' beliefs and motivational factors.

This deficiency has severe repercussions: A significant number of patients, particularly those with chronic illnesses, find it challenging to comply with their prescribed treatments.

Half of patients do not take their treatment as prescribed[1]

In 2003, the WHO released a seminal report that has since served as a key resource for those exploring the issue of adherence to long-term therapies. This comprehensive report spanned a variety of chronic conditions, including hypertension, diabetes, HIV, and epilepsy.

The report's principal conclusions were stark and concerning. It revealed that, regardless of the seriousness of the illness, a significant number of patients–up to 50%–fail to follow their physician's prescribed treatment regimen.

> *"Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments"*

The above quote from the WHO report resonates like a punchline.

In the midst of extensive efforts to develop new medications, one must question how the simple yet critical task of ensuring patients properly adhere to their existing prescriptions was overlooked. Is it not imperative to gain a deeper understanding of the patient, looking beyond the illness itself?

A decade and a half later, the OECD released a benchmark publication that reaffirmed the need for public health policies to prioritize medication adherence:[2]

1. Brown MT, Bussell JK. Medication adherence: WHO cares? Mayo Clin Proc. 2011 Apr;86(4):304-14. doi: 10.4065/mcp.2010.0575. Epub 2011 Mar 9.
2. Khan, R. and K. Socha-Dietrich (2018), "Investing in medication adherence improves health outcomes and health system efficiency: Adherence to medicines for diabetes, hypertension, and hyperlipidaemia", OECD Health Working Papers, No. 105, OECD Publishing, Paris, https://doi.org/10.1787/8178962c-en. Last accessed 07/07/2023.

- National health policy agendas should explicitly recognize the importance of adherence.
- Research indicates that characteristics of the health system, particularly the quality of the patient–provider relationship, prescription refill processes, and direct costs to patients, are significant factors.
- Patients with chronic illnesses often feel excluded from decisions regarding their treatment, leading to resistance.

Across the life sciences sector, the mission to improve care and address unmet needs is universal. Yet in 2019, Abbott took a bold step beyond the conventional. Recognizing the urgent need to tackle non-adherence in emerging markets, we launched a pioneering, non-commercial initiative, one that would challenge assumptions, reshape conversations, and place the patient experience at the center of care.

In the next pages, we will explore how this initiative came to life, its vision, its evolution, and the impact it continues to make in transforming patient engagement across the globe.

At Abbott, we call it “a:care”

The issue of medication non-adherence is particularly acute in low-to-middle-income countries, where the combination of limited health literacy, restricted access to healthcare, brief interactions with medical professionals, and the need for patients to pay for treatments out-of-pocket exacerbates the challenge.

Addressing non-adherence is a longstanding endeavor. Numerous pharmaceutical companies have introduced both offline and online patient aids, such as educational pamphlets and medication reminders, often integrated into marketing initiatives. Yet, the longevity of these programs is rarely considered, and seldom do they undergo rigorous clinical evaluation to establish their efficacy.

In tackling any medical issue, it is essential to adopt a logical approach that seeks to comprehend and confront the underlying causes rather than merely treating the symptoms. This principle is especially pertinent in the context of medication adherence, where understanding the foundational issues can lead to more effective and sustainable solutions.

> *“Non-adherence to medication is a complex issue that can’t be fixed with simple solutions”*
>
> *(Prof. Weinman)*

The initial phase of our exploration aimed to comprehend the reasons behind patients’ lapses in taking their medications, despite facing severe or even life-threatening health issues.

It raises the following question: How does one inadvertently neglect to take medication that alleviates pain?

Furthermore, the inconsistency in medical research regarding the effectiveness of adherence-enhancing strategies, like pill reminders, raises questions. What truly motivates–or demotivates–patients to follow their treatment regimens?

Initiating this investigative quest necessitates a transition from concentrating on the medical condition to gaining a profound insight into the patients themselves, exploring their individual experiences with their health challenges.

With half of the patients not adhering to their prescribed treatments, the quest to understand medication non-adherence is akin to spotlighting not just an elephant but perhaps a mammoth in the room. The issue is far from novel. For centuries, the medical field has made remarkable strides in comprehending, diagnosing, and treating diseases. Yet, in this pursuit, it may have occasionally overlooked the most critical element–the patient.

> *“It is far more important to know what person the disease has than what disease the person has”*
>
> *(Hippocrates)*

To gain a deeper insight into patients’ experiences with their conditions and to comprehend why traditional medical approaches have not effectively reached half of the patient population, it is essential to adopt unconventional thinking and incorporate diverse expertise.

Examining the consumer world offers a parallel perspective. For many years, the prevailing economic theory was that consumers behaved rationally, acting on their needs by choosing the most cost-effective products available to satisfy those needs.

But are we that rational?

No, according to Daniel Kahneman and Amos Tversky. They challenge the notion of human rationality through their work. They assert that our thinking is subject to cognitive biases and heuristics, leading us to make decisions that may seem illogical.

Intriguingly, behavioral scientists like Richard Thaler have delved into these patterns of irrationality, offering analyses and explanations for the seemingly illogical nature of our decision making. Kahneman and Thaler's pioneering contributions to behavioral economics were recognized with the Nobel Prize,[3,4] marking a significant and enduring shift in economic theories.

Is treating a disease the same as treating a patient?

Clinical guidelines typically advocate for a systematic approach to patient management. This process begins with an accurate diagnosis, is followed by the prescription of medical and pharmacological treatments that are substantiated by the strongest medical evidence, and concludes with the establishment of proper follow-up care.

While this method is undoubtedly effective for addressing specific diseases, a question emerges of whether it is equally suitable for managing patients as individuals. Are patients solely defined by their conditions?

Consider the management of type 2 diabetes, for instance. A primary intervention often involves weight management. The guidelines suggest a low-calorie diet for individuals who are overweight or obese to facilitate a significant weight reduction, averaging about 10 kg for a moderately obese person.

This recommendation is grounded in solid scientific evidence, making it a logical piece of advice for managing the disease from a purely clinical standpoint.[5]

Maintaining weight loss over an extended period presents a formidable challenge. Studies indicate that approximately 80% of individuals who achieve substantial weight loss are unable to sustain it for a full year. Furthermore, a meta-analysis of various intervention studies reveals that, on average, dieters tend to regain more than half of the weight they initially lost within 2 years.[6]

3. https://www.nobelprize.org/prizes/economic-sciences/2002/kahneman/biographical/
4. https://www.nobelprize.org/prizes/economic-sciences/2017/thaler/facts/
5. IDF Clinical Practice Recommendations for managing Type 2 Diabetes in Primary Care, International Diabetes Federation, 2017 https://idf.org/media/uploads/2023/05/attachments-63.pdf. Site last accessed 14/07/2023.
6. Unexpected Clues Emerge About Why Diets Fail, Scientific American, 13/01/2020 https://www.scientificamerican.com/article/unexpected-clues-emerge-about-why-diets-fail/ site last accessed 14/07/2023.

In some instances, despite the strong evidence backing these guidelines, pressuring patients who have asymptomatic conditions like type 2 diabetes to lose weight can heighten their frustration. This approach may sometimes prove to be counterproductive, as it could demotivate some of them and may even cause them to discontinue their care altogether.[7]

> *"We cannot solve our problems with the same level of thinking that created them"*
>
> *(Albert Einstein)*

Our exploration began with an endeavor to discern the predictability of seemingly irrational behaviors and to determine how insights from behavioral science could inform the development of novel strategies to influence patient behavior.

One of the primary goals of the initiative was to address the widespread issue of medication non-adherence in emerging countries, where the burden of chronic disease is rising and healthcare systems often face significant resource constraints. To tackle this challenge, Abbott launched a bold and innovative approach, drawing on the expertise of leading behavioral scientists and psychologists.

Ironically, despite the fact that a substantial number of patients fail to follow their prescribed treatments, experts in behavioral science and psychology are still rarely featured at major medical conferences, whether international or local. As a result, these disciplines are often seen as peripheral to mainstream medicine, rather than integral to improving patient outcomes.

To build a solution that could truly make a difference, the a:care initiative recognized the importance of involving the right stakeholders from the outset.

Given the diversity of patient populations and the complexity of adherence behaviors, the most effective starting point was to engage those who interact with patients every day: doctors, pharmacists, and nurses. These HCPs are uniquely positioned to influence behavior, build trust, and bridge the gap between medical advice and patient action.

7. Boye KS, Shinde S, Kennedy-Martin T, Robinson S, Thieu VT. Weight Change and the Association with Adherence and Persistence to Diabetes Therapy: A Narrative Review. Patient Prefer Adherence. 2022 Jan 6;16:23-39.

Consequently, Abbott's a:care inaugural action was to heighten awareness of medication non-adherence and to facilitate the integration of behavioral science, thereby revolutionizing the manner in which patients are approached and managed.

When constructin a solution for an issue that has not been previously identified.

The subsequent phase involved the creation of a suite of methods and tools designed to assist HCPs in:

- Evaluating the degree and risk of non-adherence in each patient;
- Implementing personalized strategies to effectively tackle the issue.

An unprecedented educational program for HCPs

The a:care educational program comprises a sequence of four online conferences featuring eminent experts in both medicine and behavioral science. The masterclasses have garnered the participation of 45,000 HCPs as of 2024.

The inaugural masterclass conducted by Dr. Kate Wolin, served as an introduction to the concept of adherence, defining it from a scientific perspective. It underscored the extent of non-adherence and its profound implications for patients, public health, and society at large. Dr. Wolin elucidated the primary behavioral factors contributing to non-adherence and methods for their identification. She also delved into patient decision-making processes regarding treatment adherence.

The second masterclass, led by Prof. Weinman, was designed to shed light on the various behavioral frameworks that elucidate the nature of adherence.

These frameworks include:

- Patient behavioral decision-making framework, also known as COM-B (capability, opportunity, and motivation);
- Health Belief Model;
- Theory of Planned Behavior;
- Transtheoretical model.

During the third masterclass, Dr. Pruitt discussed a robust, research-backed methodology for altering patient behavior. The session equipped healthcare practitioners with practical tools to evaluate their patients' medication adherence levels and strategies to enhance it.

Dr. Pruitt guided participants through various tactics designed to gently encourage patients towards better adherence, ensuring more consistent compliance with their medication regimen.

Finally, Prof. John Piette shed light on the most recent advancements in digital patient support programs, illustrating their beneficial impact on patient adherence.

He delved into the realm of mobile health, explaining its significance, and presented the substantiated benefits of text messaging as an effective instrument for enhancing patient adherence to treatment protocols.

The masterclasses proved to be significantly influential for those who attended. A study conducted on a sample of 130 HCPs who participated in the event was showcased at ESPACPOMP (International Society for Medication Adherence) 2023. The findings revealed the following:[8]

- 91% of the attendees recognized that the masterclasses offered valuable perspectives on medication adherence;
- 98% reported an increased confidence in pinpointing patients who were not adhering to their medication regimens;
- 74% observed a discernible shift in their patients' adherence behaviors;
- 64% of the HCPs implemented motivational interviewing techniques following the masterclasses.

8. Abstracts of the 27th Annual Meeting of ESPACPOMP (International Society for Medication Adherence), the International Society for Medication Adherence, Budapest, Hungary, 30 November–1 December 2023. Int J Clin Pharm 46, 328–353 (2024). https://doi.org/10.1007/s11096-023-01688-5.

An overview of the a:care masterclasses can be accessed online. Additional content is available as well, including a masterclass by Kevin Dolgin on managing pandemics using behavioral science, which was conducted during the early stages of the COVID-19 outbreak. This particular session, along with others, is also hosted on the a:care professional platform.

Transitioning from masterclasses to the world's largest congress on adherence

Consider a 52-year-old woman managing type 2 diabetes, hypertension, and epilepsy. She would likely consult with a general practitioner, a neurologist, an endocrinologist, and a gynecologist. Each specialist might view her through the lens of their expertise: Is she a "diabetic patient with epilepsy" or an "epileptic patient with diabetes"? Ensuring cohesive medical communication among these diverse specialists is crucial, despite the compartmentalization inherent in the medical field.

The a:care Congresses are large-scale online events created specifically for HCPs in emerging countries. These gatherings bring together experts in behavioral science and clinicians from all medical fields to tackle one of the region's most urgent healthcare challenges: medication adherence.

Rather than staying within the boundaries of individual specialties, the congresses promote a shared approach encouraging collaboration across disciplines to reflect the real-world complexity of healthcare in emerging countries. The goal is to equip professionals from emerging countries with practical, science-based tools that help them better support their patients and improve long-term treatment outcomes.

The inaugural congress in 2021 saw the participation of 10,000 HCPs and featured presentations from 15 leading experts.

The following year, the attendance rose to 15,000 HCPs. The congress received the endorsement of 65 medical societies worldwide, spanning a multitude of specialties. A panel of 49 experts representing every continent convened to adopt a holistic view of the patient, integrating universal adherence theories with specific cultural and demographic considerations.

The most recent a:care Congress, which took place in October 2024, had 20,000 participants out of 75,000 registered attendees.

> *"If I had an hour to solve a problem I'd spend 55 minutes thinking about the problem and 5 minutes thinking about solutions"*
>
> *(Einstein)*

Enhancing medication adherence involves educating physicians about the underlying causes. Unfortunately, despite many patients struggling to adhere to their prescribed treatment plans, medical education often focuses on diagnosing diseases and prescribing the best treatments, while neglecting to consider the patient as a whole person.

As a result, many physicians tend to underestimate the proportion of their patients who will not adhere to their medication–a phenomenon known as optimistic bias, which will be explored further in this book. When physicians anticipate adherence challenges, their go-to solution is often traditional pill reminders, which are generally effective only for those patients who are already motivated to take their medication. Sadly, these motivated individuals represent just a small fraction of the patient population.

Abbott is offering tools that fall into three distinct categories:

- **Assessing the risk of non-adherence.**

Evaluating the likelihood of non-adherence is a critical aspect of patient care. Regrettably, studies indicate that physicians' ability to predict whether a patient will follow their treatment plan is no better than random chance. To enhance clinical practice, doctors' toolkits should include evidence-based behavioral risk calculators that are simple to use during patient consultations.

One of the pioneering tools in this domain is called a:care Insight. This behavioral assessment instrument utilizes the "SPUR" algorithm, which was assessed in multiple published studies[9,10,11,12,13,14,15]. It offers a personalized evaluation of a patient's potential risk of non-adherence, providing valuable insights that enable physicians to proactively address these risks.

A:care Insight is readily accessible for use worldwide.

- **Improving the communication with the patient**

The a:care professional platform offers a collection of articles aimed at deepening the understanding of non-adherence issues across various medical conditions.

Additionally, it provides tools that assist patients in visualizing their health status more clearly.

Recent research has demonstrated that enabling cardiovascular patients to visualize their arteries through cardiac imaging–regardless of the presence of subclinical atherosclerosis–can foster engagement and motivate behavioral changes.[16]

These changes contribute to an improved cardiovascular risk profile and enhance adherence to primary prevention pharmacotherapy.

In line with these findings, we have introduced a cardiovascular risk calculator. This tool is grounded in the 2021 European Society of Cardiology (ESC) Guidelines for the prevention of cardiovascular disease (CVD) in clinical practice. It is designed to facilitate discussions between physicians and patients, illustrating the positive impact of managing blood pressure, regulating lipid levels, and adopting healthier lifestyles on reducing cardiovascular risk. The a:care non-HDL risk calculator is readily accessible for use: https://acarepro.abbott.com/tools/non-hdl-risk-calculator/

9. de Bock E, Dolgin K, Arnould B, Hubert G, Lee A, Piette JD. The SPUR adherence profiling tool: preliminary results of algorithm development. Curr Med Res Opin. 2022 Feb;38(2):171-179.
10. Wells JS, El Husseini A, Okoh S, Jaffar A, Neely C, Crilly P, Dolgin K, Kayyali R. SPUR: psychometric properties of a patient-reported outcome measure of medication adherence in type 2 diabetes. BMJ Open. 2022 Sep 6;12(9):e058467.
11. Wells J, Mahendran S, Dolgin K, Kayyali R. SPUR-27 - Psychometric Properties of a Patient-Reported Outcome Measure of Medication Adherence in Chronic Obstructive Pulmonary Disease. Patient Prefer Adherence. 2023 Feb 19;17:457-472.
12. Tugaut B, Shah S, Dolgin K, Rebibo Seror H, Arnould B, Laporte ME, Lee A, Nabec L, Kayyali R, Wells J, Piette JD, Hubert G. Development of the SPUR tool: a profiling instrument for patient treatment behavior. J Patient Rep Outcomes. 2022 Jun 6;6(1):61.
13. de Bock E, Dolgin K, Kombargi L, Arnould B, Vilcot T, Hubert G, Laporte ME, Nabec L, Reach G. Finalization and Validation of Questionnaire and Algorithm of SPUR, a New Adherence Profiling Tool. Patient Prefer Adherence. 2022 May 12;16:1213-1231.
14. Wells J, Wang C, Dolgin K, Kayyali R. SPUR: A Patient-Reported Medication Adherence Model as a Predictor of Admission and Early Readmission in Patients Living with Type 2 Diabetes. Patient Prefer Adherence. 2023 Feb 19;17:441-455.
15. Dolgin K. The SPUR Model: A Framework for Considering Patient Behavior. Patient Prefer Adherence. 2020 Jan 16;14:97-105.
16. Whitmore K, Zhou Z, Chapman N, Huynh Q, Magnussen CG, Sharman JE, Marwick TH. Impact of Patient Visualization of Cardiovascular Images on Modification of Cardiovascular Risk Factors: A Meta-Analysis. JACC Cardiovasc Imaging. 2023 Apr 18:S1936-878X(23)00150-X.

- **Coaching the patient after the consultation**

Simple pill reminders are not sufficient to improve medication adherence, especially in cases of intentional non-adherence, where patients consciously choose not to follow treatment. However, non-intentional non-adherence—such as forgetting doses, misunderstanding instructions, or being overwhelmed by complex regimens—is also widespread and often underestimated. To address both types, Abbott has released the mobile app my a:care, which aims to improve adherence through motivational interventions, behavioral support, and personalized guidance.

The mobile application my a:care was assessed through a proof-of-concept clinical trial in dyslipidemia. The primary endpoint of this proof-of-concept study on recently diagnosed dyslipidemic patients is encouraging, with potential benefits on blood lipids[17].

> *"The journey of a thousand miles begins with one step"*
>
> *(Lao Tzu)*

Enhancing medication adherence is an ambitious, long-term endeavor. Achieving such a goal necessitates a comprehensive transformation of healthcare systems and, crucially, a shift in mindsets. We acknowledge that this represents one of the most formidable challenges in the field of medicine.

Success in this area has the potential not only to elevate population health but also to yield significant economic benefits.

This book draws on the extensive knowledge gained throughout the a:care journey and the conferences organized by Abbott. It has multiple objectives: to raise awareness among HCPs about this critical medical issue, to enhance their understanding of why some patients remain uncontrolled, when it comes to their medical outcomes, and to provide guidance on addressing these challenges.

17. Pongchaiyakul C and Driessen S (2025) Evaluating the effect of mobile applications "My A:Care" and "Smart Coach" on adherence to lipid-lowering treatment in patients with dyslipidemia: a prospective, randomized, open-label clinical study. Front. Digit. Health 7:1502990. doi: 10.3389/fdgth.2025.1502990.

The time has come for the medical community to confront this issue directly and to focus on the “other-half-of-patients”–the ones who don’t take their treatment correctly–who are often overlooked. It is crucial that we all acknowledge and address this long-ignored problem.

An elephant in the hospital

Adherence to long-term therapy is defined by the "extent to which a person's behavior–taking medication, following a diet, and/or executing lifestyle changes–corresponds with agreed recommendations from an HCP."[18]

Notably, this definition moves away from the previously common term "compliance." The term "compliance" suggests a hierarchical dynamic where the doctor, presumed to know best, issued directives that the patient was expected to follow, often within a context of vulnerability and trust.

The widespread issue of non-adherence underscores the need to refine this concept to better represent a collaborative agreement between the doctor and the patient, rather than a one-sided mandate.

The three pillars of medication adherence

"Adherence to medications" is the process by which patients take their medication as prescribed. It is further divided into three quantifiable phases: initiation, implementation, and discontinuation.[19]

- **Initiation**

Initiation occurs when the patient takes the first dose of a prescribed medication.[20,21]

18. World Health Organization. (2003). Adherence to long-term therapies: evidence for action. World Health Organization. https://apps.who.int/iris/handle/10665/42682 - last accessed 09/01/2025.
19. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, Dobbels F, Fargher E, Morrison V, Lewek P, Matyjaszczyk M, Mshelia C, Clyne W, Aronson JK, Urquhart J; ABC Project Team. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol. 2012 May;73(5):691-705.
20. Jimmy, Beena, and Jimmy Jose. "Patient medication adherence: measures in daily practice." Oman Medical Journal vol. 26,3 (2011): 155-9.
21. Abhijit S. Gadkari & Colleen A. McHorney (2010) Medication nonfulfillment rates and reasons: narrative systematic review, Current Medical Research and Opinion, 26:3, 683-705.

It is indeed a paradox that a patient would go through the process of scheduling an appointment, traveling to the doctor's office, waiting for their turn, consenting to an examination, and paying for the consultation, only to neglect filling their prescription. According to the OECD, between 4% and 31% of patients who are prescribed medications for diabetes, hypercholesterolemia, or hypertension do not fill their initial prescription.[22]

In general, medical research further narrows this range, indicating that 20%–30% of patients do not fill their initial prescriptions.[23]

Research indicates that approximately 18%–34% of patients do not proceed with filling their second prescriptions for medications related to diabetes, cholesterol, or hypertension, as reported by the OECD.[22] This phenomenon of not fulfilling a prescription is referred to as primary non-adherence.

- **Implementation**

Implementation is the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen, from initiation until the last dose.

- **Discontinuation**

Discontinuation occurs when a patient stops taking the prescribed medication for whatever reason(s).

Persistence is defined as the length of time between initiation and the last dose, which immediately precedes discontinuation. Maintaining long-term treatment adherence is a significant challenge. HCPs should not assume that patients will automatically adhere to their treatment plans. Regrettably, non-adherence should be considered the norm.

All HCPs have a role to play to help patients form habits by applying the right behavioral strategies.

22. Khan, R. and K. Socha-Dietrich (2018), "Investing in medication adherence improves health outcomes and health system efficiency: Adherence to medicines for diabetes, hypertension, and hyperlipidaemia", OECD Health Working Papers, No. 105, OECD Publishing, Paris, https://doi.org/10.1787/8178962c-en. Last accessed 07/07/2023.

23. Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock SJ, Wines RC, Coker-Schwimmer EJ, Rosen DL, Sista P, Lohr KN. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review. Ann Intern Med. 2012 Dec 4;157(11):785-95.

> *"If you feel bad at 10 miles, you're in trouble. If you feel bad at 20 miles, you're normal. If you don't feel bad at 26 miles, you're abnormal"*
>
> *(Rob de Castella, Australian world champion marathon runner)*

The extent of non-compliance and non-persistence is alarming.

For those who do fill the first prescription, only 50 to 70% are taking their medications regularly (i.e, at least 80% of the time) and less than half of these patients are still continuing to take their medications within 2 years of the initial prescription.[24]

When patients obtain their medications but fail to take them, this is known as secondary non-adherence. Unfortunately, the percentage of patients who both fill their prescriptions and adhere to their treatment as prescribed for the intended duration is significantly lower than one would reasonably anticipate.

Very few patients with chronic diseases take their medicines as prescribed

In a group of newly diagnosed patients with either diabetes, hypertension or high blood cholesterol

4–31% of patients will not fill their first prescription

A further **18–34%** of patients will not fill their second prescription

59–67% of patients will self discontinue their medication within 2 years

30–50% of patients will fill their prescriptions but won't take them regularly

Khan R and Socha-Ditrich K. Investing in medication adherence improves health outcomes and health system efficiency. Adherence to medicines for diabetes, hypertension, and hyperlipidaemia. OECD health working paper No. 105, OECD publishing Paris. 2018

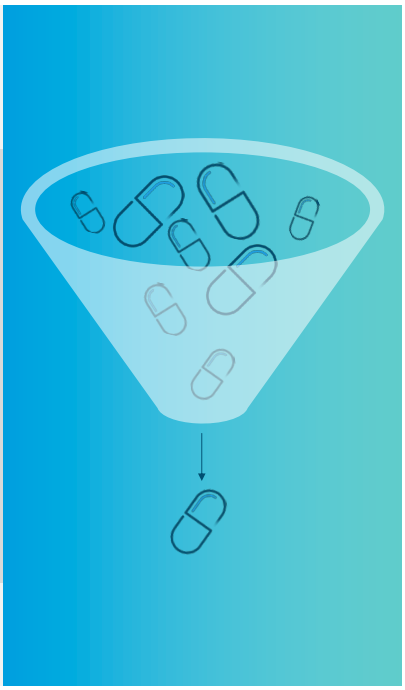
24. Khan, R. and K. Socha-Dietrich (2018), "Investing in medication adherence improves health outcomes and health system efficiency: Adherence to medicines for diabetes, hypertension, and hyperlipidaemia", OECD Health Working Papers, No. 105, OECD Publishing, Paris, https://doi.org/10.1787/8178962c-en. Last accessed 07/07/2023.

What is happening after prescription

For every 100 prescriptions written

- 50–70 are filled at the pharmacy
- 48–66 are picked up from the pharmacy
- 25–30 are taken properly
- 15–20 are refilled as prescribed

National association of chain drug stores, pharmacies: Improving health, reducing costs, July 2010. Based on IMS health data



The burden of non-adherence is massive!

It is estimated that inadequate adherence to medication regimens is responsible for nearly 200,000 premature deaths annually in Europe. Furthermore, it is believed to incur costs of approximately EUR 125 billion each year due to preventable hospitalizations, emergency care, and outpatient visits.[25]

In the US, the estimated financial impact ranges from USD 105 billion to USD 300 billion annually. [26,27]

Non-adherence is associated with at least 10% of hospitalizations and 10% of total US healthcare costs. The three most prevalent chronic conditions–diabetes, hypertension, and hyperlipidemia–stand out as the diseases with the highest avoidable costs, for which every extra USD spent on medications for patients who do adhere can generate between USD 3 and USD 13 in savings on avoidable emergency department visits and inpatient hospitalizations alone.[25]

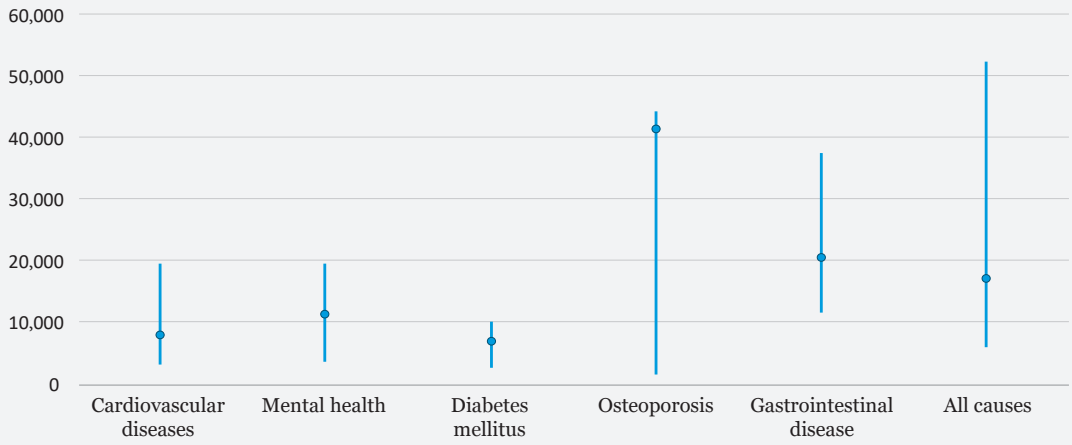
In the field of cardiology, research has demonstrated that adherence to medication regimens is correlated with net reductions in overall healthcare costs for conditions such as diabetes, hypertension, and hypercholesterolemia.

25. Khan, R. and K. Socha-Dietrich (2018), "Investing in medication adherence improves health outcomes and health system efficiency: Adherence to medicines for diabetes, hypertension, and hyperlipidaemia", OECD Health Working Papers, No. 105, OECD Publishing, Paris, https://doi.org/10.1787/8178962c-en. Last accessed 07/07/2023.

26. Iuga AO, McGuire MJ. Adherence and healthcare costs. Risk Manag Healthc Policy. 2014 Feb 20;7:35-44.

27. Medication Adherence: Importance, Issues and Policy: A Policy Statement from the American Heart Association https://www.heart.org/-/media/Files/About-Us/Policy-Research/Policy-Positions/Clinical-Care/Med-Adherence-Exec-Summary.pdf Last accessed 23/07/2023.

Unadjusted costs of non-adherence

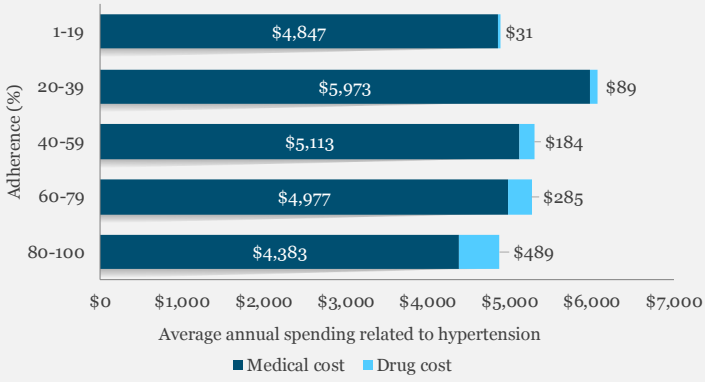


Adapted. Cutler RL, Fernandez-Llimos F, Frommer M, et al. Economic impact of medication non-adherence by disease groups: a systematic reviewBMJ Open 2018;8:e016982. doi: 10.1136/bmjopen-2017-016982

Total healthcare cost comparison across disease groups (US)[28]

Impact of non-adherence on direct costs

Hypertension average spending by adherence level*



*Adapted Michael C. Sokol, MD, MS, and others, Impact of Medication Adherence on Hospitalization Risk and Healthcare Cost, June 2005, [Accessed 29 June 2020] http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.566.9487&rep=rep1&type=pdf

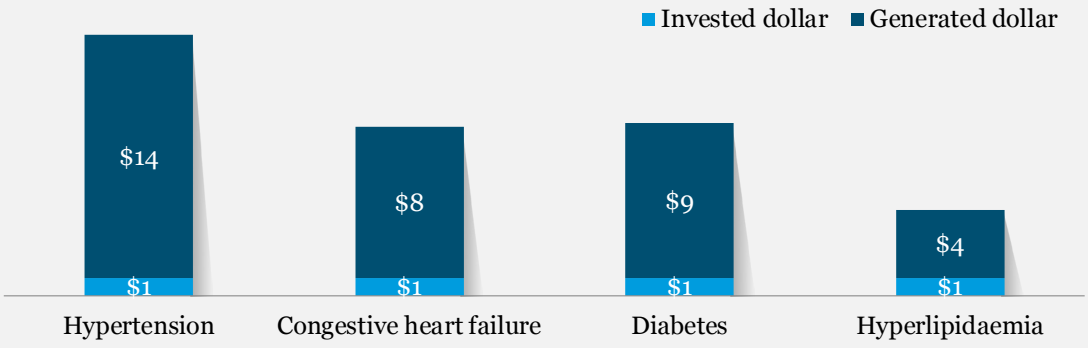
The issue of non-adherence becomes even more frustrating when considering that it may be deliberate in approximately 80% of cases.[29] However, improving this situation is worth the effort as any dollar invested in this area yields benefits for healthcare systems.

28 Cutler RL, Fernandez-Llimos F, Frommer M, Benrimoj C, Garcia-Cardenas V. Economic impact of medication non-adherence by disease groups: a systematic review. BMJ Open. 2018 Jan 21;8(1):e016982.

29. Medication Nonadherence Increases Health Costs, Hospital Readmissions, Nov 20, 2018, https://physicians.dukehealth.org/articles/medication-nonadherence-increases-health-costs-hospital-readmissions Last accessed 26/07/2023.

Medication adherence is cost effective

The average cost–benefit ratios from adherence*



*Adapted. Rabia Khan and Karolina Socha-Dietrich: Investing in medication adherence improves health outcomes and health system efficiency: Adherence to medicines for diabetes, hypertension, and hyperlipidaemia , OCDE Study, Sep 2018, https://doi.org/10.1787/18152015 [Accessed 29 June 2020], , https://www.oecd-ilibrary.org/social-issues-migration-health/investing-in-medication-adherence-improves-health-outcomes-and-health-system-efficiency_8178962c-en

Building and rebuilding trust in HCPs is essential. Studies show a strong correlation between trust in HCPs and improved medication adherence. For example, studies on asthma, stroke survivors, and oncology patients across different countries and conditions found that trust in HCPs was a strong predictor of medication adherence.

There is a strong correlation between trust in HCPs and improved medication adherence

1. Wu D, et al. patient trust in physicians matters-understanding the role of a mobile patient education system and patient-physician communication in improving patient adherence behavior. field study. j med internet res. 2022;24(12).
2. Fan Q, et al. impact of beliefs about medication on the relationship between trust in physician with medication adherence after stroke. patient educ couns. 2022;105(4):1025-1029.
3. Fan Q, et al. The mediating role of trust in physician and self-efficacy in understanding medication adherence in severe asthma. Respiratory Medicine. 2021; 190: 106673

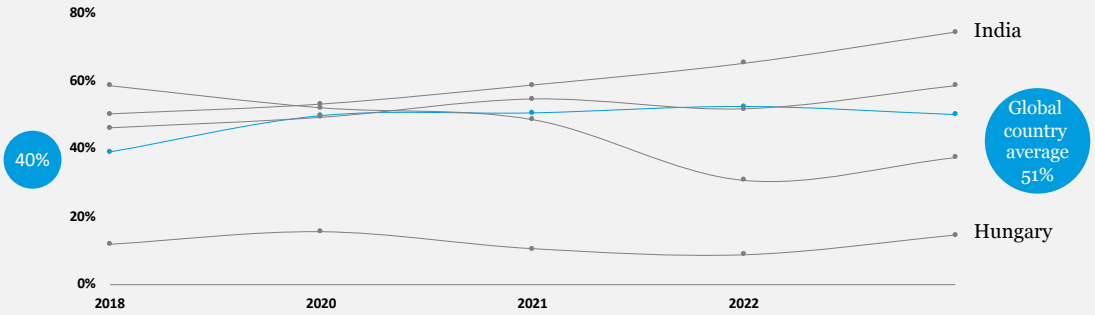
A global survey conducted in 2023 found that only 51% of people worldwide trust their country's healthcare system to provide the best treatment. In some countries, this trust is even lower; for instance, only 15% of people in Hungary trust their healthcare system to provide the best treatment.

For HCPs, this lack of trust in the healthcare system raises concerns about how likely people are to trust their HCPs or follow their advice.

Half of the global population trusts the healthcare system in their own country

Percentage who responded "agree" to the statement

I trust the healthcare system in my country to provide me with the best treatment



IPSOS global health service monitor 2023: A 31 country global survey. Available at: https://www.ipsos.com/sites/default/files/ct/news/documents/2023-09/Ipsos-global-health-service-monitor-2023-web.pdf.

Healthcare institutions and international medical societies are increasingly dedicated to addressing non-adherence

A WHO report from 2003 marked a turning point in acknowledging the importance of medication adherence. This landmark report highlighted a model that outlines the multifaceted aspects of adherence:[30]

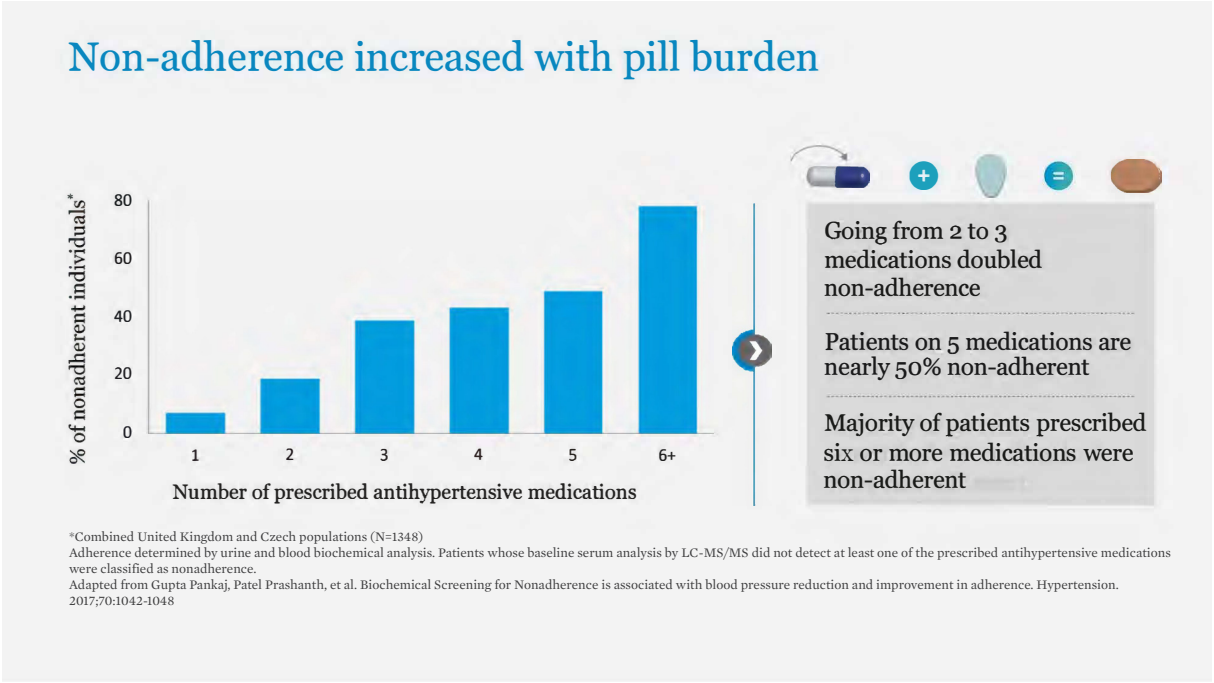
- Social and economic factors;
- Healthcare system-related factors;
- Patient-related factors;
- Therapy-related factors;
- Condition-related factors.

A working paper published by the OECD 15 years later revealed that, regrettably, advancements in this area have been minimal, and there is still much work to be done. In recent years, prominent medical societies, such as the European Society of Hypertension and the International Society of Hypertension (ISH), have focused on hypertension and revised their guidelines to underscore the issue of non-adherence. Notably, non-adherence is now recognized as a potential cause of "resistant hypertension."[31]

A summary of adherence and resistant hypertension as per the 2020 ISH Global Hypertension Practice Guidelines is available as a podcast by ISH President-Elect Maciej Tomaszewski.

At the a:care Congress in 2022, ISH Past President Prof. Alta Schutte emphasized that the goal of controlling blood pressure has not been met, as non-adherence rates are 10% for a single pill and escalate to 80% when six pills are prescribed. Merely offering potent medications to lower blood pressure is insufficient if patients do not take them.[32]

30. World Health Organization. (2003). Adherence to long-term therapies: evidence for action. World Health Organization. https://apps.who.int/iris/handle/10665/42682 - last accessed 07/07/2023.
31. de Jager RL, van Maarseveen EM, Bots ML, Blankestijn PJ; SYMPATHY investigators. Medication adherence in patients with apparent resistant hypertension: findings from the SYMPATHY trial. Br J Clin Pharmacol. 2018 Jan;84(1):18-24.
32. https://acarepro.abbott.com/congress/congress-session/session-ish-awareness-non-adherence/ last accessed 23/07/2023.



In 2021, the American Heart Association issued a policy statement to increase awareness about medication non-adherence.[33] It highlighted that, according to a cross-sectional survey, among over 24,000 adults with chronic conditions such as hypertension, diabetes, and hyperlipidemia, 62% had forgotten to take their medications, and 37% had depleted their medication supply within the span of 1 year.

These sobering data necessitate immediate policy and systems solutions to support patients in adherence.

Changing mindsets is a challenging task. Despite the fact that half of all patients do not follow their prescribed treatments, most medical conferences still treat adherence as a secondary issue, dedicating few or no sessions to it. Behavioral science experts are seldom featured speakers at such events. Often, the clinical cases discussed involve patients with complex comorbidities, rather than those who are non-adherence due to intricate belief systems.

33. Piña IL, Di Palo KE, Brown MT, Choudhry NK, Cvengros J, Whalen D, Whitsel LP, Johnson J. Medication adherence: Importance, issues and policy: A policy statement from the American Heart Association. Prog Cardiovasc Dis. 2021 Jan-Feb;64:111-120.

In the field of economics, Nobel Prizes have been awarded to individuals like Kahneman and Thaler for their work in elucidating seemingly irrational consumer behaviors and developing methods to predict them. In contrast, the medical field remains predominantly focused on diagnosing conditions and selecting treatments based on scientific evidence and guidelines, thereby overlooking the fact that patients are more than just their conditions.

It is imperative for HCPs to recognize that the responsibility for change does not lie solely with the patient in forming new habits. It is equally important for professionals to reevaluate and transform approaches to patient care. Now is the time to begin addressing the needs of “the other half of patients”, the ones who don’t take their treatment as prescribed.

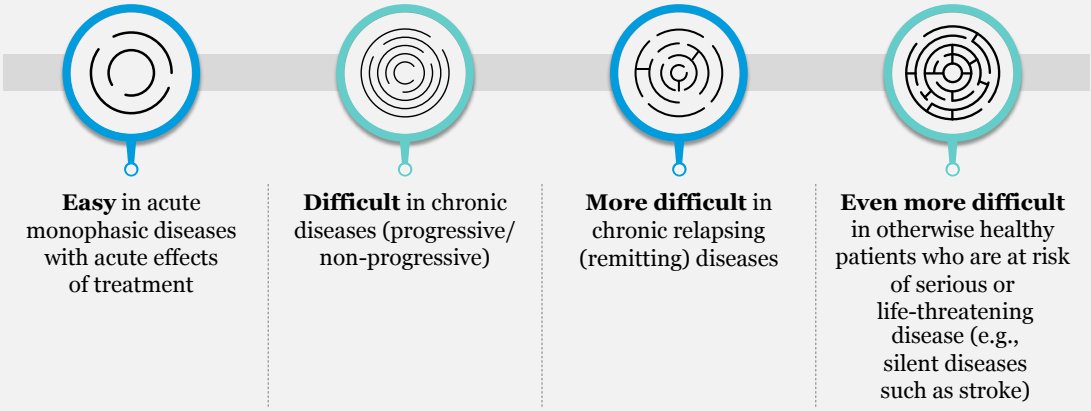
Avoiding acute crises with silent disorders

At the a:care Congress 2021, Prof. Michael Strupp, a neurology expert at the Ludwig Maximilians University Hospital in Munich, Germany, discussed his hands-on experience with patient adherence.

Adherence tends to be more straightforward in cases of acute monophasic diseases that respond rapidly to treatment, such as pneumonia. In contrast, it becomes more challenging for patients with chronic conditions, whether these are progressive or not. For instance, individuals with neurological disorders like amyotrophic lateral sclerosis or diabetic retinopathy may struggle with adherence because the benefits of treatment are not immediately apparent.

The difficulty increases further in chronic relapsing—remitting diseases such as multiple sclerosis, where patients often find it hard to maintain their medication regimen following an isolated clinical episode. The most complex scenario arises with otherwise healthy individuals who are at risk of severe, life-threatening events—such as those with atrial fibrillation, where the threat of stroke or heart attack may not feel urgent enough to motivate consistent adherence to treatment.

Compliance, adherence, and persistence

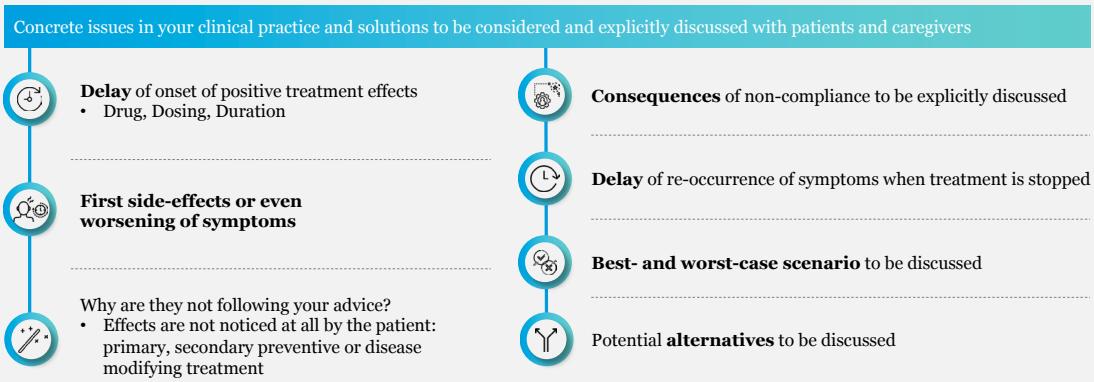


Prof. Strupp advocates for vertigo a proactive engagement with patients, emphasizing the need to inform them about the delayed onset of positive treatment effects. It is common for patients to initially experience side effects or even a temporary exacerbation of symptoms, such as during balance training exercises.

Effective communication is crucial, especially when patients might not notice the impact of primary or secondary prevention treatments, or disease-modifying therapies, unless these are combined with additional symptomatic treatments. It is important to clearly outline the repercussions of non-adherence. A frequently overlooked aspect is the delay in symptom recurrence when a treatment is discontinued.

Patients must be made aware of this potential delay, and the possible outcomes–both best and worst-case scenarios–of adhering to their medication regimen should be discussed. This discussion should also cover alternative treatments, which may be less effective and carry a higher risk of side effects.

Compliance, adherence and persistence



While COVID-19 posed significant challenges, it also provided the impetus for the advancement of remote patient management. Physicians are encouraged to embrace this technology, which facilitates regular patient consultations and the prompt assessment of treatment responses, side effects, and urgent health events.

The convenience of telemedicine for patients is clear, as it eliminates the need for travel, and both patients and doctors have adapted to this technological shift. Nevertheless, it is imperative for doctors to respond swiftly to patient communications, aiming for a response time of 1–2 h to foster a positive doctor–patient relationship.

Moreover, remote patient examinations using high-quality smartphones can be an effective tool. Observing patients' eye movements and walking patterns can provide insights into the side effects of medications, such as antiepileptic drugs.

Engaging with patients attentively is essential–they are the primary source of genuine feedback.

One additional measure to improve CAP

Remote management of your patient!

- Frequent consultations of your patients if possible
- Evaluation of side-effects, effects and acute events
- Convenient for the patient: no traveling
- Doctors and patients are already used to technology
- Covid: challenge and catalyst

Acting on the unseen: How do we help patients to remain adherent when they are asymptomatic?

Non-adherence is commonly associated with asymptomatic diseases like hypertension and diabetes, where the lack of symptoms might lead patients to forget or deem their medication as non-essential. However, the factors contributing to non-adherence are far more intricate, as evidenced by its prevalence even in symptomatic and painful conditions.

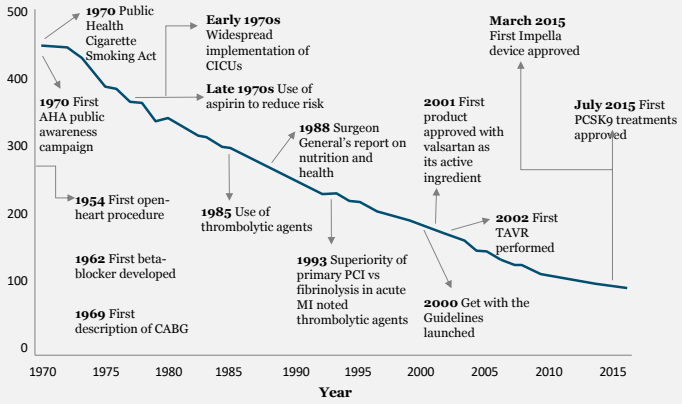
During the a:care Congresses in 2021 and 2022, Profs. Markus Schlaich and Lale Tokgözoğlu delivered lectures focused on elucidating and understanding the complex issues related to non-adherence in CVDs.

Dyslipidemia

CVD is the leading cause of mortality in most parts of the world, despite significant improvements over the past 20 years. Cardiovascular medications have played a crucial role in these improvements.

Ischemic heart disease mortality over time with selected medical advancements and public initiatives

Age-adjusted Mortality



- CV medications are responsible for half of the 50% reduction in mortality from CHD over the past 20 years[2]
- Poor adherence to treatment of chronic diseases is a worldwide problem of striking magnitude[1]
- 125,000 deaths per year in the US are due to medication non-adherence[3]

CV= Cardiovascular, CHD= Coronary Heart Disease

1. Mensah GA, Sorlie PD, Fine LJ, et al. Decline in cardiovascular Mortality: Possible Causes and Implications. Circulation Research. 2017;120(2): 366-380;
2. McClellan M, Brown N, et al. Call to action; Urgent Challenges in Cardiovascular Disease. Circulation. 2019;139:e44-54;
3. Benjamin RM, Medication adherence: helping patients take their medicines As Directed - Public Health reports 2012

However, poor adherence to treatment for chronic diseases, especially in the cardiovascular arena, is a worldwide problem of striking magnitude. In the US alone, 125,000 deaths per year are due to medication non-adherence. Adherence to long-term therapy for chronic illnesses averages about 50% in developed countries, and unfortunately, it is much lower in developing countries.

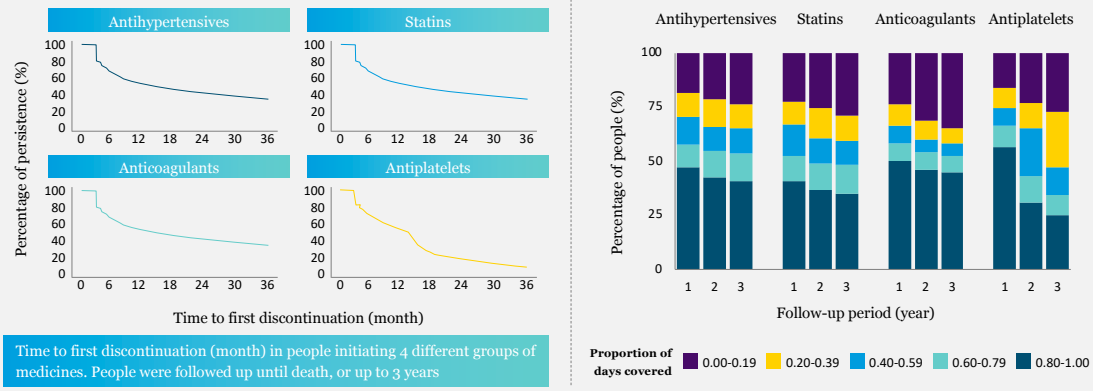
For example, in China, Gambia, and the Seychelles, only 43%, 27%, and 26% of patients with hypertension adhered to their antihypertensive medications, respectively. According to a study, 80% of non-controlled hypertensives were non-adherence.

Studies from Australia on patients with coronary artery disease show that about 15% discontinue their medication within 90 days, and about 50% discontinue within the first year. High adherence, defined as more than 80% drug coverage, is seen in about 50%–60% of patients in the first year, but this proportion decreases in subsequent years.

Persistence to cardiovascular medicines significantly declines following initiation

Using Australian national dispensing

Adults (≥18 years) initiating antihypertensives, statins, oral anticoagulants, or antiplatelets in 2018



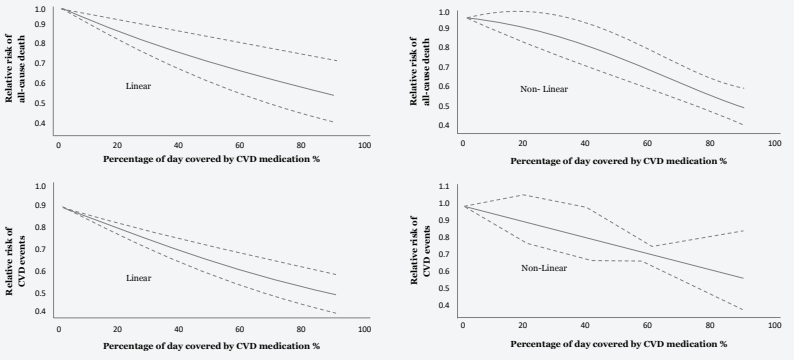
Time to first discontinuation (month) in people initiating 4 different groups of medicines. People were followed up until death, or up to 3 years

De Oliveira Costa J, et al. Persistence and Adherence to Cardiovascular Medicines in Australia. Journal of the American Heart Association. 2023;12(13):e030264.

Meta-analyses of 18 studies across several countries show a dose—response relationship between cardiovascular medication adherence and the risk of cardiovascular events and mortality. A 20% increase in medication adherence is associated with an 8%–12% reduction in cardiovascular mortality.

Poor adherence is dose-dependently associated with significantly increased risk of cardiovascular events and all-cause mortality in patients with CAD

Countries involved: Canada, China, Finland, France, Israel, Italy, UK and USA



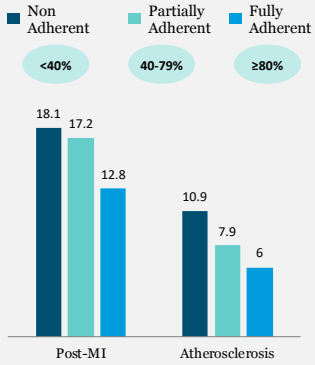
Dose–response relationship (linear and nonlinear) of cardiovascular medication adherence and cardiovascular events. The solid line and the dashed lines represent the estimated relative risk and the 95% confidence interval, respectively

CAD: coronary arterial disease; CV: Cardiovascular disease.
Chen C et al. Adherence with cardiovascular medications and the outcomes in patients with coronary arterial disease: "Real-world" evidence. Clin Cardiol. 2022;45(12):1220-1228.

In the US, patients with full adherence have lower cardiovascular events and healthcare costs related to myocardial infarction, stroke, and cardiovascular admissions compared to those with partial or non-adherence. Factors contributing to low medication adherence include inadequate patient education, high drug costs, side effects, complex medication regimens, poor family support, and comorbidities such as depression and dementia.

Impact of medication adherence on long term CV outcomes and cost

Adherence levels and MACE (Hospitalizations per 100 patient-years)



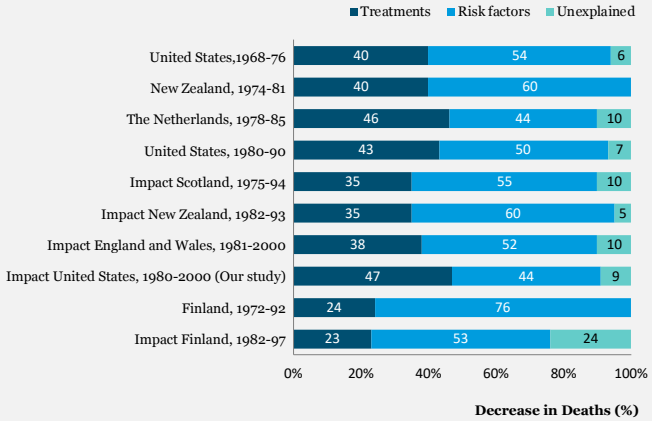
- Database of a large health insurer for patients hospitalized for MI or with atherosclerotic disease in USA
- Proportion of days covered (PDC) for statin and ACE inhibitors
- Outcome: Composite of all-cause death, MI, stroke, or coronary revascularization

	Post-MI Cohort (Per Patient Per Year)			ATH Cohort (Per Patient Per Year)		
	Non-adherent	Partially Adherent	Fully Adherent	Non-adherent	Partially Adherent	Fully Adherent
MI	$844.46	$774.09	$404.64	$396.03	$297.02	$181.51
Stroke	$178.49	$133.87	$89.24	$168.62	$116.74	$77.82
Revascularization	$3,375.21	$3,070.50	$2,531.41	$1,863.60	$1,353.33	$1,064.91
Angina and CV atherosclerosis	$1,432.86	$1,527.12	$1,093.50	$1,772.64	$1,236.72	$865.71
All-cause ED visits	$256.97	$219.56	$182.64	$181.65	$132.43	$109.29
Cardiac-related ED visits	$14.77	$12.80	$13.29	$10.34	$6.89	$4.92
Outpatient visits to cardiologist	$639.38	$657.47	$645.19	$411.83	$423.24	$424.32
Outpatient visits to cardiologist with CV testing	$558.76	$553.16	$576.67	$446.69	$436.41	$446.69

Bansilal S et al. Assessing the Impact of Medication Adherence on Long-Term Cardiovascular Outcomes. J Am Coll Cardiol. 2016;68(8):789-801.

There are several reasons for this, but rising indirect costs and out-of-pocket spending represent particular challenges for low-income countries. The impact of poor adherence grows as the burden of chronic disease increases worldwide.

Attribution of treatment and risk factors changes in deaths from coronary heart disease



- Adherence to long-term therapy for chronic illnesses averages 50% in developed countries and is lower in developing countries[1]
- In China, the Gambia and the Seychelles, only 43%, 27% and 26% of patients with hypertension adhere to their antihypertensive medication. 80% of noncontrolled HTN are nonadherent[2]
- Indirect costs are rising, and this out-of-pocket spending represents a particular challenge for low-income patients[3]
- The impact of poor adherence grows as the burden of chronic disease grows worldwide[2,3]

HTN= Hypertension

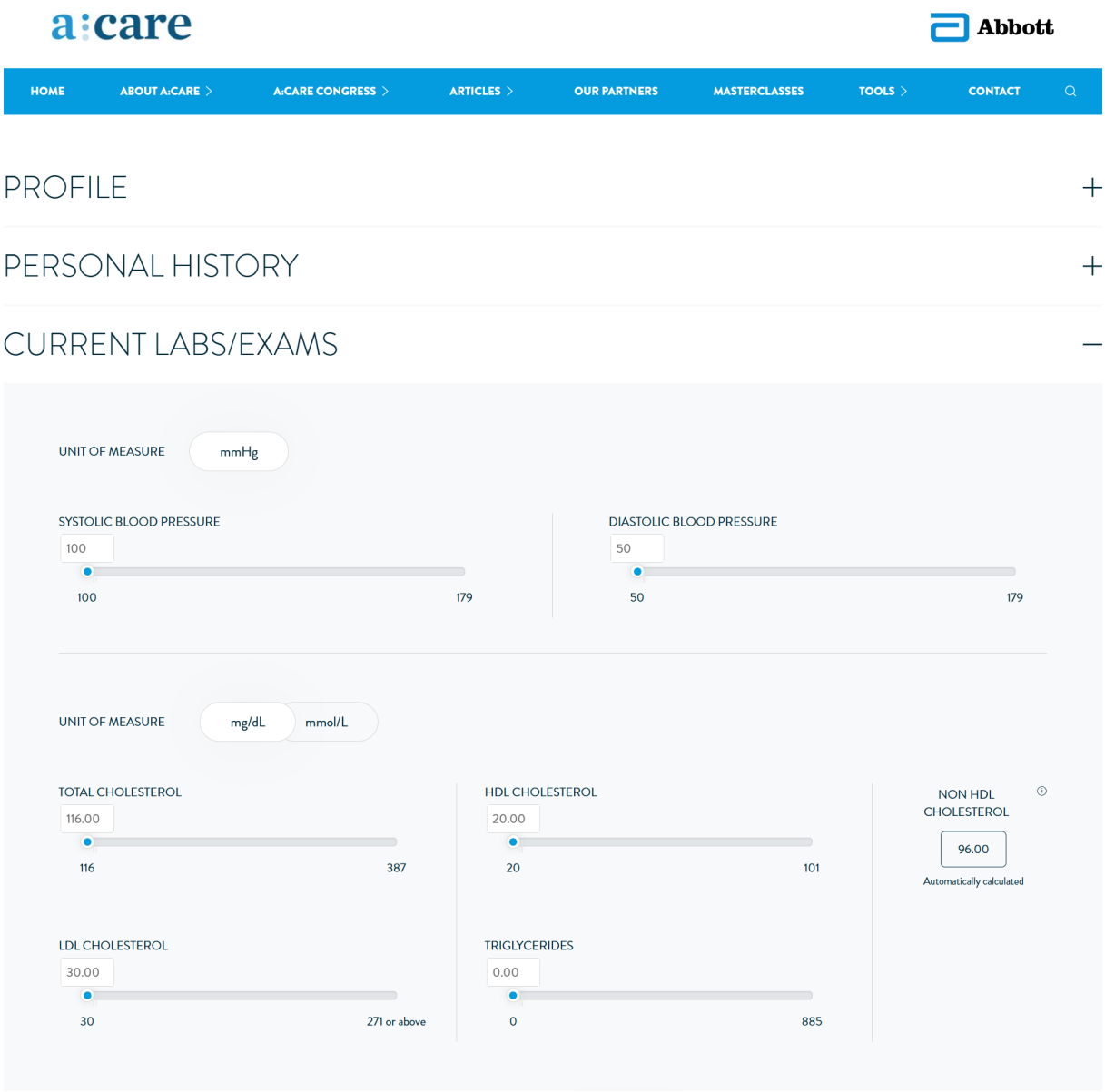
1. Ford ES, Ajani UA, et al. Explaining the decrease in U.S. Deaths from Coronary Disease, 1980-2000. The New england Journal of Medecine. 2007;356:2388-98; 2. World Health Organization. Adhrence to long-term therapies – Evidence for action. 2003; 3. McClellan M, Brown N, et al. Call to action; Urgent Challenges in Cardiovascular Disease. Circulation. 2019;139:e44-54

One of the first steps to improve the health of populations is to reach the goals recommended in various clinical guidelines.

