OCTOBER 2023

senzo

FUTURE DIAGNOSTICS

# AMR

## The Next Pandemic?

**Antimicrobial resistance threatens not just our healthcare, but modern medicine itself. Discover what needs to happen from better diagnostics to new antibiotics.**

About Senzo: Senzo Health is a diagnostics technology company developing future testing solutions for healthcare and industry, based in London, Cambridge and the USA.

Senzo Health | London | Pennsylvania | Cambridge | www.senzo.com | info@senzo.com

**“Antimicrobial resistance will affect everybody, regardless of where they live, their health, economic circumstances, lifestyle or behaviour.”**
WHO

**“Antibiotic resistance undermines much of modern health care, which relies on access to effective antibiotics to prevent and treat infections…”**
SCIENCE

**“We estimate that without antimicrobials, the rate of postoperative infection is 40-50% and about 30% of those with an infection will die.”**
BMJ

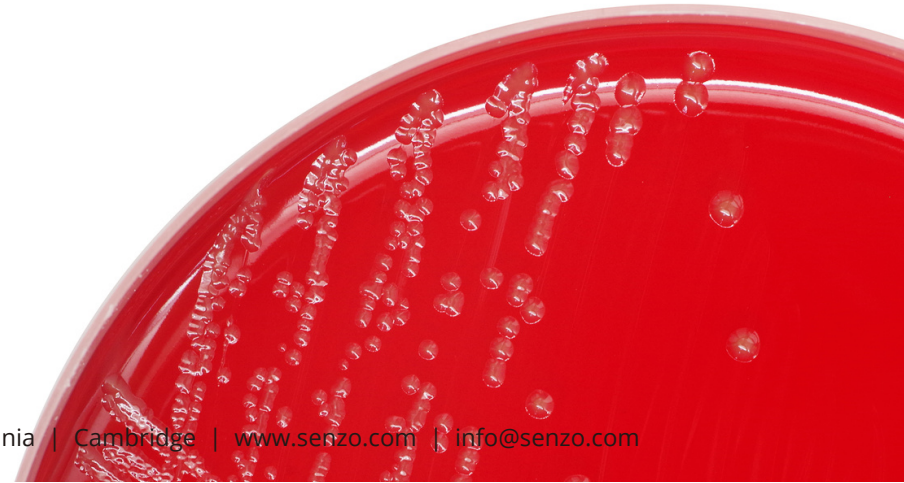
**“it is clear that “the existing classes of antibiotics are probably the best we will ever have.”**
BMJ

**“Almost as soon as antibiotics were discovered, we knew that bacteria were able to develop resistance against them.”**
BMJ

**“…we could enter a post-antibiotic era, where simple surgical procedures, such as total hip replacements or caesarean sections, can no longer be safely performed, due to the risk of infections.”**
PHARMO ECONOMICS

**“Lower respiratory infections accounted for more than 1·5 million deaths associated with resistance in 2019, making it the most burdensome infectious syndrome.”**
LANCET

**“The emergence and spread of new forms of resistance continues to alarm CDC experts, especially resistance shared among germs through genetic mobile elements…”**
CDC



# AMR: Global Status

## A Pervasive Threat

A 2022 report, “Modeling The Effects On Antimicrobial Resistance (AMR)”, highlighted the potential reality of a "post-antibiotic era", where even basic surgical procedures like hip replacements or cesarean sections could become unsafe due to the elevated risk of infections [18]. Research published in the British Medical Journal found that in a scenario devoid of effective antimicrobials, postoperative infection rates could soar to between 40-50%, with an estimated 30% of those infected subsequently succumbing to such infections [16].

Whilst this is a worst-case scenario, there is little doubt that AMR poses a fundamental risk to modern medicine, certainly on the scale of the recent Covid-19 pandemic albeit at a pace more similar to climate change [4, 5]. Notwithstanding, as the World Health Organization puts it, AMR represents "a profound threat to human health"[3].

As the British Medical Journal writes, “Almost as soon as antibiotics were discovered, we knew that bacteria were able to develop resistance against them. This is not necessarily a problem, as long as there are other antimicrobials to take their place. During the latter half of the 20th century this was the predominant situation, but no longer.”[16] "Greater use of antibiotics during the past 50 years has exerted selective pressure on susceptible bacteria and may have favored the survival of resistant strains."[14].

