This presentation is intended for educational purposes only. Abbott has directly engaged the presenter for the preparation of this presentation and/or its delivery. The statements of fact and opinions expressed in this presentation and displayed on the slides are solely those of the presenter and not necessarily those of nor should they be attributed to Abbott. Abbott does not assume any responsibility for, nor does it guarantee the accuracy, completeness or reliability of the information/content provided herein and expressly disclaims liability in relation to the content herein. This presentation may not be modified, duplicated or redistributed in whole or in part without the express written permission of Abbott and/or presenter. The Abbott name and logo are trademarks/intellectual property of Abbott Laboratories Inc. and its affiliates and are used by permission.

Abbott

a:care

TOWARDS A SHIFT OF PARADIGM FROM TREATING DISEASES TO TREATING PEOPLE

Raising awareness on non-adherence

Prof. Alta Schutte
Faculty of Medicine and Health, University of New South Wales
Professorial Fellow, The George Institute for Global Health Immediate
Past President, ISH
Sydney, Australia

International Society of Hypertension

Financial disclosure

Prof. Alta Schutte has received speaker honoraria for lectures from Servier, Abbott, Aktiia, Omron, Sanofi, Sun Pharmaceuticals and Medtronic.

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)

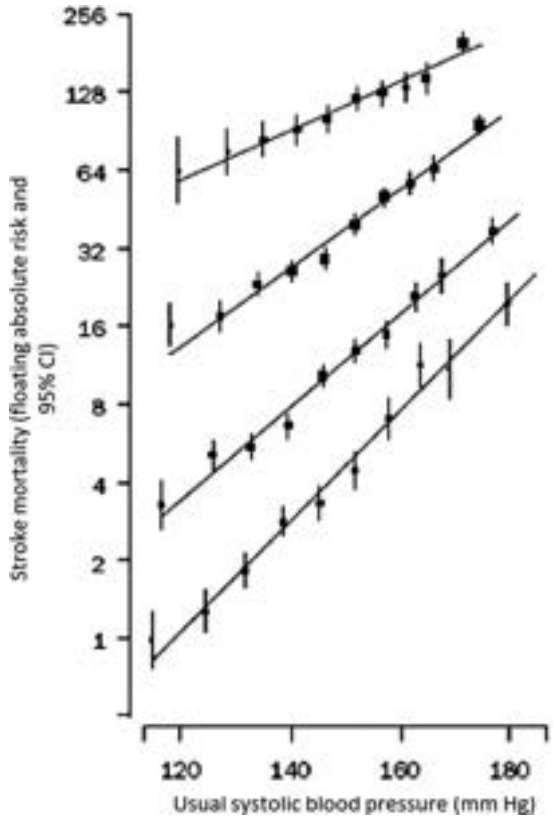
10.8 million deaths/year

= 29,589 DEATHS/DAY

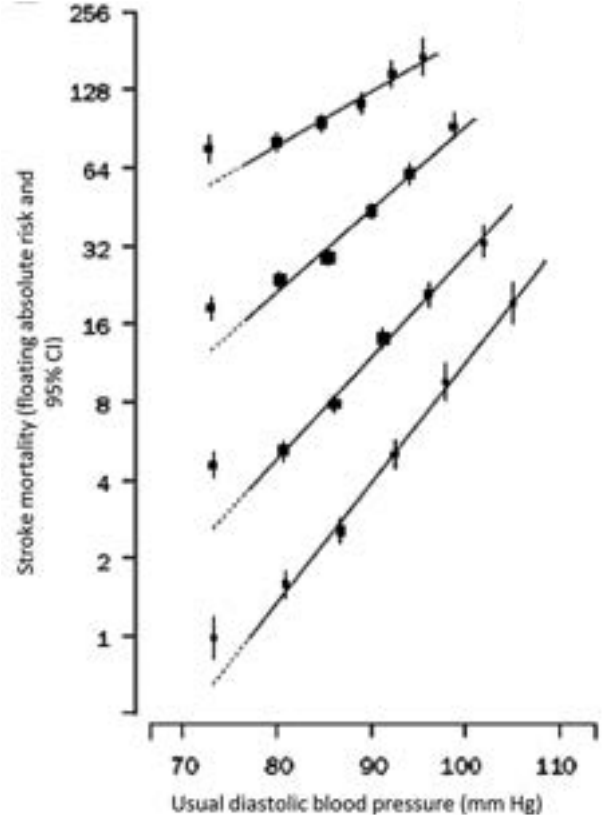
Murray JL, Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396:1223-49