The a:care non-HDL risk calculator is a publicly accessible tool that evaluates the cardiovascular risk of patients, whether they are apparently healthy or have other health conditions. This calculator is based on the 2021 ESC Guidelines for the prevention of CVD in clinical practice,[34] as well as the SCORE2 and SCORE2-OP metrics.

It calculates an individual's 10-year risk of cardiovascular events based on various factors, including country risk levels, lipid profiles, blood pressure, existing health conditions, and lifestyle choices. The calculator serves as an aid in patient communication, illustrating the potential benefits of managing lipid levels or the positive effects of quitting smoking, for example.

34. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, Benetos A, Biffi A, Boavida JM, Capodanno D, Cosyns B, Crawford C, Davos CH, Desormais I, Di Angelantonio E, Franco OH, Halvorsen S, Hobbs FDR, Hollander M, Jankowska EA, Michal M, Sacco S, Sattar N, Tokgozoglu L, Tonstad S, Tsioufis KP, van Dis I, van Gelder IC, Wanner C, Williams B; ESC National Cardiac Societies; ESC Scientific Document Group. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021 Sep 7;42(34):3227-3337.



a:care non-HDL risk calculator

Merely prescribing the appropriate treatment does not suffice to reduce cardiovascular risk unless patients comply with the medication regimen as directed.

Findings from the EUROASPIRE IV study indicate that a considerable proportion of coronary patients with dyslipidemia remain insufficiently managed, and a substantial segment of those undergoing lipid-lowering treatment are not achieving the targeted LDL-C levels.[35]

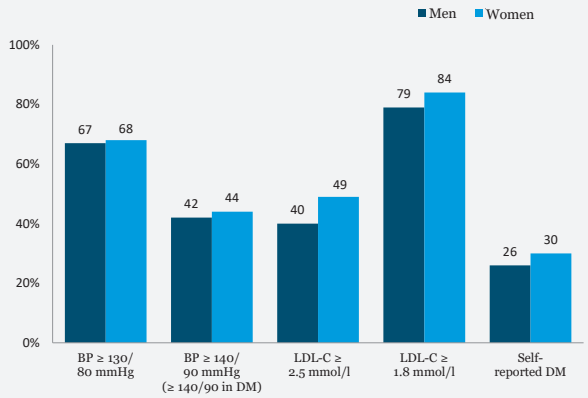
35. Ž. Reiner, G. De Backer, Z. Fras, K. Kotseva, L. Tokgözoglu, D. Wood, D. De Bacquer. Lipid lowering drug therapy in patients with coronary heart disease from 24 European countries – Findings from the EUROASPIRE IV survey. Atherosclerosis, Volume 246, 2016, Pages 243-250, ISSN 0021-9150.

Statins

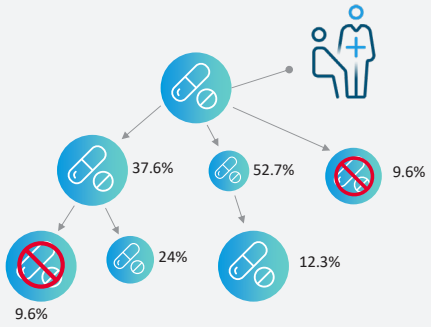
Statins are one of the most important weapons we have for cardiovascular prevention, but they are probably one of the least adhered-to drugs. For example, when the EUROASPIRE IV patient journey was published, we saw that patients with coronary artery disease were all prescribed a statin at hospital discharge. However, at six months, only 37% were still taking the same dose, half had reduced their dose, and 10% had completely stopped the medication. Further follow-up showed the situation worsened over time.

Attaining targets in CAD patients from 24 European countries EA IV[1]

Prevalence (%)



EUROASPIRE IV statin therapy at discharge: instead of escalating Rx to get to goal, de-escalate at FU[2]



CAD= Coronary Artery Disease, IV= Intravenous, EA= EUROASPIRE

1. Kotseva K, Wood D, De Bacquer D, et al. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. European Journal of Preventive Cardiology. 2016, Val 23(6) 636-648; 2. Reiner Z, De Backer G, Fras Z, et al. Lipid lowering drug therapy in patients with coronary heart disease from 24 European countries – Findings frome the EUROASPIRE IV survey. Atherosclerosis. 2016: 243-250

> “Non-adherence is the new cardiovascular risk factor”
>
> *(Prof. Tokgözoğlu)*

Statin compliance and adherence is a major problem worldwide. In the US, about 12% of patients do not even fill their prescriptions, which may be due to a lack of understanding of the benefits of therapy, denial, financial reasons, or health literacy issues. This highlights the importance of shared decision making and getting patients on board once a prescription is written.

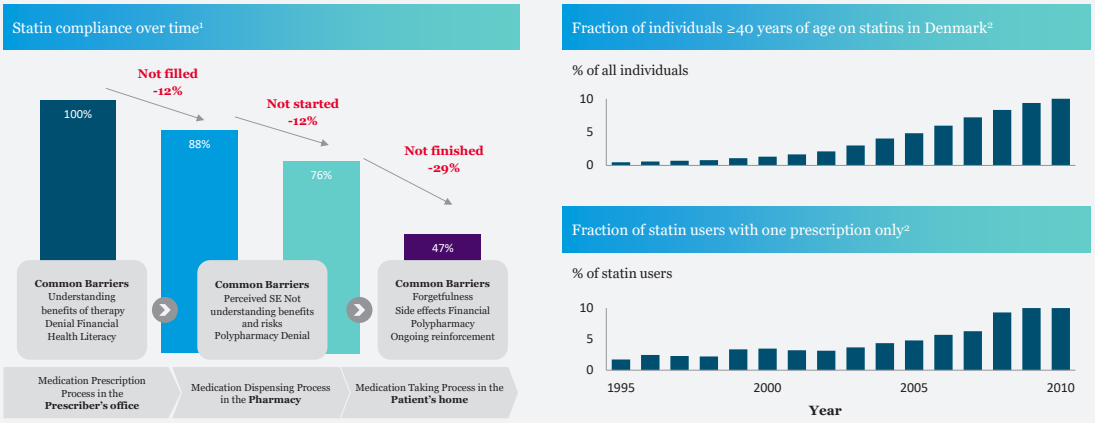
Another barrier is that 12% of patients who get the medication do not start it, possibly due to perceived side effects, lack of understanding of benefits and risks, polypharmacy (more than 10

prescribed medications), or denial. Teamwork involving pharmacists, family members, or nurses can help patients understand the importance of starting the medication.

Once patients start the medication, about 30% do not finish it due to forgetfulness, side effects, financial reasons, polypharmacy, and lack of ongoing reinforcement. From the beginning, about 50% of patients are lost.

A nationwide study from Denmark, where electronic health records are well kept, showed that over time, the fraction of individuals over 40 years of age on statins increased, but so did the fraction of statin users with only one prescription, highlighting the relevance of the problem.

Statin compliance and adherence



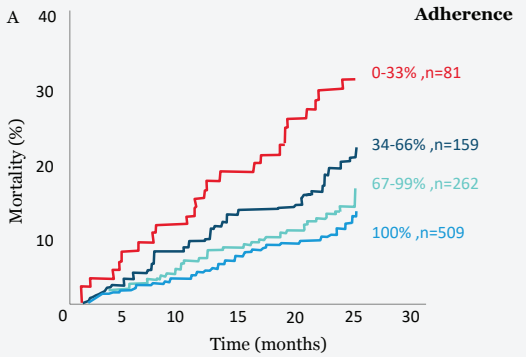
1. Cohen JD, Aspry KE, Brown AS, et al. Use of health information technology to improve statin adherence and low-density lipoprotein cholesterol goal attainment in high-risk patients: Proceedings from a workshop. Journal of Clinical Lipidology. 2013; 7, 573–609;
2. Stroes ES, Thompson PD, Corsini A, et al. Statin-associated muscle symptoms: impact on statin therapy-European Atherosclerosis Society Consensus Panel Statement on Assessment, Aetiology and Management. European Heart Journal. 2015; 36, 1012-1022

There are significant consequences of poor adherence, including compromised treatment effectiveness, increased healthcare costs, higher risk of adverse effects, and loss of work productivity for patients and family caregivers. The disease or fatality may also exacerbate. For example, a study of about 1,000 patients with chronic disease and polypharmacy showed that mortality in the non-adherence group was significantly higher compared to the adherent group, as polypharmacy is a cause of non-adherence.

Consequences of failure to identify and remediate poor adherence

- Compromised effectiveness of treatment
- Increased health care costs
- Increased risk of adverse effects
- Lost work productivity for patients and/or family caregivers
- Exacerbation of disease or fatality

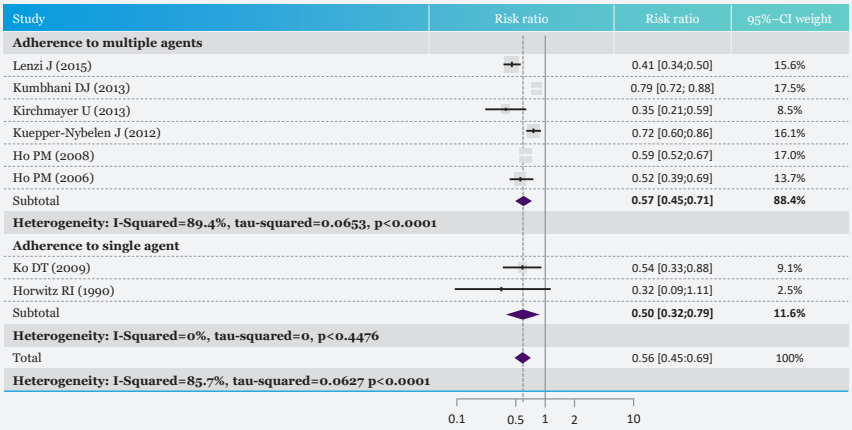
1011 patients with chronic disease on polypharmacy



Wu JYF, Leung WYS, Chang S, et al. Effectiveness of telephone counselling by pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial. BMJ. 2006 Sep 9;333(7567):522

A meta-analysis of over 100,000 patients comparing those with good versus poor medication adherence found that good adherence to cardiovascular medications (beta-blockers, ACE inhibitors or angiotensin receptor blockers, anti-platelets, and statins) was associated with a lower risk of all-cause mortality, cardiovascular mortality, cardiovascular hospitalization, and myocardial infarction. Simply adhering to the treatment regimen can significantly decrease these cardiovascular endpoints.

A meta-analysis in CAD patients with good vs. poor medication adherence n=106,000



Forest plot of the risk ratio of all-cause mortality between patients with good medication adherence and those with poor adherence.

- Good adherence to CV medications (B-blockers, ACEi/ARB, antiplatelets, and statins) was related to lower risk of all-cause and CV mortality, cardiovascular hospitalization/ myocardial infarction

Du L, Cheng Z, Zhang Y, et al. The impact of medication adherence on clinical outcomes of coronary artery disease: A meta-analysis. European Journal of Preventive Cardiology 2017, vol24: 962–970

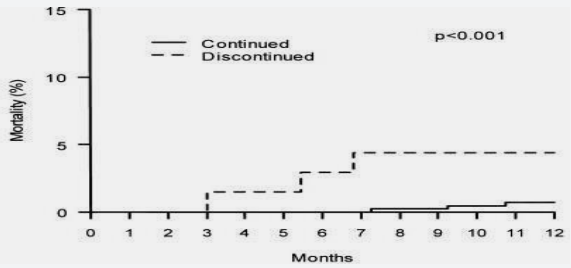
Another example comes from the PREMIER registry, where nearly one out of every seven patients who suffered a myocardial infarction and were treated with a drug-eluting stent had ceased taking thienopyridines within 30 days. The study found a significant correlation between the early discontinuation of thienopyridine treatment and an increase in subsequent mortality rates.[36,37]

Prematurely stopping therapy is associated with subsequent mortality

1 in 7 patients with heart attack who receive a stent are no longer taking clopidogrel by 30 days

1 in 6 patients who receive a stent do not fill clopidogrel prescription

Kaplan-Meier mortality curves 1 to 12 months after MI, by thienopyridine therapy at 1 month after MI



N at risk							
Continued	431	431	431	431	430	429	420
Discontinued	68	68	67	66	65	65	62

Spertus JA, Kettelkamp R, Vance C, et al. The origin is at the time of the patient's heart attack, but the lines begin at the 1-month assessment point. Circulation. 2006 Jun 20;113(24):2803-9. Ho PM, Tsai TT, Maddox TM, et al. Circ Cardiovasc Qual Outcomes. 2010 May;3(3):261-6

The study concluded that patients who stopped thienopyridine therapy by 30 days were more likely to die during the next 11 months (7.5% versus 0.7%, P < 0.0001; adjusted hazard ratio = 9.0; 95% confidence interval = 1.3 to 60.6) and to be rehospitalized (23% versus 14%, P = 0.08; adjusted hazard ratio = 1.5; 95% confidence interval = 0.78 to 3.0).

Consequently, cardiologists face the challenge of devising effective strategies to evaluate and address patient non-adherence.

In a comprehensive meta-analysis, the authors noted that the absolute risk difference linked to suboptimal medication adherence for CVD was 13 per 100,000 CVD deaths annually, and approximately 9% of all CVD cases in the EU may be ascribed to poor adherence. Additionally, data amalgamated from roughly 2 million individuals suggest that consistent adherence to cardiac medications is associated with a 20% reduction in CVD risk and a 35% decrease in all-cause mortality risk, regardless of most clinically significant patient and study characteristics.[38]

36. Spertus JA, et al. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: results from the PREMIER registry. Circulation. 2006 Jun 20;113(24):2803-9.

37. Ho PM, Tsai TT, Maddox TM, et al. Circ Cardiovasc Qual Outcomes. 2010 May;3(3):261-6.

38. Chowdhury R, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. Eur Heart J. 2013 Oct;34(38):2940-8.

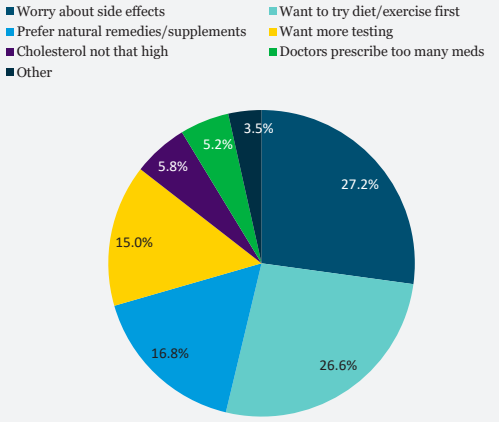
Factors contributing to the decision of statin treatment discontinuation

A few years ago, researchers aimed to understand why patients decided to stop statin treatments. Surprisingly, it was not because doctors advised them to stop. Most of the reasons were related to negative information about statin treatment from TV programs, non-believers, and relatives, as well as a lack of sufficient information on high cholesterol and related risks.

Some patients believed that after finishing one box of medication, the treatment was complete, and they preferred to switch to non-drug alternatives. Many did not believe in long-term treatments, and some did not consider high cholesterol a disease that required treatment.

Patient co-payments and reimbursements were minimal reasons for non-adherence, especially since 90% of the population has health insurance. Therefore, the issue is not the cost but the patients' perceptions, which we need to address through shared decision making.

Surveys on patient perspectives[1,2]



Factors contributing to the decision of statin treatment discontinuation (n = 532)[2]

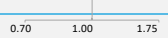
Treatment discontinuation reason	Yes	
	n	%
Negative information about statin treatment	213	40.0
Negative information about statin treatment in TV programs	175	32.9
Patients' lack of sufficient information on high cholesterol and related risks	163	30.6
Negative information about statin treatment heard from the relatives of the patient relatives of the patient	155	29.1
Completion of the treatment as considered by the patient	149	28.0
Switching to non-drug alternatives	139	26.1
Negative information about statin treatment in newspapers	117	22.0
Disbelief in long-term treatment	87	16.4
Not considering high cholesterol as a disease that needs treatment	78	14.7
Considering treatment to be inefficient	74	13.9
Chronically forgetting to take the medicine	61	11.5
Patient copayment contribution	30	5.6
Lack of complete reimbursement by Social Security Institute	14	2.6
High drug costs	13	2.4
Difficulty in payment	13	2.4

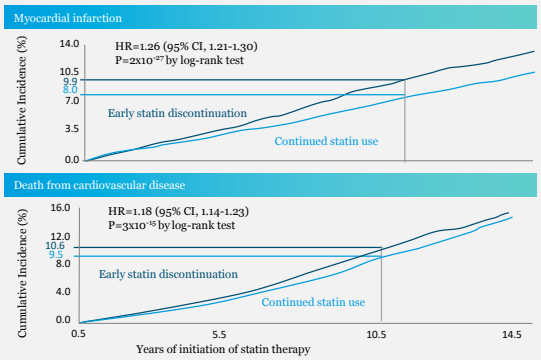
1. Tarn DM, Pletcher MJ, Rosqui R, et al. Primary nonadherence to statin medications: Survey of patient perspectives Preventive. Preventive Medicine Reports 22. 2021. 101357;
2. Tokgözoglu L, Ramazan Ö, Altindag R, et al. Patient characteristics and statin discontinuation-related factors during treatment of hypercholesterolemia: an observational non-interventional study in patients with statin discontinuation (STAY study). Turk Kardiyoloji Dernegi Arsivi. 2016;44(1):53-64

Media is a powerful mediator of medication adherence worldwide. A study from Denmark showed that every time there was a negative nationwide news story about statins, adherence fell. More interestingly, this discontinuation increased the risk of myocardial infarction and even death. This study, published in 2016, highlighted that the situation has not improved since then.

Media is a powerful mediator of medication adherence: Effects of media on statin use and CV mortality

Predictor		P-value
Odds ratio for early statin discontinuation with 95% confidence interval		
Negative nationwide statin-related news story	1.09 (1.06-1.12)	9×10^{-9}
Neutral nationwide statin-related news story	0.98 (0.96-1.01)	0.16
Positive nationwide statin-related news story	0.92 (0.90-0.94)	7×10^{-15}
Odds ratio for early discontinuation of antihypertensive medication with 95% confidence interval		
Negative nationwide statin-related news story	1.15 (1.09-1.21)	4×10^{-7}
Neutral nationwide statin-related news story	1.00 (0.96-1.03)	0.82
Positive nationwide statin-related news story	1.01 (0.98-1.04)	0.39
Odds ratio for early discontinuation of insulin use with 95% confidence interval		
Negative nationwide statin-related news story	1.00 (0.83-1.20)	0.99
Neutral nationwide statin-related news story	1.05 (0.92-1.21)	0.45
Positive nationwide statin-related news story	1.02 (0.91-1.15)	0.74





Individuals	No. Of statin users at risk			
Early statin discontinuation	84,800	26,865	4,534	828
Continued statin use	4,24,000	1,47,083	31,735	6,465

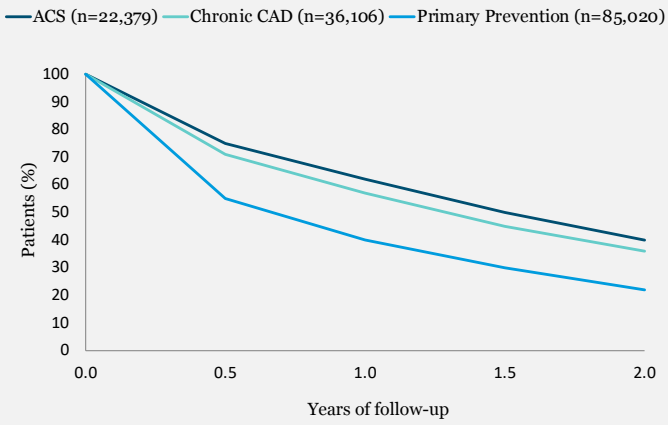
Fallgaard Nielsen S and Nordestgaard BG. Negative statin-related next stories decrease statin persistence and increase myocardial infarction and cardiovascular mortality: a nationwide prospective cohort study. European Heart Journal. 2016; 37, 908-916

Discontinuation of statin therapy is more common in primary prevention because healthy patients do not perceive a risk. However, even in secondary prevention, where patients have had an acute coronary syndrome or myocardial infarction, statin discontinuation remains a problem.

Several factors contribute to this issue, both patient and physician related.

A large meta-analysis identified independent predictors of discontinuation, including older age, lower socioeconomic status, depression or dementia, and polypharmacy. Patients who had not experienced an acute event like a heart attack in the previous year were also more likely to discontinue their medication, having forgotten the severity of their condition.

Discontinuation of statin therapy in primary or secondary prevention of CAD[1,2]



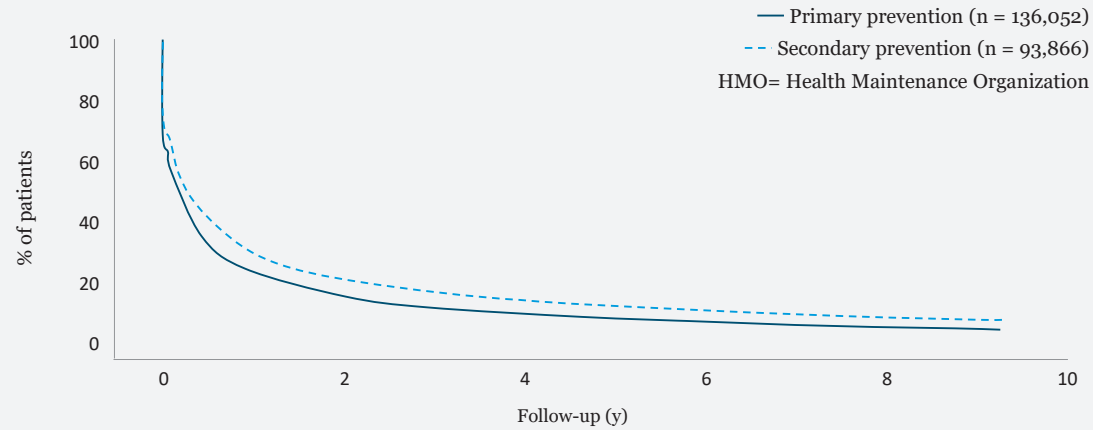
Independent predictors of statin therapy discontinuation[2]

- Older age (≥75 years)
- Lower socio-economic status
- Depression or dementia
- ≥ 10 prescribed medications
- No acute events in previous 12 months

1. Jackevicius Cynthia A, Mamdani Muhammad, Tu Jack V. Adherence With Statin Therapy in Elderly Patients With and Without Acute Coronary Syndromes. JAMA. 2002;288:462-467;
2. Benner Joshua S, Glynn Robert J, Neumann Peter J et al. Long-term Persistence in Use of Statin Therapy in Elderly Patients. JAMA. 2002;288:455-461.

Persistence with statin therapy declines even further after 2 years. A study with the longest follow-up from an HMO cohort in Israel showed that even in secondary prevention, adherence drops significantly over time, similar to primary prevention.

Long term treatment persistence with statin therapy in an HMO cohort in Israel n=229,918



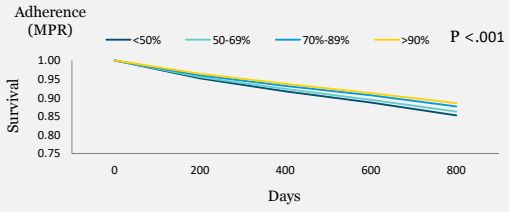
Chodick G, Shavel V, Gerber Y et al. Long-term persistence with Statin Treatment in a Not-for-Profit Health Maintenance Organization: A Population-Based Retrospective Cohort Study in Israel. Clinical Therapeutics. 2008;30:2167-79

Even after a myocardial infarction, patients stop their medication. Several studies have shown the impact of non-adherence on cardiovascular and total mortality. Both non-adherence and discontinuation were again related to increased mortality rates.

Impact of statin adherence on CVD and mortality outcomes

ASCVD pts on statin n=3,47,104[1]

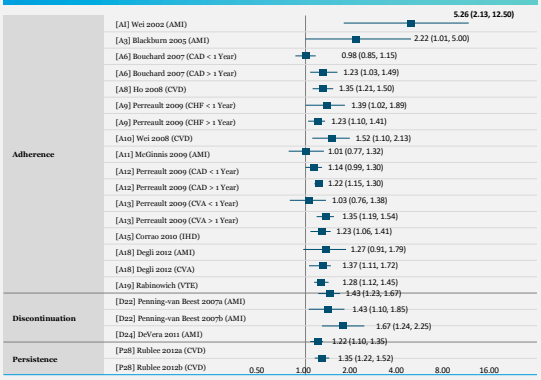
Survival curves by statin adherence level as defined by Medication Possession Ratios (MPRs)



No. at Risk				
	3,47,104	3,25,772	3,04,209	2,29,681

Plotted values include point estimates and 95% confidence intervals. There is a dose-response association between adherence and survival, with the greatest survival among the most adherent patients

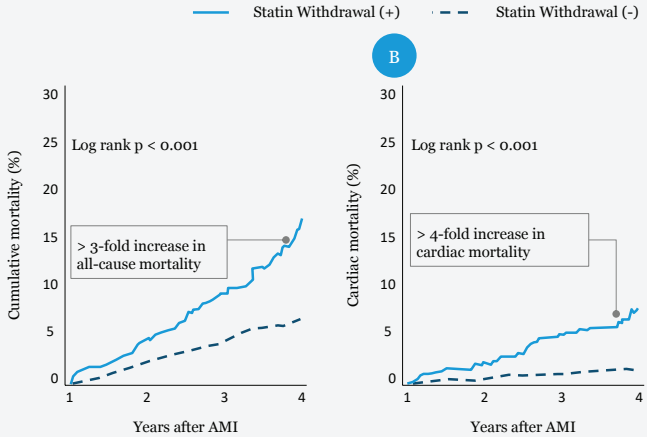
In meta-analysis RR 1.22 to 5.26 for CVD and 1.25 to 2.54 for death[2]



1. Rodriguez F, Maron D, Knowles JW, et al. Association of Statin Adherence With Mortality in Patients With Atherosclerotic Cardiovascular Disease. JAMA Cardiology. 2019;4(3):206-213;
2. De Vera M, Bhole V, et al. Impact of statin adherence on cardiovascular disease and mortality outcomes: a systematic review. British Journal of Clinical Pharmacology. 2014; 78: 684–698

A large registry study from Korea demonstrated that after 4 years, statin withdrawal was associated with higher mortality and cardiovascular mortality.

Poor statin adherence even occurs after MI



- 3,807 patients in the Korean multicenter registry
- Patients were prescribed statin at discharge and were divided into 2 groups on the basis of statin withdrawal history; 603 patients had a history of statin discontinuation and 3,204 patients continued statin therapy. The primary outcome was mortality from any cause
- The duration of follow-up was 4 years after AMI. Statin withdrawal was associated with higher mortality than continued statin treatment (hazard ratio 3.45, 95% confidence interval 2.81 to 4.24, p <0.001), primarily as the result of increased cardiac mortality (hazard ratio 4.65, 95% confidence interval 3.14 to 6.87, p <0.001)

Kim MC, Cho JY, Jeong HC, et al. Impact of Postdischarge Statin Withdrawal on Long-term Outcomes in Patients With Acute Myocardial Infarction. American Journal of Cardiology. 2015;115:1-7

What about older adults? If one is over 75, do they still need to continue taking cardiovascular medications, including statins? A study from Denmark examined the cumulative incidence of major cardiovascular events in both primary and secondary prevention. It showed that discontinuing statins, even after age 75, leads to an increased risk of cardiovascular events.

Statin discontinuation and CV events in older people

Figure 1. Cumulative incidence curve for the outcome of major adverse cardiovascular events in the primary prevention cohort[1]

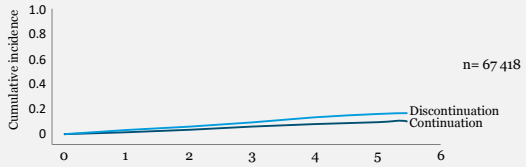
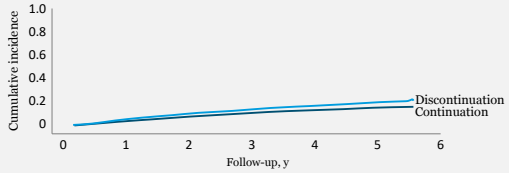
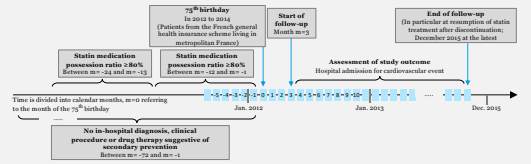


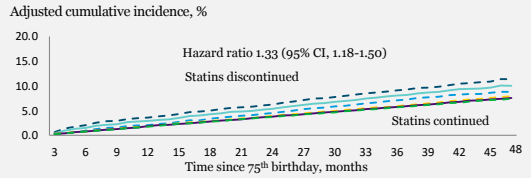
Figure 2. Cumulative incidence curve for the outcome of major adverse cardiovascular events in the secondary prevention cohort[1]



Study design[2]



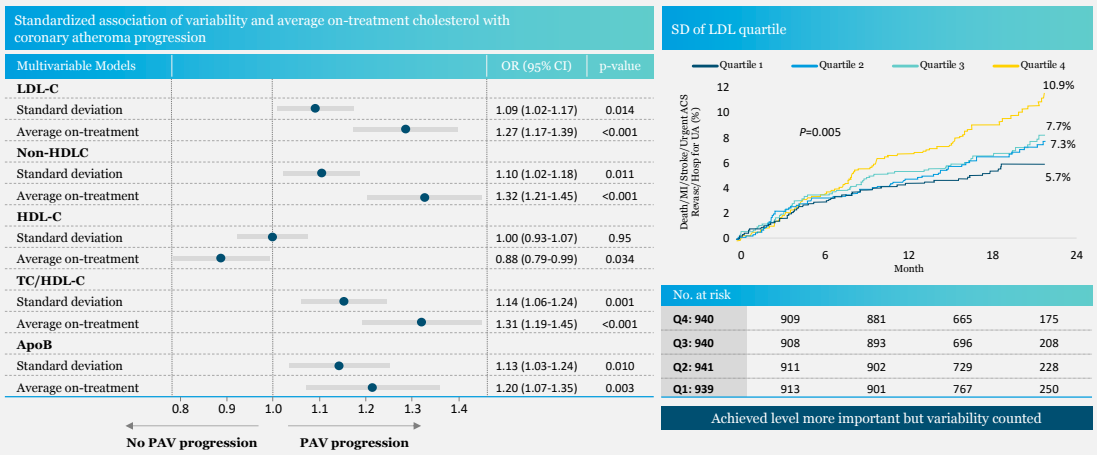
Principal result[2]



1. Thompson W, Morin L, Jarbol DE, et al. Statin Discontinuation and Cardiovascular Events Among Older People n Denmark. JAMA Network Open. 2021;4(12):e2136802;
2. Giral P, Neumann A, et al. Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide population-based cohort study in France. European Heart Journal. 2019; 40 :3516–3525

An intravascular ultrasound study found that lower LDL cholesterol levels are associated with fewer cardiovascular events. However, this study also showed that day-to-day variability in drug intake, even among patients who had achieved better LDL levels, mattered. Skipping doses occasionally can affect the progression of atherosclerotic plaque.

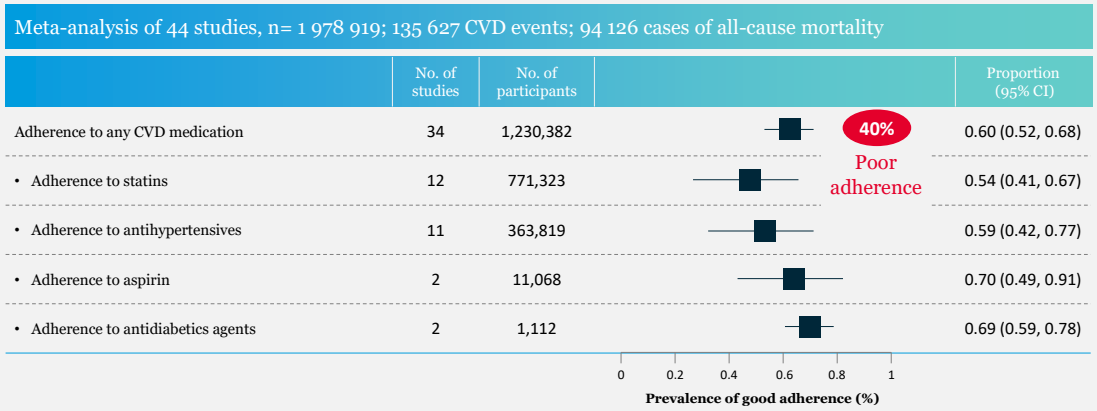
Visit-to-visit cholesterol variability correlates with coronary atheroma progression and clinical outcomes n=4,978



Clark D 3rd, Nicholls SJ, St John J et al. Visit-to-visit cholesterol variability correlates with coronary atheroma progression and clinical outcomes. European Heart Journal. 2018 Jul 14;39(27):2551-2558.

The largest meta-analysis, involving 44 studies and about 2 million patients, examined the prevalence of good adherence to cardiovascular medications. It looked at adherence to statins, antihypertensives, aspirin, and antidiabetic agents, all of which protect against CVD. Poor adherence was observed in 40% of individuals.

Prevalence of good adherence (>80%) to CV medications among participants in prospective studies



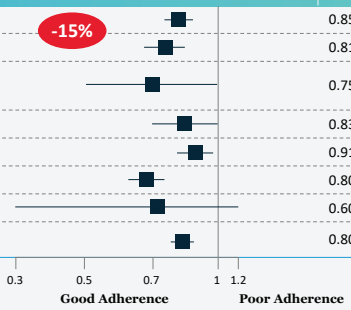
Chowdhury R, Khan H, Heydon E, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. European Heart Journal. 2013;34:2940–48

There was substantial non-adherence across all drug groups. For example, adherence to statins was associated with a 15% decrease in cardiovascular outcomes. The analysis concluded that one in 10 cardiovascular events in Europe could be attributed to poor adherence to vascular medications alone, highlighting that non-adherence is indeed a cardiovascular risk factor.

Relative risks for any cardiovascular disease in good vs. poor adherence (<80%)

Meta-analysis of 44 studies, n= 1 978 919; 135 627 CVD events; 94 126 cases of all-cause mortality

	No. of studies	No. of participants	No. of CVD events	RR (95% CI)
1. Adherence to statins	17	1,055,920	96,216	0.85 (0.81, 0.89)
2. Adherence to antihypertensive agents	13	552,143	36,186	0.81 (0.76, 0.86)
• ACE inhibitors/Angiotensin receptor blockers	4	68,781	4,643	0.75 (0.55, 1.01)
• Beta-blockers	4	90,402	10,774	0.83 (0.71, 0.98)
• Calcium channel blockers	1	9,168	2,249	0.91 (0.82, 1.01)
• Multiple agents	7	443,264	22,714	0.80 (0.73, 0.89)
3. Adherence to aspirin	3	15,253	2,274	0.60 (0.31, 1.16)
4. Adherence to any CVD medication	33	1,615,126	135,627	0.80 (0.77, 0.84)



9% of all CVD events in Europe could be attributed to poor adherence to vascular medications alone

Chowdhury R, Khan H, Heydon E, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. European Heart Journal. 2013;34:2940–48

The benefits of enhancing medication adherence have also been documented in developing countries.

In developing nations, patients needing lipid-lowering drugs for secondary CVD prevention frequently face avoidable health issues due to poor medication adherence. It is therefore necessary to investigate different approaches to enhance adherence, which could lead to both cost reductions and the fulfillment of therapeutic objectives.

In conclusion, non-adherence to cardiovascular therapies is a preventable risk factor that is often underestimated by clinicians. Once HCPs write the prescription, they assume it will be taken, but non-adherence to statins and antihypertensive drugs is much more common than we think. The benefits of therapy seen in randomized clinical trials will only be replicated in real life if patients adhere to the prescribed treatment regimen, achieve and maintain the goals recommended in various guidelines.

Conclusion

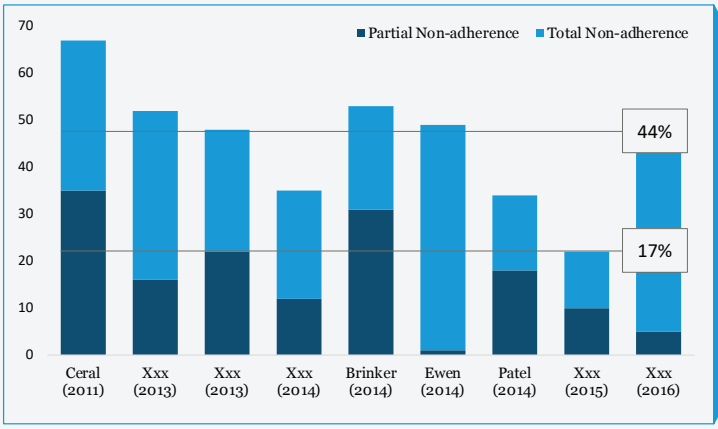
Hypertension

The WHO reports that around 1.28 billion adults aged 30–79 worldwide suffer from hypertension, with the majority (two thirds) residing in low- and middle-income countries. Out of these, only about one in five adults (21%) has their hypertension under control.[39]

Considering resistant hypertension, which refers to patients whose condition remains uncontrolled despite taking at least three antihypertensive medications, the rate of non-adherence in randomized controlled trials is alarmingly high, affecting 30%–50% of patients. This is particularly significant given that monitoring in trials is generally more stringent than in typical clinical practice. Such substantial levels of non-adherence can even influence the results of the clinical trials themselves.

39. Hypertension, https://www.who.int/news-room/fact-sheets/detail/hypertension Last accessed 11/10/2023.

Non-adherence with prescribed antihypertensive drug in clinical studies



30 to 50% non-adherence rate is consistent between clinical trials and medical practice

Poor and dynamic adherence introduces variability to trial endpoints

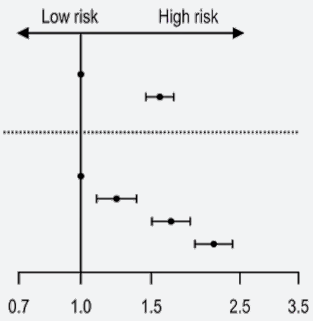
Not easily controlled, even with rigorous trial design

Berra E, Azizi M, Capron A, Høieggen A, Rabbia F, Kjeldsen SE, Staessen JA, Wallemacq P, Persu A. Evaluation of Adherence Should Become an Integral Part of Assessment of Patients With Apparently Treatment-Resistant Hypertension. Hypertension. 2016 Aug;68(2):297-306

The issue of non-adherence in a typically asymptomatic condition like hypertension results in grave adverse consequences. An examination of a South Korean National Health Insurance Service health information database, which tracked approximately 400,000 patients with hypertension over a decade, revealed that the multivariable-adjusted hazard ratio for cardiovascular events in non-adherence compared to adherent patients was 1.57 (95% confidence interval, 1.45–1.71). This analysis also identified a dose—response relationship between the level of medication adherence and the risk of cardiovascular events.

Adherence to antihypertensive medication and incident CV events in young adults with hypertension

Composite CVD events				
Group	Events	Person-yrs	Rate*	HR (95% CI)
Adherence group				
Adherent	855	447,564	191.0	1.00 (reference)
Nonadherent	2,147	761,129	282.1	1.58 (1.45-1.71)
Proportion of days covered, quartile				
Q4, highest	522	300,596	173.7	1.00 (reference)
Q3	662	307,239	215.5	1.23 (1.10-1.38)
Q2	841	300,825	279.6	1.68 (1.51-1.88)
Q1, Lowest	977	300,034	325.6	2.15 (1.93-2.40)

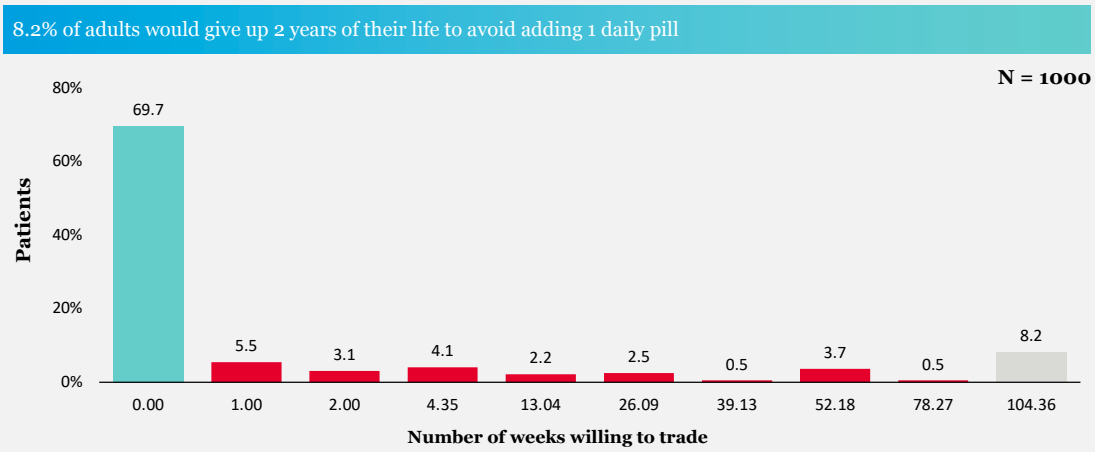


Cardiovascular disease (CVD) risk associated with nonadherence to antihypertensive medication

Lee H, Yano Y, Cho SMJ, Heo JE, Kim DW, Park S, Lloyd-Jones DM, Kim HC. Adherence to Antihypertensive Medication and Incident Cardiovascular Events in Young Adults With Hypertension. Hypertension. 2021 Apr;77(4):1341-1349

The complexity of a treatment regimen, including the quantity of pills, can deter patients from adhering to it over an extended period. For example, a study in the US involving over 1,000 individuals with hypertension revealed that 30% of the participants would opt to forfeit months of their lifespan rather than consume an extra pill. Moreover, 8.2% indicated they would be willing to forgo over 2 years of life instead of increasing their pill burden.

~30% of Adults Would Rather Die Early than **Take** Lifelong Polypharmacy



Hutchins R., et al. Quantifying the Utility of Taking Pills for Cardiovascular Prevention. Circ Cardiovasc Qual Outcomes March 2015; 8: 155-63.

Heart failure

> *"Good adherence matters, even with placebo"*

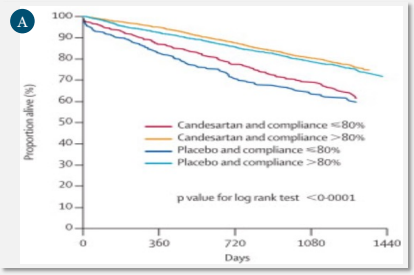
Proper adherence to medication is linked to a reduced mortality risk in patients with chronic heart failure, regardless of the treatment they are assigned, even if that treatment is a placebo!

The researchers of the CHARM study on heart failure deduced that adherence serves as an indicator of commitment to beneficial treatments beyond the medications provided in the study, or to other compliant behaviors that influence the outcome.[40]

Adherence is a Behavior ...
Adherence to Placebo is a good Behavior!

Good adherence was associated with lower all-cause mortality in all patients HR 0·65, 95% CI 0·57–0·75)

The adjusted HR for good adherence was similar in the candesartan (0·66) and placebo (0·64) groups



Numbers at risk				
Candersartan and compliance ≤ 80	493	426	380	249
Candersartan and compliance > 80	3310	3137	2891	1967
Placebo and compliance ≤ 80%	435	359	306	209
Placebo and compliance > 80%	3361	3106	2864	1951

Granger BB, et al. Adherence to candesartan and placebo and outcomes in chronic heart failure in the CHARM program: double-blind, randomized, controlled clinical trial. Lancet. 2005 Dec 10;366(9502):2005-11

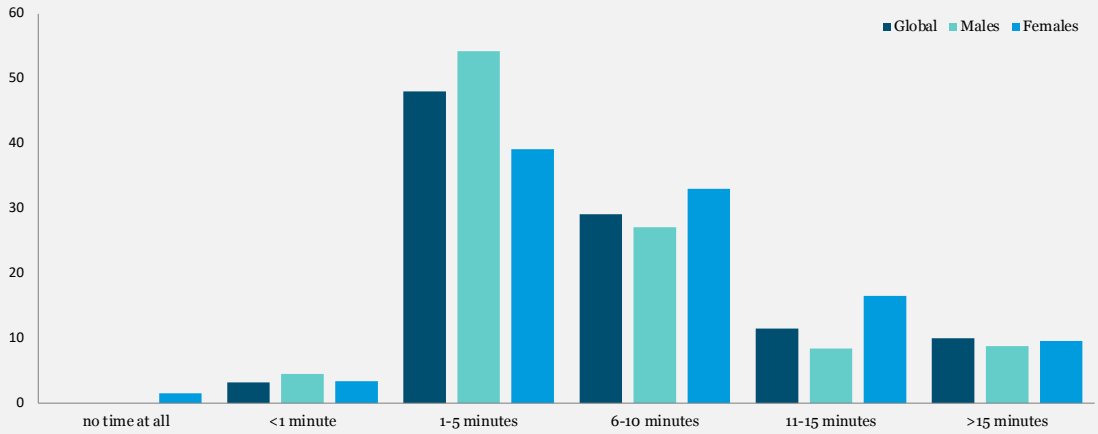
The drivers of non-adherence in CVDs

Several factors contribute to patients not adhering to their prescribed antihypertensive treatments, including a limited understanding of the disease and the necessity of treatment, apprehension about potential or experienced side effects, doubts about the efficacy of the treatment, fear of stigma related to the disease, and the complexity of the medication regimen.[41] Regrettably, even in specialized institutions like the European Society of Hypertension Centres of Excellence, physicians typically allocate less than 5 minutes to discuss chronic treatments with their patients.

40. Granger BB, et al. Adherence to candesartan and placebo and outcomes in chronic heart failure in the CHARM program: double-blind, randomized, controlled clinical trial. Lancet. 2005 Dec 10;366(9502):2005-11.

41. Poulter NR, Borghi C, Parati G, Pathak A, ToliD, Williams B, Schmieder RE. Medication adherence in hypertension. J Hypertens. 2020 Apr;38(4):579-587.

Time spent by physicians talking with patients about their use of medications—A survey of ESH Centers of Excellence



Burnier M, Prejbisz A, Weber T, et al. Hypertension healthcare professional beliefs and behaviour regarding patient medication adherence: a survey conducted among European Society of Hypertension Centres of Excellence. Blood Pressure. 2021 Oct;30(5):282-290.

Monitoring adherence in CVDs

There are various methods to assess non-adherence, ranging from straightforward questionnaires to comprehensive laboratory tests.[42] Some of these methods are outlined below:

- **Clinical judgment**

Several clinical studies have shown that regrettably, physicians' ability to gauge their patients' adherence levels is no more accurate than random chance, often resulting in an overestimation (positive bias). Furthermore, patients themselves frequently struggle to provide precise accounts of their adherence to medication regimens.[43]

- **Self-report tools**

These approaches are cost effective, straightforward to apply, and offer prompt feedback. They ascertain adherence levels either through direct questioning or by evaluating behavior. Nonetheless, while these methods are highly specific, they have a tendency to overestimate adherence, with biases that can reach up to 20%.[44,45]

42. Kronish IM, Ye S. Adherence to cardiovascular medications: lessons learned and future directions. Prog Cardiovasc Dis. 2013 May-Jun;55(6):590-600.
43. Zeller A, Taegtmeyer A, Martina B, Battegay E, Tschudi P. Physicians' ability to predict patients' adherence to antihypertensive medication in primary care. Hypertens Res. 2008; 31:1765–71.
44. Voils CI, Hoyle RH, Thorpe CT, Maciejewski ML, Yancy WS Jr. Improving the measurement of self-reported medication nonadherence. J Clin Epidemiol. 2011; 64:250–4.
45. Stirratt MJ, et al. Self-report measures of medication adherence behavior: recommendations on optimal use. Transl Behav Med. 2015 Dec;5(4):470-82.

The effectiveness of self-reported adherence measures can be improved by utilizing validated scales, accurately evaluating the intended construct, enhancing estimation accuracy, aiding memory recall, minimizing the influence of social desirability bias, and using technological means for administration. In terms of practical application, this method is particularly feasible in low- and middle-income countries.

The a:care Insight tool is accessible at no cost to physicians. It operates on a patient questionnaire analyzed by the SPUR engine, functioning as a behavioral risk calculator. This tool assists physicians in evaluating the likelihood of non-adherence and offers insights on how to tackle it.

- **Physiologic or laboratory markers**

Assessing the blood concentrations of drugs or their metabolites is a precise method, yet it is not applicable to all medications and is significantly influenced by their pharmacokinetics. Additionally, this method is costly.

- **Pharmacy refill data**

Pharmacy refill data is an objective measure that can be scaled for large populations. However, its implementation is challenging outside of a closed pharmacy system. It facilitates the calculation of the Proportion of Days Covered (PDC), which is the total number of pills dispensed from the first to the last refill, divided by the number of days between refills.

- **Pill counts**

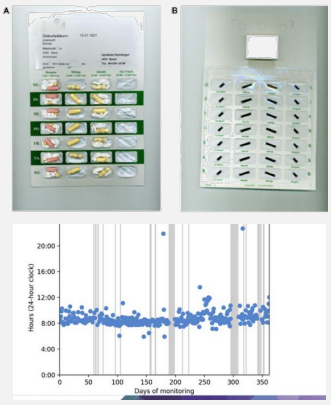
Pill counts are also objective, but they are time consuming, particularly when a patient is prescribed multiple medications simultaneously. Moreover, there is a possibility for patients to manipulate the count.

- **Electronic medication monitor**

Electronic medication monitors represent one of the most reliable methods. They are objective, accurate, and provide detailed data on daily usage patterns. Nonetheless, they may be confusing for patients who must also adapt to using the technology. These devices are costly and not easily incorporated into regular clinical care, which is why they are primarily utilized in clinical trial settings. Additionally, just opening the medication packet does not ensure that the medication is actually taken.

Electronic monitoring systems show 97% accuracy

- Multicompartmental pillbox will transmit a signal to a receiver and into a computer shared with physician and emailed texted to patient showing date and time
- Smart electronic packaging/device monitoring is 97% accurate, ahead of pill counts (60%), and patient self-reporting and electronic patient diaries (27%)
- Does not guarantee pill is swallowed



1. Isabelle Arnet*, Philipp N. Walter and Kurt E. Hersberger. Polymedication Electronic Monitoring System (POEMS) – a new technology for measuring adherence (2013). Frontiers in Pharmacology. 4(26):1-6.
2. Helen L. Figge. Electronic Tools to Measure and Enhance Medication Adherence. US Pharm 2010;36(4)(Compliance & Adherence suppl):6-10.
3. Vrijens B. Digital Medication Adherence in Clinical Trials. Clinical and Medical Research, 2021;13(1):58-89.

One of the most sophisticated monitoring systems involves the use of ingestible sensors.[46] A study that tested an ingestible sensor combined with a pill to accurately track medication intake in patients at high risk of CVD who were participating in a CVD prevention and rehabilitation program found that only 57% of patients were actually adherent, even though 90% reported they were adhering to their treatment regimen. This study demonstrates that self-reporting tools are not as effective as more advanced methods. It also indicates that patients continue to exhibit non-adherence even when they are aware that their medication intake is being closely monitored.

46. Thompson D, Mackay T, Matthews M, Edwards J, Peters NS, Connolly SB. Direct Adherence Measurement Using an Ingestible Sensor Compared With Self-Reporting in High-Risk Cardiovascular Disease Patients Who Knew They Were Being Measured: A Prospective Intervention. JMIR mHealth uHealth. 2017 Jun 12;5(6):e76.

Adherence measurement using ingestible sensor

- The sensor emits a signal when it encounters the acidic environment of the stomach, detectable by an externally worn patch and linked software app
- Longitudinal adherence data in the form of daily progress charts for sensed dosing events as compared with scheduled dosing are visible to patients
- Self reported adherence 90%
- Sensor reported adherence 57% despite motivated and select patients!
- We really need to educate and convince our patients

Thompson D, Mackay T, Matthews M, Edwards J, Peters NS, Connolly SB. Direct Adherence Measurement Using an Ingestible Sensor Compared With Self-Reporting in High-Risk Cardiovascular Disease Patients Who Knew They Were Being Measured: A Prospective Intervention. JMIR mHealth uHealth. 2017 Jun 12;5(6):e76.

Interventions to improve medication adherence in patients with CVD's

Various strategies can be readily employed to enhance medication adherence.

Interventions to improve adherence

- Assess each patient's needs and offer individualized solutions
- Make pill-taking easier for the patient
- Improve patient—practitioner communication in a blame-free environment
- Educate patients
- Offer motivational interviewing
- Involve patient in decision making/empower the patient
- Implement guideline recommendations
- Use single-pill combinations
- Establish a collaborative team-based care approach, including nurses and pharmacists
- Use reminders (memory cues, blister packaging, pill counters, MEMS)
- Use e-Health technology as a supportive tool

MEMS, medication event monitoring systems

Poulter NR, Borghi C, Parati G, Pathak A, Toli D, Williams B, Schmieder RE. Medication adherence in hypertension. J Hypertens. 2020 Apr;38(4):579-587.

In low-to-middle-income countries, interventions that incorporate multiple components are found to be more successful than those with a single focus.[47] Technological interventions, including mobile phone calls, electronic pillboxes, and interactive SMS reminders, prove to be more effective than standard reminders. The impact on medication adherence is greater when interventions target both the patient, through methods like reminders, and the HCP, through approaches like team-based care.

> *"Reconsidering treatment prescription through a patient-centered approach"*

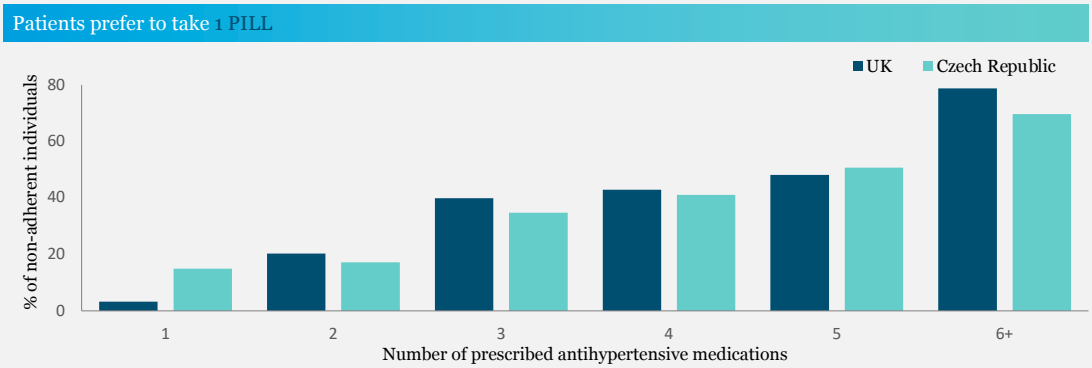
The management of hypertension and CVDs extends beyond merely selecting the appropriate drugs tailored to each patient's profile; it also encompasses the manner in which patients adhere to their treatment regimens. For example, it is recognized that the likelihood of non-adherence escalates with an increase in the number of medications prescribed.

The use of fixed-dose combinations, which blend several medications for cardiovascular prevention–including cholesterol-lowering drugs and one or more agents to reduce blood pressure, with or without the addition of acetylsalicylic acid–has been demonstrated to enhance medication adherence.

47. Ogungbe O, Byiringiro S, Adedokun-Afolayan A, Seal SM, Dennison Himmelfarb CR, Davidson PM, Commodore-Mensah Y. Medication Adherence Interventions for Cardiovascular Disease in Low- and Middle-Income Countries: A Systematic Review. Patient Prefer Adherence. 2021 Apr 29;15:885-897.

Patients prefer to take less pills

Non-adherence to antihypertensive medicines in the real world- according to number of medicines



Gupta P, et al. Risk Factors for Nonadherence to Antihypertensive Treatment. Hypertension. 2017 Jun;69(6):1113-1120.

Over the past decade, three extensive studies have demonstrated that the polypill approach is effective in aiding the prevention of cardiovascular conditions in patients with preexisting CVDs:[48]

- **Indian Polycap study (CVD or type 2 diabetes):**

- ramipril, atenolol, hydrochlorothiazide, simvastatin, and aspirin (supplemented by potassium) in a single capsule (half-dose of the drugs)

- **UMPIRE trial (cardiovascular disease) in which two polypill strategies were used depending on the extent of baseline comorbidities:**

- aspirin, simvastatin, atenolol, and lisinopril

- aspirin, simvastatin, lisinopril, and hydrochlorothiazide

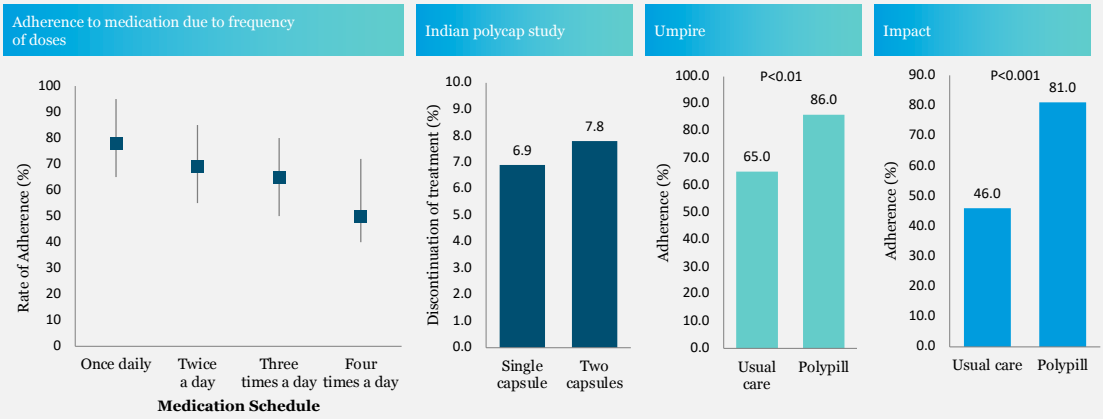
- **IMPACT trial (established CVD or high cardiovascular risk) in which two polypill strategies were used:**

- aspirin, simvastatin, lisinopril, and atenolol

- aspirin, simvastatin, lisinopril, and hydrochlorothiazide

48. Coca, Antonio & Agabiti-Rosei, Enrico & Manolis, Athanasios & Redón, Josep & Mancia, Giuseppe. (2017). The polypill in cardiovascular prevention: Evidence, limitations and perspective-position paper of the European Society of Hypertension. Journal of Hypertension.