# Quantifying the Impact

The threat of AMR is not merely academic; it manifests in startling statistics. “Antimicrobial resistance will affect everybody, regardless of where they live, their health, economic circumstances, lifestyle or behaviour.”[3] Currently, resistant organisms account for over 650,000 infections and over 30,000 attributable deaths in Europe each year, with 1.2m deaths globally[18]. “One pathogen–drug combination, methicillin-resistant S aureus (MRSA), caused more than 100,000 deaths attributable to AMR in 2019, while six more combinations each caused 50,000–100,000 deaths…”[5]

# The Drying Well of Antibiotics

The paucity of new antibiotics hitting the market is clear. "A rapid decrease in the number of new drugs approved and numerous withdrawals on quality and safety grounds" are pivotal factors contributing to the shrinking reservoir of effective antibiotics [16]. Due to this, as written in the British Medical Journal, "the existing classes of antibiotics are probably the best we will ever have."[16]

“Almost as soon as antibiotics were discovered, we knew that bacteria were able to develop resistance against them”

# Contributors and Consequences

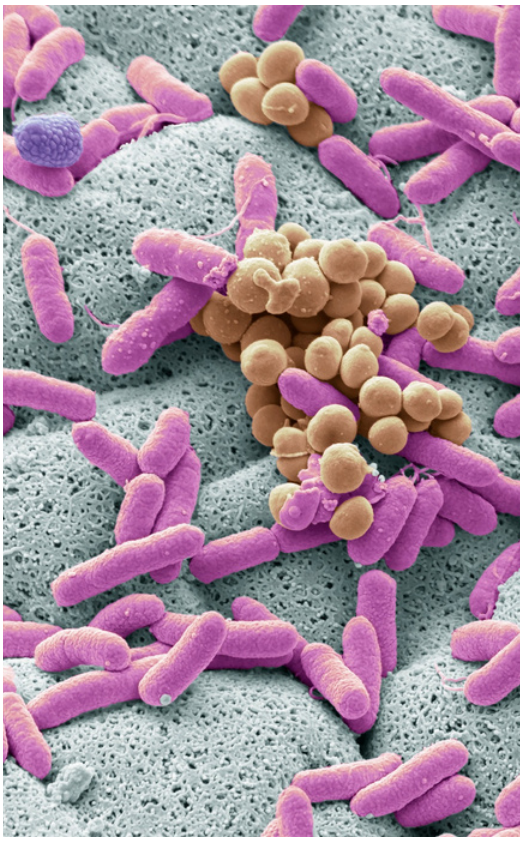
AMR isn't only the consequence of antibiotic usage in healthcare, but is also caused by the "uncontrolled use of antibiotics in both the health and agriculture sectors"[1]. Due to the complex drivers of AMR, modeling the exact trajectory of antibiotic resistance and the minute alterations in antibiotic consumption remains a complex task [17, 18], and what is hard to measure, is hard to fix, especially when a global response is required.

> "we could enter a post-antibiotic era, where simple surgical procedures, such as total hip replacements or caesarean sections, can no longer be safely performed"
>
> The Opportunity Of Point-Of-Care Diagnostics In General Practice: Modelling The Effects On Antimicrobial Resistance

## The Struggle for Collective Action

Organizations such as the Center for Disease Control and the World Health Organization highlight that despite numerous initiatives aimed at tackling AMR, progress has been slow, attributed to factors such as inadequate monitoring, reporting, and, crucially, a lack of acknowledgement on the urgency to act amongst stakeholders.[3] "This resistance to antimicrobial medicines is happening in all parts of the world for a broad range of microorganisms with an increasing prevalence that threatens human and animal health."[3] The emergence and spread of new forms of resistance continue to heighten the alert level amongst experts, underscoring the need for intensified, collective action across all sectors. [2]

# Causes of AMR



## Misuse of Antibiotics

AMR is caused by the use of antibiotics with the rate of AMR correlated to the amount of antibiotics used. One complex challenge presented in combating AMR within healthcare is the notable misuse and over-prescription of antibiotics. This is particularly clear in cases of respiratory tract infections (RTIs). According to the 2020 paper 'Efficacy And Safety Of Rapid Tests To Guide Antibiotic Prescriptions For Sore Throat', "Between 50% to 70% of pharyngitis cases are treated with antibiotics, despite the majority of cases being viral in origin"[9]. "Evidence shows a high rate of unnecessary antibiotic prescriptions in primary care in Europe and the United States. Given the costs of widespread use and associated antibiotic resistance, reducing inappropriate use is a public health priority"[11]. Another study found that "Even though bacteria are estimated to cause a minority of community-acquired acute respiratory tract infection (CA-ARTI) cases in Europe, CA-ARTIs account for around 40% of antibiotic prescriptions by general practitioners (GPs) in the Netherlands."[18]

"...resistant organisms are estimated to account for 1.27 million deaths globally."