Polypill: Possible to track by biomarkers; increases adherence significantly-Solution for LMIC



Coca, Antonio & Agabiti-Rosei, Enrico & Manolis, Athanasios & Redón, Josep & Mancia, Giuseppe. (2017). The polypill in cardiovascular prevention: Evidence, limitations and perspective-position paper of the European Society of Hypertension. Journal of Hypertension. 35. 2. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005 Aug 4;353(5):487-97.

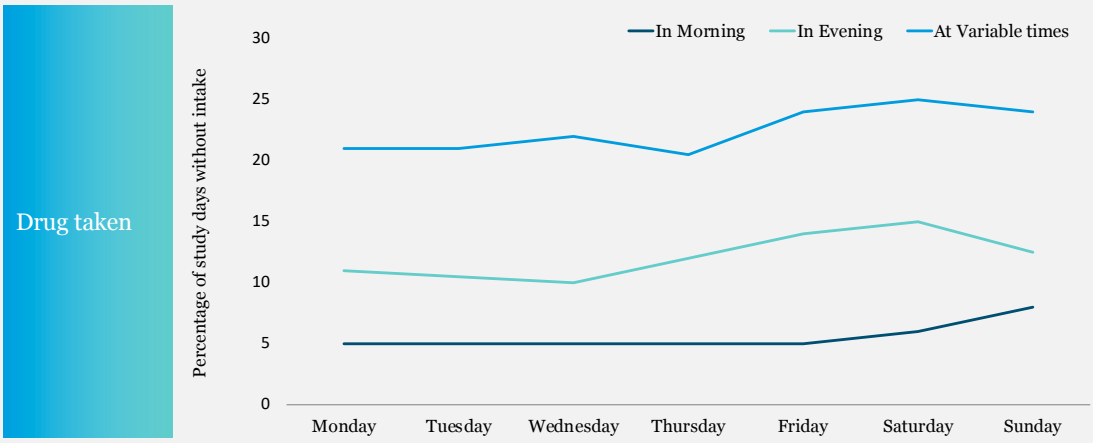
Therefore, in 2023 the WHO decided to add these treatments in its list of essential drugs.[49]

Adherence to medication is also inversely related to the frequency of dosing. Patients who are prescribed medication four times a day tend to have an average adherence rate of approximately 50%.

Finally, a study on hypertension indicates that the time of day when medication is taken also affects adherence to the medication regimen.

49. WHO endorses landmark public health decisions on Essential Medicines for Multiple Sclerosis, World Health Organization 26,07/2023 https://www.who.int/news/item/26-07-2023-who-endorses-landmark-public-health-decisions-on-essential-medicines-for-multiple-sclerosis last accessed 31/07/2023.

Relevance of timing of antihypertensive therapy



Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. BMJ. 2008 May 17;336(7653):1114-7.

Medications that require administration at a consistent time each morning are more likely to be taken compared to those that must be taken at varying times throughout the day. Additionally, the specific day of the week plays a role. The highest number of missed doses for morning medication occurs on Sundays, while evening doses are most frequently missed on Saturdays.

> *“Influencing adherence to cardiovascular medications when patients “feel fine”*

As previously mentioned, failing to adhere to treatment and advice for cardiovascular conditions can result in severe consequences, such as

- Heart attacks or strokes;
- Aneurysms;
- Heart failure;
- Weakened and narrowed blood vessels in the kidneys;
- Thickened, narrowed, or torn blood vessels in the eyes;

- Metabolic syndrome;
- Cognitive impairments;
- Dementia.

Given these potential complications, one might wonder why patients would not do everything possible to avoid them. The challenge lies in the extensive list of recommendations, which includes

- Eating a well-balanced, low-salt diet;
- Limiting alcohol consumption;
- Engaging in regular physical activity;
- Managing stress;
- Maintaining a healthy weight;
- Quitting smoking;
- Adhering to prescribed medications;
- Limiting caffeine intake;
- Collaborating with HCPs.

Moreover, and perhaps more significantly, there are numerous patient-related factors to consider:

- The "I feel fine" mentality, where patients may question the need for treatment when they experience no symptoms, especially if the only noticeable effects are the treatment's side effects.
- A lack of awareness among many patients about the potential complications of their condition, or a tendency to view such complications as distant future concerns.
- An inability of patients to discern whether their medication is effective.
- A tendency among some patients to normalize non-adherence, thinking that missing a few days of medication is inconsequential, not realizing that short-term lapses can lead to long-term non-adherence.

Lastly, the sheer volume of tasks required of patients can be overwhelming, making it unsurprising that they might feel defeated before even beginning.

> *What can HCPs do to improve adherence to recommendations for hypertension control*

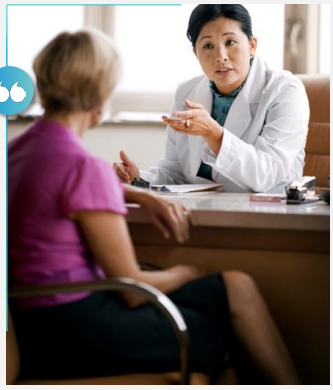
Begin with manageable steps. Customize your guidance to suit the patient.

Choose a single, achievable action for the patient, such as taking one pill daily or implementing a dietary change. Next, harness the patient's emotions and values to boost their intrinsic motivation.

Abandon attempts to persuade through logic, demands, threats, commands, shaming, judgment, criticism, blame, warnings, directives on what the patient "should" do, or expressions of disagreement. These tactics are ineffective. Instead, engage the patient's emotions, aspirations, values, and wishes to enhance their commitment to your recommendations, and remember to ask open-ended questions to facilitate discussion.

How to use patient's emotions/values to enhance intrinsic motivation to adhere to advice

Ask open-ended questions



- If you were to take this medicine, how might things be better for your family?
- What long-term benefits for you and your family do you see from taking this medicine?
- If you were taking this medicine, how might it impact your future and the things you could do in your life?
- How important is it for you to live a long, healthy life and see your children grow up?

HCPs can enhance patient adherence by engaging in meaningful two-way communication and genuinely listening to patients' feedback. Utilizing open-ended questions facilitates a space for dialogue.

It is important to align with patients' current capabilities. Ensuring that patients feel confident in their ability to follow recommendations is crucial. Therefore, advice should be customized to suit their individual needs.

Instructing patients directly on what actions to take tends to be ineffective. Instead, posing open-ended questions that resonate with the patient's emotions and values proves to be a more effective strategy.

Dr. Sheri D. Pruitt's lecture is fully available on the a:care Pro website.

Improving medication adherence with motivational interviewing: Example of a heart failure patient

At the a:care Congress in 2021, Prof. Athul Pathak discussed the benefits of motivational interviewing in aiding patients with cardiovascular issues, specifically focusing on heart failure.

Heart failure presents a unique challenge due to its progressive and often initially asymptomatic nature, only becoming apparent upon diagnosis or patient decompensation. Additionally, these patients frequently contend with other health conditions such as chronic kidney disease, diabetes mellitus, and obesity.

Consequently, individuals with heart failure must manage additional treatments to address these comorbidities alongside their heart-failure therapy.

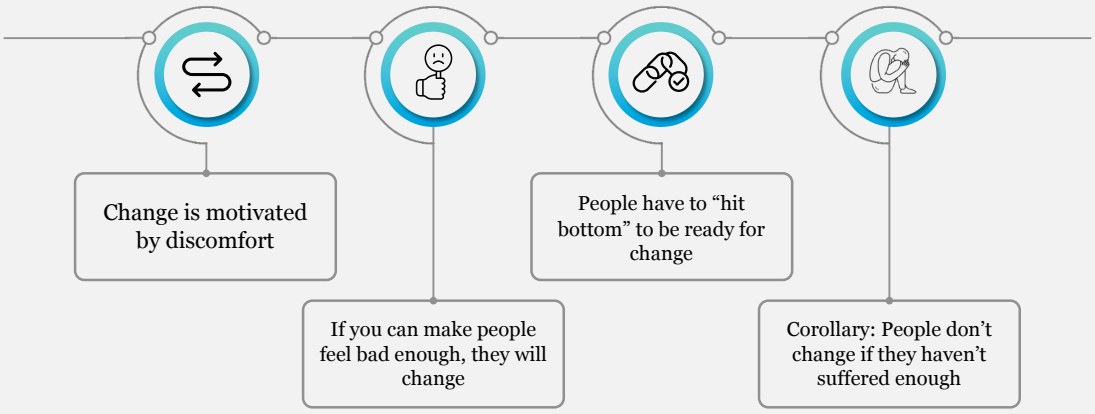
Patients encounter a particular dilemma: While certain medications like diuretics are effective in alleviating symptoms, they do not necessarily reduce mortality rates. Conversely, the four primary drugs proven to extend patient survival—beta-blockers, RAAS inhibitors, mineral receptor antagonists, and SGLT-2 inhibitors–may not significantly alleviate symptoms and could potentially cause adverse side effects.

> *“Heart failure patients cannot perceive the risk/benefit ratio of the treatments they take”*
>
> *(Prof. Pathak, a:care Congress 2021)*

Physicians often encounter challenges with patients who appear unwilling to alter their lifestyle habits. It is crucial to assess a patient’s stage of readiness for change.

Traditionally, the advice for change is deferred until the patient’s condition deteriorates.

Traditional approach

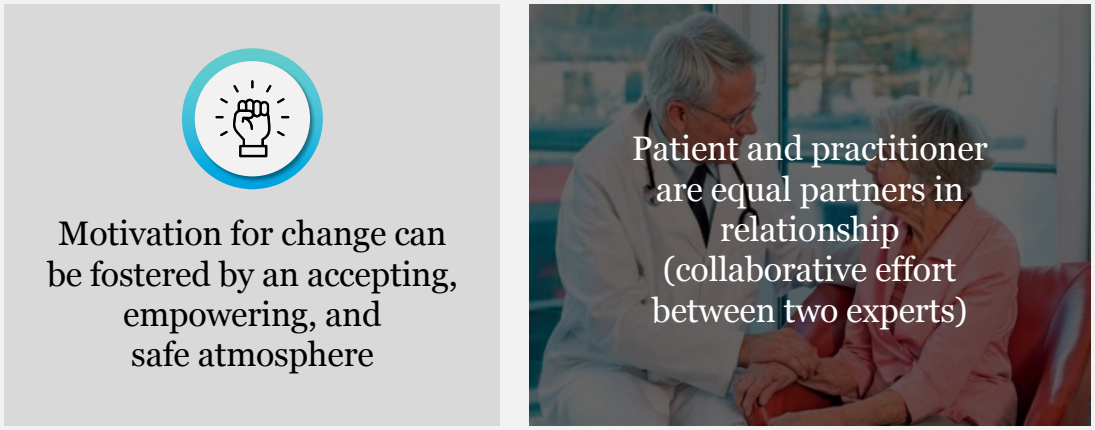


Sources: Slide adapted by Jeanne Obert, 2006, from Miller, W.R., & Rollnick, S. (2002). Motivational Interviewing: Preparing people for change. New York: Guilford Press

There is a belief that "a patient who resists change simply has not endured enough to be sufficiently motivated." According to this view, "the patient must confront harsh realities and reach rock bottom to be prepared for change." However, this method is generally ineffective.

An alternative is to modify the physician's approach. Doctors should recognize themselves as equal partners in their relationship with patients. Creating a supportive, empowering, and non-threatening environment can nurture the motivation to change.

Another approach: motivating!

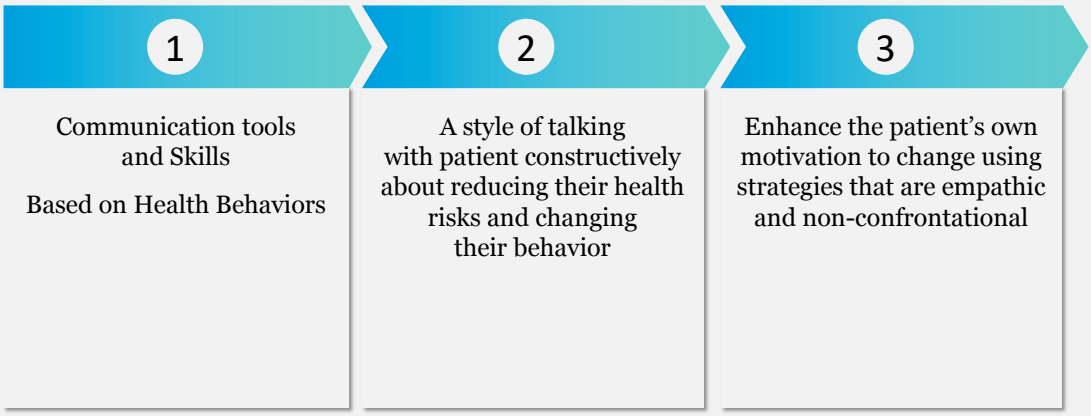


Sources: Slide adapted by Jeanne Obert, 2006, from Miller, W.R., & Rollnick, S. (2002). Motivational Interviewing: Preparing people for change. New York: Guilford Press

Motivational strategies rest on three foundational pillars:

- Utilizing communication tools and skills derived from health behavior theories and practical experience;
- Embracing a new style of dialogue and interaction with the patient;
- Establishing a motivational method that is empathetic and non-confrontational.

What are motivational strategies?



Sources: Slide adapted by Jeanne Obert, 2006, from Miller, W.R., & Rollnick, S. (2002). Motivational Interviewing: Preparing people for change. New York: Guilford Press

These strategies are designed to address the patient's hesitations:

- "Should I take my medication?"
- "Is it necessary for me to adhere to a low-salt diet?"
- "Do I need to engage in daily physical activity even if I feel extremely tired?"

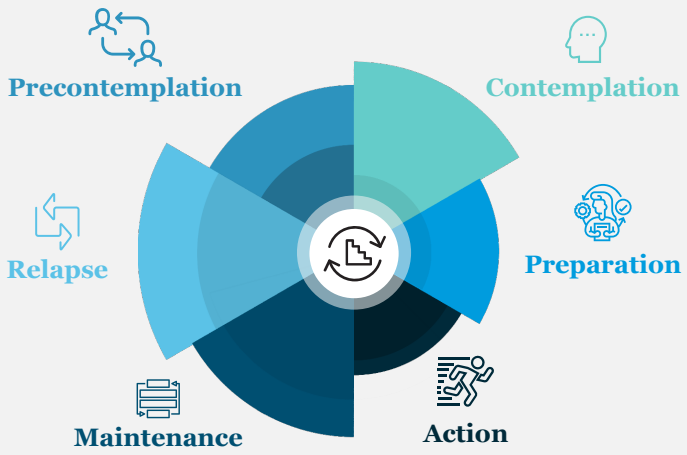
The goal is to work collaboratively with the patient to understand their challenges and set a shared objective for change.

> *"Motivation requires knowledge about stages of change"*

Realizing the need for change and grasping the methods of implementing it is not an instantaneous process. It typically requires time, patience, organization, and strategic planning. Individuals commonly experience various "stages" as they come to acknowledge their issues.

Motivational interviewing serves as a technique to assist individuals in progressing through these stages of change.

Stages of Change



Prochaska, J. O., & DiClemente, C. C. (1982). Transtheoretical therapy: Toward a more integrative model of change. Psychotherapy: Theory, Research & Practice, 19(3), 276–288.
Sources: Slide adapted by Jeanne Obert, 2006, from Miller, W.R., & Rollnick, S. (2002). Motivational Interviewing: Preparing people for change. New York: Guilford Press

Patients may be in a state of denial regarding their illness, or they might not view the condition as severe enough to warrant altering their habits. This is known as the **precontemplation** stage.

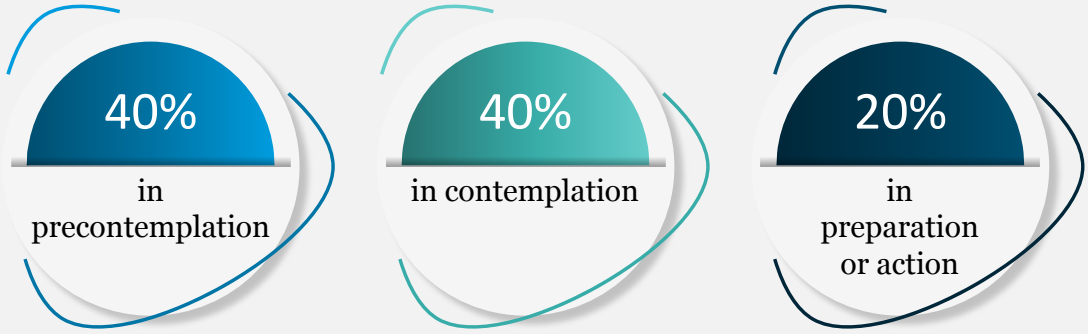
Others may be in a state of ambivalence. While they recognize the need for change, they do not take steps to initiate it and may require encouragement. This is the **contemplation** stage.

During the **preparation** stage, patients are ready to change. They consider the advantages over the drawbacks of the new behavior. They communicate with their doctor about their proactive steps, such as identifying low-salt products at the supermarket and enlisting their partner's support.

Following this is the **action** stage, where the patient actively changes their behavior with the hope of sustaining it, leading to the maintenance stage.

Ultimately, the process may culminate in the **termination** stage or a **relapse**. For example, a patient might dine out, consume seafood, and end up in the hospital the following day. Physicians should understand that this is part of the journey, not a setback. It is an opportunity to recognize and prepare for potential risks in the future.

For any behavioral problem at a given time, there are (in the population at large)



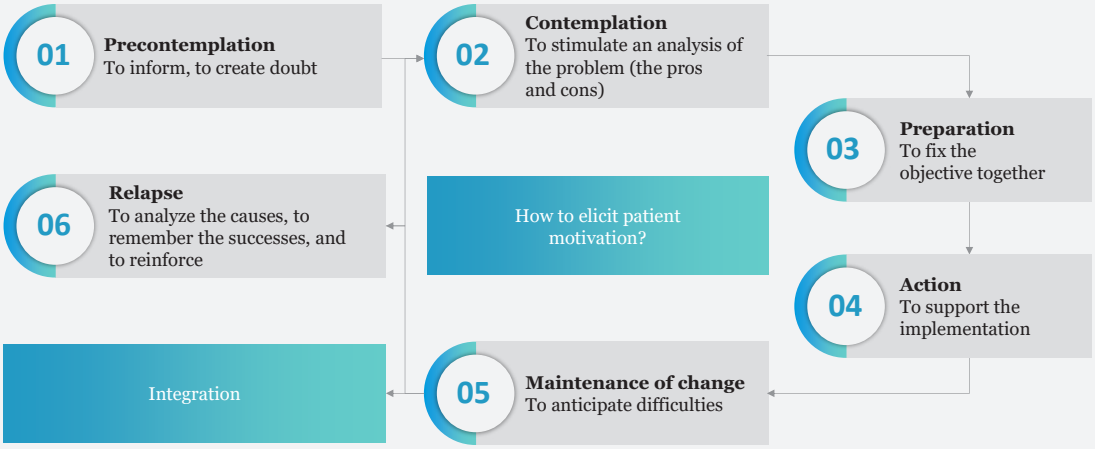
Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot. 1997 Sep-Oct;12(1):38-48.

In approximately 40% of cases, physicians may encounter difficulties with patients who are not prepared to change because they are in the denial phase (precontemplation). For these patients, physicians can primarily provide information, acknowledging that the motivational process may be postponed.

Physicians might prefer to invest their time in patients who are either indecisive (contemplation stage) or those who are prepared to take action.

After HCPs recognize the various stages of change, they can implement tailored approaches accordingly.

The stages of motivation



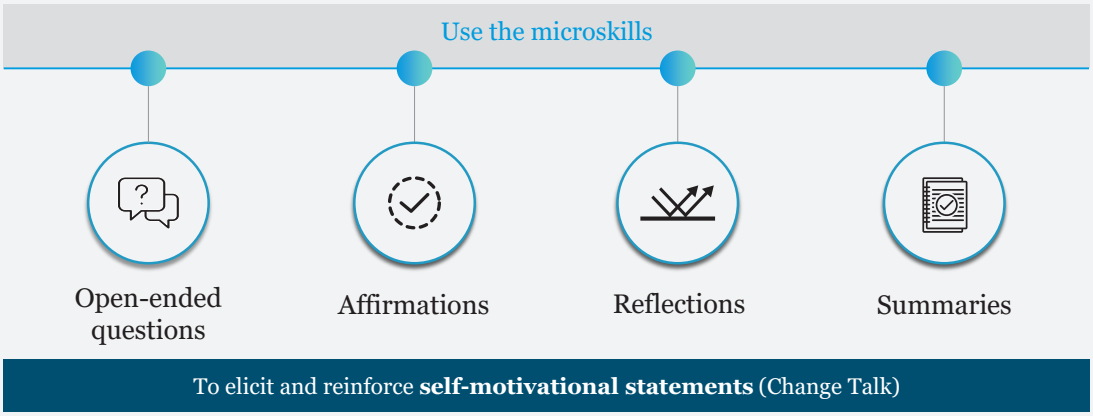
Patients in denial about their health condition can be time intensive. Efforts to persuade a patient who is not ready to make a change, such as quitting smoking, can prove to be highly challenging. Often, the more one attempts to convince such a patient, the more they may resist, reducing the effectiveness of the conversation.

For those in the **precontemplation** stage, it is beneficial to provide informational resources like flyers or website links, acknowledge their current state of unreadiness, and schedule a follow-up appointment to progress further.

When dealing with patients in the **contemplation** stage who are uncertain about changing, it is important to assist them in weighing the advantages and disadvantages of the new behavior. This helps transition them to the preparation stage, where physicians can collaboratively set realistic goals with the patients. It is advisable to aim for modest, attainable goals rather than overly ambitious ones, even if the patient has high expectations. Establish a shared goal with the patient, offer support and guidance during the implementation, and prepare for potential challenges in maintaining the new habit. Recognize that relapses may occur; when they do, it is essential to examine the reasons, recall past successes, and bolster the positive progress.

Building motivation using OARS (the microskills)

How can I help patients?



Open-ended questions

To foster patient motivation, it is effective to employ open-ended questions that elicit more than a simple "yes" or "no" response. Here are some reformulated examples:

- Instead of asking, "Are there good things about not taking the pills?" you might say, "What are the benefits you see in not taking the pills?";
- Rather than "Are there bad things about using drugs?" consider "Could you share some downsides you've experienced with using drugs?";
- Swap "Do you have concerns about your heart failure?" with "It seems you have concerns about your heart failure. What specific worries do you have?";
- And instead of "Do you worry a lot about having heart failure?" ask "What aspects of having heart failure are most troubling to you?".

Affirmations

Consistently recognize and value the efforts your patients are making. Express gratitude for their presence at the appointment. Acknowledge their endeavors and commend the solutions they are developing. Maintain a positive attitude to enhance your patients' motivation.

OARS: Affirmation

- Thanks for coming today
- I appreciate that you are willing to talk to me about your heart failure
- You are obviously a resourceful person to have coped with those difficulties
- That's a good idea
- It's hard to talk about....I really appreciate your keeping on with this

Reflective listening

Always engage in active listening with your patient:

- Verify that you have accurately comprehended the patient's perspective;
- Emphasize the patient's mixed feelings regarding their substance use;
- Guide the patient toward a deeper acknowledgment of their issues and worries;
- Support any declarations that suggest the patient is contemplating change;
- Employ repetition, rewording, and paraphrasing to reinforce understanding.

Summarize

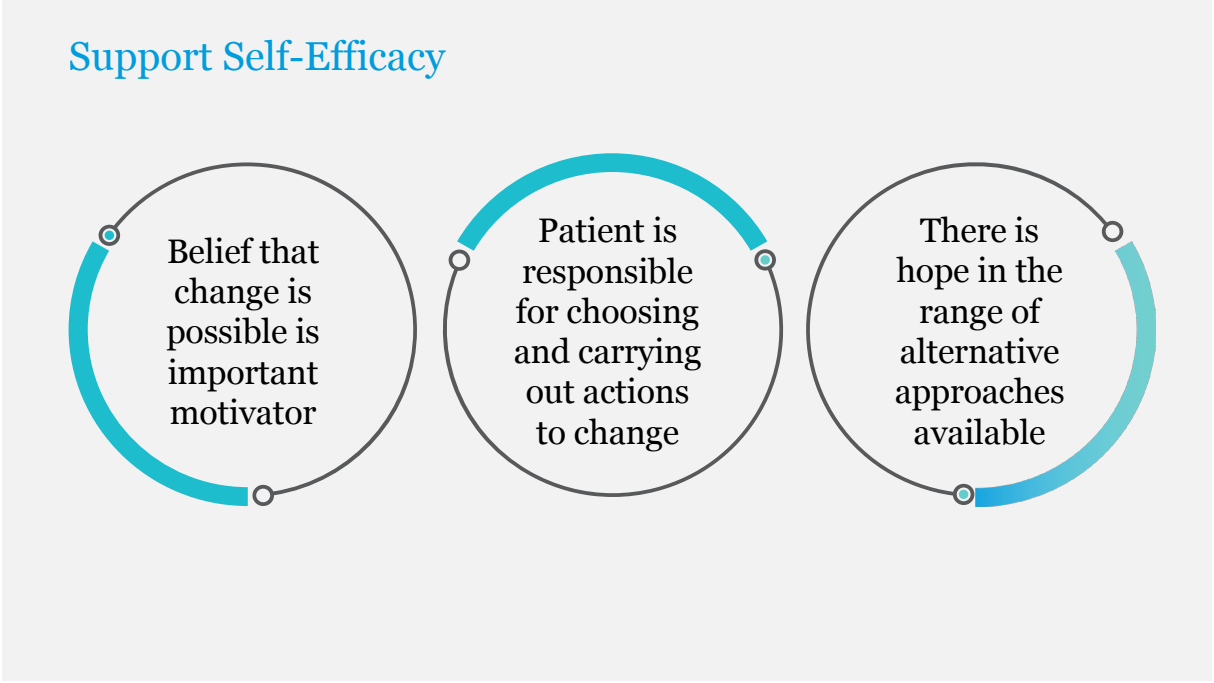
Summarizing plays a crucial role in jointly reviewing previous discussions, ensuring accurate understanding of the patient's statements and readying them for the next steps. It involves compiling various reflective thoughts into a cohesive overview.

"Four principles of motivational interviewing"

The responsibility for developing new behaviors does not rest solely on the patient if you aim for successful outcomes. Here are four principles of motivational interviewing:[50]

- **Express empathy.** Refrain from passing judgment and demonstrate your understanding of the patient's struggles.
- **Develop discrepancy.** Set objectives and assist the patient in recognizing that certain behaviors do not align with these goals. It is vital to establish a contrast between the patient's current state and where they need to be.
- **Avoid argumentation** to minimize resistance. Acknowledge and adapt to the patient's reluctance.
- **Support self-efficacy.** Encourage self-respect and foster confidence.

Adhering to these four principles will enhance your rapport with patients and contribute to improved health results. The goal is to encourage a shift in the patient's perspective and dialogue.



50. Motivational Interviewing (MI) - Rolling with Resistance – University of Missouri - https://health.mo.gov/living/healthcondiseases/chronic/wisewoman/pdf/MIRollingwithResistance.pdf Last accessed 17/11/2023.

To discern whether your patient is prepared to embrace change, look for the following indicators:

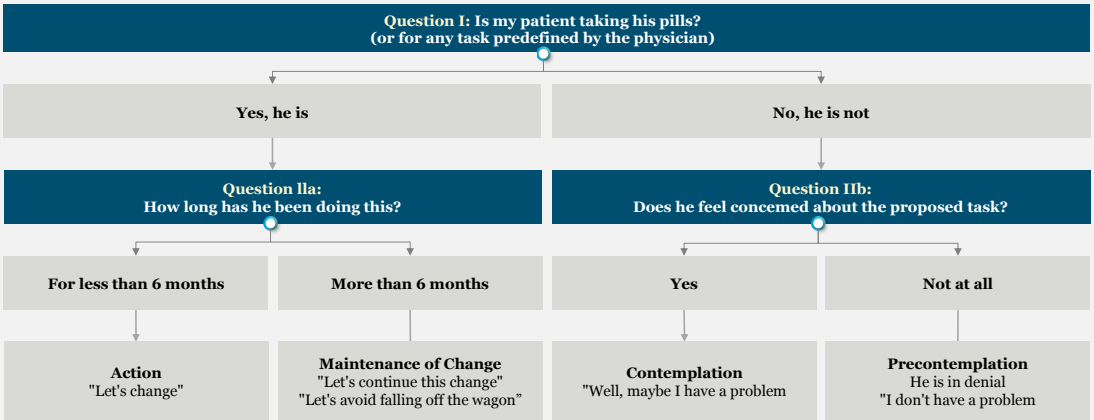
- A decrease in resistance;
- A reduction in queries about the problems;
- An increase in inquiries about how to change;
- Statements that reflect self-motivation;
- The discovery of new solutions to their issues;
- A forward-looking outlook;
- Active experimentation with change.

If these signs are absent, it may be necessary to reconsider whether the guidance provided is effective.

For a straightforward evaluation of your patient's readiness to change, consider employing a structured approach or algorithm tailored to assess their progress on the **change journey.**

The tool

Motivational stage



Systematic reviews and meta-analyses have demonstrated that motivational strategies can be more effective than conventional advice giving across different areas, including diet, exercise, and medication adherence.

Furthermore, some studies have revealed statistically significant improvements in direct health indicators like blood pressure, cholesterol levels, and body mass index when motivational techniques are employed.[51]

Impact of motivational interviewing on clinical parameters

Effect measure	*n*	Estimate of Effect (variation)	p-value (95% CI)
Body mass index	1140	0.72	0.0001 (0.33 to 1.11)
HbA1c (%GHb)	243	0.43	0.155 (-0.16 to 1.01)
Total blood cholesterol (mmol/l)	1358	0.27	0.0001 (0.20 to 0.34)
Systolic blood pressure (mm Hg)	316	4.22	0.038 (0.23 to 8.99)
Number of cigarettes/day	190	1.32	0.099 (-0.25 to 2.88)
Blood alcohol content (mg%)	278	72.92	0.0001 (46.80 to 99.04)
Standard ethanol content (units)	648	14.64	0.0001 (13.73 to 15.55)

Rubak S, Sandbaek A, Lauritzen T, Christensen B. Motivational interviewing: a systematic review and meta-analysis. Br J Gen Pract. 2005 Apr;55(513):305-12.

Heart failure serves as an ideal case of a chronic condition where the use of motivational tools can significantly enhance patient adherence. To achieve this, it is essential to initiate change within the patients, but the process begins with self-transformation on the part of the HCP.

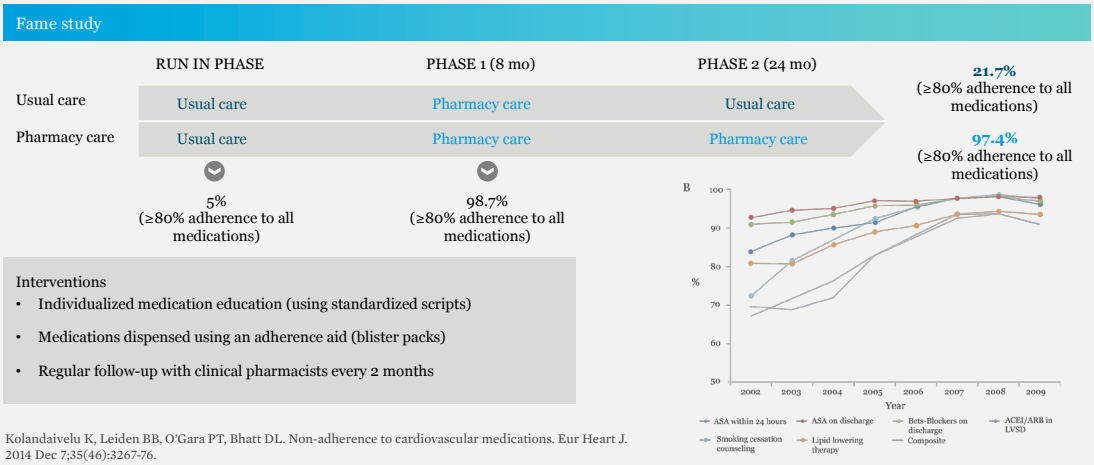
Pharmacy care improves adherence

Pharmacy involvement is crucial in enhancing medication adherence. In the US, a detailed pharmacy care initiative was launched, encompassing personalized medication instruction, the use of adherence aids like blister packs, and consistent consultations with clinical pharmacists. This program aimed to boost medication adherence among military healthcare recipients over the age of 65 who were taking a minimum of 4 medications daily for conditions such as high blood pressure and dyslipidemia.

51. Rubak S, Sandbaek A, Lauritzen T, Christensen B. Motivational interviewing: a systematic review and meta-analysis. Br J Gen Pract. 2005 Apr;55(513):305-12.

This study was conclusive as after 8 months, the percentage of patients who adhered to all chronic medications at a rate of at least 80%–the threshold generally recognized for satisfactory medication adherence–soared from 5.0% to 98.7% (P < .001). Even more significant was the sustained impact observed after 24 months; patients who returned to standard care maintained a positive outcome, with 21.7% continuing to adhere to their treatment regimen. Among those who received ongoing pharmacy care, nearly all (97.4%) remained compliant with their medication.

Pharmacy care improves adherence: In FAME, elderly patients with coronary risk factors were randomized to usual care vs. a multi-component program



Kolandaivelu K, Leiden BB, O'Gara PT, Bhatt DL. Non-adherence to cardiovascular medications. Eur Heart J. 2014 Dec 7;35(46):3267-76.

Furthermore, patient engagement is vital, and the adoption of technology-driven programs has been shown to substantially improve adherence rates. These include interventions such as SMS, automated educational responses, phone calls, and text message reminders.[52,53]

52. 1. Cohen, J.D., Aspry, K., Brown, A.S., Foody, J.A., Furman, R., Jacobson, T.A., Karalis, D.G., Kris-Etherton, P.M., Laforge, R., O'Toole, M.F., Scott, R.D., Underberg, J.A., Valuck, T., Willard, K., Ziajka, P.E., & Ito, M.K. (2013). Use of health information technology (HIT) to improve statin adherence and low-density lipoprotein cholesterol goal attainment in high-risk patients: proceedings from a workshop. Journal of clinical lipidology, 7 6, 573-609.

53. Ismail, Sophia & Tsoli, Stergiani & Chowdhury, Rajiv. (2017). Therapy-related strategies to improve adherence to diabetic medications. Medicographia. 39. 289-297.

Patient engagement essential even for pharmacy care and for most other methods to work! (1/2)

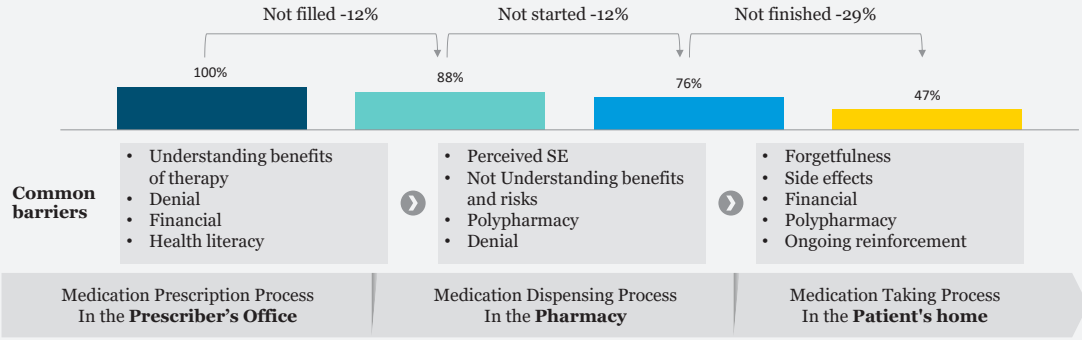
Technology-based programs increase patient engagement

	Measurement	Intervention arm	Control arm	P-value
SMS and automated behavioral education response	≥80% PDC	62.8%	49.4%	<0.001
SMS, automated education response and optional interactive personalized message	≥80% PDC	60.0%	49.4%	0.002
Automated telephone call followed by education letter	Proportion of dispensed medication	42.3%	26.0%	<0.001
Automated text reminders	≥80% medication use	91.0%	75.0%	<0.001

1. Cohen, J.D., Aspry, K., Brown, A.S., Foody, J.A., Furman, R., Jacobson, T.A., Karalis, D.G., Kris-Etherton, P.M., Laforge, R., O'Toole, M.F., Scott, R.D., Underberg, J.A., Valuck, T., Willard, K., Ziajka, P.E., & Ito, M.K. (2013). Use of health information technology (HIT) to improve statin adherence and low-density lipoprotein cholesterol goal attainment in high-risk patients: proceedings from a workshop. Journal of clinical lipidology, 7 6, 573-609.
2. Ismail, Sophia & Tsoli, Stergiani & Chowdhury, Rajiv. (2017). Therapy-related strategies to improve adherence to diabetic medications. Medicographia. 39. 289-297.

Patient engagement essential even for pharmacy care and for most other methods to work! (2/2)

Statin compliance over time



1. Cohen, J.D., Aspry, K., Brown, A.S., Foody, J.A., Furman, R., Jacobson, T.A., Karalis, D.G., Kris-Etherton, P.M., Laforge, R., O'Toole, M.F., Scott, R.D., Underberg, J.A., Valuck, T., Willard, K., Ziajka, P.E., & Ito, M.K. (2013). Use of health information technology (HIT) to improve statin adherence and low-density lipoprotein cholesterol goal attainment in high-risk patients: proceedings from a workshop. Journal of clinical lipidology, 7 6, 573-609.
2. Ismail, Sophia & Tsoli, Stergiani & Chowdhury, Rajiv. (2017). Therapy-related strategies to improve adherence to diabetic medications. Medicographia. 39. 289-297.

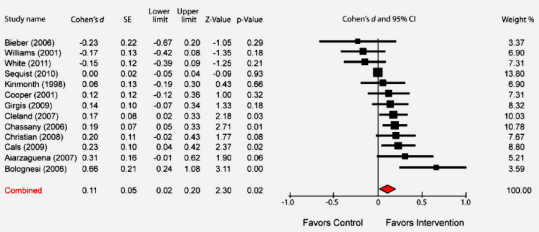
Patient motivation is required for even the most sophisticated methods

A recent meta-analysis has once again questioned Dr. House's patient management style, highlighting the importance of establishing a strong rapport between the physician and the patient as a key factor in achieving superior health outcomes. It emphasizes that a patient cannot be reduced to merely a collection of symptoms on a chart; a holistic approach is crucial.

You need patient motivation for even most sophisticated methods

- New nucleic acid-based therapies with once yearly injections, new medications with less side effects or FDC and new technologies are helpful
- Shared decision making with the patient is the key!
- Nothing about me without me!

  – Valerie Billingham



Kelley JM, Kraft-Todd G, Schapira L, Kossowsky J, Riess H. The influence of the patient-clinician relationship on healthcare outcomes: a systematic review and meta-analysis of randomized controlled trials. PLoS One. 2014 Apr 9;9(4):e94207.

Raising awareness of non–adherence: Perspectives from the International Society of Hypertension

This session of the a:care Congress 2022 was held by Prof. Schutte.

First, let us highlight the main findings from the Global Burden of Disease study, a prominent global investigation comparing various risk factors for death. This study consistently finds that raised systolic blood pressure is a leading cause of death worldwide, accounting for approximately 10.8 million deaths annually. Raised blood pressure is often the primary reason patients visit clinics.

Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019

GBD 2019 Risk Factors Collaborators*

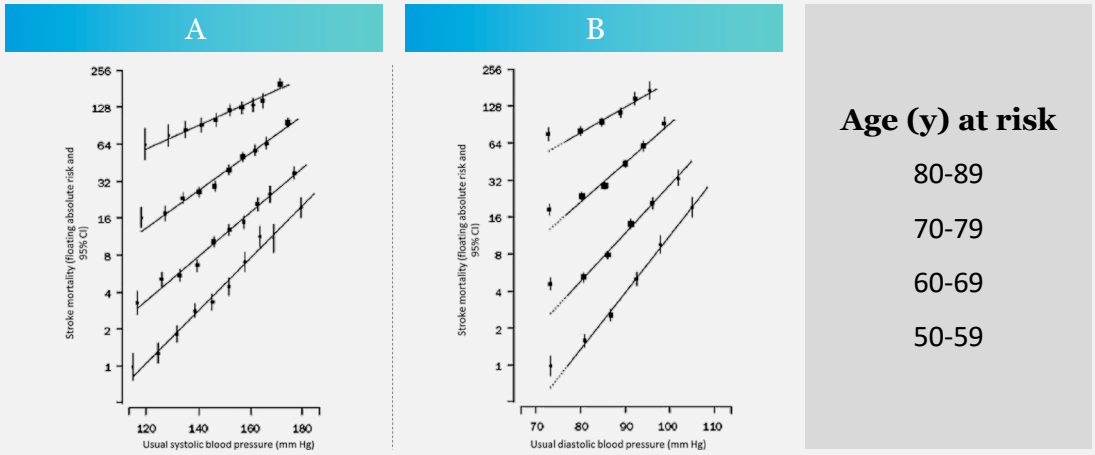
In 2019, the leading level 2 risk factor globally for attribute deaths was high systolic blood pressure. Which accounted for 10.8 million (95% uncertainty interval [UI] 9.51-12.1) deaths (19.2% [16.9-21.3] of all deaths in 2019)

10.8 million deaths/year
= 29,589 DEATHS/DAY

Murray JL, Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396:1223-49

The high contribution to mortality is due to the strong linear relationship between raised blood pressure and outcomes such as stroke and myocardial infarction across different age groups. If blood pressure is not managed with medication, the risk remains high, underscoring the importance of adherence.

Absolute risk of stroke mortality in relation to blood pressure

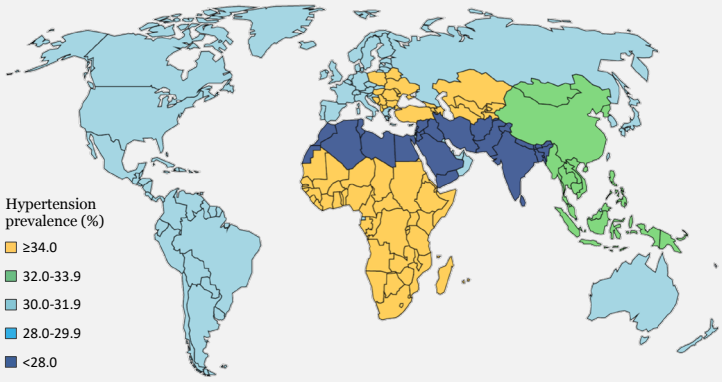


Wilbert S. Aronow, Jerome L Fleg, et al. ACCF/AHA 2011 Expert Consensus Document on Hypertension in the Elderly. Circulation. 2011;123:2434-2506

From a global standpoint, we need to emphasize the challenges faced in low- and middle-income countries. Data from 2010 estimated that 1.4 billion people worldwide have hypertension, with over 1 billion from low- and middle-income regions. These numbers have likely increased. In these regions, a significant proportion of people with raised blood pressure reside, placing a major burden on health systems already strained by other conditions.

Hypertension prevalence by world region in 2010 (1/2)

A Men



1.39 billion estimated with hypertension in 2010

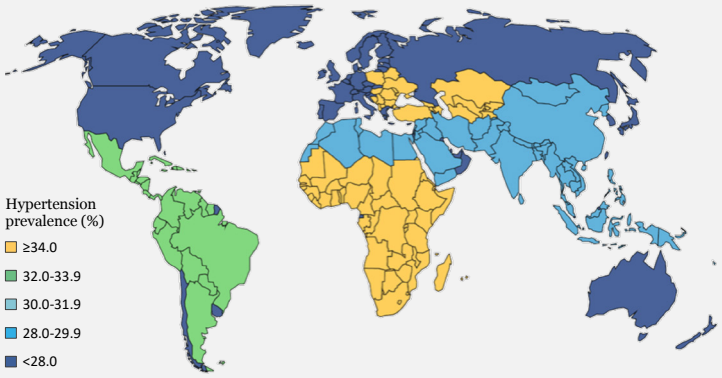
349 million from HIC

1.04 billion from LMIC

1. Mills Katherine T, Stefanescu Andre and Jiang He. The global epidemiology of hypertension. Nature Reviews Nephrology. 2020;16:223-237; 2.Mills Katherine T. Kelly Tanika, et al. Global Disparities of Hypertension Prevalence and Control. Circulation. 2016;134:441-450

Hypertension prevalence by world region in 2010 (2/2)

B Women



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1. Mills Katherine T, Stefanescu Andre and Jiang He. The global epidemiology of hypertension. Nature Review Nephrology. 2020 volume 16, Issue 4; 2.Mills Katherine T. Kelly Tanika, et al. Global Disparities of Hypertension Prevalence and Control. Circulation. 2016;134-441-450

Deaths due to high systolic blood pressure are significantly higher in low- and middle-income countries compared to high-income countries. This disparity highlights the challenges in managing a common, often asymptomatic condition like hypertension.

Circulation Research

Hypertension compendium

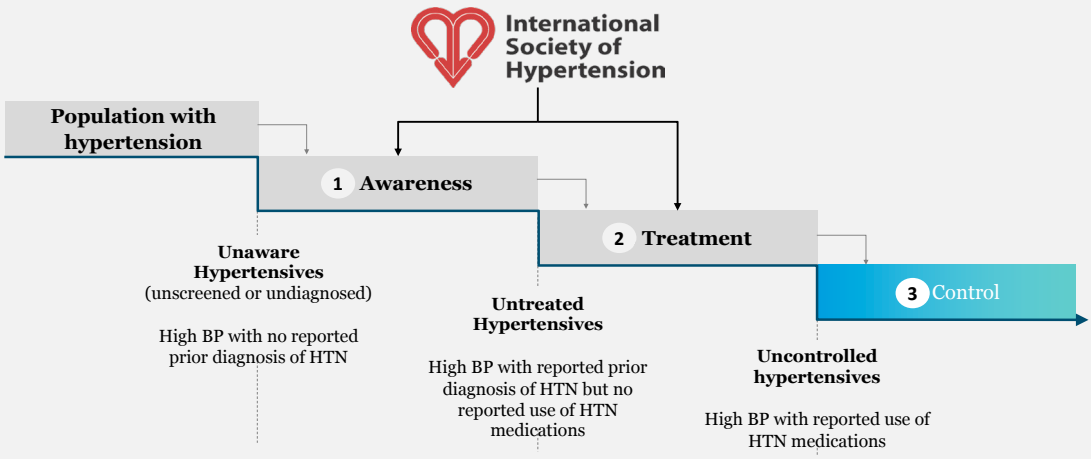
Age-standardized deaths (per 100 000 with 95% CIs) due to CVD, high SBP, and high sodium intake according to World Bank income classification of countries in 2019

	World Bank income classification of countries			
	High income	Upper middle income	Lower middle income	Low income
Deaths due to CVD	133 (118-142)	267 (24-283)	313 (287-337)	304 (270-340)
CVD deaths due to high SBP	64 (54-74)	143 (121-164)	172 (149-197)	167 (142-192)
Deaths due to high SBP	**72 (61-83)**	**153 (131-175)**	**187 (162-213)**	**184 (157-211)**
Deaths due to diet high in sodium	9 (1-24)	35 (11-69)	22 (3-58)	26 (3-71)

CVD indicates cardiovascular disease; and SBP, systolic blood pressure

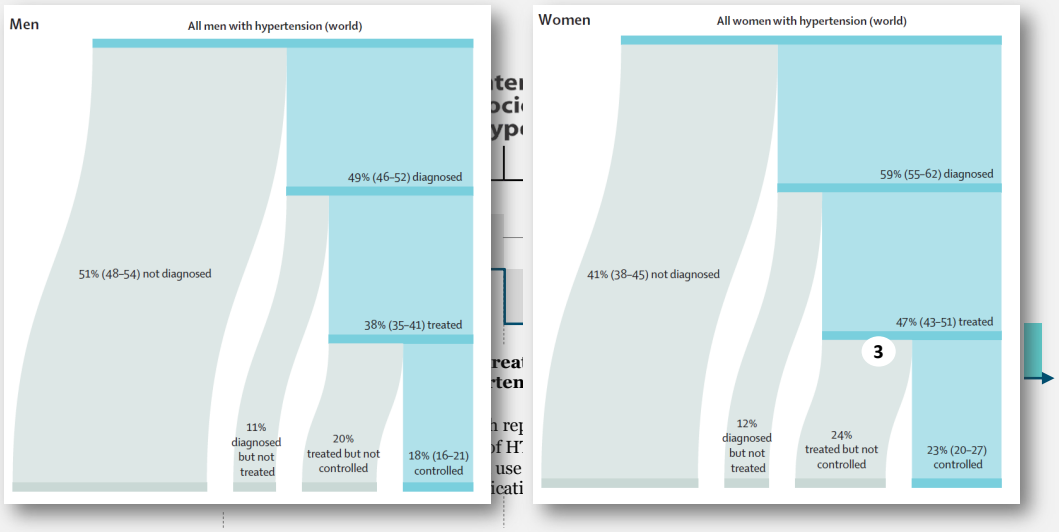
Schutte Aletta E, Venkateshmurthy Srinivasapura Nikhil, et al. Hypertension in Low- and Middle-Income Countries. Circulation Research. 2021;128:808-826

The hypertension cascade illustrates the steps needed to control blood pressure: awareness, treatment, and control. Many people are unaware of their condition, and even those who receive treatment may not be adequately managed. Non-adherence to medication is a critical issue, leading to uncontrolled hypertension.



Ezzati Majid. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet 2021;298:957-80

Globally, 51% of men with hypertension are not diagnosed, and only 18% of those diagnosed have their condition controlled. For women, 23% have controlled hypertension, but nearly 80% remain uncontrolled.

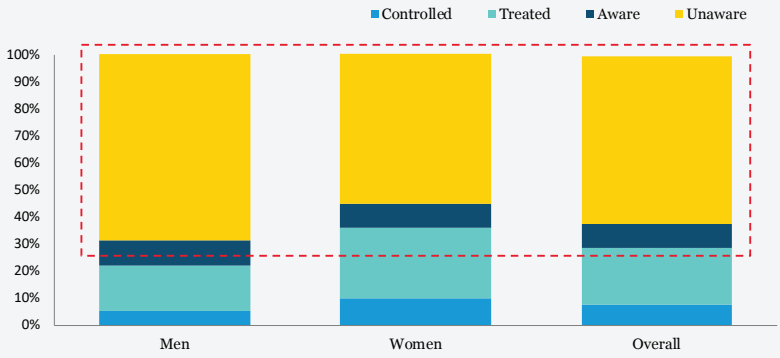


In low- and middle-income countries, control rates are about 10%.

The Lancet

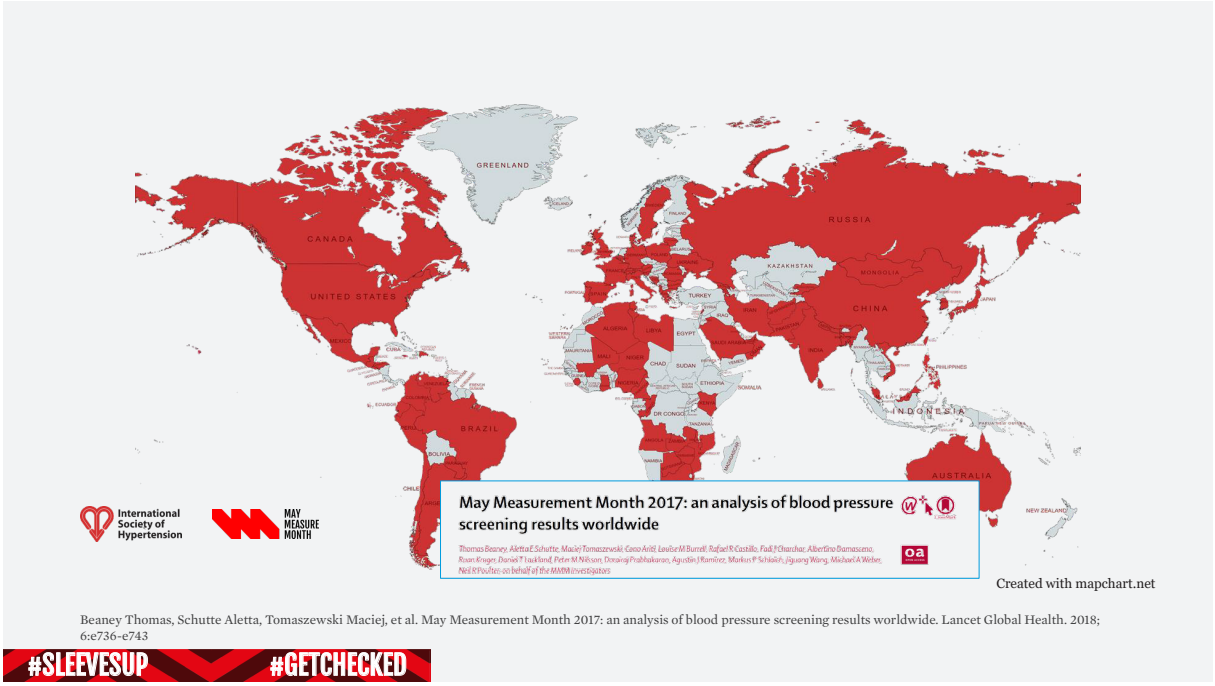
GOALS
Every adult should know their blood pressure[1]

Sex-specific hypertension awareness, treatment and control in Low/Middle Income Countries (LMIC) in 2010[2]



1. Olsen Michael H, Angell Sonia Y, et al. A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: the Lancet Commission on hypertension. The Lancet. 2016;388:2665-712;
2. Adapted from Mills Katherine T. Kelly Tanika, et al. Global Disparities of Hypertension Prevalence and Control. Circulation. 2016;134:441-450

The ISH has initiated several projects to address these issues, focusing on improving awareness and treatment. One notable initiative is the global awareness campaign “May Measurement Month,” which started in 2017. This campaign involves volunteers measuring blood pressure worldwide, with over 100 countries participating and about 5 million people measured so far.



Beaney Thomas, Schutte Aletta, Tomaszewski Maciej, et al. May Measurement Month 2017: an analysis of blood pressure screening results worldwide. Lancet Global Health. 2018; 6:e736-e743

#SLEEVESUP #GETCHECKED

In addition to raising awareness, ISH has also focused on improving treatment. In 2020, the ISH released the Global Hypertension Practice Guidelines. Recognizing the significant challenges in low- and middle-income regions, these guidelines include both essential and optimal standards of care.

Essential standards represent the minimum required to manage hypertension effectively, while optimal standards apply to high-resource settings with access to advanced management tools like ambulatory blood pressure monitoring. These guidelines are designed to be clear and concise, suitable for use by clinicians, nurses, and community health workers.

International Society of Hypertension

Guidelines[1]

2020 International Society of Hypertension global hypertension practice guidelines

Thomas Unger[a], Claudio Borghi[b], Fadi Charchar[c,d,e], Nadia A. Khan[f,g], Neil R. Poulter[h], Dorairaj Prabhakaran[i,j,k], Agustin Ramirez[l], Markus Schlaich[m,n], George S. Stergiou[o], Maciej Tomaszewski[p,q], Richard D. Wainford[r,s,t], Bryan Williams[u], and Aletta E. Schutte[v,w]

Clinical practice guidelines[2]

2020 International Society of Hypertension Global Hypertension Practice Guidelines

Thomas Unger, Claudio Borghi, Fadi Charchar, Nadia A. Khan, Neil R. Poulter, Dorairaj Prabhakaran, Agustin Ramirez, Markus Schlaich, George S. Stergiou, Maciej Tomaszewski, Richard D. Wainford, Bryan Williams, Aletta E. Schutte

The ISH guidelines committee extracted evidence-based content presented in recently published extensively reviewed guidelines and tailored **ESSENTIAL** and **OPTIMAL** standards of care in a practical format that is easy-to-use particularly in low, but also in high resource settings – by clinicians, but also nurses and community health workers, as appropriate

1. Unger Thomas, Borghi Claudio, et al. 2020 International Society of Hypertension global hypertension practice guidelines. Journal of Hypertension. 2020;38:982-1004;
2. Unger Thomas, Borghi Claudio, et al. 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension. 2020;75:1334-1357

Returning to the guidelines, we need to address why we are not more successful in managing hypertension despite having effective and affordable treatments available globally. Numerous clinical trials since the 1960s have provided robust evidence supporting these treatments. So, what is going wrong?

Several reasons need to be considered to identify why the current treatment strategy has failed to achieve better BP control rates (1/2)

1 Efficacy of pharmacological therapies

Are the best available treatments, in whatever combination, incapable of controlling BP in most patients? The evidence from RCTs demonstrating that BP control can be achieved in most recruited patients, and that no more than 5–10% of these patients exhibit resistance to the selected treatment regimen, suggests that ineffective drug therapy is not the source of the problem

2 Physician or treatment inertia

(I.e., failure to adequately uptitrate treatment). Evidence suggests that inertia. contributes to suboptimal BP control, with many patients remaining on monotherapy and/or suboptimal doses, despite inadequate BP control

3 Patient adherence to treatment

Evidence is accumulating that adherence is a much more important factor than previously recognized. Studies using urine or blood assays for the presence or absence of medication have shown that adherence to treatment is low. This is supported by studies in the general population in which adherence to treatment, based on prescription refilling, was <50% of the treatment in half of the patients. Poor adherence has also been shown to be associated with increased cardiovascular risk in various studies

4 Insufficient use of combination treatment

BP is a multiregulated variable depending on many compensating pathways. Consequently, combinations of drugs, working through different mechanisms, are required to reduce BP in most people with hypertension. Thus, monotherapy is likely to be inadequate therapy in most patients. Indeed, almost all patients in RCTs have required combinations of drugs to control their BP

Williams Bryan, Giuseppe Mancia, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. Journal of Hypertension. 2018;36:1953-2041

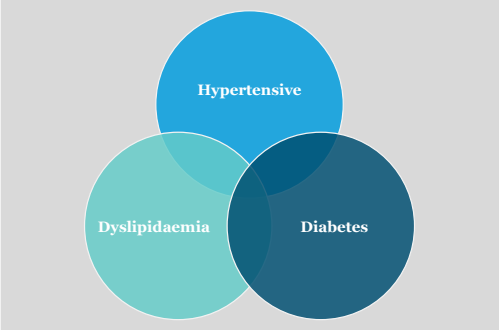
Firstly, the efficacy of the therapies is not the problem. The data clearly show that the treatments are effective. One major issue is physician inertia–doctors often prescribe medication at diagnosis but fail to adjust or intensify treatment if blood pressure remains uncontrolled.

Another critical factor is patient adherence to treatment. Studies consistently show that about 50% of patients are non-adherence, significantly increasing their risk of cardiovascular events like strokes and heart attacks.

Several reasons need to be considered to identify why the current treatment strategy has failed to achieve better BP control rates (2/2)

5 Complexity of current treatment strategies

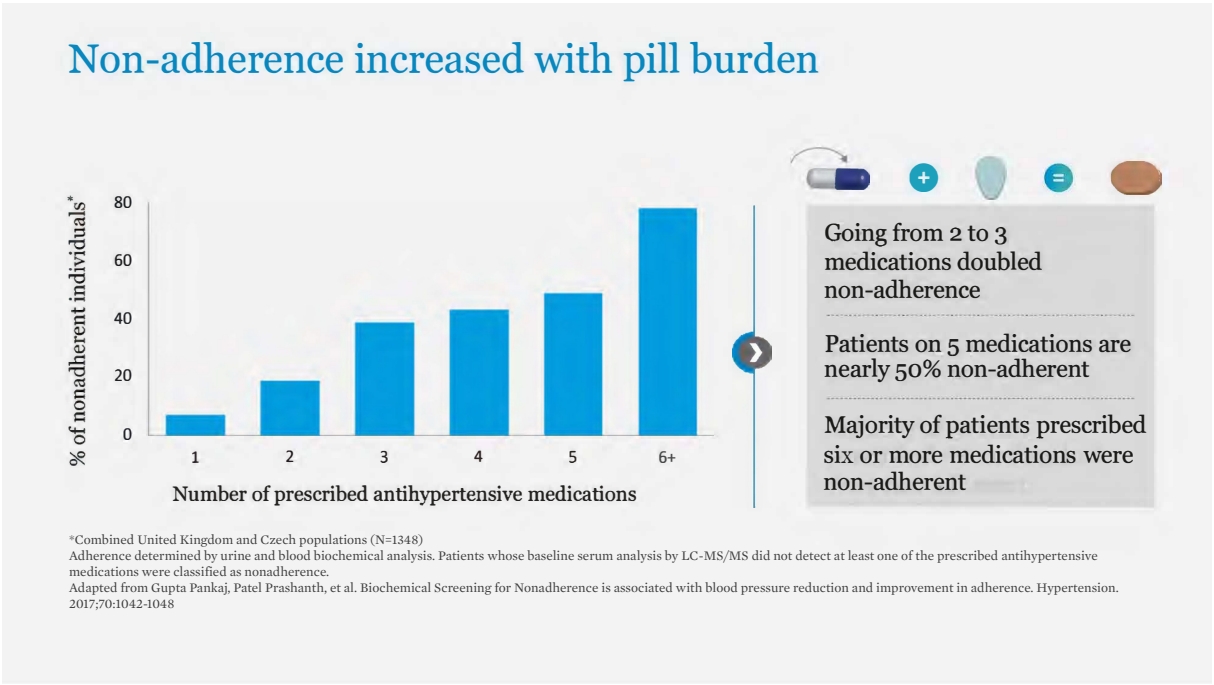
There is also evidence that adherence to treatment is adversely affected by the complexity of the prescribed treatment regimen. In a recent study, adherence to treatment was strongly influenced by the number of pills that a patient was prescribed for the treatment of hypertension. Nonadherence was usually less than 10% with a single pill, rising to 20% with two pills, 40% with three pills, and very high rates of partial or complete nonadherence in patients receiving five or more pills



Williams Bryan, Giuseppe Mancia, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. Journal of Hypertension. 2018;36:1953-2041

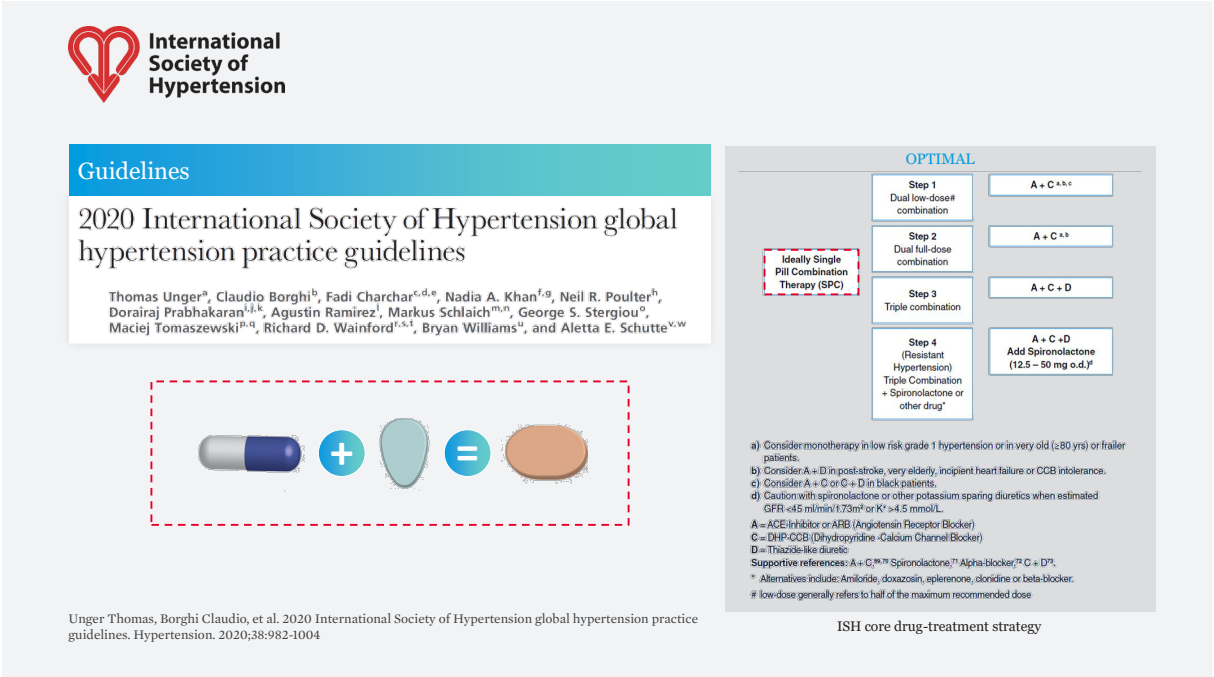
Additionally, there is insufficient use of combination treatments. Many patients require more than one drug to control their blood pressure, yet monotherapy is often prescribed.

The complexity of treatment regimens also poses a challenge. Patients with hypertension often have other conditions, leading to multiple medications, which can be overwhelming and reduce adherence. Studies show that adherence drops significantly as the number of medications increases.



*Combined United Kingdom and Czech populations (N=1348)
Adherence determined by urine and blood biochemical analysis. Patients whose baseline serum analysis by LC-MS/MS did not detect at least one of the prescribed antihypertensive medications were classified as nonadherence.
Adapted from Gupta Pankaj, Patel Prashanth, et al. Biochemical Screening for Nonadherence is associated with blood pressure reduction and improvement in adherence. Hypertension. 2017;70:1042-1048

To address this, the ISH guidelines emphasize single-pill combination therapy, which simplifies the regimen and improves adherence. Evidence supports this approach, showing that fixed-dose combinations favor adherence. For example, a meta-analysis of various trials consistently found that single-pill combinations improved adherence.



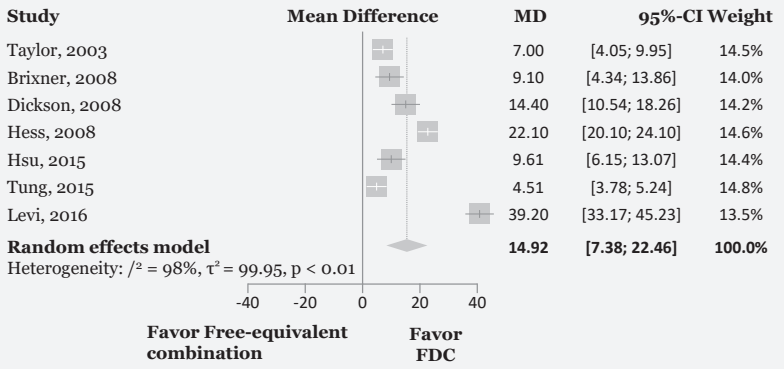
Unger Thomas, Borghi Claudio, et al. 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension. 2020;38:982-1004

ISH core drug-treatment strategy

In summary, non-adherence is a global issue affecting both high- and low-income countries. By focusing on simplified treatment regimens and improving awareness and management strategies, we can better support patients in controlling their hypertension.

Single-pill combination is one approach to improve medication adherence

Forest plot for medication adherence. CI, confidence interval; FDC, Fixed-dose combination; MD, mean difference

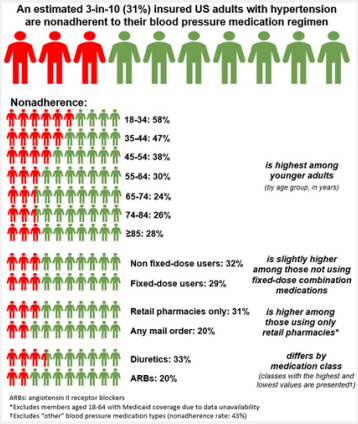


Du Li-Ping, Cheng Zhong-Wei, et al. The impact of fixed-dose combination versus free-equivalent combination therapies on adherence for hypertension: A meta-analysis. Journal of Clinical Hypertension. 2020;38:982-1004

A study conducted in the US revealed that three out of 10 insured US. adults with hypertension were non-adherence to their medication. Notably, younger adults had the highest likelihood of non-adherence, with six out of 10 adults aged 18–34 not following their prescribed treatment. This is particularly challenging because hypertension often has no symptoms, and patients may stop taking their medication due to side effects, feeling fine beforehand.

For many years non-adherence was under-recognized in patients with hypertension

A global phenomenon affecting both high and low income countries



De Terline Diane Macquart, Kane Adama, et al. Factors associated with poor adherence to medication among hypertensive patients in twelve low and middle income Sub-Saharan countries. PLOS One. 2019,14(7):e0219266
Chang Tiffany E, Ritchey Matthew D, et al. National Rates of Nonadherence to Antihypertensive Medications Among Insured Adults With Hypertension, 2015. Hypertension. 2019;74(6):1324-1332

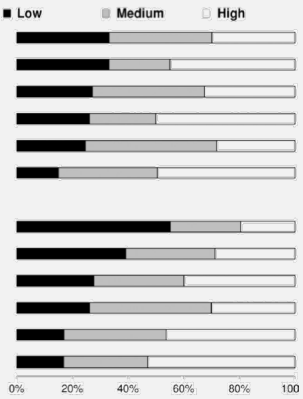
The study also found that adherence was slightly better among those using single-pill or fixed-combination therapy.

Focusing on low- and middle-income countries, there is significant variation in adherence rates. Some countries perform better than others despite similar income levels. For example, the Democratic Republic of the Congo faces particularly low adherence rates. Common reasons for non-adherence in these regions include the high cost of treatment, side effects, and forgetfulness. In some cases, medications cost more in low-income countries than in high-income ones, and patients often have to pay out of pocket, making it difficult to prioritize medication, especially when they have no symptoms.

For many years non-adherence was under-recognized in patients with hypertension

A global phenomenon affecting both high and low income countries

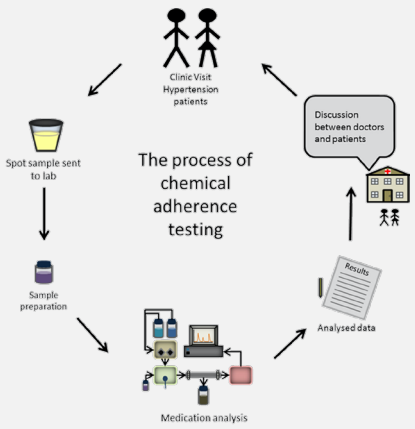
Countries	N	Low adherence, n(%)
MIDDLE INCOME COUNTRIES		
Côte d'Ivoire	295	98 (33.2%)
Congo	178	59 (33.1%)
Cameroun	375	102 (27.2%)
Mauritania	84	22 (26.2%)
Gabon	89	22 (24.7%)
Senegal	160	24 (15.0%)
LOW INCOME COUNTRIES		
Dem. Rep. of the Congo	261	144 (55.2%)
Benin	250	98 (39.2%)
Mozambic	148	41 (27.7%)
Niger	80	21 (26.3%)
Togo	106	18 (17.0%)
Gabon	89	22 (24.7%)

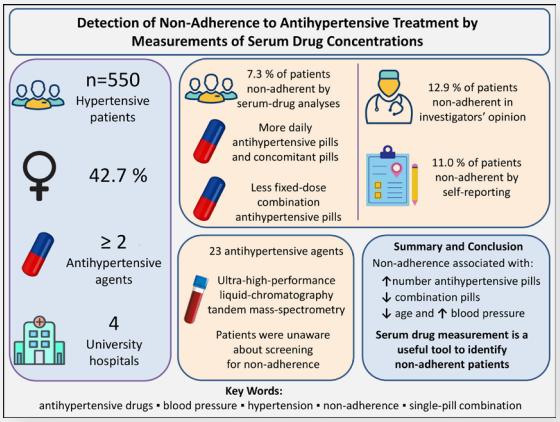


De Terline Diane Macquart, Kane Adama, et al. Factors associated with poor adherence to medication among hypertensive patients in twelve low and middle income Sub-Saharan countries. PLOS One. 2019,14(7):e0219266
Chang Tiffany E, Ritchey Matthew D, et al. National Rates of Nonadherence to Antihypertensive Medications Among Insured Adults With Hypertension, 2015. Hypertension. 2019;74(6):1324-1332

In high-income countries, new methods are being used to verify medication adherence, such as analyzing urine and blood samples. These techniques can detect whether patients have taken their medication, leading to more informed discussions between doctors and patients.

For instance, a study found that 7.3% of hypertensive patients were non-adherence, particularly those taking multiple pills daily and those not using fixed-dose combination therapy. Non-adherence was also more common among younger patients and those with higher blood pressure.





1. Dan Lane, Alexander Lawson, et al. Nonadherence in Hypertension: How to Develop and Implement Chemical Adherence Testing. Hypertension., Volume: 79, Issue: 1, Pages: 12-23 ;
2. Bergland Ola Undrum, Halvorsen Lene V, et al. Detection of nonadherence to antihypertensive treatment by Measurement of Serum Drug Concentration. Hypertension. 2021;78:617-628

To summarize:

- Hypertension is the leading cause of death globally, affecting over 1.4 billion people;
- The ISH has implemented several initiatives, including the “May Measurement Month” campaign and the Global Hypertension Practice Guidelines, to address non-adherence;
- Antihypertensive medications are effective, widely available, and low cost, but non-adherence remains a significant challenge, affecting about half of patients with hypertension;
- Non-adherence is a widespread issue in both low- and high-income countries, and it is now considered a cardiovascular risk factor;
- Non-adherence is more common among young adults, those not using single-pill combination therapies, and in low-income countries where treatment costs and side effects are major barriers.

Take home messages

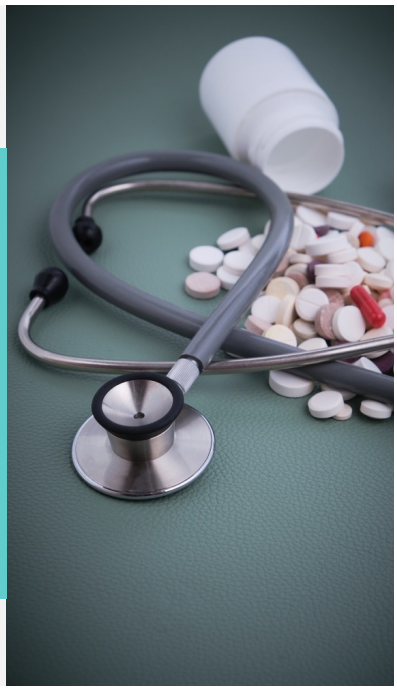
Hypertension is the leading cause of death globally, affecting over **1.4 billion people**[1]

The **International Society of Hypertension** has implemented actions to improve aspects of the hypertension cascade–including the MMM global awareness campaign and the 2020 ISH Global Guidelines (with SPCs)

Antihypertensive **medications** are highly effective, low cost and widely available. But **non-adherence** is a major challenge, **affecting approx. 45%** of patients with hypertension

Awareness of the challenge of non-adherence needs to be raised with health practitioners and patients–both in **high and low- and middle-income countries**

Non-adherence was **more common among young adults, people not using SPCs**. In LMICs the **high cost of treatment, forgetfulness and perceived side effects** were main contributors



1. Egan BM., Kjeldsen SE. et al. The global burden of hypertension exceeds 1.4 billion people. Journal of Hypertension. 2019: 37(6):1148-1153.

The paradox of non-adherence to treatment in oncology

Advancements in medicine and cancer treatments have greatly enhanced survival rates for many types of cancer. At the a:care Congress 2022, Prof. Enrique De Madaria highlighted that improved treatment efficacy and advancements in galenic formulations have transformed gastrointestinal cancers from fatal diseases to manageable chronic conditions. Despite these medical achievements, the issue of treatment non-adherence in oncology remains prevalent, driven by various cancer-specific factors.

Over the past decades, we have witnessed significant changes in oncology treatments. In the past, treatments were primarily based on intravenous chemotherapy, administered in healthcare facilities. These treatments often had frequent and intense adverse events, low efficacy, and progressive disease symptoms in many cancers.

Medical treatments in oncology

In the past	Currently
Based on IV chemotherapy	Frequent use of oral/subcutaneous drugs
Drug provided by healthcare facilities	Drug acquisition by the patient
Administered in healthcare facilities	Administered by the patient
Frequent and intense adverse events	Some drugs with few adverse events
Low efficacy, progressive disease symptoms	High efficacy, cancer as a chronic disease

Currently, we are seeing a shift towards the frequent use of oral and subcutaneous drugs. These medications are acquired and administered by the patients themselves, often with fewer adverse events and higher efficacy. As a result, cancer is now seen as a chronic disease in many cases. However, this shift has paradoxically led to decreased adherence to these medications.

Studies addressing adherence to oral oncological treatments are quite heterogeneous, with different sample types and sizes, assessment methods, definitions of adherence, types of drugs (hormonal therapy, chemotherapy, immunotherapy), and healthcare systems. Up to one third of these studies have a high risk of bias.

Adherence in oral oncological treatments

Heterogeneity of studies

- Different samples (type, size)
- Different assessment methods for adherence (some of them linked to biases)
- Different definitions for adherence
- Different types of drugs: hormonal therapy, chemotherapy, immunotherapy...
- Different healthcare systems

1/3 studies with high risk of bias

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

Adherence rates in oral oncological treatments vary. For endocrine treatments like breast or prostate cancer, poor adherence rates are 12% in the first week, 15% at 6 months, 40% at 1 year, and up to 50% at 5 years. For non-endocrine antineoplastic drugs, baseline poor adherence is up to 36%, and at 1 year, it is 41%.

Adherence in oral oncological treatments

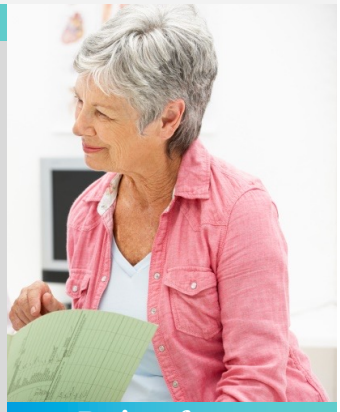
Oral oncological treatment	Poor adherence
Endocrine treatment (breast, prostate)	1 week: 12%
	6 months: 15%
	1 year: 23-40%
	5 years: Up to 50%
Nonendocrine antineoplastic drugs	Baseline: Up to 36%
	1 year: 27 to 41%

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

Risk factors for non-adherence to oral antineoplastic therapies are varied and sometimes contradictory. Demographic factors such as age, gender, marital status, education, employment status, and income level can influence adherence.

Risk factors for non-adherence to oral antineoplastic therapies (1/7)

Demographic factors
Age (younger, older)
Sex (male, female)
Race (black, white)
Not married/no partner/living alone
Less education
Employment status
Lower annual income or financial status



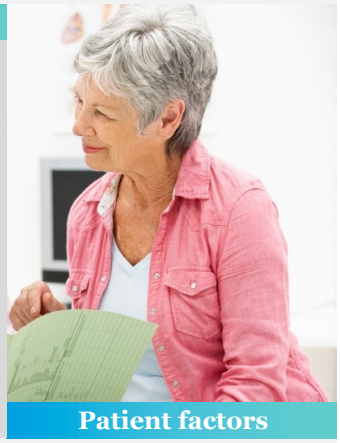
Patient factors

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

Psychosocial and cognitive factors, including social support, depression, anxiety, quality of life, and health literacy, also play a role.

Risk factors for non-adherence to oral antineoplastic therapies (2/7)

Psychosocial and cognitive factors
Lower social support
Higher depression or antidepressant use
Higher anxiety
Higher quality of life
Forgetting to take dose
Worse verbal memory



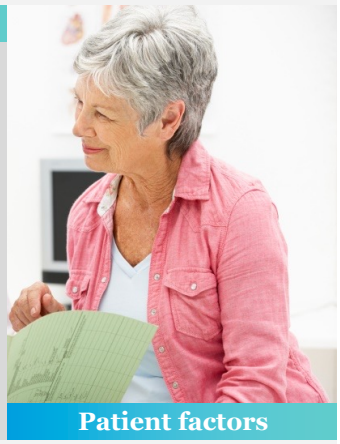
Patient factors

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

Health risk and perception factors, such as family history of cancer, use of alcohol and cigarettes, and perceived necessity of medication, are important as well.

Risk factors for non-adherence to oral antineoplastic therapies (3/7)

Health risks and perceptions factors
No family history of cancer
Use of alcohol and cigarettes
Greater concerns or negative emotions related to medication
Lower perceived necessity of medication
Less satisfaction with information received
Less self-efficacy in long-term medication behavior
Less knowledge of disease and treatment



Patient factors

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

Disease factors, including comorbidities, disease duration, risk class, tumor stage, and severity, can affect adherence.

Risk factors for non-adherence to oral antineoplastic therapies (4/7)

Disease factors

Comorbidities (more or few)	Higher cancer complexity	Suboptimal treatment/ cytogenic response or less hormone suppression
Longer duration of time since diagnosis	Worse disease severity marker	Cancer recurrence
Lower disease risk class at diagnosis	Tumor size (larger ductal cancers, smaller, unknown)	Worse survival/higher all-cause mortality
Lower tumor stage	Node-negative breast cancer	
Diagnosis of incurable cancer	Lymph node involvement	

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

Risk factors for non-adherence to oral antineoplastic therapies (5/7)

Treatment factors: Medication

Higher dose	Duration of treatment (shorter or longer)
Greater toxicity/side effects/symptoms/adverse events	Adjuvant chemotherapy (presence/absence)
Medications/concomitant prescriptions (more/fewer) disease risk class at diagnosis	Combination of hormone therapy and/ or radiation and/or chemotherapy
Delay of hormone treatment	Hormone replacement therapy

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

Treatment factors, such as dosage, side effects, and treatment duration, are also significant.

Risk factors for non-adherence to oral antineoplastic therapies (6/7)

Treatment factors: Utilization factors

More long-term care received

More outpatient visits, ED visits, urgent care, hospitalizations

More tests and procedures

No attendance at regular follow-up appointments or rehabilitation program

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

Utilization factors, including long-term care, outpatient visits, emergency department visits, hospitalizations, and follow-up appointments, influence adherence.

Risk factors for non-adherence to oral antineoplastic therapies (7/7)

Treatment factors: Utilization factors

Not seeing/less frequent/poor communication with oncologist

More consultations/visits with oncologist

Shorter duration of visits (initial and follow-up) with doctor

Having a doctor with more years of professional experience

Having a doctor not practicing in a university or teaching hospital

Greater prescription, medical, healthcare, and out-of-pocket costs

Not receiving low-income subsidy

No use of mail-order pharmacy

Shorter duration between prescription refills

Non-oncologist writing prescription

Greer Joseph, Amoyal Nicole, et al. A Systematic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist 2016;21:354-376

A real-world study on patients with metastatic colorectal cancer compared adherence to two different treatments: trifluridine + tipiracil (TT) versus regorafenib. The TT treatment had better tolerance, leading to higher adherence rates. Patients on TT had better medication possession ratios and higher proportions of days covered, indicating better adherence.

Toxicity and adherence

Example: Trifluridine+Tipiracil (TT) VS. Regorafenib (TT Better tolerance)

Adherence (≥80%)	Persistence	Discontinuation
Medication possession ratio: TT OR 2.47 Proportion of days covered: TT OR 2.77	TT 83%, Regorafenib 68%	TT HR 0.76

Data on adherence must be taken into account!

Patel Anuj K, Barghout Victoria, et al. Real-Word Adherence in Patients with Metastatic Colorectal Cancer Treated with Trifluridine plus Tipiracil or Regorafenib. The Oncologist 2020

It is important to note that adherence in real clinical practice can differ from that in randomized controlled trials, where patients are closely monitored. Real-world data on adherence must be considered to understand the true impact of these treatments.

What about adherence to oral chemotherapy medications among gastrointestinal cancer patients? A study from Japan examined 117 patients with gastrointestinal cancer and found that only 56% had good medication adherence. This may seem high for patients receiving treatment for such a serious disease with a typically poor prognosis, but it highlights a significant paradox.

Adherence to oral chemotherapy medications among GI cancer patients

117 patients with GI cancer › Only 56% good medication adherence ›

Factors associated to non-adherence

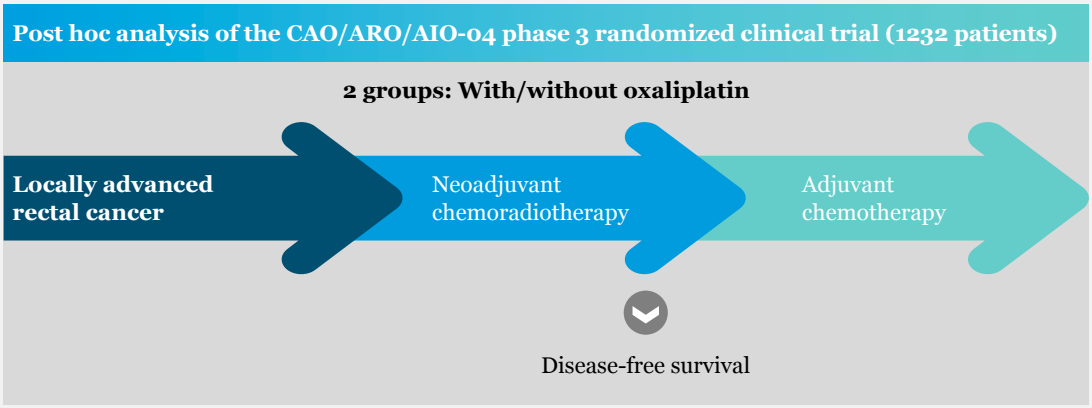
- History of patient-caused treatment interruptions due to worsening of symptoms
- Diarrhea
- Pain
- Taking oral chemo every 8 h
- Diminished sense of priority for medication

Hirao Chieko, Mikoshiba Naoko, et al. Adherence to oral chemotherapy medications among gastroenterological cancer patients visiting an outpatient clinic. Japanese Journal Clinical Oncology. 2017;1-9

Factors associated with non-adherence included a history of patient-caused treatment interruptions due to worsening symptoms like diarrhea and pain, the need to take oral chemotherapy every 8 h, and a diminished sense of priority for medication.

Outcomes and adherence (1/2)

Example: Association of treatment adherence with oncologic outcomes for patients with rectal cancer



Diefenhardt Markus, Ludmir Athan, et al. Association of Treatment Adherence With Oncologic Outcomes for Patients with Rectal Cancer. JAMA oncology 2020;6:1416-1421

Another study explored the association between treatment adherence and oncologic outcomes, which are crucial for our patients.

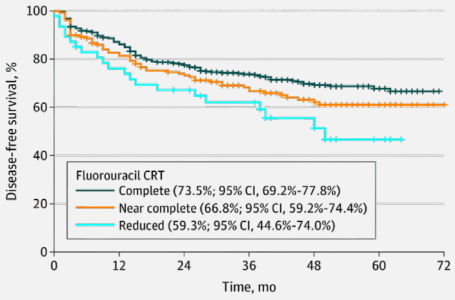
This post-hoc analysis of a phase three randomized clinical trial involved over 1,200 patients with rectal cancer. The patients were divided into two groups, with and without oxaliplatin. Those with locally advanced rectal cancer received neoadjuvant chemoradiotherapy followed by adjuvant chemotherapy. The main outcome variable was disease-free survival.

The study found that decreased adherence to therapy was significantly associated with reduced disease-free survival, a trend not observed in neoadjuvant chemotherapy.

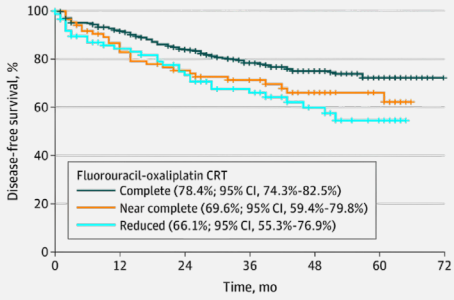
Outcomes and adherence (2/2)

Neoadjuvant treatment

A Neoadjuvant fluorouracil CRT



B Neoadjuvant fluorouracil-oxaliplatin CRT



No differences in adjuvant chemo

Diefenhardt Markus, Ludmir Athan, et al. Association of Treatment Adherence With Oncologic Outcomes for Patients with Rectal Cancer. JAMA oncology 2020;6:1416-1421

In conclusion, we are experiencing a fascinating time in oncology with targeted and highly effective treatments that are easier to administer and safer. However, this progress is accompanied by adherence problems. Studies on this topic are heterogeneous and sometimes biased, but it is clear that non-adherence is frequent. We need to understand more about the factors associated with non-adherence, which are complex and involve patient, disease, and treatment factors. Addressing adherence must be an integral part of managing neoplastic diseases.

Conclusions, the paradox of non-adherence to treatment in oncology

We are experiencing a fascinating time in oncology: Targeted and highly effective treatments, easier to administer and safer

However, this is associated with adherence problems

Studies are heterogeneous, some of them biased, but nonadherence is frequent

The causes of nonadherence are complex, involving patient, disease, and treatment factors

Data on adherence must be considered and addressed with the patient. Strategies to improve adherence must be part of the management of neoplastic diseases

Consequences of non-adherence to narrow therapeutic index drugs

Depending on its intensity and the context in which it occurs, a single seizure can have profound social and medical consequences for patients, significantly impacting their quality of life. For medications with narrow therapeutic indices, even a single missed dose can trigger a seizure and lead to preventable adverse events.

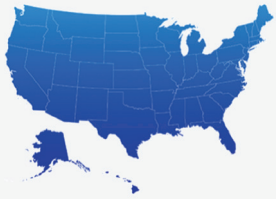
During the a:care Congress 2022, Prof. Pavel Klein highlighted the substantial costs associated with non-adherence to anti-seizure medication and the limited flexibility that narrow therapeutic indices offer for adherence. He emphasized the double burden of this healthcare challenge and underscored the critical need for clinicians to support patients in their adherence efforts.

Epilepsy affects about 1% of the global population, roughly 65 to 70 million people. In the US, there are about 3.5 million people with epilepsy, with approximately 150,000 new cases each year.

Epilepsy

~1% of world population

65 million
people worldwide suffer from epilepsy[1]



3.4 million people in the US have epilepsy, with **150,000 new cases** per year[1,2]

1. Mehndiratta MM., Wadhai SA. International Epilepsy Day - A day notified for global public education & awareness. Indian J Med Res. 2015, 141: 143-144.
2. Centers for Disease Control and Prevention website: Epilepsy Data and Statistics | CDC – visited on 2nd September 2022

Let us focus on drugs with a narrow therapeutic index. These drugs have a narrow range between too low a dose, which lacks efficacy, and too high a dose, which causes toxicity. This is particularly true for anti-seizure medications, previously known as antiepileptic drugs, where the therapeutic range is often very narrow.

Missing a dose can quickly put a patient into the sub-therapeutic range, leading to seizures.

Here are some examples of anti-seizure medications with short half-lives: levetiracetam, lamotrigine, carbamazepine, valproic acid, lacosamide, oxcarbazepine, topiramate, and brivaracetam, with half-lives ranging from 7–17 h. Older medications like phenytoin and phenobarbital have longer half-lives of 20–24 h. Some newer medications, such as zonisamide (50–70 h), perampanel (105 h), and cenobamate (60 h), have very long half-lives.

Narrow therapeutic index drugs

- Have low dose/blood level range of efficacy without toxicity
- Too low a dose: Lack of efficacy; too high a dose: Toxicity
- Antiepileptic drugs (AEDs) = Antiseizure medications (ASMs): A narrow range between too low and too high
- Missing medication may result in uncontrolled disease/seizures, because there is little margin for error i.e., in a patient with epilepsy, missing medications may result in seizure
- With ASMs with short half life, **missing a single dose may result in seizure**[1]

ASM half life: Short	ASM half life: Longer	ASM half life: Very long
Levetiracetam: 7-8 hours Lamotrigine: 12 h Carbamazepine: 12-17 h Valproic acid: 6-17 Lacosamide 7-9 h Oxcarbazepine: 8-11 h Topiramate: 7-9 h Brivaracetam: 7-9 h	Phenytoin: ~20 h Phenobarbital: ~ 24 h	Zonisamide: ~50-70 h Perampanel: 105 h Cenobamate: 60 h

1. Cramer JA, Yan T, et. al. Risk of hospitalization among patients with epilepsy using long versus short half-life adjunctive antiepileptic drugs. Epilepsy Behav. 2020; 102:106634

Non-adherence to anti-seizure medications differs from non-adherence to other medications, like statins, because seizures are paroxysmal disorders. Antiseizure medications prevent the spread of an electrical event in the brain, which, if uncontrolled, can lead to a seizure.

Seizures can result in catastrophic, life-changing consequences, including loss of awareness, job loss, car accidents, injuries, and even death. Missing a single dose can result in loss of seizure control and the aforementioned consequences.

Why does non-adherence with antiseizure medications (ASMs) differ from non-adherence with other medications?

- Seizures are a paroxysmal disorder
- Antiseizure medications prevent spread of brief, spatially confined electrical instability to adjacent brain with longer duration, i.e., a seizure
- Seizure is a sudden loss of control of motor activity or behavior that can result in catastrophic, life changing consequences
  - Loss of awareness, loss of job
  - Car accidents, loss of driving
  - Injury
  - Seizure continuation, i.e., status epilepticus, with high mortality
  - Death (e.g., during seizure or after seizure, with sudden unexplained death in epilepsy, drowning)
- Missing a single ASM dose may result in loss of seizure control, seizure and the above consequences

Hovinga CA, Asato MR, et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: survey of patients with epilepsy and physicians. Epilepsy Behav. 2008;13(2):316-22

Here are a few examples from Prof. Klein's practice:

A 31-year-old woman with cryptogenic right temporal lobe epilepsy started having seizures at age 28. She had focal seizures with bilateral tonic-clonic seizures, a normal examination, and a normal MRI. She was on levetiracetam 2,000 mg/day without side effects. After forgetting her medication for 2 days, she had two seizures at work, resulting in hospitalization, intubation, and ICU admission for 2 days. She ultimately lost her job.

A 40-year-old man with idiopathic generalized epilepsy had bilateral tonic-clonic seizures since his teens. He was a bodybuilder and personal fitness trainer on levetiracetam and primidone without side effects. Due to disease denial and belief in his strength, he was noncompliant. One night, he had a seizure while asleep, fell out of bed, and broke his spine, resulting in lumbar spinal cord compression, paraparesis, urinary and fecal incontinence, and residual paralysis and impotence after 4 months of rehabilitation.

A 36-year-old man with focal seizures secondary to a previously resected meningioma was seizure-free on carbamazepine and lamotrigine, with mild fatigue as the only side effect. He was very religious and believed that "God will take care of me." Six months after stopping his medication, he had a tonic-clonic seizure while crossing a road, was hit by a car, and suffered traumatic brain injury with intracranial hemorrhage, resulting in permanent memory issues.

These cases illustrate the catastrophic consequences of non-adherence. Estimates of non-adherence in epilepsy vary from 20% to 95%, depending on the study population, definitions of adherence, and methods of measuring non-adherence.

Methods for measuring adherence in epilepsy, like self-reports, electronic bottle tops, pharmacy records, and therapeutic drug monitoring, all have shortcomings. Self-reports and pill counts are indirect and subjective, while electronic bottle tops and pharmacy records are objective but indirect measures of drug ingestion. Therapeutic drug monitoring is both direct and objective but must account for pharmacokinetic and diurnal variability.

Incidence and mode of ascertainment of non-adherence with antiseizure medications (ASMs)

Estimates vary from 21-95%

- Different study populations, different definitions of adherence, different methods to measure non-adherence may account for the wide variability

All available methods to assess adherence are hampered by shortcomings

- Self-reports are indirect and subjective
- Pill-counts
- Electronic bottle-tops and
- Pharmacy records are objective, but indirect measures of drug ingestion
- Therapeutic drug monitoring is both direct and objective, but pharmacokinetic and diurnal variability must be taken into account

Brodtkorb E, Samsonsen C, Sund JK, Bråthen G, Helde G, Reimers A. Treatment non-adherence in pseudo-refractory epilepsy. Epilepsy Res. 2016;122:1-6

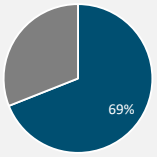
A study in Scotland found that 69% of children under 16 had at least 10% non-compliance with their medication at some point. In the US, a study found that 39% of adults were non-adherence to the point of having 80% or less drug possession.

Non-adherence

Missing AED doses is a persistent challenge among children, adolescents, and adults

Children and adolescents <16 years

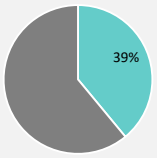
- Population-based study of patients aged <16 years with a diagnosis of epilepsy and receiving AEDs from the Tayside Children's Epilepsy Database in Scotland
- Adherence to AEDs was calculated based on medication dispensing data



Patients with an Adherence Index of <90%[1] (N=320)

Adults

- Retrospective analysis of adults in a US managed care population (aged ≥21 years) with a diagnosis of epilepsy (primary or non- primary) or non-febrile convulsions and ≥2 AED prescription claims over the 5-year study period
- AED adherence was calculated based on prescription drug claims



Patients with a Nonadherence medication possession ratio of <80%[2] (N=10,892)

The number one reason for breakthrough seizures is a missed dose
Risk for breakthrough seizures rises when plasma levels fall outside of therapeutic range[3]

1. Shetty J., Greene SA., et al. Adherence to antiepileptic drugs in children with epilepsy in a Scottish population cohort. Child Neurol. 2016;58:469-474,
2. Davis KL., Candrilli SD., et al. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. Epilepsia. 2008;49:446-454,
3. Specht U, Elsner H., et al. Postictal serum levels of antiepileptic drugs for detection of noncompliance. Epi Behav. 2003;4:487-495

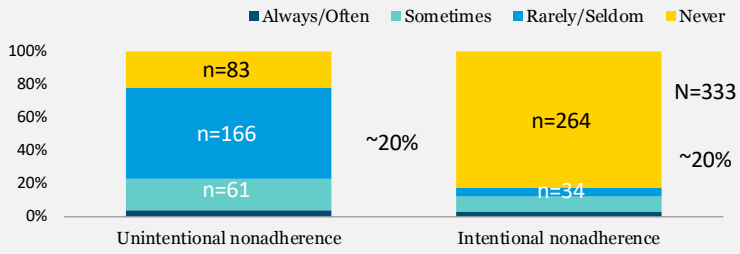
The number one reason for breakthrough seizures is a missed dose, with the risk increasing when plasma levels fall outside the therapeutic range. A study on epilepsy control showed that 40% of patients with non-refractory epilepsy had unintentional non-adherence, like forgetting to take their medication.

Incidence of non-adherence in epilepsy

Non-refractory epilepsy

- 40% unintentional non-adherence
- 30% intentional non-adherence[1]

Refractory epilepsy



- One in five rarely, sometimes, or often **consciously decide** not to take the AED as scheduled
- One in five sometimes or often **forget** to take the AEDs as scheduled

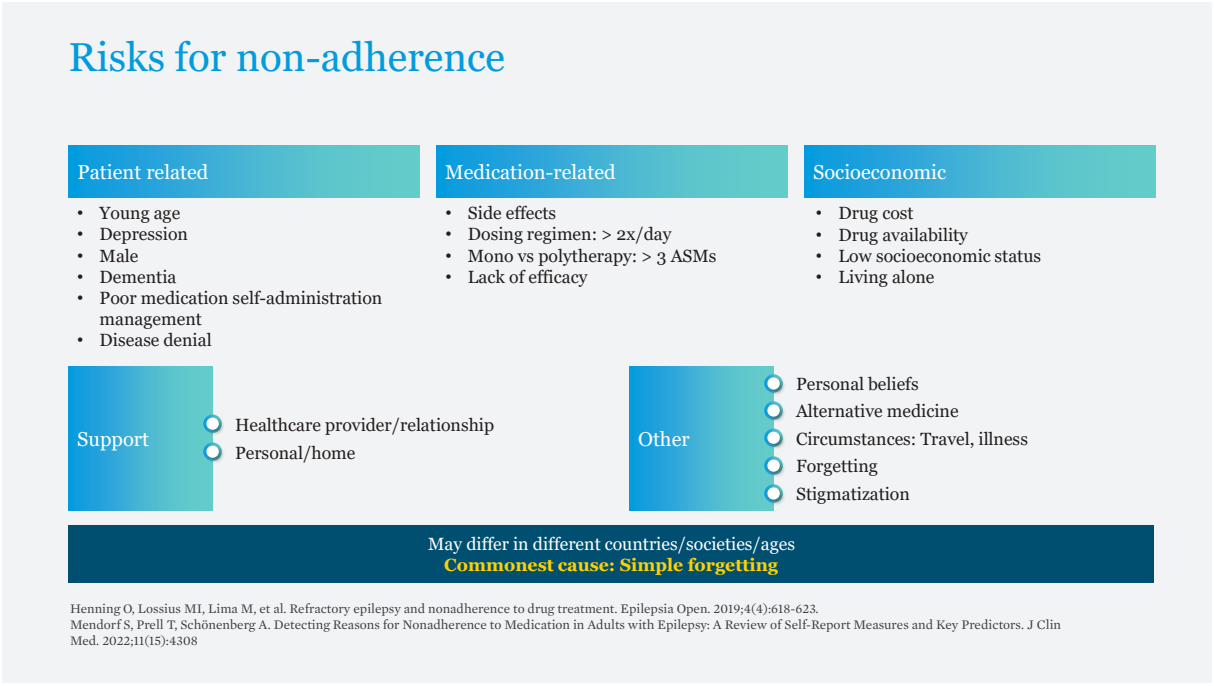
1. Henning O, Johannessen Landmark C, Nakken KO, Lossius MI. Nonadherence to treatment regimens in epilepsy from the patient's perspective and predisposing factors: Differences between intentional and unintentional lack of adherence. Epilepsia. 2019;60(5):e58-e62,
2. Henning O, Lossius MI, Lima M, et al. Refractory epilepsy and nonadherence to drug treatment. Epilepsia Open. 2019;4(4):618-623

Thirty percent of patients exhibited intentional non-adherence, which is quite astonishing. These patients deliberately chose not to take their medications, similar to what has been observed in studies on diabetes and statins.

On the right side of the figure, we see patients with refractory epilepsy. The bright yellow represents patients who always take their medications, while the various shades of blue indicate patients who, at some point, either frequently or less frequently, do not adhere to their medication regimen. Unintentional non-adherence accounts for almost 80% of these patients, with 20% frequently or always missing their medications.

Intentional non-adherence, where patients choose not to take their medications on purpose, is seen in 20% of patients with uncontrolled epilepsy. These startling numbers present a significant challenge in ensuring effective treatment.

The risk factors for non-adherence are similar to those discussed in the previous chapters. Patient-related factors include young age, a sense of invincibility, depression, male gender, dementia, poor medication self-management, and disease denial. Medication-related factors include side effects, dosing regimens requiring more than twice-daily administration, polytherapy, and lack of efficacy.



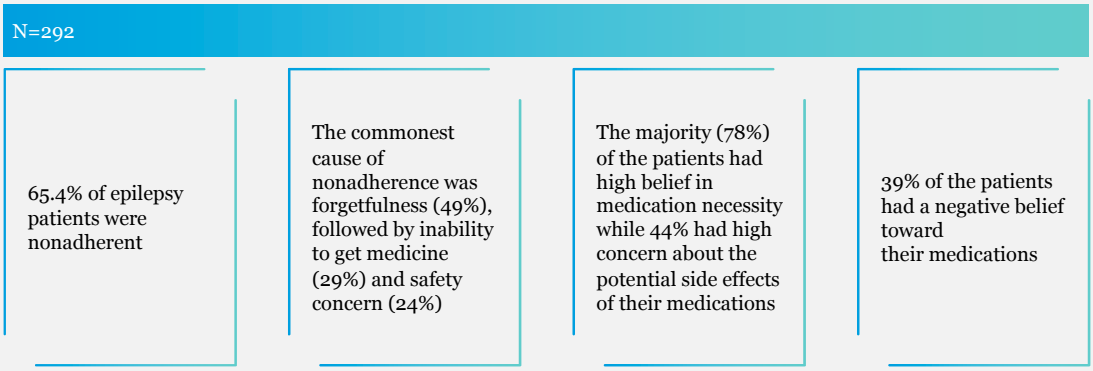
Henning O, Lossius MI, Lima M, et al. Refractory epilepsy and nonadherence to drug treatment. Epilepsia Open. 2019;4(4):618-623.
Mendorf S, Prell T, Schönenberg A. Detecting Reasons for Nonadherence to Medication in Adults with Epilepsy: A Review of Self-Report Measures and Key Predictors. J Clin Med. 2022;11(15):4308

Socioeconomic factors such as drug costs, availability, low socioeconomic status, and living alone also play a role. Support systems are crucial, and HCP relationships, as well as personal and home support, are very important. Other factors include personal beliefs about the worth of the medication and the medical system, belief in alternative medicines, circumstances like travel or

intercurrent illness, forgetfulness, and stigmatization, which may vary across different countries, societies, and ages. The most common cause, however, is simple forgetfulness.

A study from Ethiopia involving almost 300 patients with epilepsy found that 65% were non-adherence, a staggering number. The most common cause of non-adherence was forgetfulness (about 50%), followed by the inability to obtain medication (30%) and safety concerns (24%). Most patients (almost 80%) had a high belief in the necessity of medication, but a significant proportion (45%) were concerned about side effects. Additionally, 39% had a negative belief towards their medications, reinforcing points made in previous talks.

Risks for non-adherence: Ethiopia



Comorbidity, seizure in the last 3 months, low medication necessity, high medication concern belief, and negative medication belief were predictors of medication non-adherence

Niriayo YL, Mamo A, Gidey K, Demoz GT. Medication Belief and Adherence among Patients with Epilepsy. Behav Neurol. 2019;2019:2806341

Comorbidities in the last 3 months, low perceived necessity of medication, higher concern about side effects, and negative beliefs about medication predicted non-adherence.

Another study from the University of Cincinnati evaluated adherence in 124 children aged 2–12 with newly diagnosed epilepsy using electronic monitors. It found that 58% of patients had persistent non-adherence during the 6 six months of therapy. Socioeconomic status was the sole predictor of whether a patient would be adherent or non-adherence.

Risks for non-adherence: Children

University of Cinncinatti
124 children aged **2-12** with newly diagnosed epilepsy
Objective adherence measures using electronic monitors

58% Had persistent non-adherence during the first 6 months of therapy

26%	13%	13%	7%
Mild non-adherence	Moderate non-adherence	Severe early non-adherence	Severe delayed non-adherence

Adherence pattern for most patients was established in the first month of therapy
Socioeconomic status was the sole predictor

Modi AC, Rausch JR, Glauser TA. Patterns of nonadherence to antiepileptic drug therapy in children with newly diagnosed epilepsy. JAMA. 2011;305(16):1669-1676.

In a study of 661 patients, 71% reported missing doses, and 45% reported having a seizure after a missed dose at some point during treatment. Seizures are a common consequence of non-adherence in patients with epilepsy and medications with a narrow therapeutic index.

Consequence of ASM non-adherence

Seizures!

N=661, postal survey

Dose omissions were reported by 71%

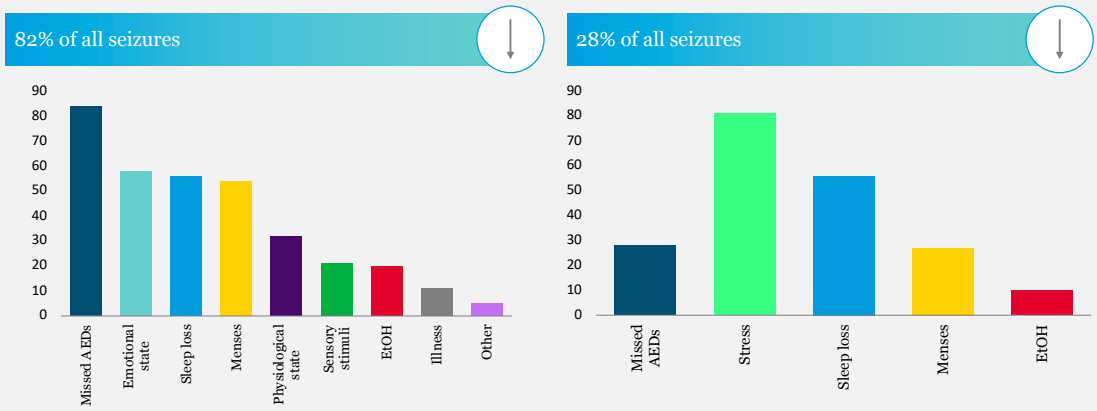
45% of patients reported a seizure after a missed dose at some time during treatment

Cramer JA, Glassman M, Rienzi V. The relationship between poor medication compliance and seizures. Epilepsy Behav EB. 2002;3(4):338-342.

Several studies have examined the triggers for breakthrough seizures in patients with established epilepsy. A study from Yale in the 1980s found that missed anti-seizure medication was the most common cause of breakthrough seizures (82%), followed by emotional state and sleep deprivation

(60% each). A similar study at Georgetown found that 28% of breakthrough seizures were due to non-adherence, with stress and sleep loss also being significant factors.

Non-compliance is a common trigger of seizures in epilepsy



Mattson RH, Adv Neurol 1991;55:453-60
Klein P et al. Epilepsia 2000, 41; (Suppl. 7):S112

The consequences of seizures include medical issues such as injury during seizures, status epilepticus, and increased mortality; economic impacts like increased hospitalizations and ER visits; and psychosocial effects such as loss of driving privileges, job loss, impact on relationships, and self-esteem. Non-adherence is the leading cause of status epilepticus in people with epilepsy and is clearly associated with sudden unexplained death in epilepsy.

Consequences of seizures

Medical	Medico-economic	Psychosocial
Seizure breakthrough	Hospital admissions	Driving
Injury, including head injury	ER visits	Job loss
Status epilepticus	$ cost	Marriage/relationship
Mortality		Self-esteem

Non-adherence is the leading cause of status epilepticus in people with epilepsy
There is clear association with sudden death (SUDEP)

A large study by Ed Faught evaluated the consequences of non-adherence to anti-seizure medication in about 34,000 adult patients between 1997 and 2006. Using the medication possession ratio to evaluate adherence, it found that non-adherence patients had over a threefold higher hazard ratio of dying compared to adherent patients.

Consequences of ASM non-adherence: Medical

- N=33,658 Medicaid adult epilepsy patients, 1997-2006
- Medication possession ratio was used to evaluate adherence, with MPR < 0.8 defined as non-adherence
- Non-adherence was associated with an >3x increased risk of mortality compared to adherence
- Periods of non-adherence were associated with a higher incidence of ED visits (RR = 1.5), hospital admissions (RR = 1.9), MVA injuries (RR = 2.1), and fractures (RR = 1.2) than periods of adherence

Mortality in non-adherence with ASMs

	Hazards Ratio	p Value
Adherence status		
Adherent	Reference	
Nonadherent	3.32	<0.001
Untreated	0.92	0.067

Serious clinical event in non-adherence with ASMs

ED=emergency department; IRR=incidence rate ratio; MVA=Motor vehicle accident

	Non-adherent quarters (32,365 patient-years)		Adherent quarters (91,678 patient-years)	
Event	**No. of events**	**Incidence rate**	**No. of events**	**Incidence rate**
ED visits	47,859	1.48	90,562	0.99
Hospitalizations	43,167	1.34	65,913	0.72
MVA injuries	349	0.011	477	0.005
Fractures	17,419	0.54	41,039	0.45
Head injuries	11,942	0.37	46,213	0.50

Faught E, Duh MS, Weiner JR, Guérin A, Cunnington MC. Nonadherence to antiepileptic drugs and increased mortality: findings from the RANSOM Study. Neurology. 2008;71(20):1572-1578

The right side of the slide above shows other consequences evaluated at 3-month intervals, comparing non-adherence quarters to adherent quarters. Emergency room visits are higher during non-adherence quarters. Hospitalizations are also higher during these periods, with an increased odds ratio of approximately 1.5. Motor vehicle injuries are about twice as likely during non-adherence periods.

These factors significantly impact patient healthcare.

Regarding the economic consequences, the study evaluated 3-month intervals of non-adherence versus adherence. For inpatients, there was a higher incidence of hospitalization, inpatient days, and emergency room visits. The cost increases related to serious outcomes, including inpatient costs, were higher for non-adherence, with roughly USD 4,300 additional costs per quarter. Emergency room utilizations added approximately $300 in additional costs per quarter. Thus, the cost of delivering care rises with non-adherence, while there is a decline in pharmacy and outpatient care costs for obvious reasons.

Consequences of ASM non-adherence: Economical

AED non-adherence was associated

- With higher incidence of hospitalizations, inpatient days, and ED visits
- Cost increases related to serious outcomes, including inpatient cost ($4,320 additional cost per quarter) and ED services ($303 additional cost per quarter)

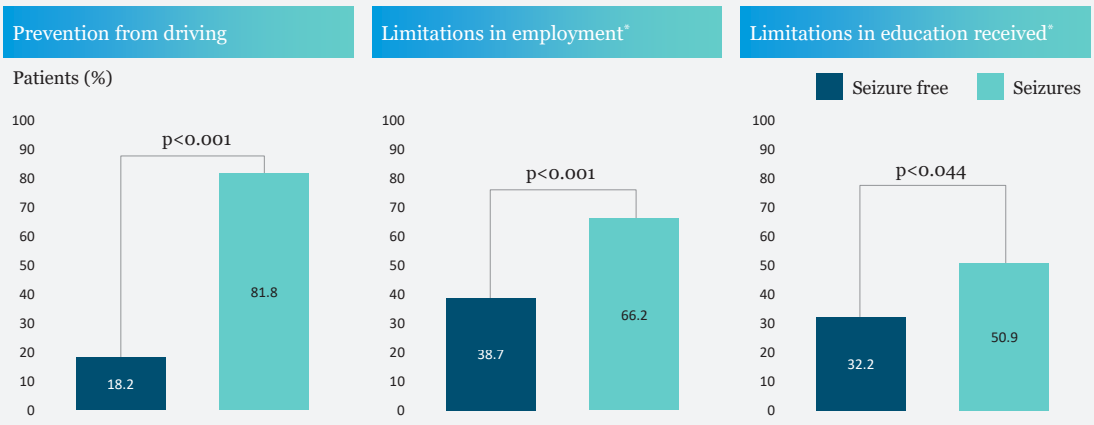
The rate during periods of nonadherence was 39% higher for hospitalizations, 76% higher for inpatient days, and 16% higher for ED visits relative to periods of adherence

	Cost associated with non-adherence with ASMS			
	Mean cost for non-adherent quarters (+SD)	Mean cost for adherent quarters (+SD)	Unadjusted incremental cost	Adjusted incremental cost
Inpatient	$1,670.57 ± $8,293	$746.14 ± $5,837	$924.43	$4,320.44
ED	$101.49 ± $1,819	$68.73 ± $3,366	$32.76	$303.44
Outpatient	$543.10 ± $1,516	$677.49 ± $1,845	-$134.39	-$75.96
Pharmacy				
• AED	$205.60 ± $313	$624.92 ± $809	-$419.32	-$187.14
• Other	$1,083.65 ± $2,158	$1,217.11 ± $2,495	-$133.47	-$280.13

Faught RE, Weiner JR, Guérin A, Cunnington MC, Duh MS. Impact of nonadherence to antiepileptic drugs on healthcare utilization and costs: findings from the RANSOM study. Epilepsia. 2009;50(3):501-509.

Additionally, there is a significant impact on the quality of life. Here are some important factors that determine the quality of life in patients with epilepsy. There was a substantial difference in driving privileges between non-adherence and adherent patients, with 82% of non-adherence patients unable to drive compared to 18% of adherent patients. Employment limitations were also notable, with 66% of non-adherence patients facing limitations compared to 39% of adherent patients. Educational limitations were significant as well, with 60% of adherent patients receiving high school, college, or post-college education compared to 32% of non-adherence patients.

Seizures reduce the quality of life



Josephson CB, Patten SB, Bulloch A, et al. The impact of seizures on epilepsy outcomes: A national, community-based survey. Epilepsia. 2017;58(5):764-771.

So, what can we do to mitigate non-adherence? There are several strategies:

- Adjust treatment to minimize patient burden. Simplify medication regimens, reduce unnecessary polytherapy, and tailor dosing to individual habits and daily routines;
- Use aids for patients with cognitive problems and memory impairment. Drug dispensers, alarms, smartphones, wristwatch alarms, social support, and regular visits from community nurses can help;
- Educate and motivate patients. Increase the frequency of outpatient visits, provide clear procedures for missed doses, involve patients in treatment decisions, and use support from epilepsy nurses and pharmacists;
- Address adverse drug reactions. Improve communication and modify treatment to minimize adverse events;
- Support patients with depression and intake barriers. Modify drug formulations and use memory aids to associate doses with daily routines;
- Consider medications with longer half-lives. These can reduce the impact of missed doses.

Mitigating against non-adherence

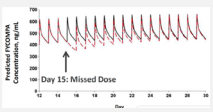
1. Adjust treatment to minimize patient burden

Methods to improve adherence to antiepileptic drug treatment

Problem areas	Interventions
Complex drug regimens	Reduction of unnecessary polytherapy and dosing frequency. Simple dosing tailored to individual habits and daily routines
Cognitive problems/memory impairment	Drug dispensers, alarms (smart phone, wrist watch). Alliance with proxies. Social support with regular visits from community nurses
Insufficient knowledge, motivation and awareness of the need for treatment. Negative attitude to pharmaceuticals	Education, increased frequency of outpatient follow-up. Clear procedures related to missed drug intake. More involvement in treatment decisions. Epilepsy nurse and pharmacist support. Telephone contacts
Adverse drug reactions	Improved communication. Treatment modification
Depressed mood	Antidepressive and cognitive treatment
Oral intake barriers (swallowing/motor and intellectual deficits/behavior/aversion to medication/intercurrent illness)	Modified drug formulations (soluble, liquid, granular, powder), as well as size and taste of tablets. Alternative routes (rectal, i.v.)

2. Memory aids: Associating doses with daily routines (toothbrushing, morning coffee), filling pill boxes

3. ASMS with long half life: reduce peak to trough level variation



ASM half life: Very long

Zonisamide: ~50-70 h

Perampanel: 105 h

Cenobamate: 60 h

Brodtkorb E, Samsonsen C, Sund JK, Bråthen G, Helde G, Reimers A. Treatment non-adherence in pseudo-refractory epilepsy. Epilepsy Res. 2016;122:1-6

For example, in the case of the previous 31-year-old patient who forgot her medication for 2 days and ended up in the ICU, Prof. Klein switched her levetiracetam to an extended-release formulation, suggested a routine to take her medication while brushing her teeth, recommended using a smartphone reminder, and added a second medication with a longer half-life for backup protection.