The Opportunity Of Point-Of-Care Diagnostics In General Practice: Modelling The Effects On Antimicrobial Resistance

# Variability in Antibiotic Prescribing

The challenges of misuse are further compounded by the significant variability in antibiotic prescribing practices globally. A study in the British Medical Journal noted the vast disparities: "Antibiotic prescribing by networks ranged from 20% to nearly 90% (53% overall), with wide variation in classes of antibiotics prescribed"[12]. This evidence signals a striking inconsistency and underscores a lack of and need for the adoption of a uniform, evidence-based approach to antibiotic prescription, particularly for RTIs.

## Antibiotic Access

A paper published in the journal 'Pharmaco Economics', demonstrated that "A major driver of antibiotic use is patients consulting for respiratory infections in primary care" [18] where access is easier. "Inappropriately high levels of antibiotics are still prescribed in primary health care for RTIs"[8]. Put another way, whilst antibiotics are essential for a safe operation within a hospital setting, their misuse is being driven in large part by prescriptions given for more minor ailments such as RTIs by community healthcare professionals. "Reducing inappropriate antibiotic use while expanding essential access is a difficult challenge, especially in low- and middle-income countries."[17]

Understanding and addressing primary care consultation patterns and prescriber behaviours is central to contending with the problem of antibiotic misuse.

# Economic Incentives

One potential solution to AMR is the development of new, more effective antibiotics to replace those which become more resistant. Unfortunately, this is not happening. As SCIENCE writes "...without government intervention, R&D for antibiotics is rarely profitable, and most major pharmaceutical companies have left the field"[17]. The economics of antibiotic discovery and development are further complicated as it, "depends on various factors: which drug and pathogen are involved, the mechanism of antibiotic resistance, the prevalence of that pathogen, the types of infections it causes and their level of transmissibility, the health burden of those infections, and whether alternative treatments are available"[17].

The challenges of misuse (usually over-prescription, but sometimes under-prescription) of antibiotics, particularly in the realm of RTIs, alongside the considerable hurdles in antibiotic research and development present an extremely difficult challenge for global healthcare to address.

“We estimate that without antimicrobials, the rate of postoperative infection is 40–50% and about 30% of those with an infection will die.”

The True Cost Of Antimicrobial Resistance, BMJ

# BURDEN

## A Current Crisis

AMR is not a future threat; it is a current healthcare emergency with current societal and economic burdens. As ‘The Lancet’ states, "Lower respiratory infections accounted for more than 1.5 million deaths associated with resistance in 2019, making it the most burdensome infectious syndrome" [5]. The paper goes on to note that there were "an estimated 4.95 million deaths associated with bacterial AMR in 2019" [5] and that “one pathogen–drug combination, methicillin-resistant S aureus (MRSA), caused more than 100,000 deaths attributable to AMR in 2019" [5].

# Healthcare Implications

AMR however threatens not just lives through illnesses that do not respond to treatment, but our entire healthcare system. As 'SCIENCE' puts it: "Antibiotic resistance undermines much of modern health care, which relies on access to effective antibiotics to prevent and treat infections associated with routine medical procedures" [17]. As The World Health Organization explains "The direct consequences of infection with resistant microorganisms can be severe, including longer illnesses, increased mortality, prolonged stays in hospital, loss of protection for patients undergoing operations and other medical procedures, and increased costs" [3].

# Economic Costs

Behind every AMR statistic is a patient requiring additional care, generating additional costs. In the United States, nearly "223,900 people required hospital care for C. difficile and at least 12,800 people died in 2017" [2]. Despite some progress, "the number of people facing antibiotic resistance in the United States is still too high. More than 2.8 million antibiotic-resistant infections occur in the United States each year, and more than 35,000 people die as a result" [2].

AMR is threatening to become a colossal socioeconomic drain. The World Health Organization warns that "AMR is a drain on the global economy with economic losses due to reduced productivity caused by sickness (of both human beings and animals) and higher costs of treatment" [3].

# Solutions


## What works

The World Health Organization makes it very clear: "Simply, here's what works. 1. Preventing infections protects everyone. 2. Improving antibiotic use in people and animals slows the threat and helps preserve today's drugs and those yet to come. 3. Detecting threats and implementing interventions to keep germs from becoming widespread saves lives." [13].