Real life experience: Follow up

31 YO W with cryptogenic right temporal lobe epilepsy stating aged 28, with focal to bilateral tonic clonic seizures, normal examination and MRI. Works as an accountant. Meds: Lev 2000 mg/day. No side effects. Forgot to take medication for 2 days> seizure x 2 at work> hospitalization, ICU for 2 days, lost job

Management	Change of levetiracetam from 1000 mg bid to Extended Release 2000 mg qhs	Suggested routine: take meds at night when brushing teeth	Smart phone reminder – just before bedtime	Addition of zonisamide to levetiracetam (long half life)

In conclusion, non-adherence to anti-seizure medications in patients with epilepsy is common and has diverse causes. It often leads to seizures with severe impacts on patients' lives and contributes to the healthcare burden of epilepsy.

Conclusion

- Non-adherence with antiseizure medications in patients with epilepsy is common
- Has diverse etiology
- Commonly leads to seizures with often severe impact on patients' lives
- Contributes to healthcare cost of epilepsy
- Mitigations efforts against it include supportive care; memory aids; simplification of treatment schedule; avoidance of medication/doses with side effects; and use of antiseizure medications with long half life

Behaviors and beliefs: The foundations of adherence

This chapter draws upon the sessions conducted by Prof. Rob Horne.

Why are beliefs so integral to adherence? It boils down to the information-action gap prevalent in medicine. While information is crucial for enabling adherence, merely providing more information does not ensure action. People must not only understand what they are doing and how to do it but also believe in it. The primary question we must ask is this: **How does the information we provide about medications resonate with patients' beliefs about those medications?**

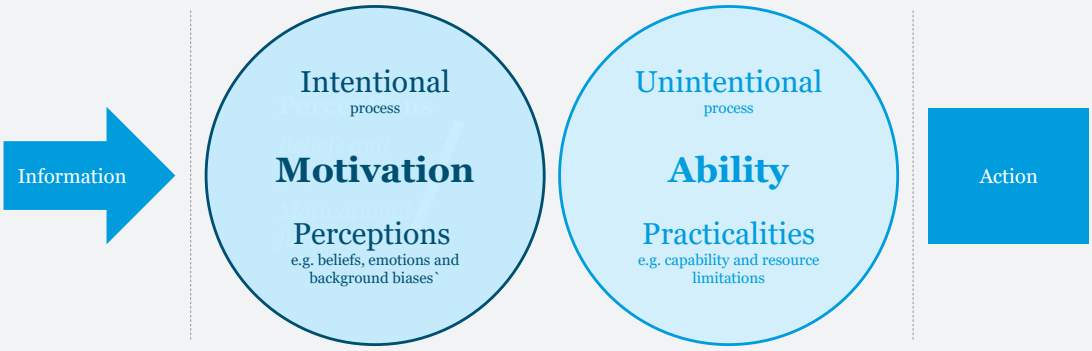
> *"The good physician treats the disease; the great physician treats the patient who has the disease"*
>
> *(William Osler)*[54]

Adherence is a multifaceted issue with numerous reasons why a patient may not take their medicine. These reasons can be distilled into two categories: they either cannot or do not want to. This simplification belies the complexity of the issue, as non-adherence can be both intentional and unintentional.

54. American college of Physicians https://www.acponline.org/about-acp/about-internal-medicine/sir-william-osler-and-internal-medicine, last accessed 12/12/2024.

The Perceptions & Practicalities Approach (PaPA)[1-2]

A framework for developing adherence support– applied in NICE Medicines Adherence Guidelines



1. Horne R. In Pharmacy Practice, 2001. Ed. by KMG Taylor & G Harding. London: Taylor & Francis [Accessed October 2021];
2. Horne, R., Cooper, V., Wileman, V., & Chan, A. (2019). Supporting adherence to medicines for long-term conditions: A perceptions and practicalities approach based on an extended common-sense model. European Psychologist, 24(1), 82–96.

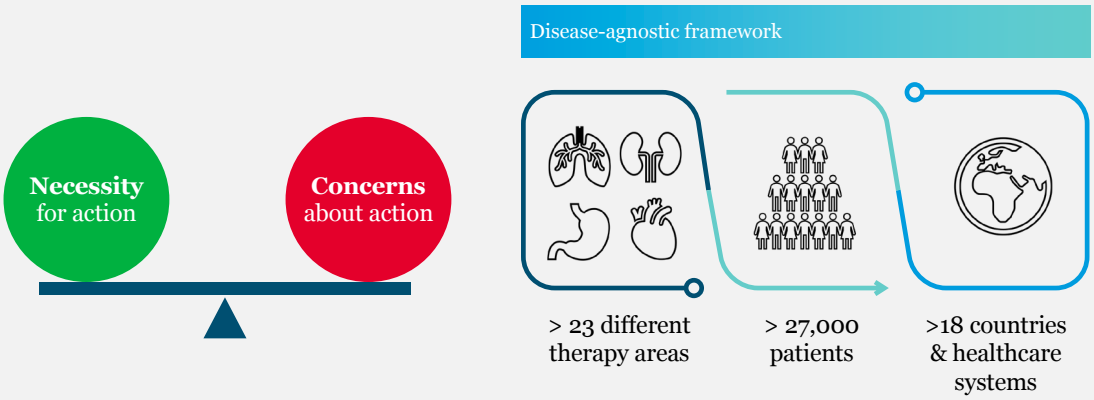
Most efforts to support adherence focus on the assumption that patients want to take their treatment but face barriers beyond their control. These are questions of ability–patients have the desire but lack the means. Barriers can include forgetfulness, complex regimens, lack of understanding, financial constraints, or difficulty establishing a routine. These practicalities are real obstacles to adherence, and while our interventions often address these issues, they do not always address the underlying motivations.

For many patients, non-adherence is not a matter of inability but rather a lack of desire. To understand this, we must examine the beliefs, emotions, and biases that influence our decisions about medications. Few interventions consider these motivational factors, yet they are crucial for anyone prescribed medication.

The challenge is to tailor support to the unique mix of perceptual and practical barriers relevant to each individual. To do this effectively, we must also acknowledge environmental factors, such as the availability of treatment, support systems, co-payments, and reminders, which can be external or internal triggers.

Ultimately, our framework of motivation and ability serves as a shorthand for understanding the patient's perspective. Let us explore the key beliefs influencing adherence. Patients can hold a variety of beliefs, but to improve adherence, we do not need to delve into their psychology. Instead, we can rely on a simple framework known as the necessity-concerns framework, which identifies two groups of beliefs fundamental to adherence.

Understanding treatment beliefs: The necessity-concerns framework (NCF)[1,2]



1. Foot H, La Caze A, Gujral G, Cottrell N. The necessity-concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. Patient Educ Couns. 2016;99(5):706-17;
2. Horne R, Chapman SC, Parham R, Freemantle N, Forbes A, Cooper V. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a metaanalytic review of the Necessity-Concerns Framework. PLoS One. 2013;8(12): e80633

Firstly, necessity beliefs are not merely about believing in the treatment's benefits or effectiveness. They are the answers to two critical questions we ask ourselves when considering medication: How much do I really need to do this to achieve something important to me? And can I get away without doing it?

The reason we pose a second question is that medicines are seldom perceived as neutral or entirely beneficial. Most patients harbor some level of concern regarding the drawbacks of taking medication. Shortly, we will delve into these concerns, but it is worth noting that this framework has been thoroughly tested and validated across various therapeutic areas, patient populations, and healthcare systems worldwide. It is a disease-agnostic framework that can be applied across different illnesses and cultures to understand the key beliefs that may influence the motivation to initiate and adhere to treatment.

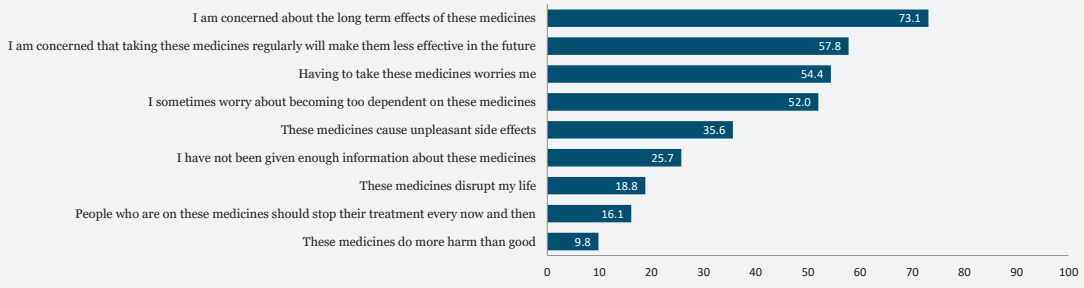
When examining concerns, it is crucial to acknowledge that they extend far beyond side effects. For instance, in a study conducted on inflammatory bowel disease in the UK, the findings, which are representative of numerous other studies in different countries and conditions, show that concerns are more widespread.[55] The graph below illustrates the percentage of respondents who agreed or strongly agreed with each listed topic.[56] For example, more than a third of patients concurred that their medicines caused unpleasant side effects. However, higher up the list, some

55. Horne R, Parham R, Driscoll R, Robinson A. Patients' attitudes to medicines and adherence to maintenance treatment in IBD Inflamm Bowel Dis. 2009;15:837–44.
56. Cooper, V. et al. Perceptions of HAART among gay men who declined a treatment offer: AIDS Care 14, 319-328, (2002).

concerns are even more common, such as worries about the long-term effects of medicines, the belief that regularly taken medicines might become less effective in the future, general apprehensions and aversions to taking medicines, and fears of becoming too dependent.

Specific concerns about medicines: Beyond side-effects

N = 1871 (a survey of 1 in 10 members of Crohn's and Colitis UK)[1,4]



Other concerns

- Personal meaning of medication: Impact on sense of self[2]
- Symbol of lack of faith[3]

1. Horne R, Parham R, Driscoll R, Robinson A. Patients' attitudes to medicines and adherence to maintenance treatment in IBD InflammBowel Dis. 2009;15:837–44;
2. Cooper, V. et al. Perceptions of HAART among gay men who declined a treatment offer: AIDS Care 14, 319-328, (2002); 3. Sherr L, Lampe FC, Clucas C, et al. Self-reported non-adherence to ART and virological outcome in a multiclinic UK study. AIDS Care 2010;22(8):939-45; 4. Speaker data.

This dependency is not akin to addiction but is often perceived as impacting how individuals view themselves and are seen by others, which can be a significant issue. Take, for example, someone who has never needed regular medication and is suddenly prescribed statins or another ongoing treatment. This person's self-perception changes; They used to see themselves as fit and healthy, but now they feel dependent on medicine for their well-being. Many patients dislike this notion and prefer to delay treatment.

Other concerns identified in our research include the possibility that medication might symbolize a lack of faith for some individuals. There are many concerns not necessarily depicted here that may act as barriers to medication adherence.

It is important to note that these concerns often operate in the background. Patients may not report them to their doctor because they fear that expressing doubts or concerns about the treatment, or admitting to not taking it, might be interpreted as a lack of trust in the clinician. Patients often hold two simultaneous beliefs: They like and trust the clinician but not the treatment. To support adherence, we must enable patients to voice these key but often concealed beliefs that act as barriers. As a reminder, the two primary beliefs are doubts about the personal need for the treatment and concerns about its potential downsides.

There may be disconnects between patient and HCP concerns

Mismatch between patient and clinician ratings of 'problems'?

Patients rank 'tolerability' side effects as severe e.g., effect on family or partner, loss of hair, fatigue and nausea and vomiting[1,2]

Experience of subjective side effects reduces adherence[3]

1. Sun CC, Bodurka DC, Weaver CB, Rasu R, Wolf JK, Bevers MW, Smith JA, Wharton JT, Rubenstein EB. Rankings and symptom assessments of side effects from chemotherapy: insights from experienced patients with ovarian cancer. Support Care Cancer. 2005 Apr;13(4):219-27;
2. Bernard M, Brignone M, Adehossi A, Pefoura S, Briquet C, Chouaid C, Tilleul P. Perception of alopecia by patients requiring chemotherapy for non-small-cell lung cancer: a willingness to pay study. Lung Cancer. 2011 Apr;72(1):114-8;
3. Fontein DB, Nortier JW, Liefers GJ, Putter H, Meershoek-Klein Kranenbarg E, van den Bosch J, Maartense E, Rutgers EJ, van de Velde CJ. High non-compliance in the use of letrozole after 2.5 years of extended adjuvant endocrine therapy. Results from the IDEAL randomized trial. Eur J Surg Oncol. 2012 Feb;38(2):110-7

There is also frequently a mismatch between how patients view the treatment and how they perceive side effects. For instance, doctors may prioritize clinically significant side effects, like those revealed through liver function tests or blood tests. However, patients are often more concerned with the subjective side effects they experience, such as headaches, nausea, or hair loss, which may be more impactful to them than clinically severe but less noticeable side effects.

Understanding the patient's perspective is essential. They do not arrive as a blank sheet upon which we can simply write a prescription. Instead, they come with preexisting ideas about the illness and its treatment. So, where do these beliefs about the necessity of treatment and concerns originate?

The key principle is the idea of "common sense fit"–treatments need to make sense to the patient.[57,58,59] To perceive a need for treatment, there must be a good fit between the patient's ideas of the problem, the illness, and the solution, the treatment. For many patients, this fit is not apparent, and merely explaining how the medicine works or how to take it is not sufficient. We need to narrate the treatment in a way that overcomes common sense defaults–prevalent ways of thinking about illness and treatment that, if unaddressed, may lead to beliefs that act as barriers to adherence.

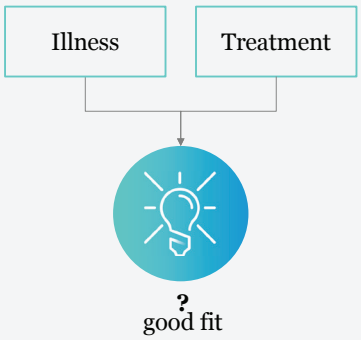
57. Horne, R., & Weinman, J. (2002). Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. Psychology & Health, 17(1), 17–32.
58. Halm EA, Mora P, Leventhal H. No symptoms, no asthma: the acute episodic disease belief is associated with poor self-management among inner-city adults with persistent asthma. Chest. 2006 Mar;129(3):573-80.
59. Hall S, Weinman J, Marteau TM. The motivating impact of informing women smokers of a link between smoking and cervical cancer: the role of coherence. Health Psychol. 2004 Jul;23(4):419-24.

Common-sense fit and common-sense defaults

Patients need to see a common-sense **fit** between their understanding of the problem (the illness) and the proposed solution (the treatment)[1-3]

For many patients that fit is not clear

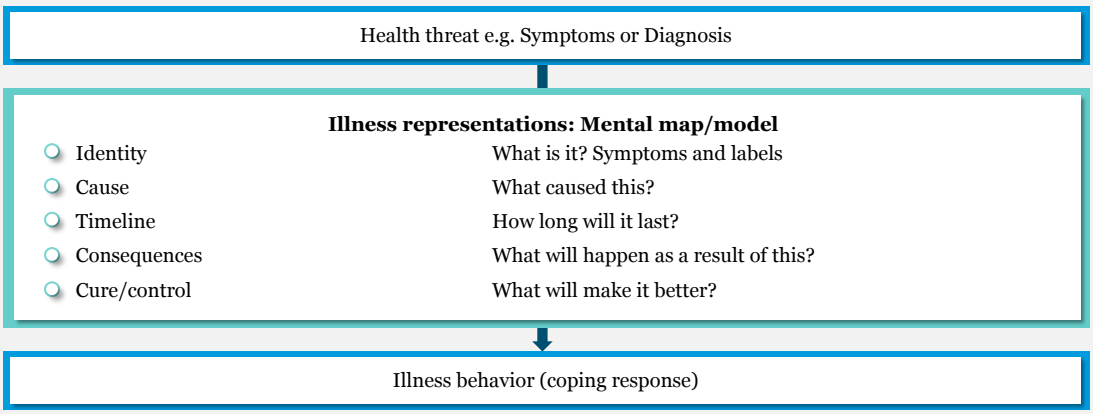
Just telling patients how the medicine works or how to take it is not enough- we need to tell 'the story' in a way that overcomes 'common-sense defaults' in the way that many people think about medicines



1. Horne, R., & Weinman, J. (2002). Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. Psychology & Health, 17(1), 17–32.
2. Halm EA, Mora P, Leventhal H. No symptoms, no asthma: the acute episodic disease belief is associated with poor self-management among inner-city adults with persistent asthma. Chest. 2006 Mar;129(3):573-80.
3. Hall S, Weinman J, Marteau TM. The motivating impact of informing women smokers of a link between smoking and cervical cancer: the role of coherence. Health Psychol. 2004 Jul;23(4):419-24.

Let us consider some examples of common sense defaults that affect patients. One critical aspect is how people conceptualize illness. We need to ask questions about the illness that resonate with us and guide our decisions regarding treatment. These are five detailed questions that all patients tend to consider when evaluating their treatment options.[60,61]

Leventhal's common-sense model: Illness perceptions

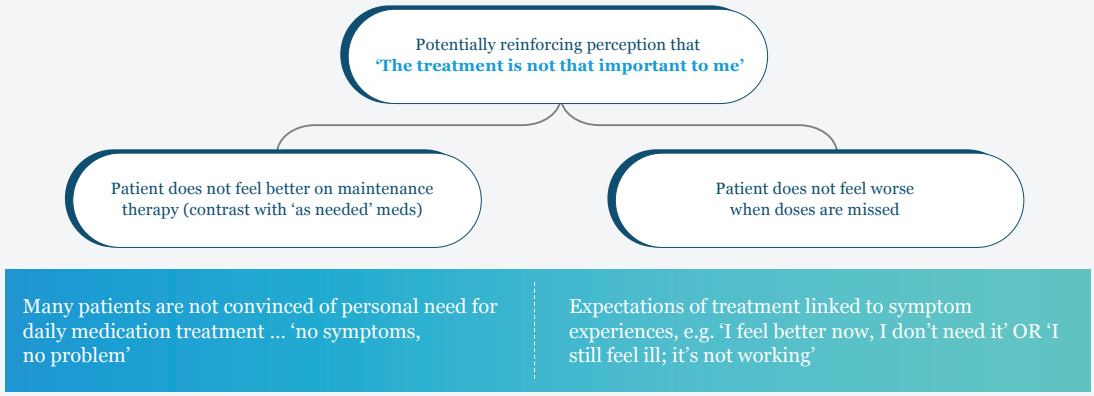


The Common-Sense Model of Self-Regulation (CSM): A Dynamic Framework for Understanding Illness Self-Management. Psychology & Health, 18 (2), 141-184; Leventhal H, Phillips LA, Burns E. Journal of Behavioral Medicine 2016; 39(6): 935-46; Petrie K, Weinman J, Sharpe N, Buckley J. Brit Med J 1996; 312: 1191-4

60. Hagger, M. S., & Orbell, S. (2003). The Common-Sense Model of Self-Regulation (CSM): A Dynamic Framework for Understanding Illness Self-Management. Psychology & Health, 18 (2), 141-184.
61. Leventhal H, Phillips LA, Burns E. Journal of Behavioral Medicine 2016; 39(6): 935-46.

It is important to note that patients often have their own understanding of their illness. This understanding may seem logical to them, even if it conflicts with medical knowledge. A typical example is the belief that "no symptoms mean no problem." Patients might think they only need treatment when they feel unwell and can stop when they feel better. While this logic is understandable, it is medically inaccurate for many chronic conditions.[62,63] Patients may not feel better on maintenance doses, and skipping doses does not necessarily make them feel worse, which can reinforce the misconception that the treatment is not crucial.

Necessity beliefs common-sense default: No symptoms, no problem![1-2]



1. Horne, R., & Weinman, J. (2002). Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. Psychology & Health, 17(1), 17–32;
2. Halm EA, Mora P, Leventhal H. No symptoms, no asthma: the acute episodic disease belief is associated with poor self-management among inner-city adults with persistent asthma. Chest. 2006 Mar;129(3):573-80

Other common misconceptions include the belief that chemicals are bad and natural products are good, that medicines accumulate in the body over time, that more potent medicines are more harmful, and that doctors overprescribe due to industry pressure, which is informed by a general mistrust of the pharmaceutical industry.

62. Horne, R., & Weinman, J. (2002). Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. Psychology & Health, 17(1), 17–32.
63. Halm EA, Mora P, Leventhal H. No symptoms, no asthma: the acute episodic disease belief is associated with poor self-management among inner-city adults with persistent asthma. Chest. 2006 Mar;129(3):573-80.

Other common – sense defaults

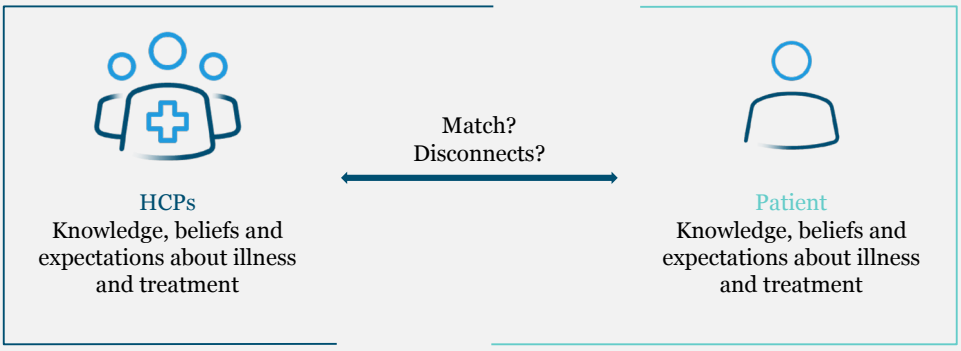
- Chemical bad, natural good
- Medicines accumulate in the body over time
- More powerful medicines are more harmful
- Suspicion of the pharmaceutical industry
- If I express a doubt or concern about the treatment the doctor will interpret it as a doubt in them

Horne Invited paper https://acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-useevidence [Accessed October 2021]

There is also the concern that expressing doubts about treatment might be interpreted by the doctor as a lack of trust.

Disconnects drive the behavioral gap

The fundamental cause of non-adherence is often a disconnect between beliefs and expectations of prescriber and patient[1,2]



1. Horne R, et al. PloS one 2013; 8(12): e80633; 2. Horne R, et al. Patient Preference and Adherence 2018; 12: 1099.

Addressing non-adherence involves a three-step process: communicating a common-sense rationale for the necessity of treatment, considering the patient's perspective; eliciting and addressing any concerns; and making the treatment regimen as simple and convenient as possible. Digital tools now offer support for clinicians, enhancing the consultation process and effectively changing beliefs about the necessity of treatment and concerns.

3-step perceptions and practicalities approach (PAPA)[1]

A 'no-blame' approach to facilitate an honest and open discussion to address

Perceptions

- Communicate a 'common-sense rationale' for why the treatment is needed – Taking account of the patients perceptions of the illness and symptom expectations. e.g. 'Why should I take this stuff when I feel well and/or my illness is controlled'
- Elicit and address CONCERNS about potential adverse consequences of the treatment – including support with side-effect management

Practicalities

- Tailor a convenient regimen and address practical barriers – Make it as easy as possible

Necessity

Concerns

Practicalities

1. Horne, R., Cooper, V., Wileman, V., & Chan, A. (2019). Supporting adherence to medicines for long-term conditions: A perceptions and practicalities approach based on an extended commonsense model. European Psychologist, 24(1), 82–96

Practicalities can be addressed through various proven techniques. The good news is that any effort to improve adherence is beneficial. The first level involves addressing practicalities to make treatment as easy as possible.

Intervention components: Practicalities

Forgetting

- Pillbox organizer
- Text reminders
- Provide feedback on adherence

Environmental/ contextual barriers

- Identify environmental/ contextual barriers
- Develop and review action plans (when, where and how to take treatment)
- Link behavior with prompts and cues

Lack of social support

- Identify potential sources of support
- Encourage use of support

1. Horne R. Compliance adherence & concordance In: Taylor K & Harding G, editors. Pharmacy Practice 2nd ed: Routledge; 2015;
2. NICE. Clinical guideline 76: Medicine adherence: involving patients in decisions about prescribed medicines and supporting adherence. London: National Institute for Health and Clinical Excellence; 2009. [Accessed October 2021];
3. Horne R, et al. Supporting Adherence to Medicines for Long-Term Conditions: A Perceptions and Practicalities Approach Based on an Extended Common-Sense Model. European Psychologist 2019 24: 82-96

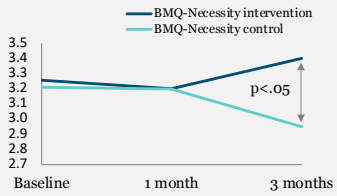
The second level includes considering key beliefs about necessity and concerns, which has a greater effect. The third level involves tailoring the approach to the individual's specific perceptions and practicalities, which is even more effective, increasing the program's efficacy and value as we move up the pyramid.

Changing necessity beliefs and concerns

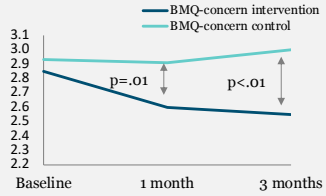
Tailoring support to address the patient's belief barriers can improve adherence[1]

In a study with inflammatory bowel disease, digital adherence support **PERSIGNIA™** reduced adherence barriers ($p<0.01$) and reported nonadherence ($p<0.05$)[2]

BMQ-necessity



BMQ-concerns



As demonstrated in the graphs

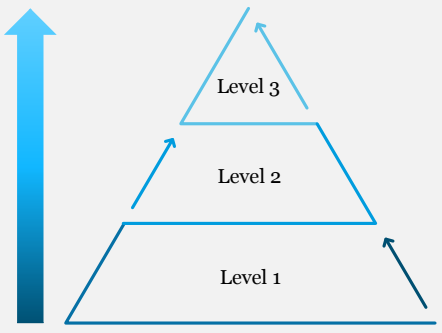
Without PERSIGNIA™, and left unchecked, necessity beliefs REDUCE over time and concerns stay the same, leading to non-adherence

With PERSIGNIA™ necessity beliefs INCREASE over time, and concerns are REDUCED – safe-guarding adherence

1. Petrie KJ, Perry K, Broadbent E, Weinman J. A text message programme designed to modify patients' illness and treatment beliefs improves self-reported adherence to asthma preventer medication. British journal of health psychology 2012; 17(1): 74-84;
2. Chapman S, Sibelli A, St-Clair Jones A, Forbes A, Chater A, Horne R. Personalised adherence support for maintenance treatment of inflammatory bowel disease: A tailored digital intervention to change adherence-related beliefs and barriers. Journal of Crohn's and Colitis. 2020;14(10):1394-404

PaPA-based interventions[1] can improve adherence and be cost effective[2-4]

Increasing program efficacy & value



Tailored PaPA
Support tailored to address individual perceptions and practicalities

Perceptions
Take account of key beliefs influencing
Motivation

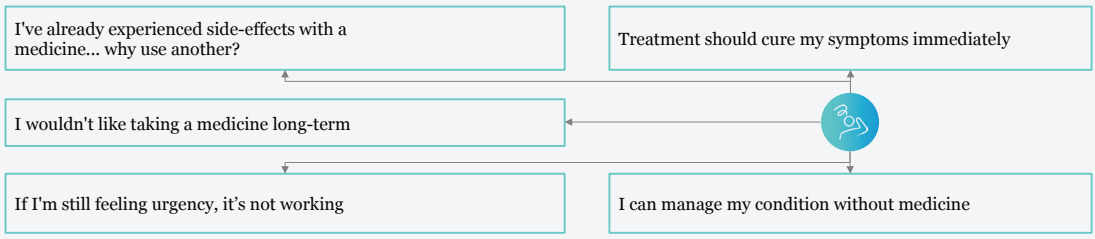
Practicalities
Simplify regimen packaging
Monitoring
Text reminders
Ability

1 Horne R, Cooper V, Wileman V, Chan A. European Psychologist 2019; 24(1): 82-96;
2. Clifford S, Barber N, Elliott R, Hartley E, Horne R.. Pharm World Sci. 2006;28(3):165-70;
3. Elliott RA, Barber N, Clifford S, Horne R, Hartley E.. Pharm World Sci. 2008;30(1):17-23; 4.Odeh M, Scullin C, Fleming G, Scott MG, Horne R, McElnay JC.. Br J Clin Pharmacol. 2019;85(3):616-25

In summary, patients come with preexisting ideas and beliefs about their condition and treatment. These are often logical from their perspective but may be incorrect medically. Understanding and addressing these beliefs and expectations is crucial for improving adherence.

Take home messages

Recognise that the patient does not come as a 'blank sheet' that we can write the prescription instructions on	These are usually logical, common-sense interpretations of the condition and treatment; they make sense from the patient's perspective, but are often mistaken from a medical perspective
Patients come with pre-existing ideas about their condition and with beliefs and expectations of treatment	Beliefs and expectations drive adherence/non-adherence



"Don't remind me to take my medication": Exploring behaviors behind medication non-adherence

> *"Patient adherence should be acknowledged as a critical healthcare issue, and a multidisciplinary approach to education and management in this area should be established"*
>
> *(Prof. Weinman)*

To raise awareness on the need to better manage adherence challenges, Prof. Weinman describes behavioral techniques for anticipating, preventing, and detecting non-adherence.

Ultimately, it is about individual patients and their behavior. Adherence is a behavior, and one common explanation for non-adherence is forgetfulness. Patients often say they forgot to take their medication.

But is this the whole story, or is there more to it? Hopefully, the picture is much bigger.

There are four key areas to cover:

- The challenge of the statement is non-adherence primarily about forgetting?
- The causes and reasons behind non-adherence, supported by evidence at the individual behavioral level.

- Practical solutions to the questions: What are the barriers to implementing these solutions in routine clinical practice and why is it not happening despite our understanding of non-adherence?
- Practical tips on managing non-adherence in day-to-day consultations.

Let us go back in time. Early explanations for non-adherence were based on the idea that patients did not understand their illness or treatment, leading to forgetfulness. Early interventions focused on providing more information and reminders, such as pillboxes. Today, many apps are based on the concept of reminding people, but do they work?

Early explanations of non-adherence

Early theories based on idea that non-adherence was result of poor communication & subsequent effects on patient understanding and memory

Early interventions mainly based on information provision, and/or reminders and these are still used. Most adherence apps are still based on reminders

Do these work? Only in those who are motivated

Choudhry NK, et al. Effect of reminder devices on medication adherence: The remind randomized clinical trial. JAMA intern med. 2017;177(5): 624-631. Speaker input.

The short answer is that reminders only work if the person is motivated to take their medication. Many people are not in that motivated state, so reminders alone are not effective.

Choudhry and colleagues, who systematically examined the effectiveness of different reminder devices across various chronic diseases, started with the idea that forgetfulness was a major contributor to non-adherence and tested three different reminder devices. The study involved over 50,000 people, divided into four groups: one with standard care and three with different reminder devices. All patients had low adherence levels at the start.

Do reminders work?

JAMA Internal Medicine | Original investigation

Effect of reminder devices on medication adherence
The REMIND randomized clinical trial

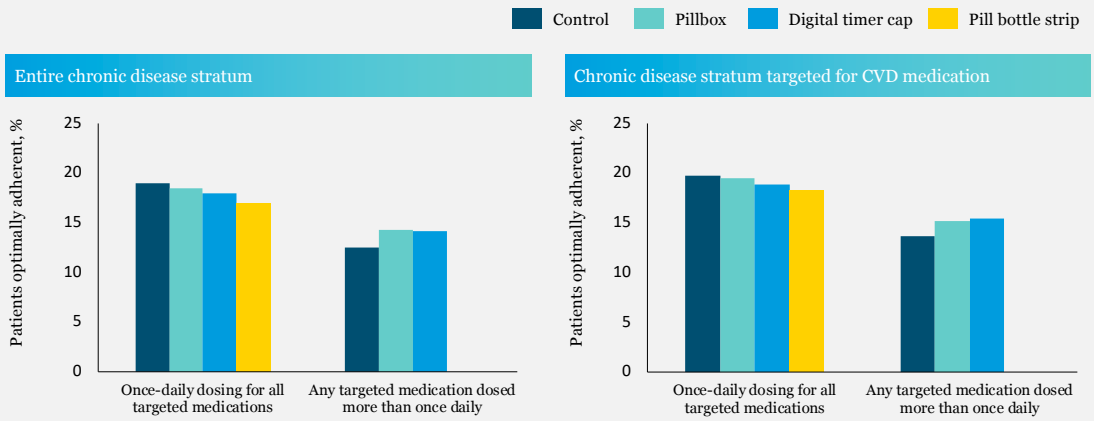
Niteesh K. Choudhry, MD, PhD; Alexis A. Krumme, MS; Patrick M. Ercole, PhD, MPH; Chairman Girdish, MPH; Angela Y. Tong, MS; Nazleen F. Khan, BS; Troyen A. Brennan, MD, JD, MPH; Olga S. Matlin, PhD; William H. Shrank, MD, MSHS; Jessica M. Franklin, PhD

Importance	Forgetfulness is a major contributor to nonadherence to chronic disease medications and could be addressed with medication devices
Objective	To compare the effect of 3 low-cost reminder devices on medication adherence
Design, setting and participants	This 4-arm, block-randomized clinical trial involved 53 480 enrollees of CVS Caremark, a pharmacy benefit manager, across the United States

Choudhry NK, et al. Effect of reminder devices on medication adherence: The remind randomized clinical trial. JAMA intern med. 2017;177(5): 624-631.

The results showed that none of the reminder devices were more effective than the control group after 12 months. This was true for both single and double daily dosing. The message from this study and others like it is that **simple reminders are not the answer for non-adherence patients.**

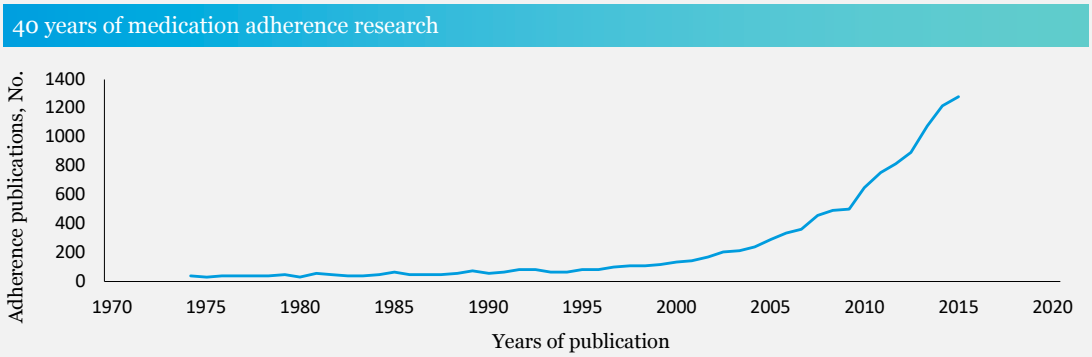
Remind trial: Results (Optimal adherence at 12 months)



Choudhry NK, et al. Effect of reminder devices on medication adherence: The remind randomized clinical trial. JAMA intern med. 2017;177(5): 624-631.

Our understanding of non-adherence has increased dramatically over the years, with a significant rise in research projects since the 1970s. There are now over 700 identified reasons for non-adherence, some more significant than others.

Adherence research over the years



Number of publications indexed in PubMed with medication adherence or compliance in the title or abstract, from 1966 to 2015

Data extracted from PubMed advanced search engine.
https://pubmed.ncbi.nlm.nih.gov/?term=(medication%20compliance%5BTitle%2FAbstract%5D)%20OR%20(medication%20adherence%5BTitle%2FAbstract%5D)&filter=years.1974-2016&timeline=expanded

There is a wealth of data on non-adherence and its causes. If we distill the key reasons, they fall into three distinct groups: **capability** issues, **opportunity** issues, and **motivational** issues. These three factors–capability, opportunity, and motivation–drive adherence **behavior**, as well as all other behaviors.

Evidence from adherence studies

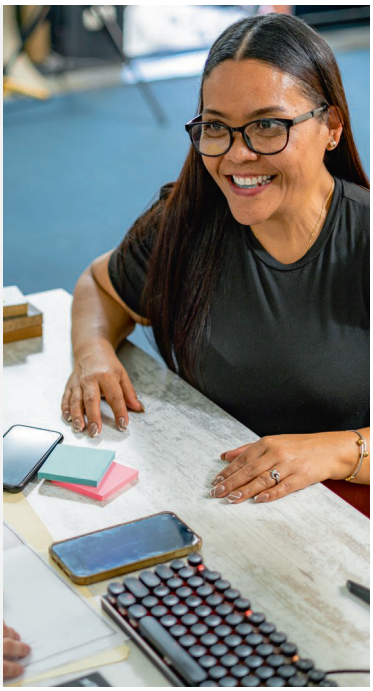
Over 700 factors have been found to influence adherence[1]

These can mostly be classified as due to Capability, Opportunity or Motivation (COM-B)[2]

Large variation in the causes of non-adherence **between** patients and **within** patients over time[1]

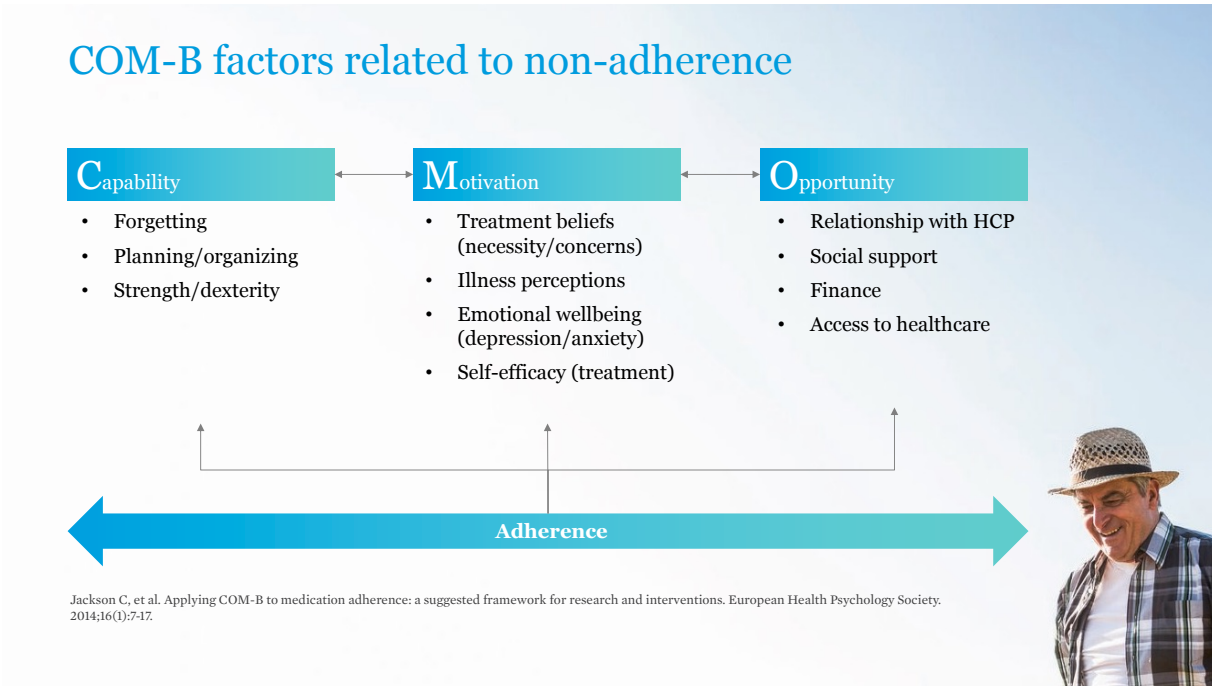
Importance of identifying the reasons for each patient and tailoring interventions to these[2]

1. Kardas P, et al. Determinants of patient adherence: a review of systematic reviews. Frontiers in pharmacology. 2013;4:91.
2. Jackson C, et al. Applying COM-B to medication adherence: a suggested framework for research and interventions. European Health Psychology Society. 2014;16(1):7-17.



To engage in a behavior, including adherence, individuals need to be capable (knowing what to do and how to do it, and being physically able to do it). Opportunity refers to external factors

that may make it difficult for patients to adhere to treatment, such as access to healthcare, financial situation, and support from peers and family. Motivation is the critical issue–whether someone actually wants to take their medication. Non-adherence is often intentional; it is not just about forgetting.

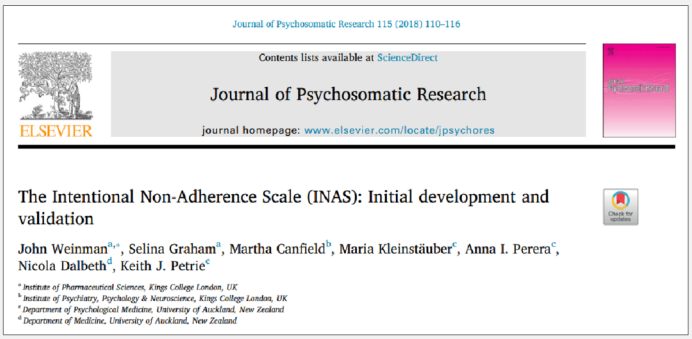


Studies show a huge variation in reasons for non-adherence between individuals. One person may struggle with capability, while another may be driven by motivational factors or limited opportunities. All three components–capability, opportunity, and motivation–are necessary for behavior. Understanding the specific reasons for each patient is crucial, as these can change over time.

Traditionally, efforts to improve adherence have focused on providing more information and reminders. However, as seen in large studies, reminders alone have little effect once a person becomes non-adherence. Motivation, based on beliefs about medicines, the condition, emotional well-being, and confidence, is a significant factor. Opportunity factors, such as the relationship with HCPs, support from the social environment, financial situation, and access to healthcare, also play a role.

Recent work has explored the impact of illness on self-identity. A major illness can affect how individuals see themselves, and some may resist taking medication as it reminds them of their illness. Understanding these complex issues, along with the capability, opportunity, and motivation factors, is essential for addressing non-adherence.

Self identity and treatment adherence



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The Intentional Non-Adherence Scale (INAS): Initial development and validation

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Resisting illness

8 items; Cronbach alpha = 0.94

- Because it reminds me I have an illness
- Because I want to lead a normal life again

Testing treatment

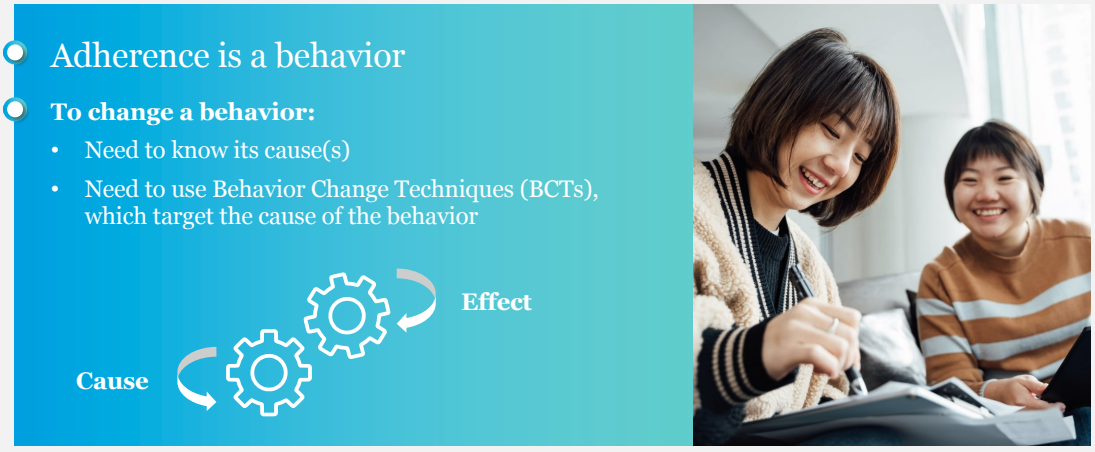
5 items; Cronbach alpha = 0.93

- To see if I can do without it
- To see if I really need it

Weinman J, et al. The Intentional Non-Adherence Scale (INAS): Initial development and validation. J Psychosom Res. 2018 Dec;115:110-116

Why is it important to understand all these causes? Why do behavioral scientists go to great lengths to identify the reasons for non-adherence? Well, adherence is a behavior, and if we want to change a behavior, we need to understand what causes it. One size does not fit all; we need to know the specific reasons for each individual's adherence problem. We use behavior change techniques, which are methods of changing behavior based on the identified reasons.

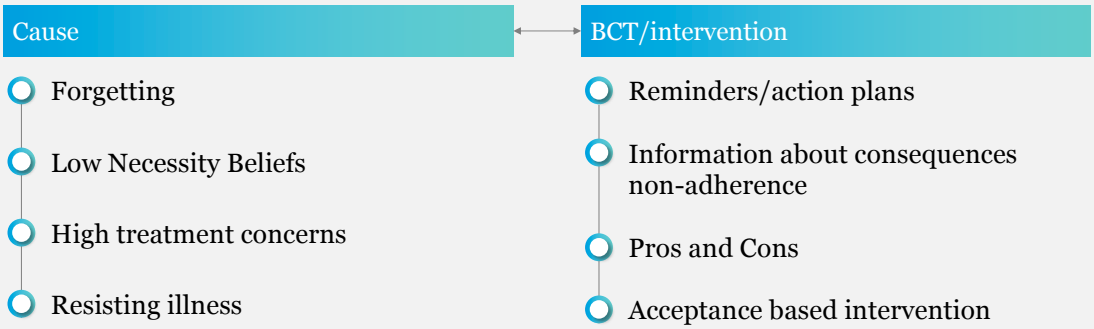
Importance of understanding causes of non-adherence



Allemann SS, et al. Matching adherence interventions to patient determinants using the theoretical domains framework. Front. Pharmacol. 2016;7:429.

For example, if a patient simply forgets to take their medication, the intervention might be to provide reminders or help them create action plans to develop a daily habit. However, about a third of non-adherence patients do not believe they need the treatment. In such cases, we need to provide more information and engage in discussions about the consequences of non-adherence to change their beliefs.

Examples of targeted BCTs for non-adherence



Patients often have concerns about treatment, such as side effects or dependency. To address these high treatment concerns, we help patients weigh the pros and cons of treatment, showing them the long-term benefits. For patients who resist the idea of being ill and taking medication, interventions focus on helping them accept their illness and the need for treatment.

In routine clinical care, HCPs can support patients by increasing awareness of the problem, detecting non-adherence in a non-threatening way, understanding the reasons for each patient's non-adherence, and using targeted behavior change interventions. A behavioral diagnosis helps understand the behavior and apply the right intervention.

Key challenges for managing non-adherence in routine clinical care

- Increase awareness of the extent of the problem
- Detecting non-adherence in a non-threatening way
- Understanding the reasons in each patient (COM-B)
- Using a targeted behavior change approach

Deal with the barriers: HCP and patient

HCPs face barriers, such as not recognizing the extent of the problem, approaching non-adherence in an accusatory manner, and lacking training in targeted interventions. Time constraints and the tendency to tell patients what to do also hinder effective behavior change.

HCP barriers to managing non-adherence in routine care

- Outside their remit “Not my job”
- Underestimate prevalence
- Approach non-adherence in a “non-friendly” manner
- Ill-equipped to manage the reasons underlying non-adherence
- Lack of time in routine appointment
- Difficult to switch off the "righting reflex"

Patients also face barriers, such as hiding non-adherence from clinicians due to fear of being reprimanded or disappointing the clinician. They may not admit to non-adherence when directly

questioned, creating a communication barrier. Discussions often focus only on capability factors, neglecting motivational and opportunity issues.

Patient barriers to managing non-adherence in routine care

- Hiding non-adherence from the clinician
- Not wishing to disappoint or get "told-off"
- Defensive in response to direct questioning re adherence
- Motivational and opportunity factors rarely addressed

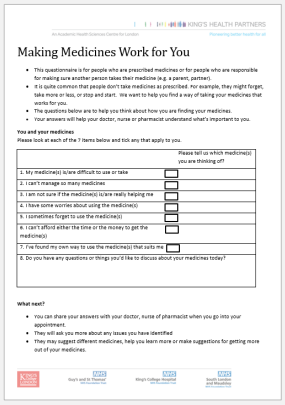
To improve detection of non-adherence, clinicians should ask about it in a non-blaming way, normalizing the possibility of non-adherence and giving patients the opportunity to discuss their challenges. Using brief screeners before consultations can help identify issues, allowing patients to bring them up during the consultation.

Detecting non-adherence

Since many patients are often reluctant to disclose non-adherence, particularly if the question is asked in a very direct way

You will be more likely to "uncover" non-adherence if you:

- Ask about adherence in a non-blaming way[1]
- Use a simple screener[2]



Making Medicines Work for You

- This questionnaire is for people who are prescribed medicines or for people who are responsible for making sure another person takes their medicine (e.g. a parent, partner).
- It is quite common that people don't take medicines as prescribed. For example, they might forget, take more or less, or stop and start. We want to help you find a way of taking your medicines that works for you.
- The questions below are to help you think about how you are finding your medicines.
- Your answers will help your doctor, nurse or pharmacist understand what's important to you.

You and your medicines

Please look at each of the 7 items below and tick any that apply to you.

	Please tell us which medicine(s) you are thinking of?
1. My medicine(s) is/are difficult to use or take	
2. I can't manage so many medicines	
3. I am not sure if the medicine(s) is/are really helping me	
4. I have some worries about using the medicine(s)	
5. I sometimes forget to use the medicine(s)	
6. I can't afford either the time or the money to get the medicine(s)	
7. I've found my own way to use the medicine(s) that suits me	
8. Do you have any questions or things you'd like to discuss about your medicines today?	

What next?

- You can share your answers with your doctor, nurse of pharmacist when you go into your appointment.
- They will ask you more about any issues you have identified
- They may suggest different medicines, help you learn more or make suggestions for getting more out of your medicines.

1. Engel T, et al. Re-phrasing the question : A simple tool for evaluation of adherence to therapy in patients with inflammatory bowel disease. United European Gastroenterology Journal. 2017;5(6):880–886.
2. Weinman J, et al. Pilot testing of a brief pre-consultation screener for improving the identification and discussion of medication adherence in routine consultations. Patient preference and adherence, 2019;13:1895.

Once non-adherence is identified, the next step is to address it with appropriate interventions.

Ask the patients to elaborate on the problem. Why do they feel they do not need the medication? What are their worries? It is important to understand the pattern of the problem. Is it occurring early in their treatment or later? Is it consistent, or do they take breaks? Understanding the nature of their adherence pattern is crucial.

After detection: What next?

Ask patient to say more about the nature and reason(s) to allow you to see the bigger picture in terms of

- Phase and pattern of the problem
- More detail about the reasons at an individual level
- Patient's level of motivation and readiness to change
- The broader context (e.g. their social situation, etc.)

Doctors also want to know their reasons for non-adherence, their level of motivation, and their willingness to change. Do they genuinely want to address the issue? It is essential to work closely with the patient and consider their broader situation, including the support they have from people around them.

Here are some basic steps for working with a patient during a consultation:

- **Check Understanding:** At the beginning, when prescribing a new medication, ensure the patient understands their treatment. Do they know why they need the medication and what it is for? If not, provide a clear rationale for the treatment.
- **Address Concerns:** Identify any worries or concerns the patient may have, either at the start or later on. Help them think more positively about the treatment.
- **Create a Practical Plan:** Work with the patient to develop a practical plan for taking their medication. Discuss when, where, and how they will take it to help them establish a regular habit. Once a habit is formed, half the battle of non-adherence is won.

- **Identify Barriers:** Help the patient think about potential barriers that might interfere with their plans.
- **Follow Up:** Always follow up with the patient. As mentioned previously, following up over time is crucial because the situation can change. Non-adherence may go away and then return.

Adherence support in the consultation: Basic steps

Check patient's understanding of treatment and, if necessary

Provide clear rationale for **necessity** of treatment

Elicit and address **concerns**

Agree practical plan for how, where and when to take treatment

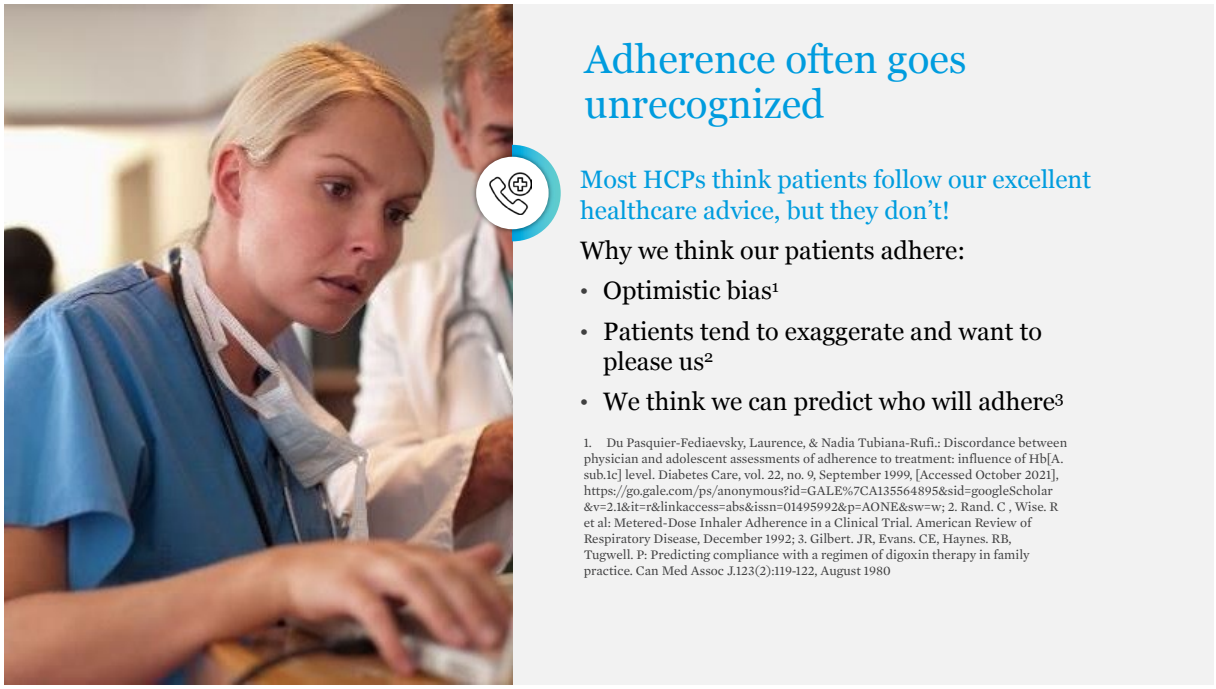
Identify any possible barriers and problem solve these collaboratively

Follow up to assess outcome

Communication strategies to increase adherence to medical advice

This chapter is based on the lecture presented by Dr. Pruitt at the a:care Congress in 2021.

The issue of non-adherence often remains undetected. One reason for this lack of recognition is that many HCPs assume their patients are following their advice, but this is not always the case. We talk about **optimistic bias**[64] when HCPs overestimate their patients' adherence to prescribed treatments. Another contributing factor is that patients may want to please their HCPs, leading them to overstate their compliance.[65]



64. Du Pasquier-Fediaevsky, Laurence, & Nadia Tubiana-Rufi.: Discordance between physician and adolescent assessments of adherence to treatment: influence of Hb[A.sub.1c] level. Diabetes Care, vol. 22, no. 9, September 1999, [Accessed October 2021], https://go.gale.com/ps/anonymous?id=-GALE%7CA135564895&sid=googleScholar&v=2.1&it=r&linkaccess=abs&issn=01495992&p=AONE&sw=w;
65. Rand. C , Wise. R et al: Metered-Dose Inhaler Adherence in a Clinical Trial. American Review of Respiratory Disease, December 1992.

Furthermore, it is a misconception that we can predict who will adhere to treatment.[66] Statistics show that about 50% of patients do not follow their treatment plans, regardless of whether they have symptomatic or asymptomatic conditions. For instance, in the context of pancreatic exocrine insufficiency, management is suboptimal, and non-adherence is linked to higher healthcare costs[67] and utilization.[68] This is often due to incorrect enzyme dosage, timing, and the high cost of treatment.

Adherence is a critical issue that must be addressed. A 2003 WHO report states, "Increasing the effectiveness of adherence interventions may have a far greater impact on health than any improvements in specific medical treatments." This suggests that enhancing patient adherence to existing medications is more crucial than developing new ones.

The question posed is whether medical care is more than just prescribing medication. It is essential to consider this, as there is much more HCPs can do. Changing communication styles is one approach. Common strategies include ordering, warning, or persuading with logic, but these are often ineffective in altering behavior.

66. Gilbert. JR, Evans. CE, Haynes. RB, Tugwell. P: Predicting compliance with a regimen of digoxin therapy in family practice. Can Med Assoc J.123(2):119-122, August 1980.
67. Brown MT, Bussell JK. Medication adherence: WHO cares?. Mayo Clin Proc. 2011;86(4):304-314. doi:10.4065/mcp.2010.0575.
68. Barkin JA, Westermann A, Hoos W, et al. Frequency of Appropriate Use of Pancreatic Enzyme Replacement Therapy and Symptomatic Response in Pancreatic Cancer Patients. Pancreas. 2019;48(6):780–786.

Common communication strategies to influence others

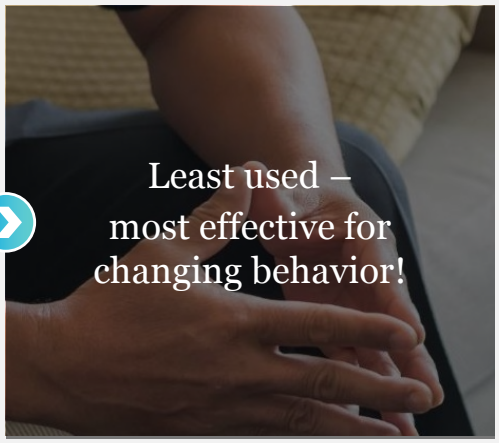
Which approach do you use?

- Ordering, directing, demanding
- Warning or threatening
- Persuading with reason, logic, argument, or lecture
- Moralizing, preaching, telling what you "should" do
- Disagreeing, judging, criticizing, blaming
- Shaming, ridiculing, labeling

Less common but more effective strategies involve being curious, non-judgmental, other focused, empathic, and collaborative. These approaches are less frequently used but have a greater impact on changing patient behavior.

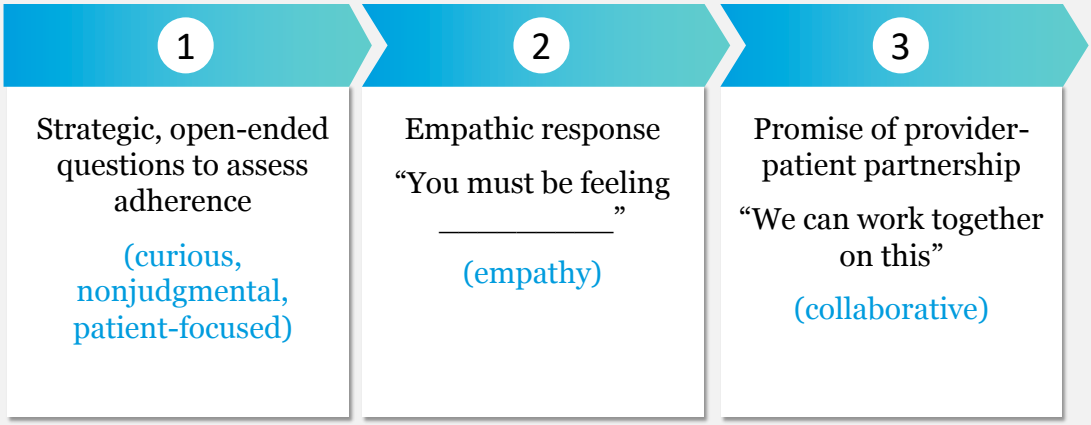
Uncommon communication strategies to influence others

- Curious
- Nonjudgmental
- Other-focused
- Empathic
- Collaborative



The slide below aims to simplify the use of these effective strategies in a three-step process.

Three steps to integrate effective communication strategies

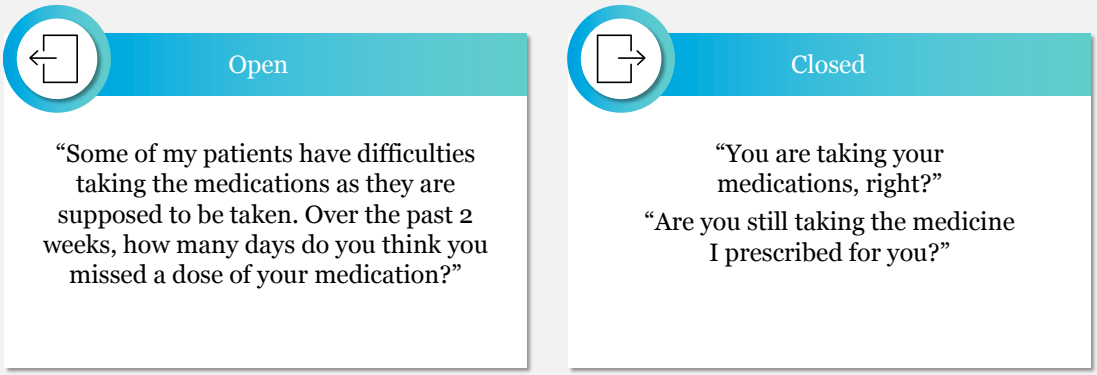


Regarding adherence, HCPs may consider the following three-step approach:

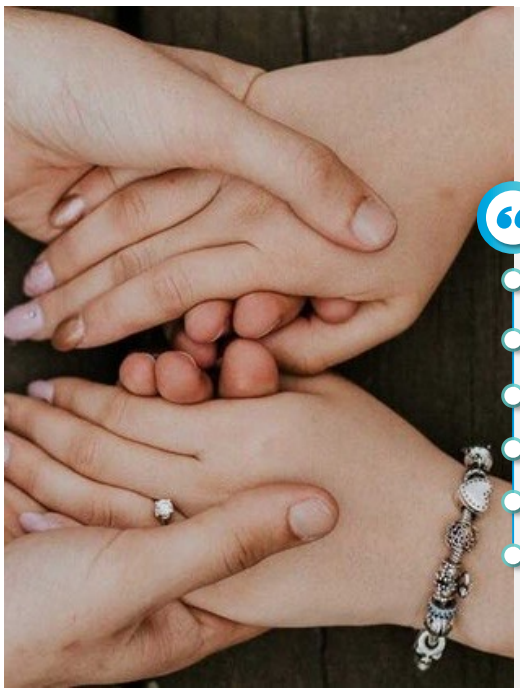
Step One: Begin with a strategic open-ended question to assess adherence. This approach allows you to be curious, non-judgmental, and patient focused. For example, instead of asking, "Are you taking your medications?" which prompts a yes or no answer, ask, "Over the past 2 weeks, how many days do you think you missed a dose of your medicine?" This type of question gives patients the opportunity to discuss their challenges openly.

Step 1: Assess adherence with open-ended questions

Examples of what to say



Step Two: Offer an empathic response. If a patient admits to struggling with their medication, respond with understanding and connection, such as “That must be very difficult for you” or “You must be feeling frustrated.” This helps to establish an emotional connection and shows the patients that you understand their perspective.



Step 2: Provide empathic responses

Examples of what to say

- This must be distressing for you
- It must be very difficult for you right now
- Things like this can be very tough
- This seems to be worrying you
- This is probably disappointing for you
- This seems to be challenging for you

Step Three: Promise a provider-patient partnership. Assure the patient that you will work together to address the issue, saying things like “We can work on this problem together” or “As your doctor, my goal is to help you with taking your medications.”

Step 3: Promise patient–provider partnership

Examples of what to say

- We can work on this problem together
- My goal as your doctor is to help you with taking your enzymes
- Let’s work together so you can be as healthy as possible

Here's how a conversation might unfold using these steps:

Provider: "Some of my patients have difficulties taking their medicines as prescribed. Over the past 2 weeks, how many times do you think you missed a dose?"

Patient: "I've missed quite a few doses. It's hard to keep track with so many pills and different times to take them."

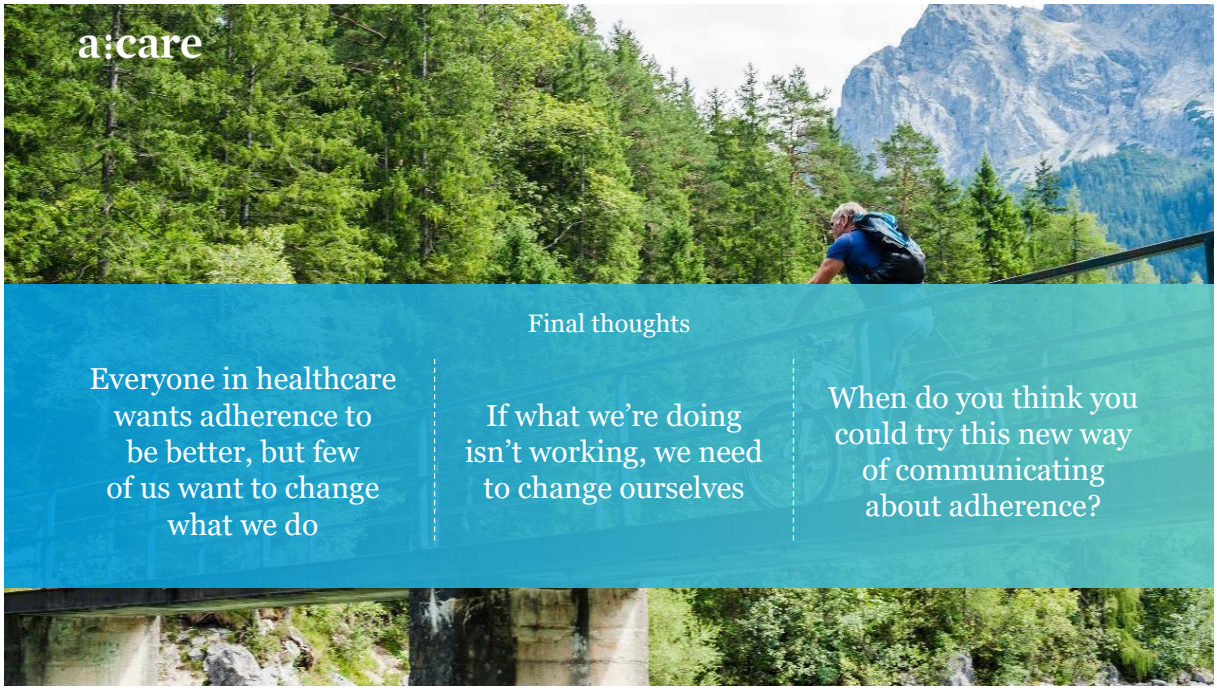
Provider: "You must be frustrated about that. Taking this treatment can be really difficult."

(After a pause to let the patient process the empathic statement)

Patient: "Yes, I am frustrated. It's hard to remember when and what to take."

Provider: "As your doctor, I want to help you be as healthy as possible. Let's work on this problem together."

In conclusion, while everyone in healthcare desires better adherence, few are willing to change their own behaviors. Communication is a behavior, and if our current methods are not effective, we need to consider changing our approach. The three steps of assessment, empathy, and collaboration offer a practical way to improve patient adherence.



Technology: AI and the physician–patient relationship

This session was handled by Dr. Evan Muse and Assoc. Prof. Ngiap Chuan Tan during the a:care Congress 2024.

To understand the future, let us take a quick look at the past. In 1922, a doctor wrote in the Journal of the American Medical Association about the revolutionary bedside telephone, which was a great convenience for night use and patient convalescence. Fast forward to today, and technology has evolved dramatically. Supercomputers that once filled entire rooms now fit in our hands or on our wrists.

Clinical Notes, Suggestions, and New Instruments

A BEDSIDE TELEPHONE

A. E. ROCKEY, M.D., PORTLAND, ORE.

The oft repeated statement that we spend one third of our lives in bed is probably true for the average person, in that one third the average physician certainly has many telephone calls. The number, of course, depends entirely on the character of his practice. It does not apply to the city specialist,

Bedside telephone.

who sees to it carefully that his name is omitted from the residence list of the telephone directory. The man doing family practice, or emergency or industrial surgery, must literally sleep with his telephone. Before the World War I was for many years surgeon to a railway, light and power company. For ten years the telephone here-with illustrated was a source of great comfort and convenience.

It combines the bell in the base with the continental type of hand telephone, with the receiver and transmitter in one

HEART BLOCK—BISHOP 1535

About this time I built a new residence just outside the city limits, and had it liberally supplied with jacks in the various sleeping and living rooms, and garage. There were twelve in all, and I paid for the equipment and installation. I knew nothing then about a service charge for jacks. It was only when pruning down overhead expenses at the time I went into military service that I discovered that I had been paying a service charge of twenty-five cents a month on each jack. In other words, for equipment which belonged to me I had paid the company about $80 for a supposed service that had not cost them one cent, as no repair had ever been required. The attention of public service commissions is invited to this. It must be a local rule of the Oregon commission. On a recent visit to Los Angeles I found twenty rooms at the Good Samaritan Hospital equipped with jacks, and the ordinary desk telephone circulating between them. The entire charge for this was one dollar a month, and no service charge for the jacks.

The Ericson phone is now made by the Federal Telephone and Telegraph Company, with the bell in the base, and recently the Western Electric has added a similar instrument to its output. That will, I fancy, do away with talk about "foreign equipment," and the medical profession, and then patients, may have an adaptable bedside telephone.

The attention of telephone companies is invited to the economic importance of this real need. The Directory of the American Medical Association contains the names of 19,250 physicians, and a list of 6,794 hospitals. It is believed that the medical profession will find this bedside telephone a great convenience to themselves for night use, and to some of their patients during convalescence.

HEART BLOCK AS A FAVORABLE INFLUENCE IN THE PROGRESS OF CHRONIC FIBRILLATION

LOUIS FAUGERES BISHOP, M.D., NEW YORK
President, Good Samaritan Dispensary, Consultant Cardiologist, Lincoln Hospital

I have already reported quite a number of examples of heart block in rheumatic hearts with mitral stenosis, in which the heart block had acted favorably in preventing the evil influence of fibrillation of the auricle.

A few days ago an illustration of another variety of the same compensating mechanism came under my observation in the person of an elderly man (Mr. L. F. H. P.) whom I saw for the first time in April, 1919, when he was 70 years of age.

Rockey AE. Clinical Notes, Suggestions, and New Instruments. A bedside telephone. JAMA. 1922;78(20)1535."

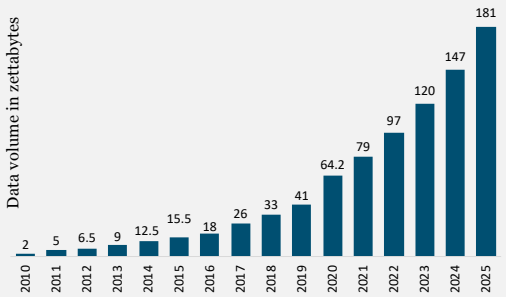
With the rise of digital medicine and mobile health, we now have sensors that monitor almost every aspect of our health, from heart rate to glucose levels, right from our homes. This data can help us treat and prevent diseases more effectively.

Looking ahead, experts predict that within the next 5–6 years, apps on our devices could potentially replace primary physicians, thanks to advancements in AI. AI is already integrated into our daily lives, from driving to work to organizing our schedules and entertainment.

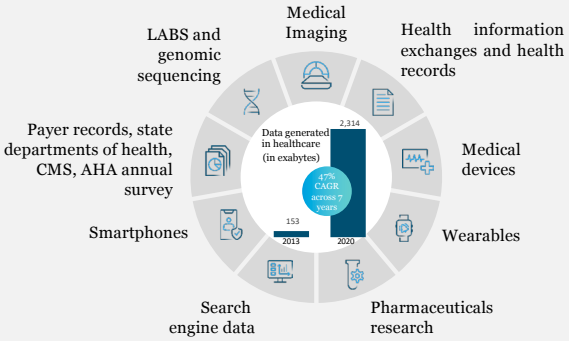
The amount of data we generate is growing exponentially, including medical data. This data, now stored digitally, can be used to create better care plans.

So much DATA!

Between the years 2010-2025, it is estimated that the total amount of data created in 1 year will have increased by 8,950%[1]

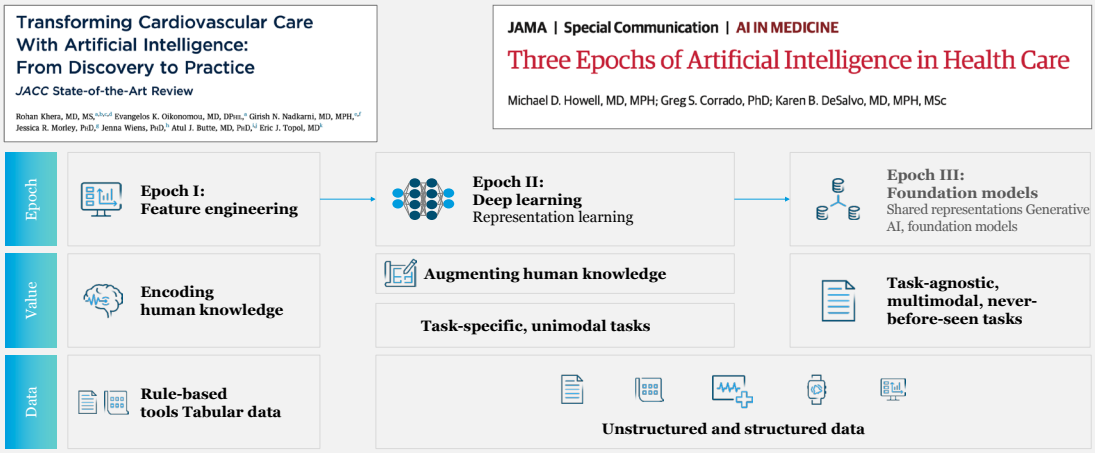


Where is all the health data coming from?[2]



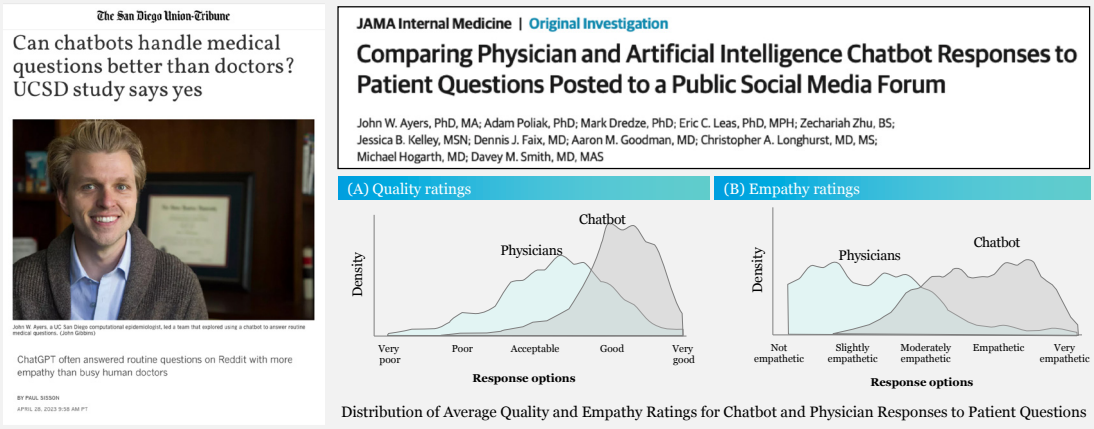
1. Duarte F. Amount of Data Created Daily. Exploding topic.2024. Available at: https://explodingtopics.com/blog/data-generated-per-day ; 2. Micron. Big Data is Informing the Healthcare Revolution. Infographic based on the Health Trends Reports Stanford Medicine 2017 « Harnessing the Power of Data in Health » Stanford Medicine 2017.

AI has progressed from basic rule-based systems to deep learning and now to large language models and multimodal AI, which can handle complex tasks and provide high-quality, empathetic insights.



1. Khera R, et al. Transforming Cardiovascular Care With Artificial Intelligence: From Discovery to Practice: JACC State-of-the-Art Review. Journal of the American College of Cardiology. 2024;84(1):97-114. 2. Howell MD, et al. Three Epochs of Artificial Intelligence in Healthcare. JAMA. 2024;331(3):242-4.

However, as we integrate AI into healthcare, we must address concerns about its impact on the doctor–patient relationship. While AI can enhance efficiency and accuracy, it must be used thoughtfully to maintain the human touch and emotional support that are crucial in healthcare.



Distribution of Average Quality and Empathy Ratings for Chatbot and Physician Responses to Patient Questions

1. Ayers JW. Can chatbots handle medical questions better than doctors? UCSD study says yest. The San Diego Union-Tribune. 2023. Available at: https://www.sandiegouniontribune.com/2023/04/28/can-chatbots-handle-medicalquestions-better-than-doctors-ucsd-study-says-yes/ ; 2. Ayers JW, et al. Comparing Physician and Artificial Intelligence Chatbot Responses to Patient Questions Posted to a Public Social Media Forum. JAMA Internal Medicine. 2023;183(6):589-96.

The overwhelming administrative tasks doctors face today can jeopardize this relationship. We spend so much time on computers, reviewing medical records, lab results, and imaging reports, that we risk losing the personal connection with our patients.

Patient–physician relationship: Threats

Physicians face overwhelming administrative tasks during a consultation

Physician

"Honestly, all that typing, printing, and confirming of test results and such, I waste a lot of time on it … sometimes I forget that, while I'm typing and looking at the screen, I'm not really looking at the patient themselves, and I end up missing information I could gather just by observing them".

Patients express dissatisfaction of not receiving enough care and attention from their physician

Patient

"I'd prefer if the physician didn't just look at the papers but lifted their head, talked to me, gave me a look, and conducted an examination if needed, which is equally important, because lately, it often seems to be reduced to just paperwork".

Čartolovni A, et al. Critical analysis of the AI impact on the patient–physician relationship: A multi-stakeholder qualitative study. DIGITAL HEALTH 2023;9:1-14.

AI has the potential to alleviate these tedious tasks, allowing doctors to focus more on patient interaction. It can speed up diagnoses, provide more accurate prognoses, and enable early intervention and preventive measures. Patients, meanwhile, hope AI will reduce wait times and overcrowding in healthcare facilities.

AI: Potential effect on the patient–physician relationship

AI: "technology that enables computers and machines to simulate human learning, comprehension, problem solving, decision making, creativity and autonomy"[1]

Physician[2]

- Alleviates tedious, repetitive, and manual tasks
- More attentive to our patients and listen to their concerns, helping them navigate their health options for treatment
- Speed up diagnosis and more accurate prognosis for early intervention/treatment and preventive measures

Patient[2]

- Less certain and more wary of the impact of AI on healthcare
- Perceive reduced wait time
- Expect increase access and reduce overcrowding in healthcare facilities

1. IMB. What is artificial intelligence (AI). Available at: https://www.ibm.com/topics/artificial-intelligence (consulted on August 30. 2024) ; 2. Čartolovni A, et al. Critical analysis of the AI impact on the patient–physician relationship: A multi-stakeholder qualitative study. DIGITAL HEALTH 2023;9:1-14.

Despite its benefits, AI also presents challenges. Doctors worry about reduced interaction with patients and the potential for deskilling in human observation and emotional recognition. Patients fear that AI might reduce the human touch and emotional support they receive from their doctors.

What are the perceived shortcomings of AI?

Physician	Patient
Fear of alienation and reduced interaction between patients and physicians	AI cannot provide emotional support or empathy to them
De-skill in observations and recognizing emotions in humans	Perceived loss of human touch
	Concern that AI could reduce communication and connection

"What I absolutely dislike is losing this contact with patients, and I believe we must fight against it, no matter how accurate any system might be"	"Well, probably, the relationship with the physician on a personal level will become less frequent. Currently, many patients can connect with a physician and develop a personal approach over time... I think that will be less and less, you know, colder"

Čartolovni A, et al. Critical analysis of the AI impact on the patient–physician relationship: A multi-stakeholder qualitative study. DIGITAL HEALTH 2023;9:1-14.

As the number of patients increases, there is a concern that AI could reduce or erode empathy and compassion, potentially affecting the doctor-patient relationship. So, how can we intelligently use AI?

Paradox of the expectations of AI

Help improve the physician's efficiency ...

BUT

It may erode the empathic and compassionate nature of the relationship between patients and physicians as a result of increased numbers of patient consultations each day due to the physician's increased efficiency.

Sparrow R and Hatherley J. High hopes for "deep medicine"? AI, economics, and the future of care. Hastings Cetn Rep 2020; 50: 14–17

According to the literature, there is no evidence that delegating certain tasks to AI will result in AI replacing physicians. AI is not expected to replace doctors anytime soon, nor will it threaten their roles, which include providing diagnoses, engaging with patients, offering consolation, and maintaining a human touch.

Intelligent application of AI

- No evidence that delegation of certain tasks to AI would result in AI replacing physicians, nor the physicians' role being threatened, because their role is not only to provide a diagnosis but to fully engage with the patients, offering consolation, consultations and more[1].
- AI-based tools have the potential to place the patient at the center of the caring process, safeguarding the patients' autonomy and assisting them in making informed decisions that align with their values[2].

1. Sezgin E. Artificial intelligence in healthcare: complementing, not replacing, doctors and HCPs. Digit Health 2023.
2. Quinn TP, et al. Trust and medical AI: the challenges we face and the expertise needed to overcome them. J Am Med Inform Assoc 2021; 28: 890–894.

AI tools have the potential to place patients at the center of the care process, safeguarding their autonomy and assisting them in making informed decisions that align with their values and preferences. To fully utilize AI, it is crucial to explain AI-enabled medical decision making clearly. Physicians must remain responsible for medical decisions, even when using AI tools. Providing clear explanations of how decisions are made is the first step in building a trusting relationship with patients.

Explain AI-enabled medical decision making is crucial

Physicians should retain ultimate responsibility in medical decision making with their patients even if they are leveraging on AI-enabled tools.

Clear explanation on how a particular decision has been made is the first step in building a trusting relationship between the physician, patient and AI.

The lack of explainability might be problematic for physicians to take responsibility for decisions involving AI systems.

The ability of a human expert to explain and reverse-engineer AI decision-making processes is still necessary.

Physician should be equipped with enhanced communication skills to explain to patients the outputs of AI-based tools that might influence their care.

Upskilling of physicians in AI is pivotal to maintain their role and responsibility as a care provider to their patients.

Speaker input.

The lack of explainability in AI can be problematic for physicians taking responsibility for AI-involved decisions. Therefore, it is essential for human experts to explain and reverse-engineer AI decisions. Physicians should be equipped with communication skills to explain AI outputs that might influence patient care. Upskilling in communication is vital for maintaining their role and responsibility as HCPs.

To mitigate risks and preserve the doctor–patient relationship, we must address the AI-driven infodemic–an epidemic of information, including fake news. Physicians should embrace informatics but neither uncritically accept nor unreasonably reject AI developments. Active engagement and contribution to the discourse are necessary, without relying entirely on AI recommendations or neglecting clinical reasoning and best practices.

Mitigating risks and preserving the patient-physician relationship

‘AI-driven infodemic’: potential creation of vast number of scientific articles, fake news, and misinformative content.

Physicians should neither uncritically accept nor unreasonably resist developments in AI but must actively engage and contribute to the discourse.

Not to rely solely upon the AI recommendations and neglect clinical reasoning and physicians’ knowledge of best xclinical practices.

Adopt a critical awareness approach to AI implementation in healthcare by applying critical thinking and reasoning.

The core values of the existing patient–physician relationship, such as trust and honesty, conveyed through open and sincere communication must be preserved.

Speaker input.

Core values such as trust and honesty, conveyed through open and sincere communication, must always be preserved. By collaborating with data scientists, Assoc. Prof. Tan and colleagues have developed AI software called ‘PERDICT AI’, which uses electronic medical records and machine learning to create modules for patient similarity, medication recommendations, and personalized care plans. This tool is being used in a randomized control trial to counsel patients with suboptimal diabetes control, emphasizing explainable AI, shared decision making, and personalized care to strengthen the doctor-patient relationship.

AI application in primary care: BRILLIANT study

Better Risk perceptIon via patient simiLarity to controL hyperglycemIa And sustaiNed by Telemonitoring (BRILLIANT RCT)

- PERDICT.AI – An AI-enabled software created from EMR data using Machine Learning, comprising three modules
  - Patient similarity
  - Medication Recommendation
  - Personalized Care Plan
- Tool to counsel adults with type-2 diabetes mellitus to optimize their glycemic control
- Three-arm randomized controlled trial
- Highlights: Explainable AI, Shared Decision Making, Personalized Care, Patient–Physician Relationship

Better Risk perceptIon via patient simiLarity to controL hyperglycemIa And sustaiNed by Telemonitoring (BRILLIANT) Clinical trial. Ongoing, available at: https://clinicaltrials.gov/study/NCT06607497 (NCT06607497)

Improving access to self-management support for patients with chronic conditions: Digital solutions

This chapter draws upon the sessions led by Prof. Piette, Dr. Vrijens, and Prof. De Madaria at the a:care Congress 2021.

The potential of integrating new patient-centric digital tools is significant, and current research indicates a wide array of self-management support goals that these tools can fulfill. Given the limited time and the extensive depth of this research area, let us focus on a few key examples.

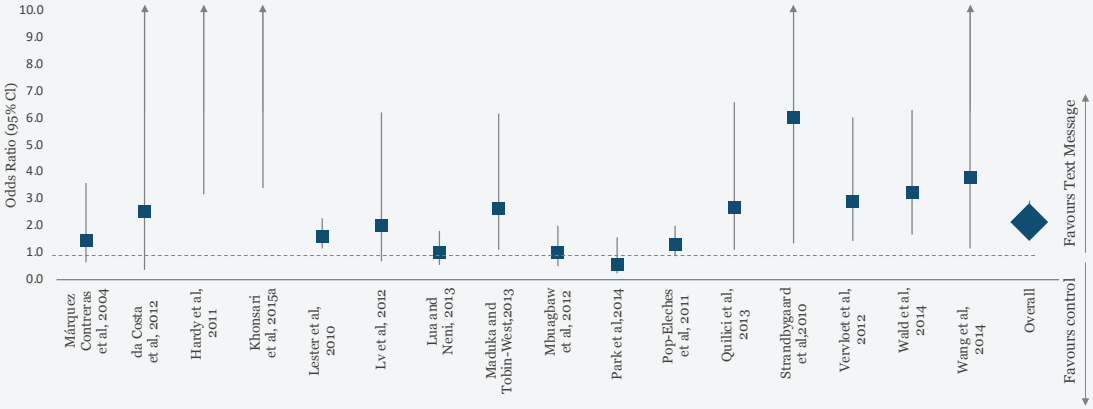
Digital solutions have undergone rigorous testing through randomized trials and meta-analyses globally, demonstrating effectiveness in various areas. For instance, they have been instrumental in enhancing medication adherence among HIV patients in Africa and in managing hypertension and CVDs in India and China. Prof. Piette's work in Latin America has similarly shown improvements in self-management and behaviors for individuals with diabetes and cardiovascular conditions.

The scope of digital solutions is vast, encompassing specialized devices like continuous glucose monitors and scales for heart failure patients. However, let us concentrate on a ubiquitous device: the mobile phone. Research has primarily focused on two communication channels: automated calls and text messaging systems. Despite the burgeoning interest in smartphones' additional functions, research in this domain is still nascent, with a few notable exceptions.

The a:care program represents a significant shift, addressing multiple conditions, cultures, and disease processes worldwide. It is a testament to the global impact of digital solutions on self-management. One of the primary goals of employing digital tools is to enhance treatment adherence. Meta-analyses reveal that text message reminders can boost medication adherence from 50% to 67.8%, or an absolute increase of 17.8%.[69]

69. Jay Thakkar, Rahul Kurup et al: Mobile Telephone Text Messaging for Medication Adherencein Chronic Disease A Meta-analysis JAMA Intern Med. 2016;176(3):340-349, 2016.

Mobile telephone text messaging for medication adherence in chronic disease a meta-analysis[9]



9. Jay Thakkar, Rahul Kurup et al: Mobile Telephone Text Messaging for Medication Adherencein Chronic Disease A Meta-analysis JAMA Intern Med. 2016;176(3):340-349, 2016, [Accessed 02 September 2020], https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2484905#:~:text=Conclusions%20and%20Relevance%20Mobile%20phone,an%20absolute%20increase%20of%2017.8%25.

Beyond adherence, digital tools are valuable for monitoring patients and gathering data between clinical visits, aiding in better decision making and early intervention to prevent complications. A notable international study involving children with nephrotic syndrome utilized a texting system for daily kidney function reporting. This approach allowed for more timely identification and treatment adjustments, reducing the average time to remission from 50 days based on clinic visits to 22 days using text data.[70]

Text Messaging for Disease Monitoring in Childhood Nephrotic Syndrome

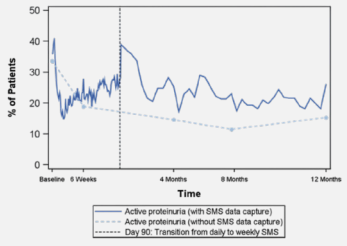


Figure 4: Percentage of patients with nephrotic range proteinuria as captured by short message service (SMS) reporting versus in-person clinic visits

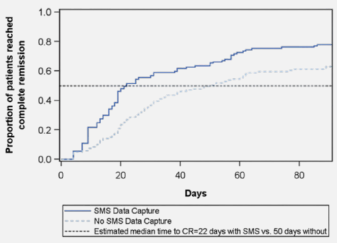


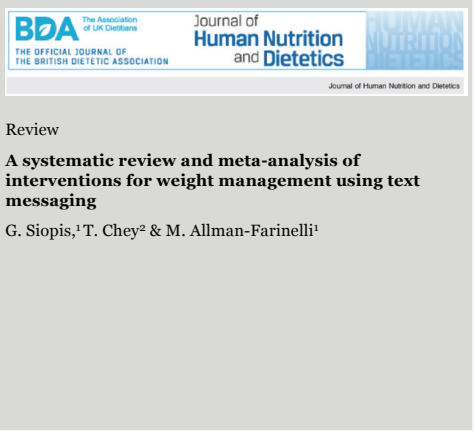
Figure 5: Time to remission after study enrolment by short message service (SMS)- captured urine protein results versus participant reporting during in-person study visits. CR, complete remission

1. Department of Pediatrics, Emory University and Children's Healthcare of Atlanta, Atlanta, Georgia, USA; 2. Department of Pediatrics and Communicable Diseases, University of Michigan, Ann Arbor, Michigan, USA; 3. Department of Pediatrics, Children's Mercy Hospital and University of Missouri at Kansas City, Kansas City, Missouri, USA; 4.Department of Pediatrics, Montefiore Medical Center, New York, New York, USA; 5.Department of Medicine and Pediatrics, University of North Carolina, Chapel Hill, North Carolina, USA; 6. Department of Pediatrics, NYU School of Medicine, New York, New York, USA; 7.Department of Health Behavior & Health Education, University of Michigan, Ann Arbor, Michigan, USA; 8.Department of Pediatrics, Cohen Children's Medical Center of New York, New Hyde Park, New York, USA; 9.Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA; 10. Department of Pediatrics, Case Western Reserve University, Cleveland Clinic Children's, Cleveland, Ohio, USA; 11. Department of Pediatrics, Mayo Clinic, Rochester, Minnesota, USA; 12. Department of Pediatrics, Seattle Children's Hospital, Seattle, Washington, USA; 12. Department of Pediatrics, Children's Hospital-LA, Los Angeles, California, USA; 14. Department of Pediatrics, Stanford University, Palo Alto, California, USA; 15. Department of Pediatrics, UT Southwestern Medical Center, Dallas, Texas, USA; and 16. Department of Pediatrics, Wake Forest University, Winston-Salem, North Carolina, USA

70. Wang CS, Troost JP, Greenbaum LA, Srivastava T, Reidy K, Gibson K, Trachtman H, Piette JD, Sethna CB, Meyers K, Dell KM, Tran CL, Vento S, Kallem K, Herreshoff E, Hingorani S, Lemley K, Oh G, Brown E, Lin JJ, Kaskel F, Gipson DS. Text Messaging for Disease Monitoring in Childhood Nephrotic Syndrome. Kidney Int Rep. 2019 May 7;4(8):1066-1074.

Patients can also report physiological data, behaviors, and symptoms via their cell phones. Lifestyle changes, such as weight loss, have been supported by text messaging, with studies indicating an average reduction of 2.5 kg.[71]

Interventions for weight management using text messaging

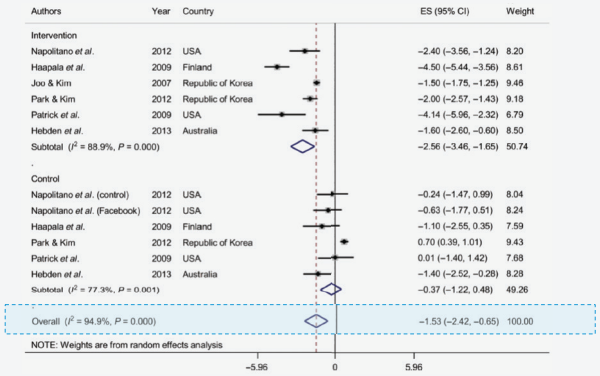


BDA The Association of UK Dietitians
THE OFFICIAL JOURNAL OF THE BRITISH DIETETIC ASSOCIATION
Journal of Human Nutrition and Dietetics
Journal of Human Nutrition and Dietetics

Review

A systematic review and meta-analysis of interventions for weight management using text messaging

G. Siopis,[1] T. Chey[2] & M. Allman-Farinelli[1]



Forest plot: mean weight change in body weight of intervention and control participants with the combined meta-regression shown below. Effect size (ES) is indicated by black diamonds; percentage weighting of each study towards the overall effect is indicated by the size of grey squares; 95% confidence interval is indicated by horizontal lines; the overall treatment effect lies at the center of the diamond with left and right endpoints indicating the 95% confidence interval (CI).

1. School of Molecular Bioscience, The University of Sydney, Sydney, NSW, Australia; 2. School of Public Health, The University of Sydney, Sydney, NSW, Australia

In the context of co-morbid conditions, including mental health challenges, mobile-based depression management resources have successfully reduced depressive symptoms.[72]

71. Siopis G, Chey T, Allman-Farinelli M. A systematic review and meta-analysis of interventions for weight management using text messaging. J Hum Nutr Diet. 2015 Feb;28 Suppl 2:1-15.

72. Twomey C, O'Reilly G, Bültmann O, Meyer B. Effectiveness of a tailored, integrative Internet intervention (deprexis) for depression: Updated meta-analysis. PLoS One. 2020 Jan 30;15(1):e0228100.

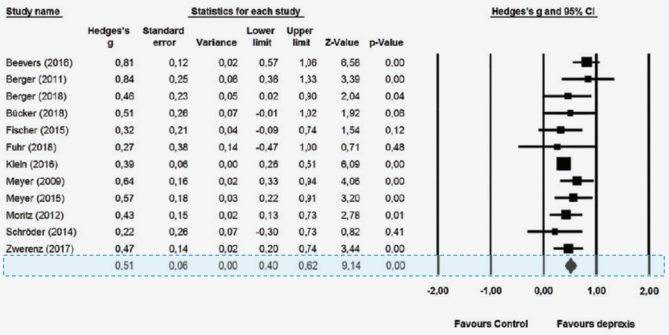
Tailored integrative Internet intervention for depression

Research Article

Effectiveness of a tailored, integrative Internet intervention (deprexis) for depression: Updated meta-analysis

Conal Twomey[1], Gary O'Reilly[1], Oliver Bültmann[2], Björn Meyer[2,3,a]

1. School of Psychology, University College Dublin, Belfield, Dublin, Ireland;
2. Research Department, Gaia, Hamburg, Germany;
3. Department of Psychology, City, University of London, London, England, United Kingdom



Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Beevers (2016)	0,81	0,12	0,02	0,57	1,06	6,58	0,00
Berger (2011)	0,84	0,25	0,06	0,36	1,33	3,39	0,00
Berger (2018)	0,48	0,23	0,05	0,02	0,90	2,04	0,04
Bücker (2018)	0,51	0,26	0,07	-0,01	1,02	1,92	0,06
Fischer (2015)	0,32	0,21	0,04	-0,09	0,74	1,54	0,12
Fuhr (2018)	0,27	0,38	0,14	-0,47	1,00	0,71	0,48
Klein (2016)	0,39	0,06	0,00	0,26	0,51	6,09	0,00
Meyer (2009)	0,64	0,16	0,02	0,33	0,94	4,06	0,00
Meyer (2015)	0,57	0,18	0,03	0,22	0,91	3,20	0,00
Moritz (2012)	0,43	0,15	0,02	0,13	0,73	2,78	0,01
Schröder (2014)	0,22	0,26	0,07	-0,30	0,73	0,82	0,41
Zwerenz (2017)	0,47	0,14	0,02	0,20	0,74	3,44	0,00
	0,51	0,06	0,00	0,40	0,62	9,14	0,00

A key takeaway is the effectiveness of cognitive behavioral therapy delivered through digital technology for depression and chronic pain management. However, we frequently observe that patients lack access to this treatment or fail to continue with it, primarily because it necessitates attending multiple in-person sessions at a clinic. Consequently, while the therapy is effective, it often remains inaccessible, it is inadequately funded by healthcare systems, and patients struggle to attend the 6–10 sessions required.

In a clinical trial, we evaluated standard cognitive behavioral therapy conducted by a psychologist in a clinic setting against the same educational content delivered through a digital tool.[73] The outcomes were strikingly similar. However, this does not suggest that digital tools are capable of supplanting our finest clinicians or that the education they provide is on par with that of a compassionate HCP employing effective communication strategies. What the trial revealed was that patients, burdened by the requirement to visit the clinic, completed only about six out of the 10 sessions. In contrast, when given access to the same material via a digital tool at their convenience and in the comfort of their homes, they engaged in approximately eight or nine sessions. Therefore, even though each digital interaction may be less impactful, the total treatment exposure was higher with the digital tool.

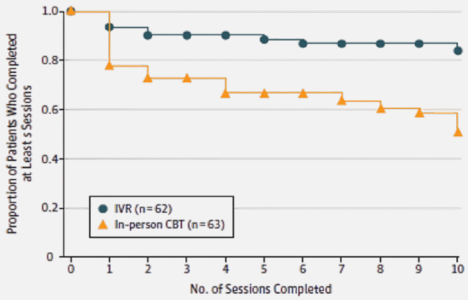
73. Heapy AA, Higgins DM, Goulet JL, LaChappelle KM, Driscoll MA, Czlapinski RA, Buta E, Piette JD, Krein SL, Kerns RD. Interactive Voice Response-Based Self-management for Chronic Back Pain: The COPES Noninferiority Randomized Trial. JAMA Intern Med. 2017 Jun 1;177(6):765-773.

JAMA Internal Medicine | Original investigation

Interactive Voice Response-Based Self-management for Chronic Back Pain

The COPES Noninferiority Randomized Trial

Number of treatment weeks by condition



CBT indicates cognitive behavioural therapy; IVR, interactive voice response

Heapy AA, Higgins DM, Goulet JL, LaChappelle KM, Driscoll MA, Czlapinski RA, Buta E, Piette JD, Krein SL, Kerns RD. Interactive Voice Response-Based Self-management for Chronic Back Pain: The COPES Noninferiority Randomized Trial. JAMA Intern Med. 2017 Jun 1;177(6):765-773.

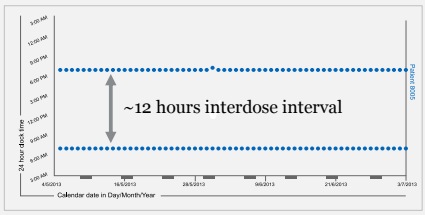
This finding is crucial as it illustrates how such resources can enhance our ability to support patients more effectively between brief face-to-face meetings.

> *"You can't manage what you don't measure"*
>
> *(Peter F. Drucker)*

Accurate measurement allows us to better understand the determinants and consequences of non-adherence and to focus on education and training, as well as incentivizing patients.

To illustrate medication intake behavior, consider this example using an electronic digital solution. The x-axis represents the days of follow-up, and the y-axis the time of drug intake. Each blue dot indicates when the patient takes their medication. Here we see a patient who consistently takes their twice-daily medication at the same time each day, with exactly 12 h between doses. This is an example of perfect adherence, though most patients will deviate from this ideal behavior.

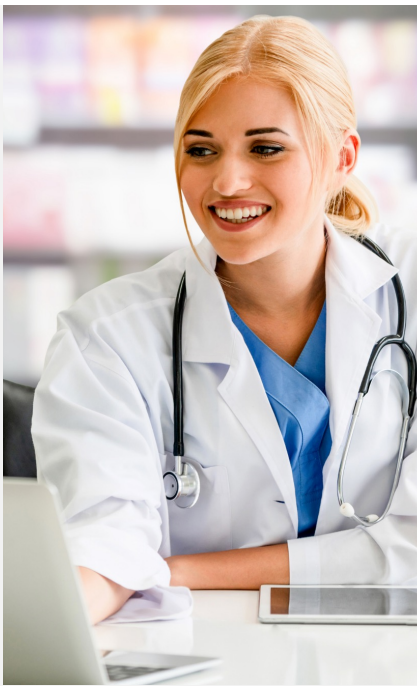
Medication Intake Behavior



You can't manage what you don't measure

Measure

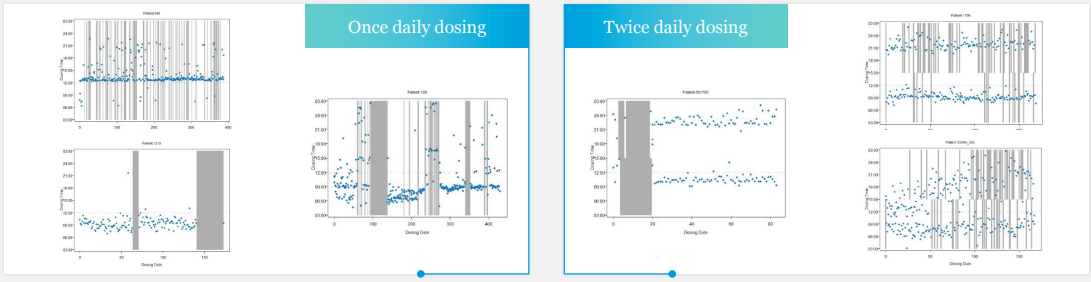
Manage



Typical deviations are observed when monitoring patients. It is important to note the "80% rule," where adherence above 80% is often considered adequate. However, even among patients with 81% adherence, we observe various deviations in behavior. Some miss doses randomly, others discontinue treatment, and some change behaviors frequently over 1 year. Once we understand these patterns, we can have focused discussions about non-adherence, enabling us to address specific issues and improve adherence.

The Unfortunate 80% Rule!

Each of these 6 patients took the same percentage (81%) of prescribed doses, which sounds good, but look

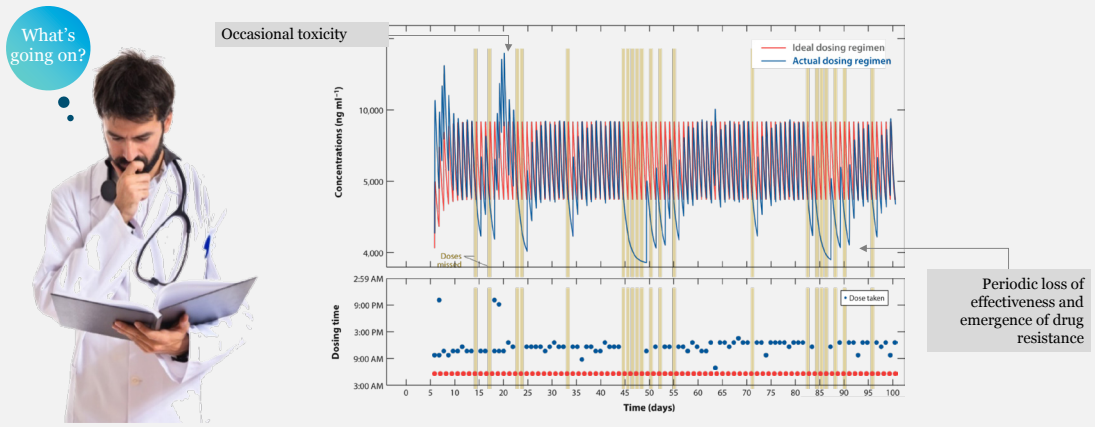


The variability in all these cases poses a significant risk to clinical success

Vrijens B et al., Assessment of medication adherence in field research, First Edition, John Wiley & Sons, Ltd., 2016

Variability in adherence poses significant risks to clinical success. Often, we assume patients take their medication perfectly, expecting blood concentration to reach and maintain a steady state. In reality, missed doses, extra doses, and breaks in treatment lead to variability in drug exposure, which can result in toxicity or reduced effectiveness and drug resistance. Therefore, measuring medication adherence is crucial to understanding both the determinants and clinical consequences.

Variable adherence creates drug-specific issues of efficacy, safety and drug resistance



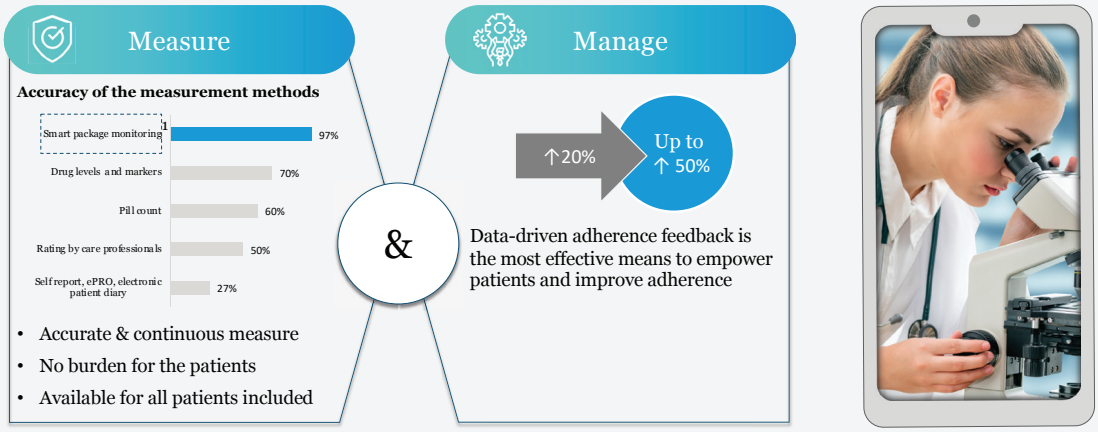
Blaschke TF, Osterberg L, Vrijens B, Urquhart J. Adherence to medications: insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. Annu Rev Pharmacol Toxicol. 2012;52:275-301.

During this session, Dr. Vrijens presented as an example a system launched over 35 years ago to monitor medication adherence using smart packages with embedded chips. These packages automatically detect when medication is removed or administered, and software analyzes and feeds back this information to HCPs and patients. This system has been used in over 70 countries for managing conditions like HIV or tuberculosis, with over 800 peer-reviewed publications demonstrating its effectiveness.

Smart packages are highly accurate, capturing 97% of adherence data, and they do not add burden to the patient. This is vital for adherence research and clinical trials, ensuring we have data for all patients, not just those who adopt new technology. Studies show that providing feedback to HCPs and having focused discussions can improve medication adherence by an average of 20%, and in some cases, up to 50%.[74,75]

74. El Alili M, Vrijens B, Demonceau J, Evers SM, Hiligsmann M. A scoping review of studies comparing the medication event monitoring system (MEMS) with alternative methods for measuring medication adherence. Br J Clin Pharmacol. 2016;82(1):268-279.
75. Demonceau J, et al. Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: a systematic literature review and meta-analysis. Drugs. 2013 May;73(6):545-62.

The Scientific Evidence



1. El Alili M, Vrijens B, Demonceau J, Evers SM, Hiligsmann M. A scoping review of studies comparing the medication event monitoring system (MEMS) with alternative methods for measuring medication adherence. Br J Clin Pharmacol. 2016;82(1):268-279.
2. Demonceau J, et al. Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: a systematic literature review and metaanalysis. Drugs. 2013 May;73(6):545-62.

The key to this intervention is empowering both patients and HCPs. It promotes self-management and patient engagement in their care. Patients are involved in monitoring their medication intake, which facilitates communication with HCPs. This communication is grounded in solid data, ensuring message consistency based on individual measurements.

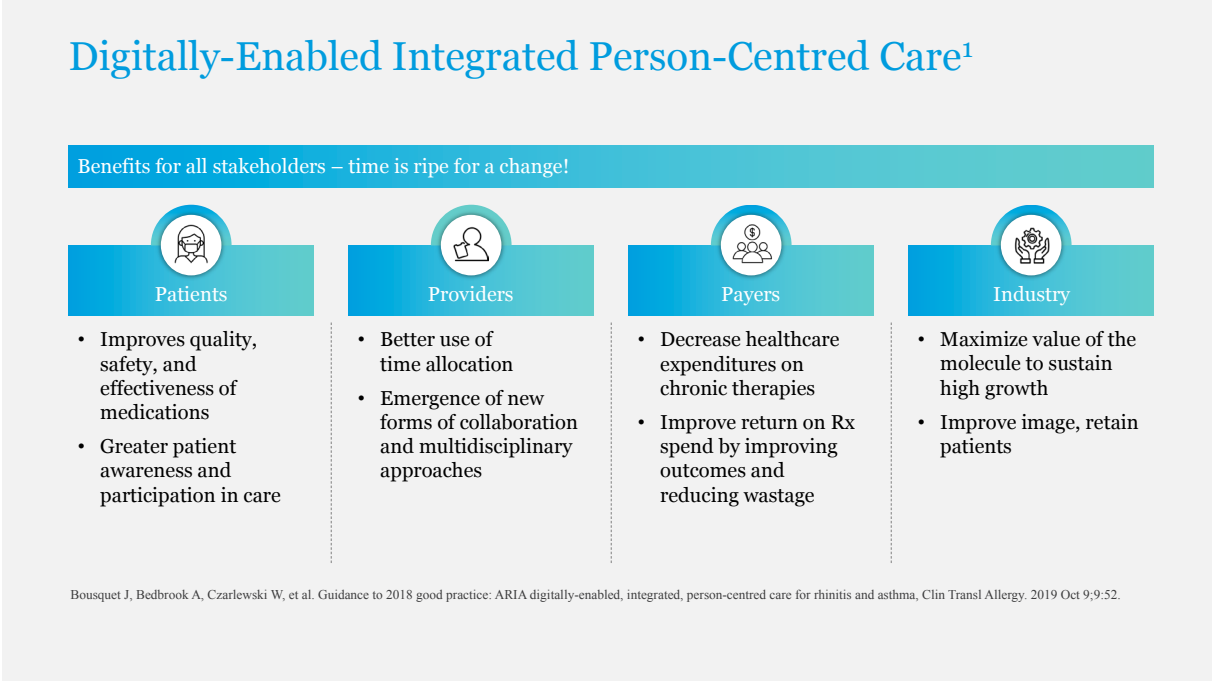
Empower Patients and HCPs

- Self-management and patient engagement in care
- Facilitate communication between the patient and providers (e.g., shared decision making)
- Consistency in the message delivered based on individual measures (e.g. multidisciplinary team)
- Individualized care based on data (e.g. rational decision rather than irrational or emotional)
- Risk stratification and prevention (e.g. set priorities and optimize HCPs' time)

A multidisciplinary team, comprising nurses, pharmacists, and physicians, is essential to address medication adherence issues. With accurate measurements, all team members can discuss the same data and deliver consistent messages, regardless of the provider.

Such an approach also enables personalized care based on data, leading to more rational decision making. This is particularly relevant when adjusting therapies for patients who do not respond to initial treatments. Often, the root cause of the issue is non-adherence. By having precise measurements, HCPs can tailor individual care plans and avoid unnecessary treatment escalation.

Moreover, such a system facilitates risk stratification and prevention, allowing us to identify at-risk patients. This ensures that HCPs can focus their time on those who need it most, which is vital for optimizing the healthcare system.



Digitally-enabled, integrated, person-centered care offers clear benefits to all stakeholders.[76] Patients experience improved quality, safety, and medication effectiveness, along with increased awareness and participation in their care. HCPs benefit from better time management and the emergence of new collaborative, multidisciplinary approaches. Payers see a reduction in healthcare expenditures on chronic therapies and an improvement in the return on prescription investments by enhancing outcomes and reducing waste. For the industry, it maximizes the value of medications, supports growth, and improves patient retention.

76. Bousquet J, Bedbrook A, Czarlewski W, et al. Guidance to 2018 good practice: ARIA digitally-enabled, integrated, person-centred care for rhinitis and asthma, Clin Transl Allergy. 2019 Oct 9;9:52.

In conclusion, every prescription and medication delivery presents an opportunity to address medication adherence. The medical world must seize every chance to tackle this critical issue, one of the most significant challenges in healthcare today.

Individualized adherence strategies and their impact on patient experience in women's health

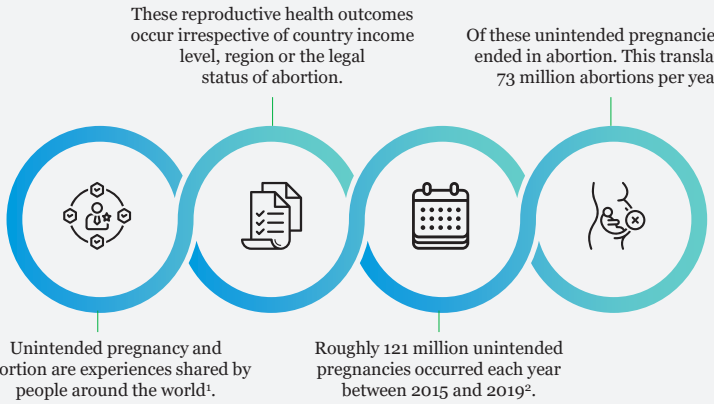
This session draws upon the lectures delivered by Profs. Johannes Bitzer, Rossella Nappi, and Horne at the a:care Congress in 2021.

The impact of non-adherence in women's health: Unintended pregnancies

Let us address first a significant health issue that is not exactly a disease but poses a substantial problem for healthcare systems: unintended pregnancies. This issue is globally recognized and transcends social classes and countries. It is estimated that approximately 121 million unintended pregnancies occurred annually between 2015 and 2019.[77]

77. Bearak J et al, Unintended pregnancy and abortion by income, region, and the legal status of abortion estimates from a comprehensive model for 1990–2019, Lancet 2020;8:e1152-61.

The pandemic of unintended pregnancies



- Unintended pregnancies have a higher risk of obstetrical complications[3]
- Negative psychosocial consequences for the woman and the newborn especially in adolescents[3]

1. RCOG and FSRH key messages on safe abortion. https://www.rcog.org.uk/globalassets/documents/global-network/projects-and-partnerships/making-abortion-safe/rcogand- fsrh-key-messages-on-safe-abortion.pdf [Accessed October 2021];
2. Bearak J et al, Unintended pregnancy and abortion by income, region, and the legal status of abortion estimates from a comprehensive model for 1990–2019, Lancet 2020;8:e1152-61; 3. Brown S and Eisenberg L (1995), The Best Intentions: Unintended Pregnancy and the Well-Being of Children and Families. National Academy Press.

There are two main concerns with unintended pregnancies: If the pregnancy is continued, it often leads to a higher risk of obstetric complications, particularly for adolescents, and negative psychosocial consequences for both the woman and the newborn. If the pregnancy is terminated, which is often the case, about half of these terminations are performed under unsafe conditions, presenting a serious health challenge.

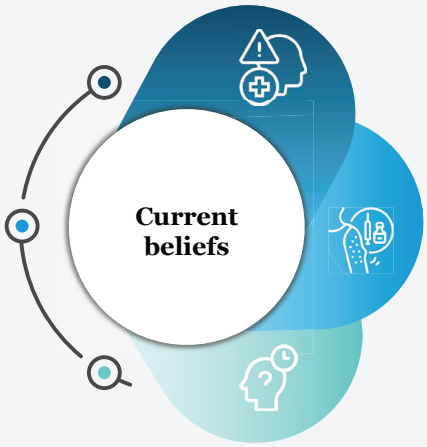
So, why do unintended pregnancies occur? Reasons include the absence of contraception due to lack of motivation or fear of health risks and side effects, discontinuation of contraception because of side effects or negative social perception influenced by the media, and non-adherence to proper contraceptive use. This boils down to behavior surrounding contraception.

Why Does It Happen?

No contraception
- Lack of motivation
- Fear of health risks and side effects

Discontinuation of contraception
- Side effects
- Bad image

Forgetting or non-adherence to proper use of the method

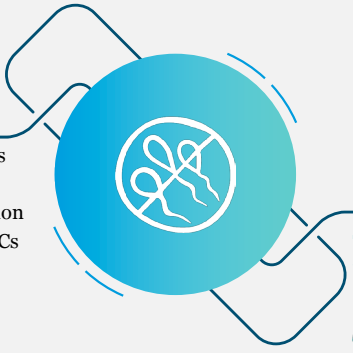


What strategies can we employ? The classical medical strategy involves developing user-independent methods, such as long-acting contraceptives like IUDs, implants, and injections. Another approach is individualization, finding the right contraception for the right woman. To achieve this, we must develop communication skills that foster patient-centered shared decision making, counseling, and care. This approach increases and maintains motivation by providing knowledge, empowering the user to make a self-determined, individual benefit–risk evaluation, and ensuring they feel the chosen method is tailored to their needs. We should partner with them in follow-up to evaluate satisfaction and provide advice.