## Prevention Versus Cure

As we know, "...antibiotic consumption is associated with the development of antibiotic resistance."[4] A report looking at the effects of antibiotic consumption on ARM stated that "Increased consumption of antibiotics may not only produce greater resistance at the individual patient level but may also produce greater resistance at the community, country, and regional levels, which can harm individual patients."[14] As such, preventing infections reduces use, preventing misuse reduces use, and preventing outbreaks reduces use. So, before we even look at the development of new and more effective antibiotics, there is a huge amount that can be done that is not being done.

The Center for Disease Control also support this prioritization: "Rapid detection and prevention strategies have helped protect people from two community-associated germs (i.e. drug-resistant tuberculosis, drug-resistant Streptococcus pneumoniae), but a stronger focus and interventions are needed."[2]

# Comprehensive Solutions

The UK government proposed the development of a comprehensive approach to tackle AMR with "New diagnostics, therapies, vaccines and interventions in use, and a full AMR research and development pipeline for antimicrobials, alternatives, diagnostics, vaccines and infection prevention across all sectors..."[4]

# Diagnostics and AMR

Coupled with reducing the initial need for an antibiotic, better and more affordable and readily available diagnostics can also assist by reducing misuse of antibiotics, a leading cause of AMR. "Based on data from five trials (2545 participants), a large reduction in prescribed antibiotics was found in the rapid test group (481/1197)"[9]. As a research paper looking at 'The Opportunity of Point-Of-Care Diagnostics In General Practice' put it, "We estimate resistance will have an upwards trend in the coming years, which can be ameliorated by such increased use of diagnostics,..."[18] with data suggesting that "Rapid testing to guide antibiotic treatment for sore throat in primary care probably reduces antibiotic prescription rates by 25%. [4,18].

"While the development of new treatments is one of these key actions, such investments must be coupled with dedicated efforts toward preventing infections in the first place, slowing the development of resistance through better antibiotic use, and stopping the spread of resistance when it does develop..."[2]

But before better diagnostics can be implemented, many will need to be invented: "...before implementation in primary healthcare, diagnostic accuracy of the POCT needs improvement and it's impact on clinical decision making should be further assessed."[8]

"Antimicrobial resistance will affect everybody, regardless of where they live, their health, economic circumstances, lifestyle or behaviour."

Worl Health Organisation

# WHAT NEXT?

The Center for Disease Control contextualizes both the challenge, urgency and necessity of the global AMR treatment: "Antibiotics are critical tools for treating common and complex infections among humans, animals, and crops, including infections that can lead to sepsis (the human body's extreme response to an infection and a medical emergency). Together, more action is needed across settings, industries, and countries to fully protect people from antibiotic resistance threats."[2]

A key contibuting solution is the development and use of fast, accurate, inexpensive diagnostics that help give healthcare professionals the ability to rule—in/rule-out a bacterial infection and more accurately and responsibly prescribe antibiotics, reducing both under or delayed prescribing of antibiotics to patients who would benefit from them, as well as over-prescribing to those who wouldn't thereby contribute to the AMR problem.

# Sources

1 A General Public Study On Preferences And Welfare Impacts Of Antimicrobial Resistance In The United Kingdom - Pharmaco Economics - 2022 - Maria Veronica Dorgali, Alberto Longo, Caroline Vass, Gemma Shields, Roger Harrison, Riccardo Scarpa, Marco Boe - https://pubmed.ncbi.nlm.nih.gov/34458962/

2 Antibiotic Resistance Threats In The United States - Center For Disease Control - 2019 - Center for Disease Control https://www.cdc.gov/drugresistance/biggest-threats.html

3 Global Action Plan On Antimicrobial Resistance - World Health Organisation - 2015 - WHO - https://www.who.int/publications-detail-redirect/9789241509763

4 Contained And Controlled. The Uk's 20-Year Vision For Antimicrobial Resistance - UK Government - 2019 - GOV.UK https://www.gov.uk/government/publications/uk-20-year-vision-for-antimicrobial-resistance

5 Global Burden Of Bacterial Antimicrobial Resistance In 2019: A Systematic Analysis - The Lancet - 2022 - Antimicrobial Resistance Collaborators - https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext

6 Enhanced Communication Skills And C-Reactive Protein Point-Of-Care Testing For Respiratory Tract Infection: 3.5-Year Follow-Up Of A Cluster Randomized Trial - Annals of Family Medicine - 2013 - Jochen W. L. Cals, MD, PhD, Leon de Bock, MD, Pieter-Jan H. W. Beckers, MD, Nick A. Francis, MD, PhD, Rogier M. Hopstaken, MD, PhD, Kerenza Hood, PhD, Eefje G. P. M. de Bont, MD, Christopher C. Butler, MD, Geert-Jan Dinant, MD, PhD, - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3601394/#:~:text=Summary%20and%20Main%20Findings&text=Patients%20managed%20by%20a%20physician,not%20observed%20for%20CRP%20testing.

7 Management Of Influenza In Adults Older Than 65 Years Of Age: Cost-Effectiveness Of Rapid Testing And Antiviral Therapy - Annals of Internal Medicine - 2003 - Michael B Rothberg, Sandra Bellantonio, David N Rose, - https://pubmed.ncbi.nlm.nih.gov/12965940/

8 Diagnostic Performance And Clinical Feasibility Of A Point-Of-Care Test For Respiratory Viral Infections In Primary Health Care - Oxford University Press - 2017 - Andrea H L Bruning, Wilhelmina B de Kruijf, Henk C P M van Weert, Wim L M Willems, Menno D de Jong, Dasja Pajkrt, Katja C Wolthersd, - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7108454/

9 Efficacy And Safety Of Rapid Tests To Guide Antibiotic Prescriptions For Sore Throat (Review) - Cochrane Library - 2020 Jérémie F Cohen, Jean-Yves Pauchard, Nils Hjelm, Robert Cohen, Martin Chalumeau, - https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012431.pub2/full/hu#:~:text=Rapid%20testing%20to%20guide%20antibiotic,no%20impact%20on%20antibiotic%20dispensing.

10 Clinical Score And Rapid Antigen Detection Test To Guide Antibiotic Use For Sore Throats: Randomized Controlled Trial Of Prism (Primary Care Streptococcal Management) - British Medical Journal - 2014 - P. Little, F.D. Hobbs, M. Moore, https://www.bmj.com/content/347/bmj.f5806

11 Clinicians' Views And Experiences Of Interventions To Enhance The Quality Of Antibiotic Prescribing For Acute Respiratory Tract Infections - PubMed - 2014 - Sibyl Anthierens 1, Sarah Tonkin-Crine, Jochen W Cals, Samuel Coenen, Lucy Yardley, Lucy Brookes-Howell, Patricia Fernandez-Vandellos, Jaroslaw Krawczyk, Maciek Godycki-Cwirko, Carl Llor, Christopher C Butler, Theo Verheij, Herman Goossens, Paul Little, Nick A Francis; GRACE/CHAMP INTRO team - https://pubmed.ncbi.nlm.nih.gov/25373834/

12 Variation In Antibiotic Prescribing And Its Impact On Recovery In Patients With Acute Cough In Primary Care: Prospective Study In 13 Countries - British Medical Journal - 2009 - C C Butler,K Hood,T Verheij,P Little,H Melbye,J Nuttall,M J Kelly,S Mölstad,M Godycki-Cwirko,J Almirall,A Torres,D Gillespie,U Rautakorpi,S Coenen,H Goossens, https://www.bmj.com/content/338/bmj.b2242

13 Aetiology Of Lower Respiratory Tract Infection In Adults In Primary Care: A Prospective Study In 11 European Countries - Clin Microbiol Infect - 2018 - M Ieven, S Coenen, K Loens, C Lammens, F Coenjaerts, A Vanderstraeten, B Henriques-Normark, D Crook, K Huygen, C C Butler, T J M Verheij, P Little, K Zlateva, A van Loon, E C J Claas, H Goossens, GRACE consortium, - https://pubmed.ncbi.nlm.nih.gov/29447989/

14 A Systematic Review And Meta-Analysis Of The Effects Of Antibiotic Consumption On Antibiotic Resistance - BMC Infectious Diseases - 2014 - Brian G Bell, Francois Schellevis, Ellen Stobberingh, Herman Goossens, Mike Pringle, - https://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-14-13

15 Superbugs: Should Antimicrobial Resistance Be Included As A Cost In Economic Evaluation? - Health Econ - 1996 - J Coast, R D Smith, M R Millar, - https://pubmed.ncbi.nlm.nih.gov/8817296/