How to improve adherence in contraception

The medical strategy

User independent methods
- Long-acting methods
- Intrauterine contraception
- Progestogen based LARCs
- Future methods

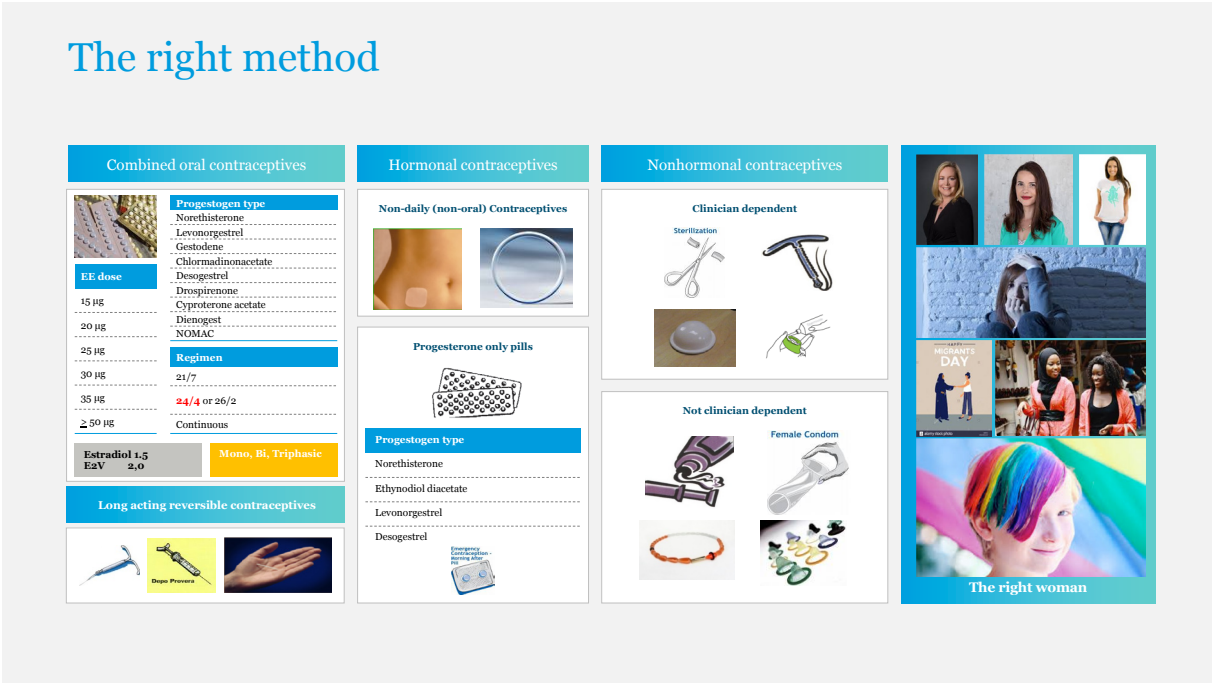


Patient centered, shared decision making based counselling and care
- Increase and maintain motivation by providing knowledge (empowerment) to the user
- Help the user to come to a self-determined, individual benefit/risk evaluation (this is my method)
- Be a partner in the follow up to evaluate the satisfaction, inform and give advice

The individualization method The right contraception for the right woman

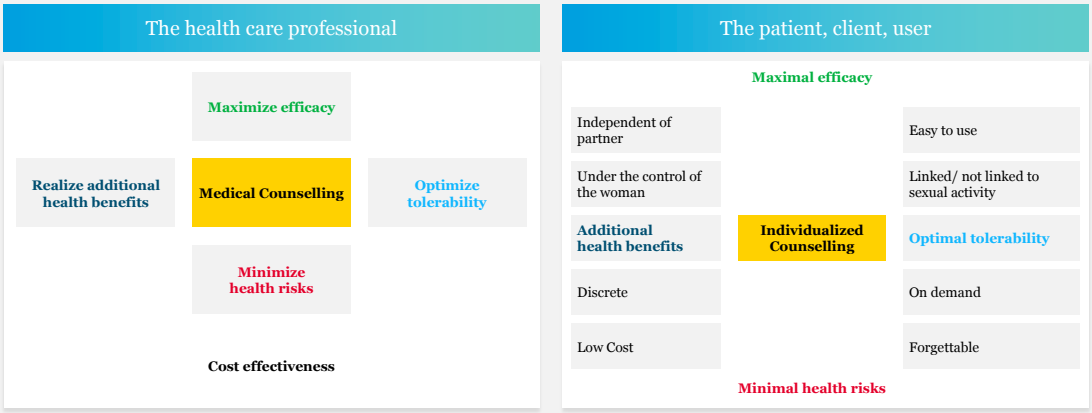
1. Mack N, et al. Strategies to improve adherence and continuation of shorter-term hormonal methods of contraception. Cochrane Database Syst Rev. 2019 Apr 23;4(4):CD004317.pub5.;
2. Bitzer J. Kontrazeptive Compliance - warum kommt es immer wieder zum Versagen der kontrazeptiven Therapie? [Contraceptive compliance - why is contraceptive failure still so frequent?]. Ther Umsch. 2009 Feb;66(2):137-43. German.

We face a challenge: On one hand, we have a vast array of contraceptive methods to prevent unintended pregnancies, both hormonal and non-hormonal, partner independent, and not requiring HCP. On the other hand, we have a diverse population of women with varying cultural, medical, social, and economic backgrounds.



The question is, how can we align these two protagonists? HCPs desire to maximize the efficacy of contraception, minimize health risks, optimize tolerability, and, if possible, realize additional health benefits while considering cost effectiveness for the patient. These four main objectives are crucial, but individual preferences, such as ease of use, discretion, and independence from a partner, are also important.

What do doctors want, what do women want?

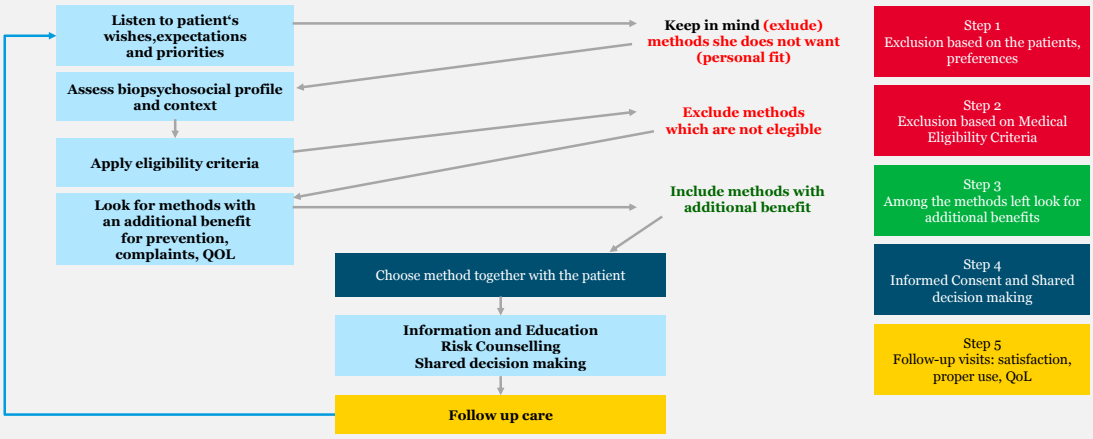


1. Merki-Feld GS, Caetano C, Porz TC, Bitzer J. Are there unmet needs in contraceptive counselling and choice? Findings of the European TANCO Study. Eur J Contracept Reprod Healthcare. 2018 Jun;23(3):183-193.
2. Bitzer J, Oppelt PG, Deten A. Evaluation of a patient-centred, needs-based approach to support shared decision making in contraceptive counselling: the COCO study. Eur J Contracept Reprod Healthcare. 2021 Aug;26(4):326-333.

To bring these two protagonists together, HCPs need expertise in contraceptive methods and communication skills. The goal is to align the method profile with the woman's profile and her context. This is achieved through the science and art of contraceptive counseling, which includes patient-centered communication, information, education, and shared decision making.

The contraceptive dialogue begins with listening to the patient's desires, expectations, and priorities, which helps us understand what they do not want and what does not align with their personal values and goals. Next, we create a medical profile and a psychosocial profile within the context, applying eligibility criteria to exclude unsuitable methods for medical or psychosocial reasons.

The Contraceptive Dialogue



We then consider the remaining methods for any additional benefits they may offer for prevention or relief of complaints. Studies have shown that if a contraceptive method improves quality of life, continuation and adherence rates are better. We aim to include methods with additional benefits among the remaining options.

Give evidence based information in a patient centered way

Inform and educate about methods in understandable way based on EBM

- Efficacy
- Health Risks
- Tolerability
- Benefits

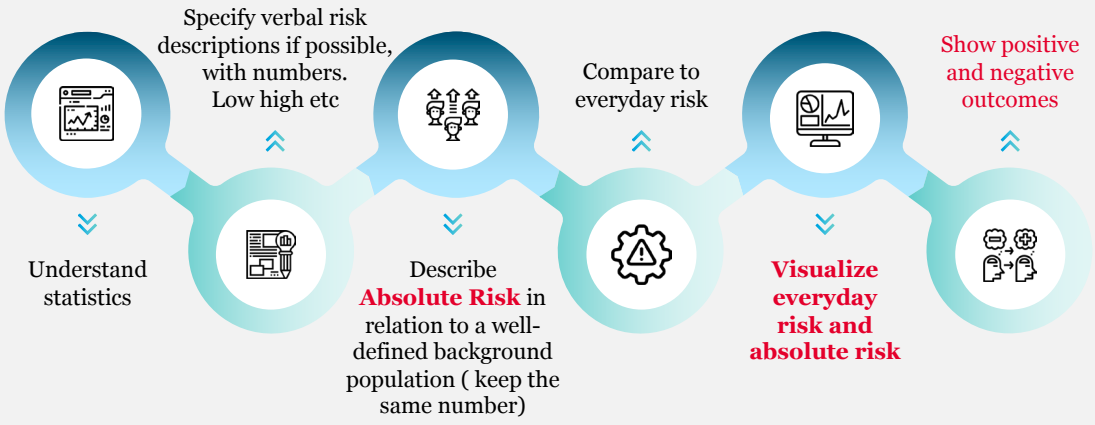
The EPE principle

- **Elicit** • Needs, knowledge, expectations, experience
- **Provide** • Small units of • information, Structurizing, • Summarizing
- **Elicit** • Understaning, Interpretation

Bitzer J, Marin V, Lira J. Contraceptive counselling and care: a personalized interactive approach. Eur J Contracept Reprod Healthcare. 2017 Dec;22(6):418-423

The final step is shared decision making, choosing the method together with the patient. To reach this goal, we apply communication skills, focusing on information, education, and risk counseling. The process involves providing evidence-based information in a patient-centered manner, understanding the statistics about the methods, and explaining risks in relation to a well-defined background population.[78] We compare these risks to everyday risks, visualizing both positive and negative outcomes.

Recommendations and guidelines for risk counselling



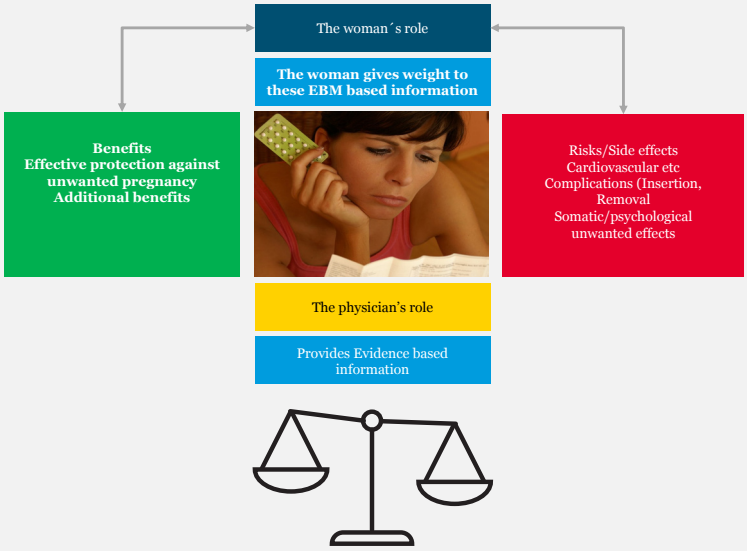
Bitzer J, Marin V, Lira J. Contraceptive counselling and care: a personalized interactive approach. Eur J Contracept Reprod Healthcare. 2017 Dec;22(6):418-423

After evaluating the benefits and risks through the lens of evidence-based medicine, the user personally weighs this information, identifying which aspects are most significant to them. This process culminates in a decision that aligns with their unique needs and expectations, an essential factor for ensuring commitment to the chosen method. The subsequent step involves arranging a follow-up with the patient to reassess whether the objectives, previously set in collaboration, have been fulfilled.

78. Bitzer J, Marin V, Lira J. Contraceptive counselling and care: a personalized interactive approach. Eur J Contracept Reprod Healthcare. 2017 Dec;22(6):418-423.

Contraceptive counselling and care is a continuous benefit/ risk evaluation-trade off

Bitzer J, Marin V, Lira J. Contraceptive counselling and care: a personalized interactive approach. Eur J Contracept Reprod Healthcare. 2017 Dec;22(6):418-423

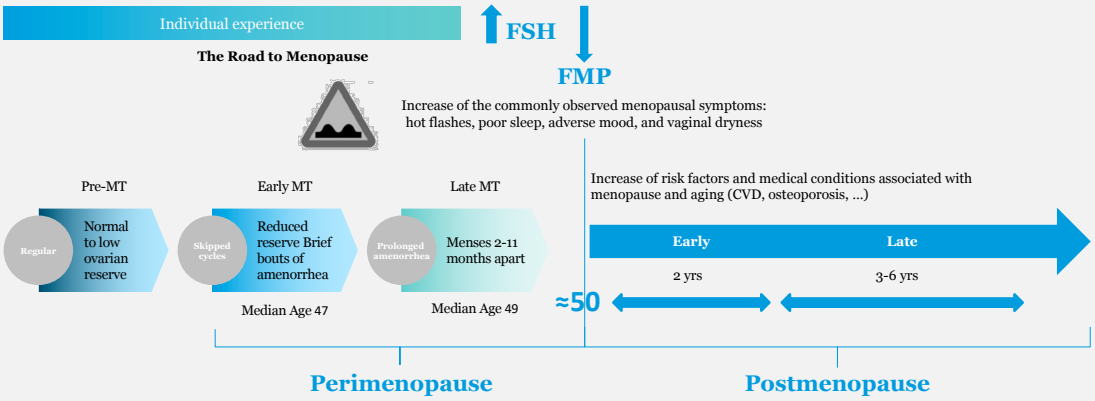


Navigating menopause with your patients

Menopause is a significant journey, and each woman experiences it uniquely. The defining feature of this phase is the irregularity of menstrual cycles, accompanied by a gradual increase in FSH levels, which begins even before the cessation of menstruation, typically around the age of 50. Women may encounter various symptoms, such as hot flashes, sleep disturbances, mood changes, and vaginal dryness. After the final menstrual period, there is an observed rise in risk factors and medical conditions associated with menopause and aging, like CVDs and osteoporosis.[79]

79. World Health Organization. Menopause. Who.int. Published October 16, 2024. https://www.who.int/news-room/fact-sheets/detail/menopause/ [Accessed November 2025].

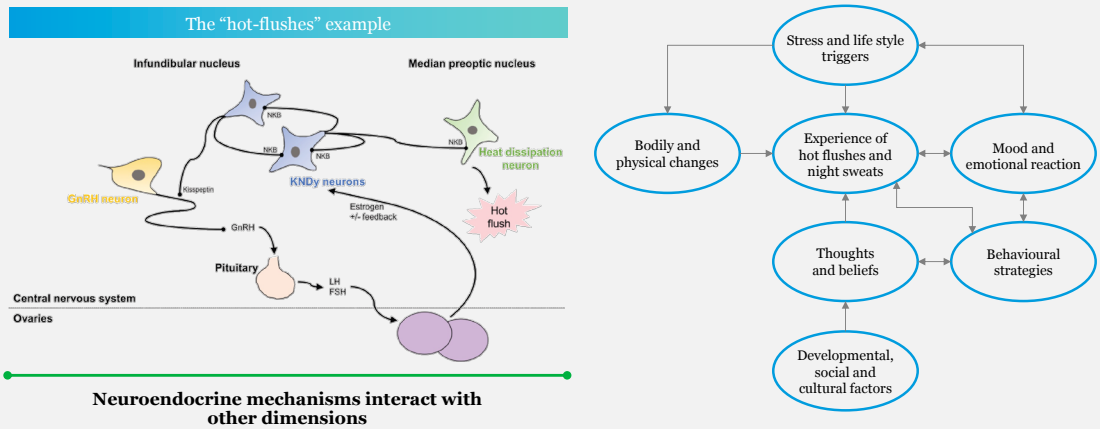
Menopause is a long journey



Santoro N. Perimenopause: From Research to Practice. J Womens Health (Larchmt). 2016 Apr;25(4):332-9. Epub 2015 Dec 10.; Harlow Sd et al.; STRAW 10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. Menopause. 2012 Apr;19(4):387-95; The NAMS. Keeping your heart healthy at menopause https://www.menopause.org/forwomen/menopauseflashes/bone-health-and-heart-health/keeping-your-heart-healthy-at-menopause [Accessed October2021]

It is important to note that menopause is not solely a biological process; it also encompasses psychosocial factors that influence symptomatology and women's approach to this life stage. For instance, hot flashes are not just a result of estrogen deficiency but are also affected by thoughts, beliefs, and behavioral strategies that women employ to manage this symptom, along with their emotional state, stress, and sociocultural factors.[80]

Menopause is a bio-psycho-socio-cultural process

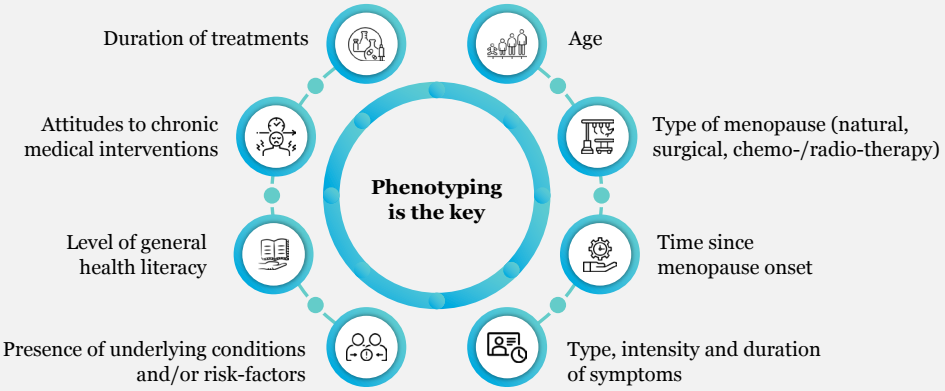


Hunter M, Rendall M. Bio-psycho-socio-cultural perspectives on menopause. Best Pract Res Clin Obstet Gynaecol. 2007 Apr;21(2):261-74. Santoro N, Roeca C, Peters BA, Neal-Perry G. The Menopause Transition: Signs, Symptoms, and Management Options. J Clin Endocrinol Metab. 2021 Jan 1;106(1):1-15.

80. Hunter M, Rendall M. Bio-psycho-socio-cultural perspectives on menopause. Best Pract Res Clin Obstet Gynaecol. 2007 Apr;21(2):261-74.

In clinical practice, we face the challenge of not having a one-size-fits-all approach to menopause. Treatment must be tailored based on age, type of menopause (whether natural, surgical, or induced by chemotherapy or radiotherapy), time since onset, symptom intensity and duration, and the presence of underlying conditions and risk factors. Additionally, varying levels of health literacy among women necessitate personalized communication based on their knowledge, attitudes towards chronic medical interventions, and readiness for long-term treatment.

There is not only one menopause!

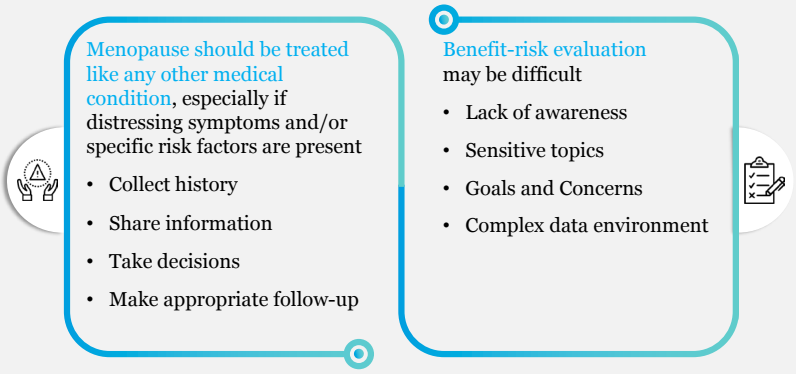


1. Genazzani AR et al. Hormone therapy in the postmenopausal years: considering benefits and risks in clinical practice. Hum Reprod Update. 2021 Aug 25:dmab026;
2. The 2017 Hormone therapy position statement of The NAMS. Menopause. 2017 Nov;24(7):728-753;
3. Baber RJ, Panay N, Fenton A; IMS Writing Group. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy. Climacteric. 2016 Apr;19(2):109-50. Epub 2016 Feb 12.;
4. Stuenkel et al. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015 Nov;100(11):3975-4011. Epub 2015 Oct 7.;
5. Berkman ND, Davis TC, McCormack L. Health literacy: what is it? J Health Commun. 2010;15 Suppl 2:9-19.

Addressing menopause in a clinical setting involves recognizing it as a personal experience that should be managed like any other medical condition, particularly when distressing symptoms or specific risk factors are present.[81] Clinicians must gather patient history, share information, make informed decisions, and conduct appropriate follow-ups. The evaluation of benefits and risks can be challenging due to a lack of awareness about the condition, and women may need to discuss sensitive topics like vaginal dryness, which vary in importance to each individual.

81. Parish SJ, Nappi RE, Kingsberg S. Perspectives on counseling patients about menopausal hormone therapy: strategies in a complex data environment. Menopause. 2018 Aug;25(8):937-949.

Specific challenges at menopause

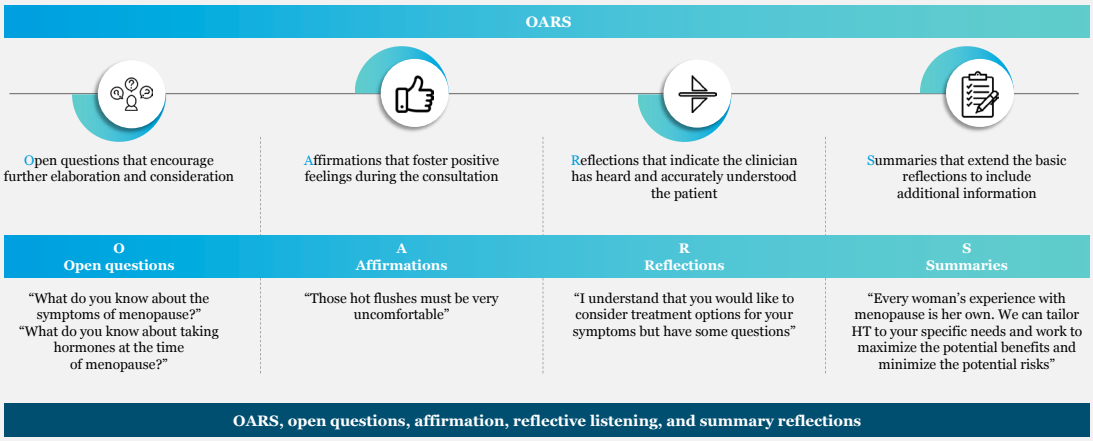


Training and competence of HCPs are fundamental to empower women

Parish SJ, Nappi RE, Kingsberg S. Perspectives on counseling patients about menopausal hormone therapy: strategies in a complex data environment. Menopause. 2018 Aug;25(8):937-949.

Effective communication in menopause management involves using the OARS model:[82] open questions, affirmations, reflections, and summaries. This model encourages elaboration, fosters positive feelings, ensures the patient feels understood, and provides comprehensive reflections on the discussion.

Successful communication at menopause



OARS, open questions, affirmation, reflective listening, and summary reflections

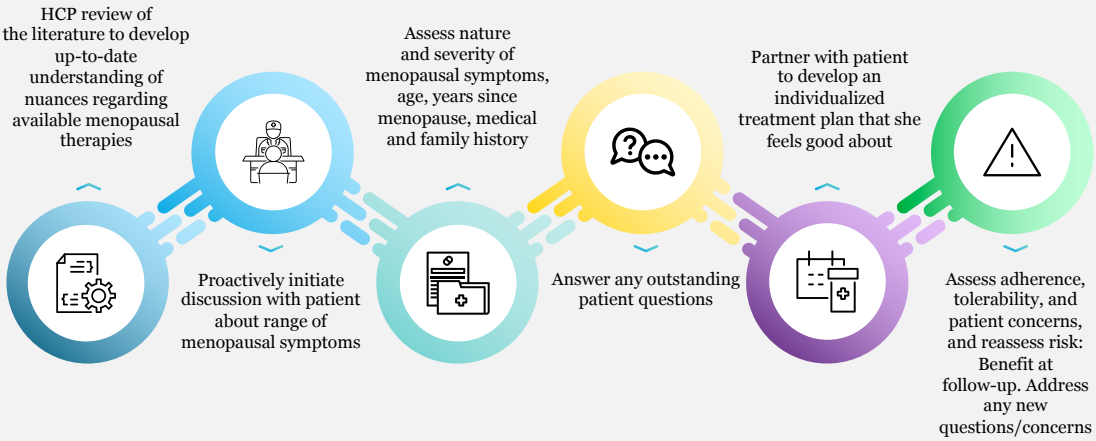
Tuccero D, Railey K, Briggs M, Hull SK. Behavioral Health in Prevention and Chronic Illness Management: Motivational Interviewing. Prim Care. 2016 Jun;43(2):191-202.; Parish SJ, et al. Perspectives on counseling patients about menopausal hormone therapy: strategies in a complex data environment. Menopause. 2018 Aug;25(8):937-949.

82. Tuccero D, Railey K, Briggs M, Hull SK. Behavioral Health in Prevention and Chronic Illness Management: Motivational Interviewing. Prim Care. 2016 Jun;43(2):191-202.

To individualize the conversation about menopausal symptom treatment, HCPs should do the following:[83]

- Stay informed about the latest literature on menopausal therapies;
- Proactively engage patients in discussions about the range and severity of symptoms;
- Assess symptoms based on age, years since menopause, and medical history;
- Answer patient questions and collaborate to develop a personalized treatment plan;
- Monitor adherence, tolerability, and patient concerns, reassessing risks and benefits during follow-up.

Individualizing discussions with women about treatment of menopausal symptoms



Parish SJ, Nappi RE, Kingsberg S. Perspectives on counseling patients about menopausal hormone therapy: strategies in a complex data environment. Menopause. 2018 Aug;25(8):937-949

Shared decision making in menopause management is complex due to its natural occurrence, the diversity of experiences, the need for communication skills, and the importance of balancing risks and benefits for personalized care. Treatment options should always consider guidelines, the context of menopausal medicine, symptom management, and chronic condition prevention.[84,85,85] Emphasizing primary prevention, a healthy diet, lifestyle adjustments, and appropriate

83. Parish SJ, Nappi RE, Kingsberg S. Perspectives on counseling patients about menopausal hormone therapy: strategies in a complex data environment. Menopause. 2018 Aug;25(8):937-949.
84. Baber RJ, Panay N, Fenton A; IMS Writing Group. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy. Climacteric. 2016 Apr;19(2):109-50.
85. Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, Santen RJ. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015 Nov;100(11):3975-4011.
86. Lobo RA, Davis SR, De Villiers TJ, Gompel A, Henderson VW, Hodis HN, Lumsden MA, Mack WJ, Shapiro S, Baber RJ. Prevention of diseases after menopause. Climacteric. 2014 Oct;17(5):540-56.

supplementation with vitamin D is crucial. It is also vital to tailor menopause hormone therapy to each woman's needs, considering type, route, dose, duration, goals, efficacy, tolerability, adherence, and other relevant factors.

Successful communication and shared decision making lead to better health outcomes during menopause. Clinicians should improve patient knowledge, align treatment with patient values, put risks and benefits into perspective, enhance treatment adherence, and increase patient satisfaction. Taking the time to present evidence clearly is essential for engaging patients in their own medical care.

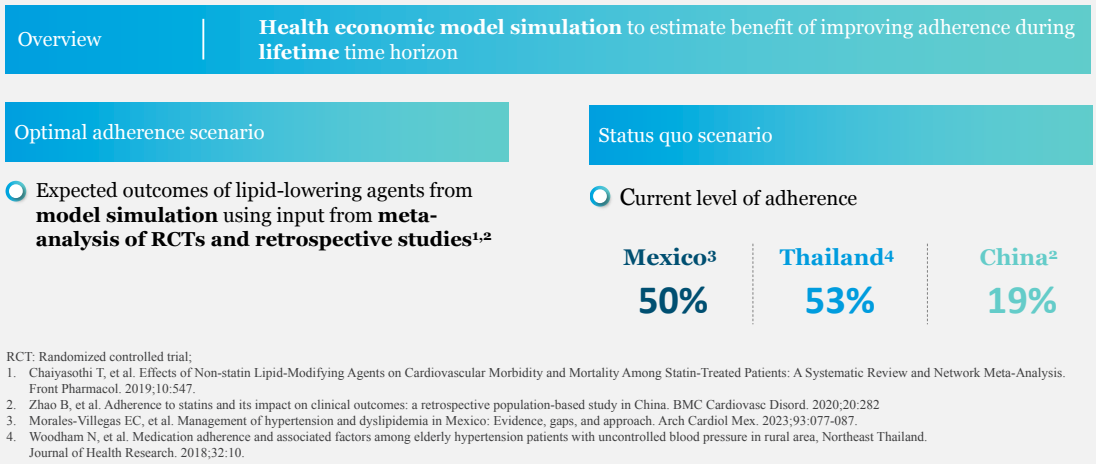
Clinical and economic benefits of improving medication adherence in emerging countries-The a:care HEOR study

During the a:care Congress 2024, Prof. Nathorn Chaiyakunapruk from the University of Utah discussed the clinical and economic benefits of improving medication adherence in emerging countries.

Expectations and reality often differ. Drugs tested in randomized controlled trials may not show the same efficacy in real-life use if patients do not take them. Simply put, drugs do not work in patients who do not take them, making non-adherence a critical issue that needs to be addressed.

Health economics studies are essential to demonstrate the clinical and economic benefits of improving adherence. This information is crucial for policymakers. An a:care HEOR study aimed to estimate the potential benefits of improving adherence in secondary CVD prevention using lipid-lowering agents in three countries: Mexico, Thailand, and China. These countries were chosen as representatives of middle-income countries in different geographical regions.

Method



RCT: Randomized controlled trial;

1. Chaiyasothi T, et al. Effects of Non-statin Lipid-Modifying Agents on Cardiovascular Morbidity and Mortality Among Statin-Treated Patients: A Systematic Review and Network Meta-Analysis. Front Pharmacol. 2019;10:547.
2. Zhao B, et al. Adherence to statins and its impact on clinical outcomes: a retrospective population-based study in China. BMC Cardiovasc Disord. 2020;20:282
3. Morales-Villegas EC, et al. Management of hypertension and dyslipidemia in Mexico: Evidence, gaps, and approach. Arch Cardiol Mex. 2023;93:077-087.
4. Woodham N, et al. Medication adherence and associated factors among elderly hypertension patients with uncontrolled blood pressure in rural area, Northeast Thailand. Journal of Health Research. 2018;32:10.

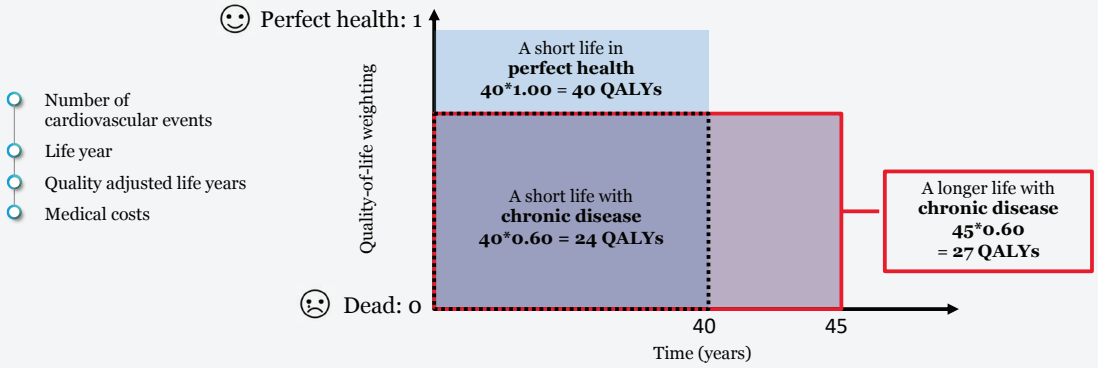
Given the objective of estimating the benefits of improving adherence, conducting lifetime clinical trials is impractical and unethical. Therefore, the authors of the a:care HEOR study used computer simulations to model the effects of improved adherence.[87] They compared the current adherence rates in Mexico (50%), Thailand (53%), and China (19%) with an optimal adherence scenario.

The simulation was based on meta-analyses of randomized controlled trials and retrospective studies. They measured outcomes such as the number of cardiovascular events prevented, life years gained, quality-adjusted life years (QALYs), and medical costs. QALYs consider both the quantity and quality of life, providing a meaningful metric for decision making and policy processes.

87. Cho JY, Wilson FA, Chaikledkaew U, Chen Y, Phrommintikul A, Diaz-Aguilera MA, Chen Z, Kim K, Chaiyakunapruk N. Projected Cost Savings With Optimal Medication Adherence in Patients With Cardiovascular Disease Requiring Lipid-Lowering Therapy: A Multinational Economic Evaluation Study. J Am Heart Assoc. 2024 Nov 19;13(22):e037792.

Method

Outcomes



Cho JY, et al. Projected Cost Savings with Optimal Medication Adherence in Cardiovascular Disease Patients Requiring Lipid Lowering Therapy: a Multi-National Economic Evaluation Study. JAHA 2024. Manuscript in Press.

Results showed that improving adherence could prevent 41, 34, and 63 cardiovascular events per 1,000 patients in Mexico, Thailand, and China, respectively. On average, each patient could gain 0.6 to 0.9 life years or QALYs. Importantly, improving adherence also resulted in cost savings in all three countries.

Result

Key findings

Result of base-case analysis from 1,000 patients in each country

Outcomes	Mexico	Thailand	China
Cardiovascular events averted			
Non-fatal CVEs	22.07	21.36	38.49
Fatal CVEs	17.91	12.67	24.47
Total CVEs	41.54	34.05	62.96
Incremental effectiveness	0.60 LY	0.59 QALYs	0.93 QALYs
Incremental direct medical costs			
Disease management cost	$226.67	$23.74	$271.96
Non-fatal CVE cost	-$401.78	-$226.78	-$523.05
Fatal CVE cost	-$223.98	-$86.63	-$300.80
Incremental direct non-medical costs	$2.71	$102.66	$9.72
Incremental indirect costs	-$15.74	-$31.93	-$148.66
Incremental costs from healthcare system perspective	-$399.09	-$289.67	-$551.90
Incremental costs from societal perspectives	-$412.12	-$218.95	-$690.84

CVE: cardiovascular events; LY: Life Year; QALY: Quality-adjusted life year
Cho JY, et al. Projected Cost Savings with Optimal Medication Adherence in Cardiovascular Disease Patients Requiring Lipid Lowering Therapy: a Multi-National Economic Evaluation Study. JAHA 2024. Manuscript in Press

In terms of cost effectiveness, they found that the interventions to improve adherence were cost saving and worth the investment. The projected cost savings and improved health outcomes highlight the importance of addressing medication adherence.

Result

Threshold analysis

Result of threshold analyses from a societal perspective

Item	Mexico	Thailand	China
Willingness-to-pay threshold	**$11,091/LY**	**$4,688/QALY**	**$18,207/QALY**
Direct medical costs			
Prevented CVE-related costs	$625.76	$313.42	$823.85
Incremental disease management costs due to increased life years	$226.67	$23.74	$271.96
Incremental direct non-medical costs	$2.71	$102.66	$9.72
Incremental indirect costs	-$13.03	-$31.93	-$148.66
Lifetime permissible expense for optimal adherence for cost saving	**$412.12**	**$218.95**	**$690.84**
Annual permissible expense for optimal adherence for cost saving	$32.58	$14.72	$57.75
Lifetime permissible expense for optimal adherence for cost-effectiveness	**$7,124.15**	**$3,421.91**	**$17,706.21**
Annual permissible expense for optimal adherence for cost-effectiveness	$563.18	$230.00	$1,480.02

CVE: cardiovascular events
Cho JY, et al. Projected Cost Savings with Optimal Medication Adherence in Cardiovascular Disease Patients Requiring Lipid Lowering Therapy: a Multi-National Economic Evaluation Study. JAHA 2024. Manuscript in Press

The analysis used reliable databases and sources, and the results were validated by relevant stakeholders. Most cost savings came from preventing cardiovascular events, which are a significant burden on healthcare systems due to poor medication adherence.

Discussion

Key take away

Projected cost savings associated with optimal adherence were highlighted:
- This study shows consistent results with **not only cost saving but improved health outcomes** in three countries from three different geographic regions
  - Our analyses rely on several network meta-analyses to ensure **generalizability**
  - Our analyses are validated by key stakeholders to ensure **relevancy**

Most cost savings comes from **prevented cardiovascular event**
- The healthcare system has been suffered from **preventable** medical costs due to **poor medication adherence**

Our model provide **a platform of health economic study** on medication adherence, which allow to estimate cost-effectiveness of newly developed adherence improving interventions such as **digital applications**

Cho JY, et al. Projected Cost Savings with Optimal Medication Adherence in Cardiovascular Disease Patients Requiring Lipid Lowering Therapy: a Multi-National Economic Evaluation Study. JAHA 2024. Manuscript in Press

In conclusion, improving medication adherence to optimal levels in CVD requiring lipid-lowering agents is not only cost saving but also prevents cardiovascular events and increases life years or QALYs in Mexico, Thailand, and China. The findings of the a:care HEOR study provide important evidence for policymakers to consider strategies to improve adherence, ultimately leading to better patient outcomes and more efficient healthcare systems.

Conclusion

1. **Improving medication adherence** to optimal levels in CVD patients requiring lipid-lowering therapy is not only **cost-saving but averting cardiovascular events** and **increasing life-years and QALYs'** in Mexico, Thailand, and China from both societal and healthcare perspectives.

2. Our findings advocate for the consideration of strategies by national healthcare systems to improve optimal adherence (e.g., digital technologies or programs leading to behavior changes) in these countries.

CVD: cardiovascular disease

Policymakers' points of view

This session was held by Dr. Miguel Angel Díaz Aguilera, from the National Center for Preventive Programs and Disease Control (Mexico City, Mexico) during the a:care Congress 2024.

CVDs remain the leading cause of death worldwide and significantly contribute to health loss and excessive healthcare costs globally. These illnesses are mainly caused by risk factors such as hypertension and hyperlipidemia. In fact, hyperlipidemia increases the risk of heart disease and stroke, and globally, high cholesterol is the third leading cause of heart disease. Overall, hyperlipidemia is responsible for 2.6 million deaths and 29 million years of life lost due to disease, disability, or early death.

CVDs

Have collectively remained the leading causes of death worldwide and substantially contribute to loss of health and excess health system costs[1]

- Hyperlipidemia increase the risks of heart disease and stroke; globally, a third of ischemic heart disease is due to high cholesterol[2]
- Overall, hyperlipidemia was attributable to cause 2.6 million deaths and 29.7 million DALYS in 2019[2]
- In 2008, the global prevalence of raised total cholesterol among adults was 39% (37% for males and 40% for females)[2]

Burden of comorbidities in hyperlipidemia, prevalence

Diabetes[3-7]	16–36%
Hypertension[4-5, 7]	62–98%
Heart failure[5,7-8]	4–21%
CKD[4-7]	3–24%

1. Vaduganathan M, et al. The Global Burden ofCardiovascular Diseases and Risk. JACC. 2022;80(25): 2361-2371 . 2. World Health Organization. Raised cholesterol, available at: https://www.who.int/data/gho/indicatormetadata-registry/imr-details/3236#:~:text=Raised%20cholesterol%20levels%20increase%20the,or%202%25%20of%20total%20DALYS. (consulted August 25th, 2024) ; 3. Bruckert E, et al. Proportion of High-Risk/Very High-Risk Patients in Europe with Low-Density Lipoprotein Cholesterol at Target According to European Guidelines: A Systematic Review Adv Ther. 2020; 37(5):1724-1736 ; 4. Steen DL, et al. Retrospective examination of lipidlowering treatment patterns in a real-world high-risk cohort in the UK in 2014: comparison with the National Institute for Health and Care Excellence (NICE) 2014 lipid modification guidelines. BMJ Open 2017;7:e013255 ; 5. Fox KM, et al. Treatment patterns and low-density lipoprotein cholesterol (LDL-C) goal attainment among patients receiving high- or moderate-intensity statins. Clin Res Cardiol. 2018; 107(5): 380–88 ; 6. Vallejo-Vaz AJ, et al. Associations between lower levels of low-density lipoprotein cholesterol and cardiovascular events in very high-risk patients: Pooled analysis of nine ODYSSEY trials of alirocumab versus control Atherosclerosis. 2019;288:85-9 ; 7. Lindh M, et al. Cardiovascular event rates in a high atherosclerotic cardiovascular disease risk population: estimates from Swedish population-based register data. Eur Heart J Qual Care Clin Outcomes. 2019;5(3):225-32; 8. Rashid M, et al. Impact of co-morbid burden on mortality in patients with coronary heart disease, heart failure, and cerebrovascular accident: a systematic review and meta-analysis Eur Heart J Qual Care Clin Outcomes. 2017; 3(1):20-36

In 2008, the global prevalence of high total cholesterol among adults was almost 40%, meaning that four out of 10 adults worldwide have this risk factor and are at risk of developing heart disease. Hyperlipidemia is often associated with other comorbidities, such as diabetes (up to 36%), hypertension (up to 98%), heart failure (up to 21%), and chronic kidney disease (up to 24%).

Despite numerous medical advances and new drug developments, the management of these cardiometabolic diseases has not improved significantly, mainly due to a lack of adherence to treatments. This affects many people, with half of the patient population not adhering to their prescribed treatments, leading to severe complications, premature deaths, and increased use of healthcare services. The three most prevalent diseases–diabetes, hypertension, and hyperlipidemia–stand out due to the magnitude of avoidable health complications, mortality, and healthcare costs.

Broad reasons behind these low rates of adherence to chronic disease medications

- The problem of poor/no adherence has rarely been explicitly included in national health policy agendas.
- Interventions tend to attribute the problem exclusively to patients, while the evidence suggests that health/social-care organization characteristics–in particular, the quality of patient-provider interaction, procedures for refilling prescriptions, or out-of-pocket costs–are lead drivers.
- Patients with chronic conditions frequently feel left out of the decision about their therapy and are inclined to rebuff.

Khan, R. and K. Socha-Dietrich. Investing in medication adherence improves health outcomes and health system efficiency: Adherence to medicines for diabetes, hypertension, and hyperlipidaemia. OECD Health Working Papers. 2018 No. 105, OECD Publishing.

Medication adherence initiatives identified from the survey responses: Organisation for Economic Co-operation and Development (OECD) countries

Country	Routine monitoring of adherence at a national level	Studies assessing non- adherence rates, drivers and impact on health outcomes and costs	Interventions to promote adherence
Australia	No	Yes	PDI, DTI
Belgium	No	Yes	No
Canada	No	Yes	PDI
Czech Rep.	No	No	No
Estonia	No	Not reported	Not reported
France	No	Yes	PDI
Hungary	No	Yes	PDI
Iceland	No	No	No
Israel	Not at a national level, but at physician level	Yes	PDI, DTI
Japan	No	Yes	PDI
Korea	No	Yes	No
Latvia	No	No	No
Norway	No	Yes	DTI, PDI
Poland	No	Work-in-progress	IC (PDI is planned)
Portugal	No	Yes	IC
Slovenia	Not at a national level, but at physician level	Yes	PDI
Sweden	Yes	Not reported	Not reported
Switzerland	No	No	PDI
Turkey	Not at a national level, but at physician level	Yes	PDI
United Kingdom	No	Yes	PDI, IC, DTI
United States	Not at national level, but at Centre for Medicare and Medicaid level	Yes	PDI, IC, DTI

Key: PDI - Provider delivered intervention with financial incentives for the HCPs. **IC** -Public information/education campaigns targeting patients **DTI -** Data & technology infrastructure.

One of the principal reasons for low adherence rates is that adherence has rarely been explicitly included in national health policy agendas. Interventions often attribute this problem exclusively to patients. However, evidence is clear that factors such as the quality of patient–provider interactions, prescription refill procedures, and out-of-pocket costs are major drivers of poor adherence. Patients with chronic diseases frequently feel excluded from decisions about their therapy and treatment, leading to poor adherence.

Current spend of health and potential benefits of improving adherence in CVD patients

Country	Current Health Expenditure per capita (Current US$)[1]	Government Health Expenditure per capita (Current US$)[1]	Out of pocket Health Expenditure per capita (Current US$)[1]
China	**$671** (5.38% GPD)	**$363** (2.91% GPD)	**$231** (34.3% CHE)
Mexico	**$611** (6.08% GPD)	**$304** (3.05% GPD)	**$253** (41.3% CHE)
Thailand	**$364** (5.16% GPD)	**$671** (5.38% GPD)	**$33** (9.04% CHE)

This study shows that patients who achieve optimal adherence can prevent CVD episodes[2]

63 in China	40 in Mexico	34 in Thailand

Incremental effectiveness per patient[2]

0.60 life-years in Mexico	0.59 QALYs in Thailand	0.93 QALYs in China

Cost savings per patient with optimal adherence[2]

$700 for China	$412 for Mexico	$316 for Thailand

The most relevant benefit of improving medication adherence in CVD patients was the improvement in health outcomes in all 3 countries, in addition to the cost savings obtained

GPD: Gross domestic product; CHE: Current health expenditure
The values shown on this slide reflect the speaker's interpretation of the data published in the references:

1. World Health Organization Global Health Expenditure database (https://apps.who.int/nha/database/country_profile/Index/en). The data was retrieved on August 06, 2024 ;
2. Cho JY, et al. Projected Cost Savings with Optimal Medication Adherence in Cardiovascular Disease Patients Requiring Lipid Lowering Therapy: a Multi-National Economic Evaluation Study. JAHA 2024. Manuscript in Press

The above slide shows the current state of health expenditure and the potential benefits of improving adherence in CVD. As Dr. Nator explained, the study involved three countries: Thailand, China, and Mexico. Government health expenditure is highest in Thailand, followed by China and Mexico. Out-of-pocket health expenditure per capita is also high, except in Thailand, where it is lower. The study found significant cost savings per patient and incremental effectiveness per patient. Most importantly, the study shows that patients who achieve optimal adherence can prevent up to 63 cardiovascular episodes in China, 40 in Mexico, and 34 in Thailand. Improving medication adherence in CVD patients leads to better health outcomes and cost savings in all three countries.

Medication adherence is a measure of the quality and effectiveness of the entire health system. It should be included as a public health policy. Policymakers should focus on improving adherence because it leads to cost savings for healthcare organizations, providing a clear incentive to improve it. Communities that benefit from better adherence should use their influence to involve all stakeholders in improving adherence.

Non-adherence factors related to the healthcare system or equipment

- **No national or local programs have been created to eliminate or reduce barriers of therapeutic adherence,** since the medical guidelines for treating chronic diseases are based mainly on pharmacological treatments, controlled diet and recommendations on a healthy lifestyle[1]
- The consequence of not addressing these diseases in a comprehensive manner is an increase in the prevalence of these diseases, affecting those who suffer from it with a poor quality of life and premature death[1]
- Health centers with inadequate infrastructure and deficient resources[2]
- Underpaid and overworked health personnel leading to short consultations lacking in quality and warmth[2]
- Inadequately trained health personnel lack of knowledge about adherence and effective interventions to improve adherence[2]

Lack of adherence has been shown to be associated with an increase in number of hospitalizations among patients, which has an impact on the increased cost of health care resources, as well as on health care personnel burnout.

1. Reyes RM. Therapeutic adherence in patients with chronic non-communicable diseases: diabetes, hypertension and obesity. Medicina y Etica. 2021;32(4): 923-945 ;
2. Ortega Cerda, et al. Therapeutic adherence: a healthcare problem. Acta méd. Grupo Ángeles. 2018;16(3):226-232.

Despite the evidence and awareness of the barriers to adherence, there are no national or local programs to eliminate or reduce these barriers. Medical guidelines still focus on pharmacological treatment, controlled diet, and lifestyle recommendations. Not addressing these diseases comprehensively leads to increased prevalence, poor quality of life, and premature death. Other factors contributing to poor adherence include inadequate infrastructure, insufficient resources, underpaid and overworked healthcare personnel, short consultations lacking quality and warmth, and inadequately trained healthcare personnel who lack knowledge about adherence and effective interventions.

Poor adherence is associated with increased hospitalizations, which significantly impact healthcare costs and resources. The good news is that there are innovative solutions to improve medication adherence. Technological innovations offer many options to enhance adherence, particularly through the fast digitalization of the health sector. Solutions targeting medication adherence directly include innovative drug designs, fixed drug combinations, long-acting drugs, subcutaneous devices, smart injectors, drug packaging with mobile app data, weekly pill organizers, wearable sensors, continuous glucose monitoring, automated appointment reminders, mobile apps with gamification, e-prescribing software, and incentive programs for HCPs.

Innovative medication adherence solutions

Technological innovation offer a multitude of options to enhance medication adherence.
In particular, fast digitization of the healthcare sector creates fertile grounds for assessing and modifying suboptimal drug taking.

Solutions targeting medication adherence directly

1. Innovative drug design
2. Smart inhalers, injectors and drug packaging
3. Data via mobile applications for (self)monitoring
4. Multidose drug packaging, weekly or monthly pill organizers
5. Smart drug organizers and dispensers
6. Wearable sensors
7. Automatized appointment reminding systems
8. Mobile/online applications
9. Mobile/online application with gamification
10. E-Prescribing software solutions
11. Incentivizing healthcare professionals

Solutions targeting medication adherence indirectly

1. Telemedicine/remote consultation options
2. Electronic prescriptions
3. Automatized prescription renewal systems
4. Decision support systems for prescribers
5. Online pharmacies and home delivery of prescription drugs (solution not universally supported due to varying legislation across countries)
6. Big Data repositories collecting prescribing and dispensing data

Mobile apps can help, remind and monitor medication intake and are useful in addressing unintentional non-adherence.

Kardas P. From non-adherence to adherence: Can innovative solutions resolve a longstanding problem?, European Journal of Internal Medicine. 2024;119:6-12.

Indirect solutions include telemedicine, remote consultations, electronic prescriptions, automated prescription renewal systems, online pharmacies, home delivery of prescription drugs, and big data repositories for prescribing and dispensing data. Mobile apps can help remind patients and monitor medication intake, addressing unintentional non-adherence. These apps are becoming essential for patient empowerment and habit modification, offering great potential for improving health behaviors such as physical activity, diet, and smoking cessation.

Adherence & health apps

- The phenomenon of apps has burst into the world of medicine, changing the paradigm of healthcare as a whole, as they allow sharing experiences in the environment that most concerns human beings, their own health, through a smartphone or tablet device.
- Apps are on the way to becoming an essential element in **patient empowerment** and **habit modification**, offering great potential for modifying behaviors that result in health benefits, such as promoting and controlling physical activity, diet, smoking cessation, etc.
- Furthermore, **apps have many potential uses in the doctor-patient relationship**, since they facilitate communication and the management of diseases, especially chronic diseases.

Lee Ventola. Mobile Devices and Apps for HCPs: Uses and Benefits. P&T. 2014;39(5):357-364 ;

In conclusion, despite the availability of effective tools, adherence remains very low. Evidence-based interventions are underused, leading to serious health and economic repercussions. There is an urgent need to change the healthcare paradigm by prioritizing adherence in national agendas. Technological innovations can help create an environment that supports and enhances adherence, contributing to patient empowerment, optimized treatment, and improved compliance with recommendations. Improving adherence has the potential to significantly decrease costs and improve clinical outcomes for patients.

Conclusion

1

Despite availability of effective tools, **adherence levels remain low,** and relevant evidence-based interventions are underused and this **leads to serious health and economic repercussions**

2

There is an **urgent need to change the paradigm of the healthcare**, putting adherence high enough in national agendas

3

Technical innovations may help that, provided that all the stakeholders get involved in creating an environment that will support and enhance adherence

Conclusion

4

Health apps contribute to the paradigm shift of the new medicine, which is undoubtedly aimed at empowerment of the patient, optimizing treatment and monitoring of their disease, improving compliance with all recommendations, pharmacological or non-pharmacological

5

Adherence to treatment is a key health behavior in people with chronic diseases, so increasing the effectiveness of adherence interventions may have a far greater impact on public health than any specific improvement in medical treatments

6

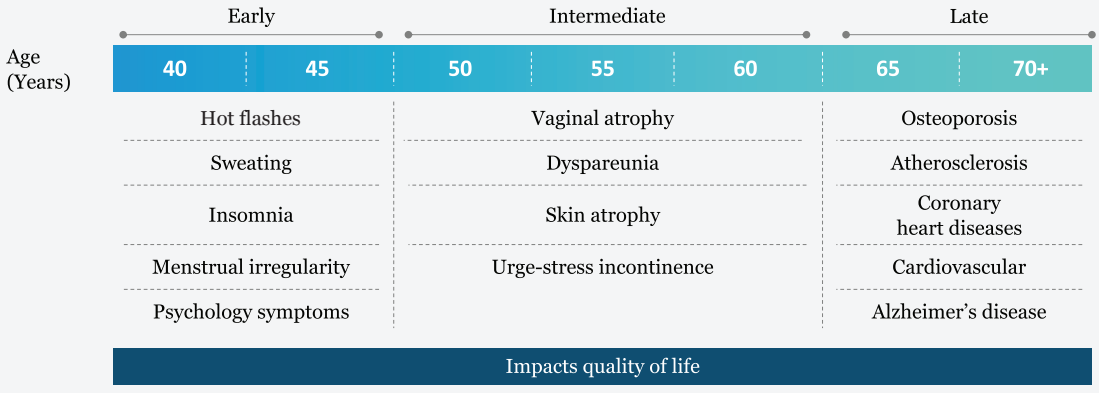
Improving adherence has the potential to **abysmally decrease costs and significantly improve the clinical condition of patients**

From treating diseases to treating patients: Changing mindsets (perspectives from the International Society of Gynecological Endocrinology)

This session was held by Prof. Tommaso Simoncini at the a:care Congress 2022.

Menopause is a significant matter of communication. It sits between being a natural condition and a disease due to its implications. Menopause occurs when the ovaries stop producing hormones like estrogen and progesterone, leading to major endocrine changes unique to women. These changes bring various consequences, some immediate and others developing over time.

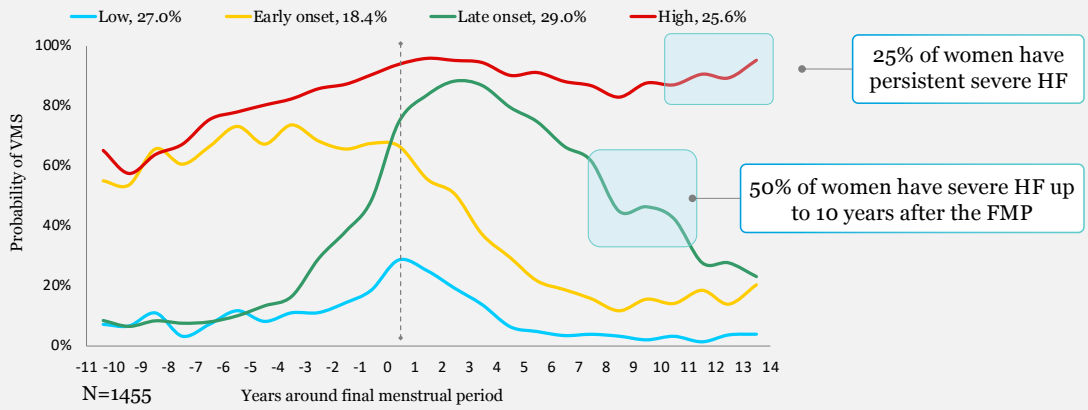
The consequences of menopause



Davis SR, Lambrinoudaki I, Lumsden M, Mishra GD, Pal L, Rees M, Santoro N and Simoncini T. Menopause. Nature Reviews Disease Primers (2015).
Zervas IM, Lambrinoudaki I, et al. Additive effect of depressed mood and vasomotor symptoms on postmenopausal insomnia. Menopause: The Journal of The North American Menopause Society. 2009; 16(4): 837-842. Monteleone P, Mascagni G, Giannini A, Genazzani AR, Simoncini T. Symptoms of menopause - global prevalence, physiology and implications. Nat Rev Endocrinol. Nat Rev Endocrinol. 2018 Apr;14(4):199-215.

Initially, women may experience well-known symptoms like hot flashes, insomnia, and sweating. Over time, they may develop vaginal atrophy, leading to pain during sexual activity, skin changes, and an increased risk of urinary incontinence. These changes also elevate the risk of CVDs, osteoporosis, and neurodegenerative disorders like Alzheimer's and Parkinson's.

Hot flashes are long lasting



Davis SR, Lambrinoudaki I, Lumsden M, Mishra GD, Pal L, Rees M, Santoro N and Simoncini T. Menopause. Nature Reviews Disease Primers (2015).
Zervas IM, Lambrinoudaki I, et al. Additive effect of depressed mood and vasomotor symptoms on postmenopausal insomnia. Menopause: The Journal of The North American Menopause Society. 2009; 16(4): 837-842. Monteleone P, Mascagni G, Giannini A, Genazzani AR, Simoncini T. Symptoms of menopause - global prevalence, physiology and implications. Nat Rev Endocrinol. Nat Rev Endocrinol. 2018 Apr;14(4):199-215.

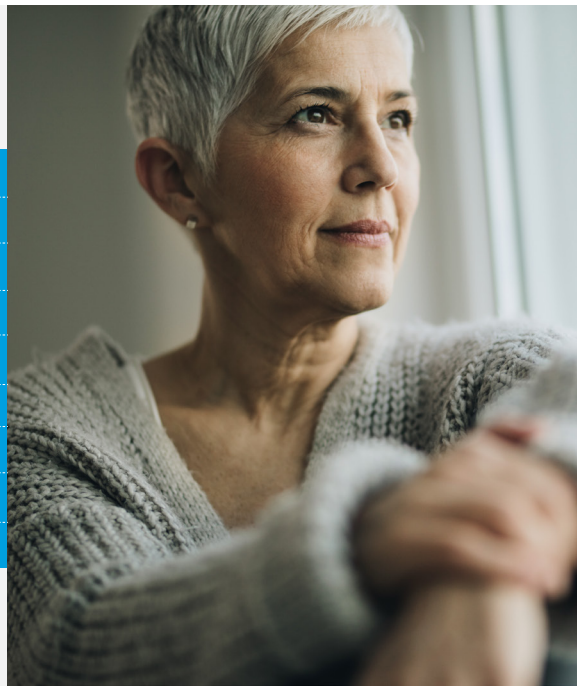
For example, hot flashes can be severe and long lasting. Studies show that about 50% of women experience severe hot flashes for up to 10 years after their last menstrual period, and 25% continue to have them indefinitely. This significantly impacts their quality of life.

Vaginal changes due to menopause can lead to dryness, painful sexual activity, and recurrent infections. These issues are not just minor inconveniences but can severely affect a woman's quality of life and relationships.

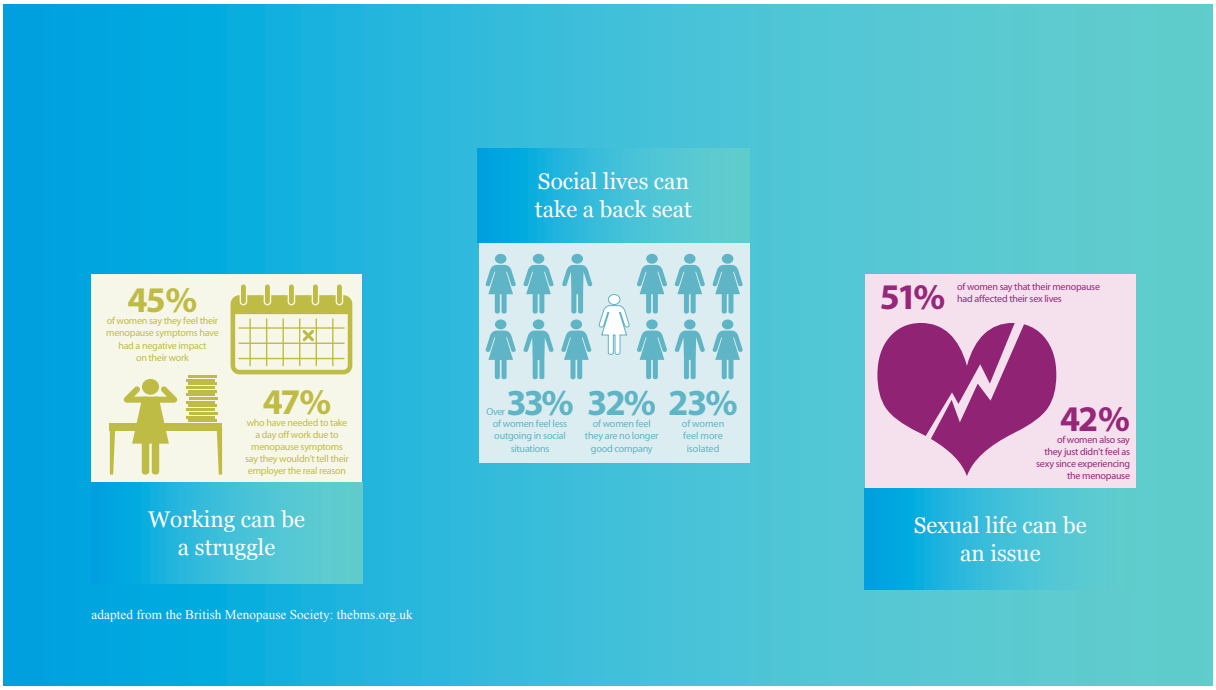
Vulvar and vaginal atrophy

- Dryness
- Itching
- Burning
- Dyspareunia
- Vaginal bleeding
- Recurrent vaginal infections
- Recurrent urinary tract infections
- Narrowing of the introitus
- Loss of elasticity and vaginal stenosis

Monteleone P, Mascagni G, Giannini A, Genazzani AR, Simoncini T. Symptoms of menopause - global prevalence, physiology and implications. Nat Rev Endocrinol. Nat Rev Endocrinol. 2018 Apr;14(4):199-215.