16 The True Cost Of Antimicrobial Resistance - British Medical Journal - 2013 - Richard Smith, professor of health system economics 1, Joanna Coast, professor of health economics2 https://www.bmj.com/content/346/bmj.f1493

17 The Challenge Of Antimicrobial Resistance: What Economics Can Contribute - SCIENCE - 2023 - Laurence S. J. Roope, Richard D. Smith, Koen B. Pouwels, James Buchanan, Lucy Abel, Peter Eibich, Christopher C. Butler, Pui San Tan, A. Sarah Walker, Julie V. Robotham, Sarah Wordsworth, https://www.science.org/doi/10.1126/science.aau4679

18 The Opportunity Of Point-Of-Care Diagnostics In General Practice: Modeling The Effects On Antimicrobial Resistance - Pharmaco Economics - 2022 - Simon van der Pol, Danielle E M C Jansen, Alike W van der Velden, Christopher C Butler, Theo J M Verheij, Alex W Friedrich, Maarten J Postma, Antoinette D I van Asselt, https://pubmed.ncbi.nlm.nih.gov/35764913/

19 Does Diagnostic Testing Always Decrease Antibiotics Prescriptions? - The European Journal of Health Economics - 2023 - Antoñanzas F, Juárez-Castelló CA, Rodríguez-Ibeas R, - https://pubmed.ncbi.nlm.nih.gov/35921019/


# About Senzo

Senzo is an In Vitro Diagnostics (IVD) company developing innovative, accurate, and accessible testing products.

Senzo was founded with the vision of utilising novel technologies, with a focus on enhanced sensitivity, to create mobile, point-of-care and self-testing products and devices with the ability to accurately, quickly, and cost-effectively conduct testing where and when healthcare professionals and patients need it most.

Senzo is creating game-changing products and systems which bring testing to the patient, eliminating the need for the current slow, expensive central-lab testing paradigms. With insights generated at the point of care, patients can make better decisions faster, and healthcare professionals can identify life-threatening diseases at an earlier stage, improving treatment outcomes and saving lives.

London:
64 Rochester Place,
London,
NW1 9JX, UK

Pennsylvania:
10 West Road,
#1011 Newtown,
PA 18940, USA

Cambridge:
IdeaSpace West,
The Hauser Forum,
3 Charles Babbage Rd, Cambridge,
CB3 0GT, UK

Online:
https://senzo.com
Email:
sales@senzo.com

# Media Requests

For journalists interested in developing further coverage on the topics discussed in this document, Senzo Health management is available for comment and interview. To coordinate please reach out to our Media Relations team at info@senzo.com.

# Important Notice

Purpose & Limitation of Use: This document is intended solely for informational and educational purposes. It is not meant to serve as, nor should it be used as, professional advice, diagnosis, treatment, or a substitute for professional judgment.
No Warranties: The information provided herein is presented 'as is', without any warranties of any kind, either express or implied, including but not limited to warranties of accuracy, reliability, or fitness for a particular purpose.
No Endorsement: Any references to specific products, procedures, or services do not constitute or imply an endorsement and the views and opinions expressed in this document do not necessarily state or reflect those of Senzo Health.
No Liability: Senzo Health shall not be liable for any direct, indirect, consequential, or other damages arising out of the access, use, or inability to use this document or any errors or omissions in its content.
Intellectual Property: All content in this document, including but not limited to text, graphics, logos, and images, is the property of Senzo Health and is protected by United Kingdom intellectual property laws.
Updates & Changes: Senzo Health reserves the right to make amendments or corrections, change, suspend, or discontinue any aspect of this document at any time without notice.
Regulatory Compliance: This document does not claim to provide guidance or information in compliance with any specific country's regulatory framework and should not be considered as such.
Use of Data: Any interpretation or use of the data and information contained in this document is at the user's own risk. Users are urged to consult with professional advisors for specific guidance tailored to their situation.
External Links: Any external links provided are for convenience only, and Senzo Health does not endorse or verify the accuracy of the information on these external sites.
Jurisdiction: These terms and conditions are governed by the laws of the United Kingdom, and any disputes arising in relation to this document shall be subject to the exclusive jurisdiction of the courts of the United Kingdom.
Indemnification: The user agrees to indemnify, defend, and hold harmless Senzo Health, its officers, directors, employees, agents, licensors, suppliers, and any third-party information providers against any losses, expenses, damages, and costs, including reasonable attorneys' fees, incurred in relation to or arising from any violation by the user of these terms and conditions.