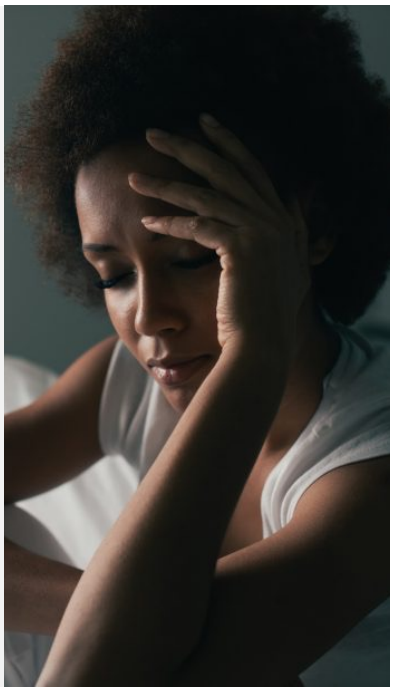
Menopause is not just about medical changes; it profoundly impacts a woman's life. Data from the British Menopause Society show that about 50% of women over 50 experience work-related issues due to menopausal symptoms. Additionally, a third of women report significant social life impacts, and about 50% face serious sexual life issues, affecting their relationships.



Menopause is a worrisome condition for many women, marking a significant life transition. It is a critical time for health and disease prevention strategies. While menopause is a natural condition, it is also a deeply personal experience that extends beyond medical aspects.

Women worry about menopause

- A time of transition towards aging
- Health and prevention begin to matter
- An important life milestone
- Is it a natural condition or is it a disease?
- For most women menopause is a personal experience, not just a medical condition

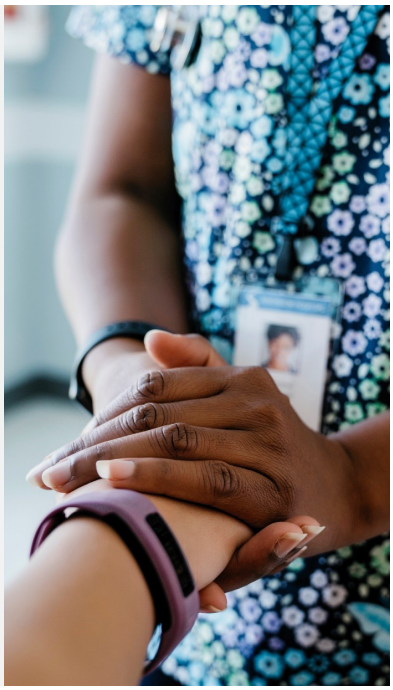


A UK survey revealed that two thirds of women feel there is a general lack of support and understanding regarding menopause. Nine out of 10 women feel unable to discuss their menopausal issues with their managers at work. One in three women consulting a general practitioner felt they did not receive correct information or were denied treatment. This is concerning, as 30% of women seeking advice or treatment do not receive appropriate care.

Do women get the support they need?

- UK survey: two thirds of women say there is a general lack of support and understanding[1]
- 9 out of 10 women say they feel unable to talk to managers at work[1]
- 1 out of 3 women consulting a GP did not receive correct information on menopause or was denied treatment[1]
- US survey: 20% of OB/GYN residents receive no lessons on menopause[2]

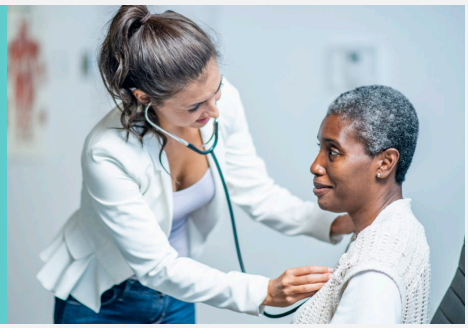
1. Nuffieldhealth.com. One in four with menopause symptoms concerned about ability to cope with life. Last update September 2017.[consulted in September 30, 2022].
2. Kling JM, MacLaughlin KL, et al. Menopause Management Knowledge in Postgraduate Family Medicine, Internal Medicine, and Obstetrics and Gynecology Residents: A Cross-Sectional Survey. Mayo Clinic Proceedings. 2019;94(2):242-253.



In the US, a recent survey found that only 20% of obstetrics and gynecology residents received education on menopause, highlighting a significant gap in teaching and awareness.

As physicians, how should we discuss menopause with our patients? While we are adept at explaining the endocrine implications and long-term consequences, identifying contraindications, and proposing personalized treatments, we often miss addressing the personal impact of menopause on a woman's life.

How we discuss about menopause with patients



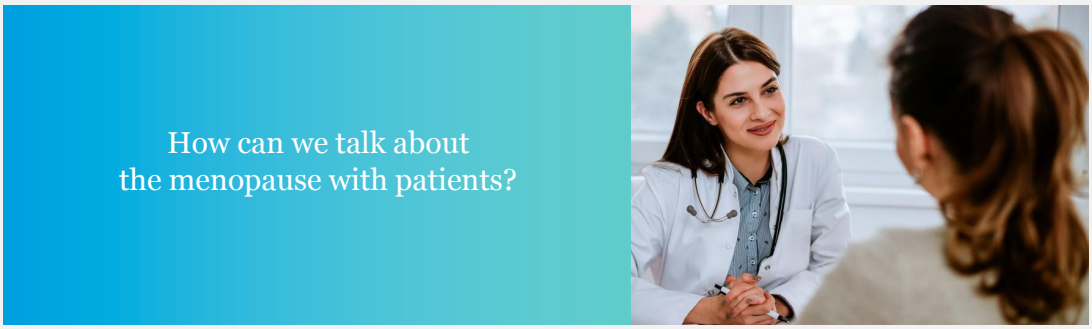
Menopause as an endocrine change

Explain the symptoms and the long-term consequences

Try to identify contraindications to treatment

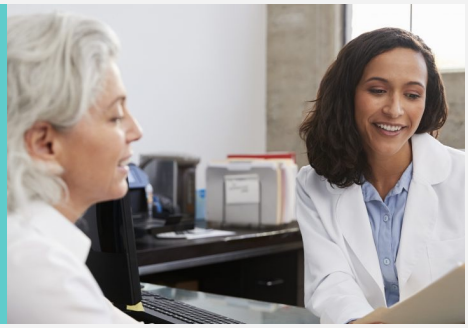
Propose a personalized treatment based on clinical issues and patient's preferences

Effective communication about menopause should go beyond medical explanations. We need to understand and address the worries and doubts that women have about menopause. This requires excellent communication skills to discuss sensitive topics such as sexuality, self-image, self-esteem, personal and professional roles, and social relationships. By doing so, we can better align our treatments with the values and attitudes of each woman, ultimately helping her more effectively.



When discussing menopause, we should start by reassuring women that it is a natural condition experienced by all women. However, we must not minimize the symptoms, as they can significantly impact quality of life. We need to encourage women to express their needs and be prepared to explain complex data and address misconceptions about menopause and its treatments. Long-term adherence to treatment is crucial, as menopause-related issues can persist and worsen over time.

How to talk menopause



Reassure-it happens to all women..

Do not minimize-however, symptoms are relevant and can ruin your life!

Help women show you their own intervention needs-what is that worries you most?

Be prepared to explain complex data correctly but plainly-address misconceptions Stress the importance of long-term adherence to interventions-things get worse over time

A comprehensive approach to menopause management involves explaining hormonal changes, medical implications, and therapeutic options. We must also break communication barriers to understand the individual impact on each woman's life, identify personalized goals, and build a lasting alliance to promote adherence to interventions.

Comprehensive menopause management

Explain hormonal changes

–

Medical implications and therapeutic options

Break communication barriers

–

Understand individual impact on life

Personalized goals, long-lasting alliance

–

Promote adherence to interventions

Scientific societies like the International Society of Gynecological Endocrinology and the International Menopause Society have made significant efforts in teaching, professional training, and providing clinical guides. However, these efforts primarily target the medical community. We need to raise awareness about menopause in the broader society and empower women to manage their health at midlife. Utilizing the internet and social media platforms can help reach women who may not be aware of these resources.

Scientific societies: Promoting education

ISGE International Society of Gynecological Endocrinology

International IMS Menopause Society

Teaching

Professional training and accreditation

IMPART
(International Menopause Society Professional Activity for Refresher Training)

Scientific societies: Clinical and social guidance

European Menopause and Andropause Society EMAS

Clinical guides

EMAS Position Statements

EMAS Menopause Essentials

EMAS Clinical Guides

EMAS Menopause & Work Day

This is why your organisation needs a menopause policy:

- Creates an open/inclusive culture
- Prevents discrimination on the basis of menopausal symptoms
- Reduces stigma
- Strengthens corporate reputation and retention of talent

Raising awareness

In summary, menopause is not a trivial problem. It disrupts the quality of life for more than 50% of women, often for many years or even the rest of their lives. Awareness and long-term adherence to treatment are essential to prevent deteriorating health and quality of life.

We have not discussed the prevention of conditions yet, but there is extensive data showing that certain treatments can prevent CVD, osteoporosis, and fractures in women. These are crucial areas that need attention.

Addressing these issues requires a collaborative effort from the medical community, HCPs, and the media to break the taboos surrounding menopause and women's health post-menopause. Misconceptions often prevent women from seeking advice and following beneficial therapies or lifestyle changes during this transition.

Scientific societies: International networking

Poor communication skills frequently lead to a lack of acceptance or discontinuation of treatment. We must improve in this area. Scientific societies play a vital role in empowering women to understand menopause and inquire about treatment options through accessible and understandable means.

Take Home Messages

- Menopause disrupts quality of life in more than 50% of women-not a trivial problem!
- Awareness and long-term adherence to treatment are of key importance to prevent deteriorating health and quality of life
- It needs a joint effort of the medical community, HCPs, and the media toward breaking taboos about menopause and women's health
- Poor communication skills are often the reason for lack of acceptance or discontinuation of treatments
- Women need to be empowered to understand menopause and ask about treatment options

Patient perspectives of adherence and how these can help us improve our practice

At the a:care Congress 2024, a session featuring Prof. Weinman and Heidi Floyd, a US patient advocate and author, provided valuable insights into adherence from a patient's perspective.

Prof. John Weinman: So, I'd like to move on to the final session this morning. I'm very pleased to welcome to the stage, as it were, Heidi Floyd. Heidi is a patient, a patient advocate, and also an author. Heidi, welcome to you, and many thanks for joining us in this interview. Good morning to you.

I really want to hear from your perspective, both in your experience as a patient and as a patient advocate, and seeing what's happening to other people. Maybe you could start by telling us a bit about your own story, your experiences of dealing with major health challenges, and the treatments that go with those challenges. Over to you.

Sure, thank you very much. It's a pleasure to be here with all of you. My experience is largely grounded in the space of breast cancer. I was a young woman when I lost my mother to breast cancer, so it was always hovering in my knowledge base. I knew that it existed, but I didn't know much about it. My mom's generation, particularly because she was a first-generation immigrant, did not discuss it. It was just known that she had it, as did her mom, and her mom before her.

So, it wasn't a terrible surprise when I discovered a lump myself. What was shocking and quite disconcerting was the fact that I had also just been informed that I was pregnant. Being in my first trimester and diagnosed with breast cancer was quite a blow. I wasn't sure what to do. I was able to locate an oncologist who understood the ramifications of treating a pregnant person and what chemotherapy could do. We went on that journey together, my oncologist and I, coupled with my OB-GYN. It was really a partnership, something I had never experienced as an average patient. I had never had to merge different practices and see how everyone would work together.

I went through my entire pregnancy getting chemotherapy on Fridays and then going to the OB-GYN on Mondays for a scan to make sure the baby was okay. That was my first diagnosis with breast cancer. We made it through the chemotherapy, and I had my son, who is now strong, healthy, and wonderful. My cancer did recur, and I am currently a cancer patient on continuing therapy.

When I had my surgery and my son, I was 36 years old. Because of the nature of my cancer, they did a complete hysterectomy, so at age 36, I was in full menopause and had no idea what that meant. It was quite a learning experience to realize at a young age, and no one discussed it with me. It was just, "We have to do this to save your life," with no questions. It was a fascinating situation.

When I completed my journey, my oncologist asked if I would consider speaking about my experience. It has helped me not only get the message out that there are continuing advancements but also that there are things being done to help the patient community. I think it's a neglected field, and we need more people advocating for what all this R&D is doing to save our lives.

So, that led you to become a patient advocate. Is that right?

Yes. When I started speaking, several people asked if I would consider joining the American Cancer Society Board of Grant Review, so I could look at grant requests from a patient's perspective. Not only that, but connecting with patients globally, on social media and in person, talking to them, and working through their issues. Not just other pregnant women with breast cancer, but in every disease space. We all pull together.

Thanks for sharing that with us. It's a huge journey you've been on. As part of that journey, you've been asked to take treatments regularly and adhere to them. Can you tell us about your experience of taking treatment and how you got on with it?

I found it fascinating that my doctor, my oncologist, and my OB-GYN took just moments–not hours, but moments-to glean things that interested me. They would talk to me about those interests, weaving them into the tapestry of my adherence. For example, my doctor knew I was a big history buff and would tell me to research the history of my chemotherapy treatment. It made it interesting for me to stay involved and on task.

We've heard that if patients feel worried about their treatment or don't have a strong sense they need to take it, it can affect adherence. Did any of those beliefs crop up in your mind, or did it all seem logical to you?

It did for me because I realized that my treatment was absolutely lifesaving, not just for myself but for my baby as well. So, for me, it was a different perspective.

I had spoken with you previously, John, about the fact that I have worked with other patients who have come to me and said, "I just can't." For example, I know one woman who came to me and said, "It's making me too tired. I can't do it. Here's a list of side effects. I don't know what to do." She was quietly stepping back from doing what she was supposed to do.

I asked her, "Have you spoken to your doctor? If not your doctor, have you spoken to any of the nurses or anyone on the medical staff? Have you told them?" She replied, "No, I don't really want to seem like a bother. I just don't think that I'll continue."

I told her, "No, no. You need to speak up." This woman happened to be a young African American woman in the breast cancer space, and I said, "You are the demographic that needs to speak out the most. You are the one that needs the most representation. Go back to your physician and tell him, 'This adherence is really challenging for me because of the timing, the weight of it, and the exhaustion.' He needs to know all of that because if he doesn't, and you don't adhere to it, it might impact people around the world. They are designing this medication, this treatment, to help your entire community. So, you need to speak up. You need to be bold."

I encouraged her to go back and sit with her physician and say, "I'm not going to take it anymore unless you can help me." It really did change the trajectory of her whole treatment. The physician had no idea that she was exhausted and couldn't handle it. It really did help a lot.

That's a powerful story. We talk about many patients who seem very reluctant to raise issues and, as you say, quietly disappear, much to the detriment of our understanding. For example, if they are in a trial and we lose those people, it really affects the outcome of the trial. Do you think this is part of a wider problem about people not feeling comfortable?

Absolutely. It's not just how you're raised but how you feel if you're uncomfortable. For example, in my mom's generation, when she called me to tell me that she had breast cancer, she whispered on the telephone in a closed room, "I have breast cancer." I was in my room with the door closed. There was some sort of stigma or shame affiliated with that disease space and with any disease. She was not native to the United States, so for her, you don't question doctors. It was considered rude. It could be a generational thing or a societal thing. You don't question what the doctor says; you just do what they say. But if you don't, you quietly go away. That's something we need to change immediately. I like to think that the next generation, my children, will not be like that. They seem much more empowered to speak up for themselves and say, "This is uncomfortable. I don't like this. I'd prefer this. Is there an alternative?" Asking questions, learning, and advocating for themselves. But there is a chasm now of patients who will not advocate for themselves and just quietly go away. They need to stand up for themselves, but there's definitely a lack of people who feel empowered to be their own health advocate.

As an advocate, what are the key things you can do to help? You talked about the young African American woman earlier. What can you do for women or anyone in that situation who feels scared and disempowered and might disappear? Give us some key tips from your perspective.

As a patient, my advice is to reach out to your community. No matter what kind of unusual part of the disease you have, there's somebody else out there who shares it with you. It's very unusual to have such an incredibly rare disease that you're the only one. Social media is pervasive; it's everywhere. You can find somebody in your disease space and talk to them. I highly recommend finding someone on the positive side of things because otherwise, you could go into a dark hole.

As far as primary care physicians and the entire medical community, including pharmacists, engaging in light conversation and building a relationship with patients will help them feel more empowered. The onus is not only on the patient but also on the medical community to reach out. They touch all of us, so everyone needs to get on board. You don't have to swarm us with 20 questions; you can just ask one at a time and make a note to ask next time. For example, "You mentioned that your daughter was doing this and that." Engaging in conversation builds a relationship, and when trust is built, communication can be more free flowing.

It's about making that personal connection. It doesn't have to be just the primary care physician. When I go to see my oncologist, at least three or four people touch me physically before I see the doctor. It's the gentleman who opens the door at the front of the cancer center, the registration nurse who hands me the pen, the lady who takes my blood pressure, and the lady who weighs me. They all have an opportunity, even if it's just moments, to ask a question. They could stage it out so that the person at the front desk asks about your family, the person who takes your blood pressure asks about your mental health because you're in a more private space, and all that information can be relayed to the doctor.

So that when the doctor rolls into the room, even though they have just a few precious moments, they've already been told everything looks clear or that the patient seems pretty happy. Or, if it's the second time the patient has mentioned feeling depressed, the doctor might not have time to ask that question because they're really focused on trying to save the life. But this could be an extra gentle avenue for the primary care physician to say, "Hey, we've heard a couple of times that you're kind of worried about depression. Can we help you?" That kind of relationship building is paramount.

And you've stressed the importance of the team in this, right? Not just the doctor?

Yes, absolutely.

Have you had experiences where you felt like just a number or where the care was impersonal?

I have, and it's interesting. Not just in the medical space, but in the real world. When my original oncologist moved, I went to a new oncologist. The nurse calling me in, in a waiting room full of people, had the clipboard and said, "Heidi Ford?" I went over, and she said, "Okay, your stage..." She didn't ask my name. I gave her my name, and then she said, "So, you're stage 3B estrogen positive." I replied, "Well, I'm not actually. I'm Heidi Floyd. I'm a patient. That disease is living within me, but I am not stage 3B."

I was also at a nonprofit event representing several types of cancer. I was carrying a box in, and a woman said, "Hey, are you breast cancer?" I thought, "I'm not all of breast cancer. I just have a little bit of it." It seems like the whole community and the whole globe look at us as if we are this disease. We're not ourselves. I'm not just a mom, a pet owner, or someone who lives in Atlanta, Georgia. I'm seen as breast cancer and then also as Heidi. We need to change that and make breast cancer secondary or tertiary. There's so much more to us than just this nasty little disease.

One of the things that can happen, and we've heard a bit about it in talks earlier, is that people are prescribed treatment and just don't think they need it. For example, about 30 years ago, I was diagnosed with high blood pressure. I was in my early 40s, a skinny person, very healthy, did a lot of sports, had a good lifestyle. I thought, "There's no way I need this treatment. It can't be right." So, I resisted it. I didn't really believe I needed it, and I probably had some worries about being dependent on the medicine I didn't think I needed.

Then something very powerful happened. My older brother, who had similar attitudes, had a huge stroke. Overnight, my attitudes changed. I suddenly got it. I could see the need for treatment and prevention.

Coming back to your situation, both yourself and the patients you've supported, do you think there are areas of cancer treatment, like continuing endocrine therapies following breast cancer surgery, where people don't have that sense of the need for treatment? Do you have a sense of that, either yourself or in fellow patients?

Yes, they do. I, myself, do not because I seem to operate a lot in the fear space. I've been around the negative side of cancer for so long. I trust my oncologist completely. If that man were to say, "Drive your car to the moon," I would try to do it. I believe him completely. When he tells me, "You have to take this medicine because it's going to keep you alive," I do that. But that's how I operate, and I assume everyone around me knows how important that is.

However, there are failures. I have many friends who say, "It's too hard, Heidi. I can't take it." There are certain medications that help if you're ER positive or PR positive. Once you're done with your main chemotherapy, there's continuing therapy you're supposed to take for 5 or 10

years. The same situation comes up: "It's too hard. The side effects are too difficult." I always advise them to talk to their doctor. Are there ways around it? Can you tweak the dosage? These doctors are geniuses; go talk to them.

I've been saying this for quite some time. However, as recently as this week, my husband fell ill last week with an ear infection. He was given penicillin, I think, for his ear. I asked, "Now, you're taking your medicine every day, right?" He said, "Oh, absolutely, absolutely."

And the other day, I went in, and there was still half a bottle left. He said, "I felt fine, so I stopped taking it." I was like, "It's my whole job! You should be taking your medicine." It just shows me that we have to keep working on this. It's pervasive.

One last area I really want to touch on is communication. You talked about it quite a lot indirectly, but let's focus on it more directly. There's a whole layer of communication among HCPs and all those people in the team. Many HCPs, doctors, and so on tell us they have very little time. They're very pushed; health systems are overloaded. What are the top three things you think people can do in that short amount of time to really get on the patient's wavelength, to really support patients, and hopefully support better adherence?

I think what we mentioned earlier about using your entire staff to glean information for you as a main healthcare professional is crucial. Glean that information and get it loaded in so that you can build that relationship without having to sit down and ask 50 questions. You don't have time to ask that many questions, but the rest of your staff might. Just get that information. If there's something repetitive or concerning, you can bring it up as the healthcare professional.

Just notice body language. If you have a patient who continually says, "I'm fine, I'm fine," and she's a metastatic breast cancer patient, she's not fine. What she's telling you is not the truth. You just have to know that. Are you addressing her by name? The takeaway, the one call to action for this session, should be to look in their eyes and know their name. Just say hello and build that relationship. It's totally worth it because you could change the trajectory of their entire life, their entire experience, and their families as well. Be a little bit more personal within the limited time you have. Make that personal connection.

Heidi, I am very grateful to you for sharing your experience and your wisdom. It's absolutely invaluable to have your view, and I think there are so many powerful messages that have come out of what you've told us this morning. It's been a great pleasure talking to you. Many, many thanks to you.

Thank you so much for having me. I love chatting with you.

Good. All right, take care. Bye.

Sharing reflections and best practices

Medication non-adherence is often referred to as a “silent pandemic”, silently undermining the potential benefits of medical treatments across all disease spectrums. The WHO estimates that in developed countries, adherence among patients with chronic diseases averages only 50%, with even lower rates in developing nations. Non-adherence not only compromises patient health but also leads to increased healthcare costs due to avoidable hospitalizations and complications.

The reasons for non-adherence are multifactorial, encompassing patient-related factors, healthcare system inefficiencies, socioeconomic barriers, and cultural influences. Understanding these factors in diverse contexts is essential for developing targeted interventions. This chapter synthesizes discussions among healthcare experts from India, Egypt, Brazil, Singapore, Turkey, and Colombia, who share their experiences and strategies in addressing medication non-adherence in their respective regions.

Experts: Prof. John Weinman – Prof. Enrique De Madaria – Dr. Shashank Joshi – Prof. Pavel Klein –Prof. Marcus Bolivar Malachias – Assoc. Prof. Zuluaga Héctor Medina – Prof. Badr Eldin Mostafa –Prof . Osman Nuri Özgirgin – Prof. Alta Schutte – Prof. Tommaso Simoncini – Assoc. Prof. Ngiap Chuan Tan

India: Addressing affordability and accessibility

Dr. Joshi highlights the unique healthcare challenges faced by India, a country with a population of approximately 1.3 billion. He points out that non-adherence to treatment in India is significantly influenced by several key factors. One of the most pressing is affordability, as a large portion of healthcare costs are paid out-of-pocket, making long-term medication financially burdensome for many patients. Accessibility also plays a major role, particularly in rural areas where healthcare facilities and pharmacies are often scarce, limiting patients' ability to obtain necessary medications. Additionally, limited health literacy contributes to widespread misunderstandings about disease management and the critical importance of adherence.

To address these challenges, Dr. Joshi proposes a multifaceted strategy. Central to his approach is the emphasis on education—he underscores the need for continuous efforts to raise awareness among both patients and HCPs through community outreach and health literacy programs. Simplifying treatment regimens is another key component, which includes reducing the number of pills by using combination therapies and considering factors like the size, taste, and shape of tablets to enhance patient acceptability. Finally, he advocates for the innovative use of technology, such as digital platforms that can support patient education, send medication reminders, and facilitate telemedicine consultations, thereby helping to overcome barriers related to accessibility.

Egypt: Empowering patients through direct communication

Prof. Mostafa sheds light on the cultural and systemic challenges surrounding treatment adherence in Egypt. One of the key issues he identifies is the reluctance of patients to openly discuss non-adherence, often due to a fear of disappointing their physicians or being judged. This dynamic can lead to underreporting and unresolved adherence problems. The diversity in educational backgrounds across the population further complicates communication, requiring HCPs to adapt their messaging to suit different levels of understanding. Additionally, inconsistent pharmaceutical packaging can create confusion about how long a treatment should last, undermining adherence.

To address these challenges, Prof. Badr advocates for a more empathetic and proactive approach. He recommends that HCPs engage in active listening and ask direct, non-confrontational questions to encourage patients to speak honestly about their adherence. He also emphasizes the

important role pharmacists can play, suggesting they be trained to offer counseling and support, as they are often the first point of contact for patients. Furthermore, he calls for collaboration with pharmaceutical companies to standardize packaging in a way that clearly aligns with prescribed treatment durations, helping to reduce patient confusion and improve adherence.

Brazil: Tackling non-adherence in CVDs

Prof. Malachias draws attention to the significant burden of CVDs in Brazil, which remain the leading cause of mortality in the country. He emphasizes that non-adherence to treatment should be considered a major risk factor, on par with conditions like hypertension and diabetes, due to its profound impact on patient outcomes. Economic constraints are a major barrier, as many patients are unable to afford the medications necessary for managing chronic illnesses. Additionally, the public healthcare system is under considerable strain, which affects the quality of interactions between patients and HCPs, as well as the consistency of follow-up care.

To address these issues, Prof. Malachias proposes several strategic interventions. He underscores the importance of continuous medical education to combat clinical inertia and ensure that HCPs consistently follow treatment guidelines. He also advocates for a team-based approach to care, involving multidisciplinary teams that include nurses and community health workers to support patient education and monitor adherence. Finally, he calls for stronger advocacy efforts aimed at improving access to affordable medications through collaboration with government bodies and health organizations.

Singapore: Preventive health and the role of family doctors

Assoc. Prof. Tan discusses Singapore's "Healthier SG" initiative, which represents a national shift from reactive disease treatment to proactive preventive health. A central theme of this approach is fostering a preventive health mindset, where individuals are encouraged to take responsibility for their well-being even in the absence of symptoms. The initiative also promotes the concept of "one patient, one family doctor," aiming to build long-term, trust-based relationships that support personalized care. Another key challenge lies in addressing common sense defaults—particularly the widespread belief that feeling well means being healthy, which can undermine adherence to preventive measures.

To support this transformation, Assoc. Prof. Tan outlines several strategic actions. Public health campaigns play a vital role in educating the population about the importance of adherence and preventive care. Technology is also leveraged through the use of digital health records and automated reminders, which help ensure continuity of care. Additionally, community engagement is emphasized, with families and local organizations being actively involved in supporting individuals' adherence to health recommendations.

Turkey: Emphasizing patient counseling and trust

Prof. Nuri Özgirgin highlights the specific challenges contributing to non-adherence in Turkey and the broader Middle East. One major issue stems from limitations within the healthcare system, particularly the time constraints during consultations, which often prevent thorough discussions about adherence. Cultural influences also play a significant role, as some patients may turn to traditional remedies or adopt fatalistic attitudes toward their health, believing outcomes are beyond their control.

To address these barriers, Prof. Özgirgin recommends a more patient-centered approach. He stresses the importance of prioritizing communication during medical consultations to build trust and better understand individual concerns. Creating a blame-free environment is also essential, as it encourages patients to speak openly about their struggles with adherence without fear of judgment. Furthermore, involving patients in shared decision making helps foster a sense of ownership and commitment to their treatment plans, ultimately improving adherence.

Colombia: Bridging infrastructure gaps

Assoc. Prof. Medina outlines the pressing challenges Colombia faces in tackling non-adherence to medical treatment. One of the primary issues is the limited time physicians have with each patient—often just 15 minutes—which restricts opportunities for meaningful education and discussion about adherence. Compounding this is the lack of robust support systems outside clinical settings, making it difficult to maintain consistent follow-up and provide ongoing patient support.

To address these gaps, Assoc. Prof. Medina proposes several strategic measures. He advocates for reforms in medical education that incorporate awareness of non-adherence, ensuring that future HCPs are better equipped to manage this issue. He also emphasizes the importance of multi-stakeholder collaboration, involving insurance companies, government agencies, and healthcare organizations in the development of comprehensive adherence programs. Additionally, he suggests adapting successful models from clinical trials, such as the COURAGE trial, which demonstrated the effectiveness of extensive patient follow-up in improving adherence outcomes.

Common themes and strategies across regions

A central theme in improving treatment adherence is the adoption of patient-centered care, which emphasizes meaningful communication and trust-building between patients and HCPs. This approach involves active listening, allowing patients to fully express their concerns and beliefs, and demonstrating empathy and compassion to foster a sense of trust. Communication must also be tailored to each individual, taking into account cultural backgrounds and varying levels of education to ensure that information is both accessible and respectful.

Education and awareness play a vital role at multiple levels. Patients need clear, comprehensible information about their conditions, the benefits of treatment, and potential side effects to feel empowered in managing their health. At the same time, HCPs must receive training that enhances their communication skills and cultural competence. Broader community outreach—through media, public health campaigns, and engagement with community leaders—helps reinforce these messages and normalize adherence as a shared goal.

Simplifying treatment regimens is another key strategy. This includes reducing the number of pills patients must take by using combination or extended-release medications, and considering patient preferences regarding the size, taste, and form of medications. Providing clear, easy-to-follow instructions further supports adherence by minimizing confusion.

Cultural competence is essential in addressing adherence challenges. This means respecting traditional beliefs and practices, and where possible, integrating them safely into treatment plans. Involving family members and caregivers in discussions can reinforce adherence, especially in cultures where health decisions are made collectively. It's also important to address stigmas and misconceptions that may prevent patients from seeking or continuing treatment.

A multidisciplinary, team-based approach enhances adherence efforts by involving pharmacists, nurses, and community health workers—professionals who often have more frequent contact with patients and can provide ongoing support. Coordinated care among various HCPs ensures that all aspects of a patient's needs are addressed.

Finally, technology offers powerful tools to support adherence. Digital reminders via apps, text messages, or automated calls help patients remember to take their medications. Telemedicine expands access to care, particularly in underserved areas, while electronic health records facilitate better tracking of adherence and communication among HCPs.

Overcoming barriers to medication adherence

Time constraints in clinical practice are a common challenge that can hinder effective communication about treatment adherence. To mitigate this, physicians can focus on conducting efficient consultations by prioritizing adherence-related discussions and delivering concise, impactful messages. Delegating certain responsibilities to other members of the healthcare team—such as nurses or health educators—can also help ensure that patients receive the necessary information and follow-up. Additionally, providing educational materials like brochures, videos, or digital content allows patients to review important information at their own pace outside the consultation.

Economic barriers also play a significant role in non-adherence, particularly when patients are unable to afford their medications. Addressing this issue involves advocating for policy changes that reduce medication costs and expand insurance coverage. Prescribing generic alternatives can offer cost-effective solutions without compromising treatment quality. Furthermore, informing patients about assistance programs that provide financial support or free medications can significantly improve access and adherence.

Psychological and behavioral factors must also be considered. Patients may harbor fears or misconceptions about their medications, which can be addressed through clear, accurate information. Techniques such as motivational interviewing can help explore and resolve ambivalence, while collaborative goal setting can empower patients by giving them a sense of ownership over their health journey.

Cultural and religious influences are equally important in shaping adherence behaviors. Developing culturally appropriate educational materials ensures that messages resonate with patients' values and experiences. Engaging religious leaders can be particularly effective in communities where they hold significant influence, helping to promote adherence in a culturally sensitive manner. Above all, respecting patients' autonomy and working collaboratively to find acceptable treatment plans fosters trust and long-term engagement.

Personalizing adherence strategies: Case studies and anecdotes

Dr. Joshi's "SMILE" approach in India offers a memorable framework for improving adherence. It begins with simplifying treatment regimens to make them more manageable for patients. He emphasizes the importance of managing care with a personalized touch—treating patients as individuals rather than just focusing on their diseases. Innovation plays a key role, with new methods and technologies being leveraged to support adherence. Continuous learning from peers and best practices is encouraged, and education remains a cornerstone—targeting patients, families, and HCPs alike.

In Singapore, Assoc. Prof. Tan champions compassionate communication, inspired by the idea that even "40 seconds of compassion" can make a meaningful difference. He advocates for brief yet impactful conversations that build rapport and show genuine interest in patients' lives. Positive reinforcement is also central to his approach, as acknowledging patients' efforts can motivate them to stay on track with their treatment.

Assoc. Prof. Medina in Colombia focuses on strengthening medical education to address adherence. He supports integrating adherence-related topics into medical curricula and emphasizes the value of mentorship and role modeling in clinical settings. His approach also involves collaboration with professional societies and academic institutions to elevate adherence as a priority in healthcare training.

Prof. Özgirgin in Turkey places strong emphasis on patient counseling. He encourages active patient involvement in treatment planning and promotes a blame-free environment where patients feel safe discussing their challenges. His strategy includes developing tailored solutions that address the unique barriers each patient may face.

In Brazil, Prof. Malachias underscores the importance of advocacy and teamwork. He calls for reducing clinical inertia by ensuring HCPs stay up to date with guidelines and take proactive steps to support adherence. He also highlights the value of multidisciplinary teams in delivering comprehensive care and stresses the need for policy engagement to improve access and affordability of healthcare services.

The role of healthcare systems and policies

Healthcare systems play a pivotal role in shaping medication adherence through a variety of structural and policy-level mechanisms. One key factor is infrastructure development, which involves creating systems that facilitate continuous patient engagement and follow-up—essential components for maintaining long-term adherence. National health programs also contribute significantly; for example, Singapore's "Healthier SG" initiative prioritizes preventive care and embeds adherence into its broader public health strategy.

Financial accessibility is another critical element. Ensuring that patients have adequate insurance coverage and reimbursement options helps remove cost-related barriers to medication adherence. Additionally, quality improvement initiatives within healthcare systems can drive better outcomes by incorporating adherence metrics into the evaluation of HCPs performance, thereby incentivizing consistent and patient-centered care.

Technological innovations and future directions

Technological advancements are opening up powerful new pathways for enhancing medication adherence. Mobile health applications are at the forefront, offering tools that help patients track their medication usage, receive timely reminders, and access educational resources—all from their smartphones. These apps empower users to take a more active role in managing their health.

Telehealth services further expand access to care by enabling virtual consultations and remote monitoring, which are especially valuable for patients in underserved or remote areas. AI is also making a significant impact by predicting which patients are at risk of non-adherence and enabling HCPs to tailor interventions accordingly. Meanwhile, data analytics allows for the examination of large datasets to uncover trends, evaluate the effectiveness of adherence strategies, and inform evidence-based decision making.

Challenges and considerations

Despite notable progress in improving medication adherence, several persistent challenges continue to hinder widespread success. One major concern is privacy—ensuring that patient data remains secure when using digital tools is essential to maintaining trust and compliance. Health literacy also varies widely among populations, and interventions must be designed to be understandable and accessible to individuals with different levels of knowledge and education.

Cultural sensitivity is another critical factor. A one-size-fits-all approach is rarely effective, and it's important to respect and adapt to the diverse cultural contexts in which healthcare is delivered. Finally, resource limitations present a significant barrier, particularly in low-income or underserved areas. Implementing effective adherence strategies in these settings requires creativity, flexibility, and a deep understanding of local needs and constraints.

Global experts' perspectives on raising awareness

During the a:care Congress 2022 panel discussion, global experts offered valuable perspectives on how collective efforts can be harnessed to improve medication adherence. Prof. Klein emphasized the importance of raising awareness at multiple levels—not only among patients but also within the medical community and society at large. He advocated for professional societies and leading medical journals to treat adherence as a priority issue. Additionally, he stressed the need to engage with key stakeholders such as insurance companies and governments, whose involvement can drive systemic change.

Prof. Simoncini highlighted the potential of scientific societies to leverage their networks to educate HCPs. However, he noted that reaching patients effectively requires collaboration with media outlets and the use of accessible, relatable language. By making adherence a topic of public discourse, patients can become more informed and actively involved in their care.

Prof. De Madaria proposed the establishment of a multi-stakeholder organization—such as an international adherence league—that could influence policy and practice at a global level. This body would work with governments, insurers, universities, and hospitals to advocate for adherence-focused programs and policies.

Prof. Horne introduced a practical framework centered on tools, training, and a "test and learn" methodology. He suggested that developing adaptable tools to address belief-related barriers,

combined with clinician training, could enhance the effectiveness of adherence interventions. Testing these strategies in diverse settings and publishing the outcomes would contribute to a growing evidence base and help identify best practices.

Implementing specific actions and individual commitments

As the discussion turned toward actionable steps, panelists shared concrete initiatives they plan to implement within their own institutions and networks to improve adherence.

Asssoc. Prof. Tan described plans to host an innovation workshop focused on asthma patients, aiming to identify barriers to adherence through creative, participatory methods such as photovoice. By involving patients directly, the workshop seeks to generate person-centered solutions that reflect real-world experiences.

Prof. Nuri Özgirgin emphasized the value of consistent counseling and regular follow-ups to reinforce adherence. He advocated for making adherence a recurring topic in clinical rounds and educational settings, ensuring that HCPs not only understand its importance but also inspire patients to stay committed to their treatment.

Assoc. Prof. Medina committed to integrating adherence education into the medical curriculum at his institution. He also highlighted the effectiveness of visual tools—such as imaging results—to help patients understand the necessity of medications, especially when symptoms are not immediately apparent.

Dr. Joshi proposed a comprehensive strategy that includes training adherence counselors within healthcare teams and patient communities, educating medical students, and incentivizing best practices. He also stressed the importance of addressing cultural myths and beliefs that may hinder adherence.

Prof. Malachias pointed to the need for region-specific research to uncover the root causes of non-adherence. By collecting and analyzing local data, more tailored and effective solutions can be developed. He also called on physicians, educators, and citizens to advocate for improved healthcare conditions and treatment access.

Finally, Prof. Mostafa shared plans to launch outreach programs through the ENT Society in Egypt. These initiatives will involve patient representative groups and pharmacists, aiming to create advocacy and stewardship programs with measurable outcomes to track progress in adherence.

Global experts' reflections on personal actions

The global experts concluded the a:care Congress 2022 by sharing their personal commitments to advancing medication adherence, reinforcing the importance of individual and collective action.

Prof. De Madaria reflected on how the conference inspired him to integrate adherence discussions into his daily clinical practice, mentoring, and guideline development. He emphasized the need to embed adherence into every educational and clinical activity to ensure it becomes a consistent priority.

Prof. Horne outlined plans to develop digital tools that work alongside clinicians to address belief-related barriers to adherence. He recognized the adaptability of these tools across different conditions and cultural settings. In addition, he stressed the importance of clinician training and the potential for global collaboration to influence health policy.

Prof. Simoncini acknowledged the innovative nature of the conference and its potential to reach a wide audience. He proposed using similar virtual platforms to explore specific topics in greater depth, thereby raising awareness and influencing decision-makers through broad engagement.

Prof. Klein shared his intention to implement a structured program at his center to assess adherence, identify causes of non-adherence, apply targeted interventions, and evaluate outcomes. He also committed to engaging professional societies and contributing to media outlets to raise awareness among both HCPs and the public.

The panel discussion underscored the multifaceted nature of medication adherence and the need for a coordinated global response. Several key themes emerged:

- **Education and Awareness:** Ongoing education for patients, HCPs, and the public is essential. Integrating adherence into medical training and using media to amplify the message can drive widespread understanding.
- **Personalized Patient Engagement:** Tailoring interventions to individual beliefs, needs, and cultural contexts enhances their effectiveness and relevance.
- **Collaboration and Networking:** Global cooperation among HCPs fosters the exchange of best practices and the development of unified strategies.
- **Utilization of Technology:** Digital tools and information systems can support adherence through reminders, monitoring, and patient engagement.

- **Policy and Advocacy:** Working with policymakers, insurers, and professional organizations can lead to systemic changes that prioritize adherence.
- **Research and Data-Driven Approaches:** Collecting and analyzing adherence data helps identify effective interventions and areas needing attention.

The collective insights and commitments shared during the congress provide a strong foundation for advancing adherence initiatives. By implementing these strategies at individual, institutional, and systemic levels, there is significant potential to improve health outcomes globally. While the challenges are complex, the solutions are within reach—through collaboration, innovation, and a steadfast commitment to patient-centered care.

Conclusion

Throughout the pages of this book, we have explored the complex, often misunderstood world of medication adherence. What began, for many of us, as a clinical issue—patients not taking their prescribed treatments—has revealed itself as something far more profound: a reflection of how we, as a global healthcare community, engage with those we serve.

Non-adherence is not simply about forgetfulness. It is not about negligence, nor can it be resolved through a single technological fix or a better reminder app. At its heart, medication non-adherence is a mirror held up to the healthcare system—a mirror that forces us to ask difficult questions. Are we truly listening to patients? Are we equipping them with the tools and understanding they need to manage their own health? Are we fostering trust, empathy, and genuine partnership in every medical encounter?

Over the past decades, medicine has advanced at an extraordinary pace. We have developed treatments that would have seemed like science fiction just a generation ago. We are harnessing the power of AI, precision medicine, and genomics. And yet, as we have seen time and again, the best treatment in the world is useless if it remains untaken. This sobering truth is both humbling and motivating. It calls us to rethink our approach—not only to adherence but to the entire philosophy of care.

From treating diseases to treating patients: this is not merely a slogan. It is a fundamental shift in mindset. It means recognizing that a patient is not an abstract "case" defined by a set of biomarkers or ICD codes. Each patient is a person—unique, with individual beliefs, fears, motivations, and life circumstances. Until we center our care models on this reality, adherence will remain elusive.

The a:care journey has shown that progress is possible. Through partnerships with leading experts in behavioral science, technology, and medicine, we have built a program that empowers HCPs to see beyond the prescription pad. We have demonstrated that when we understand the behavioral drivers of adherence—and when we equip clinicians with practical, evidence-based tools—real change can happen.

The success of the a:care Congresses, attended by tens of thousands of HCPs across the world, reflects a growing awareness that adherence must no longer be an afterthought. It must be integrated into the core of medical practice, policy, and education.

But the journey is just beginning.

As we move forward, several imperatives stand before us:

1. Elevate adherence to a public health priority

Adherence must be recognized as a critical determinant of health outcomes—on par with early diagnosis, treatment innovation, and quality of care. Global data are unequivocal: improving adherence would save hundreds of thousands of lives annually, while dramatically reducing avoidable hospitalizations and healthcare costs. Policymakers must enshrine adherence into national and international health strategies, with dedicated funding, targets, and accountability mechanisms.

This is particularly urgent in low- and middle-income countries, where barriers to adherence are compounded by structural inequities in access, affordability, and health literacy. Closing the adherence gap in these settings could have transformative effects on population health.

2. Transform medical education

The current medical curriculum remains overwhelmingly biomedical in focus. Future doctors, nurses, and pharmacists are still trained primarily to diagnose and treat disease, not to understand human behavior. This must change. Behavioral science, motivational communication, and adherence support should be taught as core competencies in all health professions education. Clinicians must learn how to partner with patients, how to recognize and address ambivalence, and how to foster intrinsic motivation for adherence.

Moreover, we must challenge the hidden curriculum that perpetuates an overly hierarchical model of care. Patients are not passive recipients of instructions; they are active agents in their own health. Cultivating a mindset of humility, curiosity, and empathy is as vital as mastering the latest therapeutic guidelines.

3. Leverage technology without losing the human touch

Digital innovation holds enormous potential to support adherence at scale. AI-driven risk stratification tools, personalized nudges, digital coaching, virtual assistants—all of these can complement traditional care. The a:care Insight tool and the my a:care app are promising examples of how technology can make adherence support more personalized, proactive, and continuous.

However, we must also guard against the risk of depersonalization. Technology must serve to deepen—not replace—the human connection between clinician and patient. The conversation in the consultation room remains irreplaceable. No app can replicate the empathy conveyed through a listening ear, a supportive word, or a compassionate gesture.

4. Foster a culture of partnership

Improving adherence is not the responsibility of any single actor. It requires a collaborative ecosystem. HCPs must work hand in hand with patients, families, community organizations, policymakers, payers, and the pharmaceutical industry. Patient associations, in particular, have a vital role to play in shaping adherence interventions that are culturally sensitive and aligned with patient realities.

At the policy level, multi-stakeholder alliances should drive national adherence action plans. Cross-sector collaboration will be key to tackling the social determinants of non-adherence, from health literacy to social isolation and financial barriers.

5. Reframe how we measure success

Too often, healthcare systems are still structured around clinical metrics—blood pressure targets, HbA1c levels, LDL cholesterol. While these are important, they do not tell the full story of patient well-being or experience. We need to broaden our measures of success to include adherence rates, patient-reported outcomes, and indicators of trust, engagement, and empowerment.

Moreover, value-based care models should explicitly reward efforts to improve adherence, recognizing that these efforts translate into better outcomes and more efficient use of health resources.

A moral imperative

Beyond the clinical and economic arguments lies a deeper, moral imperative. At its core, the quest to improve adherence is about respect for patient autonomy and dignity. Every person has the right to understand their condition, to be meaningfully involved in their care, and to be supported in achieving the best possible health outcomes.

When patients fail to adhere, it is not a "failure" on their part. It is often a signal that the system has failed to meet their needs-whether informational, emotional, financial, or logistical. Blame has no place here; empathy and partnership must guide our response.

The COVID-19 pandemic has only underscored the importance of trust in healthcare. In a world awash with misinformation and growing skepticism toward institutions, rebuilding and sustaining trust is paramount. Clinicians must be seen not only as experts but as allies—people who understand, who care, and who walk alongside patients in their health journey.

Looking to the future

As we reflect on the a:care experience, we are both encouraged and energized. The global momentum around adherence is growing. More HCPs are recognizing the centrality of adherence to their mission. More patients are speaking up about the challenges they face. More innovators are bringing creative solutions to the table.

But we must not lose sight of the scale of the task ahead. Changing mindsets—our own and those of the system—takes time, persistence, and courage. It requires us to be comfortable with complexity, to embrace humility, and to constantly learn from patients and from each other.

If there is one message we hope every reader takes from this book, it is this: every interaction matters. Every consultation is an opportunity to build trust, to explore beliefs and motivations, to offer support. Small changes in how we communicate and engage can ripple outward to create meaningful improvements in adherence-and, ultimately, in patient lives.

Together, we can create a future where adherence is not an afterthought but a foundation of care. A future where treatments do not remain trapped in the pages of a prescription but translate into better health, longer lives, and greater patient empowerment.

This is the vision we must pursue—not alone, but together. Let us walk this path with determination, with compassion, and with unwavering commitment to the people we serve.

Thank you for joining us on this journey. The next chapter begins now with you.

Slides

Supporting slides from the a:care event, which complement the book, are available for download here:

Acknowledgement: Experts

We would like to thank all the experts who contributed to the a:care journey for their invaluable support:

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Acknowledgement: Medical societies

We are grateful to the following medical societies for their unwavering support and endorsement throughout the development of a:care.

Cardiometabolic

European Atherosclerosis Society

The European Atherosclerosis Society is advancing and exchanging knowledge of the causes, natural history, treatments, and prevention of atherosclerotic disease.

International Society of Hypertension

Established in 1966, the Hypertension′ to ISH is a worldwide nonprofit scientific organization dedicated to scientific innovation and advances in medical care in the field of hypertension.

Asociación Peruana de Estudio de la Obesidad y Aterosclerosis – PERU

Asociación Peruana de Estudio de la Obesidad y Aterosclerosis is a nonprofit multidisciplinary association created to encourage the participation of health professionals in the field of obesity and atherosclerosis research.

Colegio Panamericano del Endotelio y Pared Vascular (Pan American Endothelial and Vessel Wall College) – PERU

The Pan American Endothelial and Vessel Wall College began with the desire to learn about the new frontier that will lead to the medicine of the future. Thanks to the support of different scientific societies, the great interest that the topic has aroused within the medical community and different areas of health, and the support of the pharmaceutical industry, the Pan American

Endothelium and Vessel Wall College conducts training in different locations with speakers with extensive experience in the specialized branch of the endothelium.

Corporación Grupo Chileno de Trabajo en Ateroesclerosis (ATEROS Chile) – CHILE

ATEROS Chile is a nonprofit scientific corporation that aims to research, educate, and develop programs for the prevention of atherosclerosis and its cardiovascular complications, focused on individuals, families, and communities.

Fundacion Para la Hipertension Arterial (Hypertension Foundation of Chile) – CHILE

The Hypertension Foundation of Chile's objective is to promote the comprehensive management of hypertension: promotion, prevention, early diagnosis, and follow-up of hypertension.

Instituto Cardiovascular Lezica – ARGENTINA

Instituto Cardiovascular Lezica is a CVD institute with activities related to medical assistance, research, and education.

Liga HTA Latam – CHILE

Liga HTA Latam's purpose is to democratize knowledge, teach, research, and disseminate the most relevant aspects of hypertension and cardiovascular risk.

Sociedad Chilena de HTA – CHILE

The Chilean Society of Hypertension is a nonprofit society created in 1987 with the aim of developing research, teaching, and assistance in the field of arterial hypertension, and carrying out outreach activities to the general population.

Sociedad Dominicana de Endocrinología – DOMINICAN REPUBLIC

Sociedad Dominicana de Endocrinología seeks to promote the scientific development of health professionals in the field of hormones and metabolism. The society sponsors educational programs, courses, and workshops, which seek to keep its members up to date and constantly growing.

Sociedad Latinoamericana de Ateroesclerosis Filial Chile - CHILE

SOLAT's objectives are to promote advances and disseminate scientific and technical knowledge in the field of atherosclerosis.

Sociedad Paraguaya de Endocrinología y Metabolismo – PARAGUAY

The Paraguayan Society of Endocrinology and Metabolism is a nonprofit association of specialists dedicated to the field of endocrinology. Its mission is to promote excellence in endocrine healthcare, research, and education within Paraguay.

Sociedad Peruana de Hipertensión Arterial – PERU

The Peruvian Society of Arterial Hypertension is a medical institution dedicated to promoting the prevention, diagnosis, and treatment of arterial hypertension in the population.

Central nervous system

International Vestibular Society

The Vertigo Academy International is the scientific suborganization of the International Vestibular Society that methodizes the learning program and objectives of vestibular medicine. The biannual meetings of the IVS are also presented as a part of this learning program and called the "Vertigo Academy International Meeting."

Fondazione Paolo Procacci

The Fondazione Paolo Procacci was established in 2008 with a mission to promote initiatives related to the prevention, early diagnosis, treatment, and social management of pain syndromes and associated symptoms.

The foundation supports clinical studies, research, scholarships for young researchers, healthcare professional training, and the development of pain management protocols. It aims to improve the quality of care and enhance the lives of individuals affected by pain while serving as an authoritative voice in pain-related policy matters.

Asociación Paraguaya de Psiquiatras – PARAGUAY

Asociación Paraguaya de Psiquiatras is a nonprofit association of specialists dedicated to the field of psychiatry. Its mission is to promote excellence in mental healthcare, research, and education within Paraguay.

Associação Brasileira de Dor – BRAZIL

The Brazilian Association of Musculoskeletal Pain (SBOT Pain Committee) was born due to the need for orthopedics to be represented in the Pain Committee of the Brazilian Medical

Association, which aims to evaluate doctors who are interested in the area title of acting in pain.

Sociedad Paraguaya de Psiquiatría – PARAGUAY

Sociedad Paraguaya de Psiquiatría is a nonprofit association of specialists dedicated to the field of psychiatry. Its mission is to promote excellence in mental healthcare, research, and education within Paraguay.

Gastroenterology

European Pancreatic Club

The European Pancreatic Club is a nonprofit, international scientific organization dedicated to the study of the pancreas. The EPC was founded in 1965, with the aim of bringing together basic scientists and clinicians in an informal atmosphere to promote friendship and research collaboration.

Spanish Association of Gastroenterology

The Spanish Association of Gastroenterology was founded in Madrid on December 13, 1997 with the aim of creating a new model of interaction with Spanish scientific gastroenterology. The association provides an effective professional forum for exchanging knowledge and opportunities on clinical practices and research.

CA-IHPBA Capitulo Argentino de la International Hepatopancreato

Biliary Association – ARGENTINA

The Argentine Chapter of the International Hepato Pancreato Biliary Association was founded on April 24, 1995. It is a nonprofit civil association that pursues the same goals as its parent association: to be an organization dedicated to alleviating human suffering worldwide caused by hepato-biliary-pancreatic disorders through the improvement of education, training, innovation, research, and patient care. It promotes professional excellence and ethical conduct in the specialty, both for surgeons and for doctors in general and other health professionals.

Club del Páncreas Argentina – ARGENTINA

Club del Páncreas Argentina seeks to promote excellence in the diagnosis and treatment of pancreatic disease.

Oncology

Hellenic Society for Chemotherapy – GREECE

The Hellenic Society for Chemotherapy is part of the Hellenic Institute for the Study of Sepsis, a leading, nonprofit, non-commercial organization in medical research since 2010.

Sociedad Peruana de Oncología Médica – PERU

Sociedad Peruana de Oncología Médica is a nonprofit scientific organization aimed at leading at the national-level knowledge related to cancer, its research, and medical treatment. It is part of the Medical Societies of the Medical College of Peru, as the main society to which it is legally accredited.

Osteoporosis

International Osteoporosis Foundation (IOF)

The International Osteoporosis Foundation (IOF) is the world's largest nongovernmental organization dedicated to the prevention, diagnosis and treatment of osteoporosis and related musculoskeletal diseases. IOF's network includes membership committees comprised of scientific experts, 340 patient, medical societies and universities in more than 150 countries, as well as over 1100 Fracture Liaison Services in all regions of the world. The IOF network is united in its mission to prioritize bone health and fracture prevention, striving toward a shared vision of a world free from fragility fractures, where healthy mobility is a reality for all. @iofbonehealth

Respiratory

Hellenic Institute for the Study of Sepsis

Inaugurated in July 2010, the Hellenic Institute for the Study of Sepsis is a nonprofit, non-commercial organization consisting of 14 research sites maintaining a high level of research and education actions for sepsis and systemic inflammation that are the main disorder leading to death in our world.

Hellenic Sepsis Study Group

The Hellenic Sepsis Study Group was launched in May 2006, and since then, more than 65 study sites have participated in this group. Their common goals are fostering education and research in sepsis and collaborating with groups with the same goals in Europe and further abroad.

Women's health

European Society of Gynecology

The European Society of Gynecology promotes advancements in gynecology, obstetrics, and reproductive organ medicine. It achieves this through biennial international congresses, fostering expert networking, supporting research, facilitating education, organizing meetings, and collaborating with similar entities.

International Society of Gynecological Endocrinology

The International Society of Gynecological Endocrinology is a nonprofit organization established in 1986 for the purpose of promoting science and research into all aspects of gynecological endocrinology and communication between scientists interested in these subjects.

International Society of Recurrent Pregnancy Loss

The International Society of Recurrent Pregnancy Loss is dedicated to advancing the understanding, prevention, and management of recurrent pregnancy loss. By fostering research, providing educational resources, and promoting a multidisciplinary approach, the society aims to support affected individuals and families while contributing to global improvements in care.

Federação Brasileira das Associações de Ginecologia e Obstetrician – BRAZIL

Federação Brasileira das Associações de Ginecologia e Obstetrician has in its DNA the objective of promoting, supporting, and ensuring the technical, scientific improvement and ethical aspects of the professional practice of gynecologists and obstetricians, guided by total respect for women's health and well-being.

Sociedad Chilena de Climaterio – CHILE

Sociedad Chilena de Climaterio is a medical society whose mission is promoting knowledge on the climacteric and menopause, as well as creating spaces for discussion and exchange of medical material of interest.

Sociedad de Obstetricia y Ginecología Infantil y de la Adolescencia del Perú – PERU

Sociedad de Obstetricia y Ginecología Infantil y de la Adolescencia del Perú promotes the training of medical professionals in the subspecialty of child and adolescent gynecology. The society seeks to encourage, promote, and sustain teaching and research activities in the subspecialty. It keeps the general population informed and disseminates in understandable and scientifically proven language topics related to child and adolescent gynecology.

Ukrainian Association of Gynecologists-Endocrinologists – UKRAINE

Established in 2011, the Ukrainian Association of Gynecologists-Endocrinologists is a nonprofit scientific organization dedicated to scientific education and advances in medical care in the field of women's health.

Other

Academia Nacional de Medicina – COSTA RICA

The National Academy of Medicine of Costa Rica is a permanent organization created to promote and strengthen health in all its breadth, providing an impartial space for open discussion of national and international issues that impact the health of Costa Ricans, both in direct care and in matters related to research and teaching. Its vision is to be a nationally and internationally recognized entity, made up of physicians and academics of extensive prestige and experience, for discussion and analysis of issues related to health, both in the area of care and research and teaching, in order to improve the quality of life of Costa Ricans.

Asociación Médica Guatemalteca de Atención Primaria – GUETEMALA

Asociación Médica Guatemalteca de Atención Primaria is a scientific medical society whose main objective is primary healthcare as a tool to advance access and health coverage to overcome inequality

Sociedad Chilena de Nutrición, Bromatología y Toxicología – CHILE

The Chilean Society of Nutrition, Bromatology, and Toxicology is a scientific organization that aims to bring together professionals in the area to achieve scientific communication at the national level and promote the progress of these disciplines in their various aspects.

Sociedad Peruana de Nefrologia – PERU

Sociedad Peruana de Nefrologia is a nonprofit civil association whose mission is to promote the further development of nephrology in Peru, promoting studies, research, and the teaching of this specialty.

Universidad Autónoma de Centroamérica – COSTA RICA

Universidad Autónoma de Centroamérica seeks too become an outstanding university in Costa Rica in academics, research, and social projection. Its mission is to train professionals in a framework of respect and freedom, with a discipline in logical and creative thinking and a supportive and humanistic attitude

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