Absolute risk of stroke mortality in relation to blood pressure

A



B



Age (y) at risk

80-89

70-79

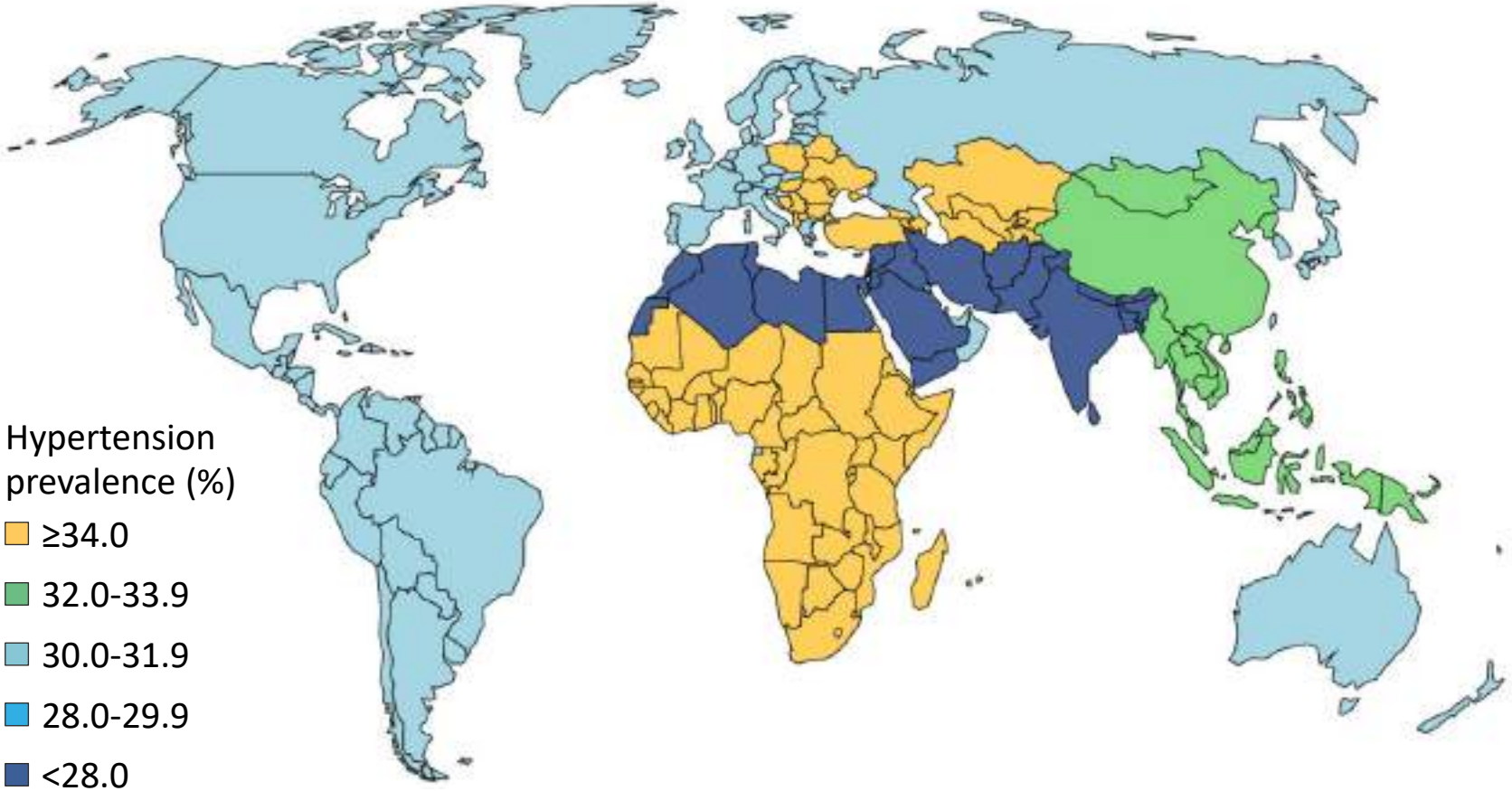
60-69

50-59

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

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

A MEN



1.39 billion estimated with hypertension in 2010

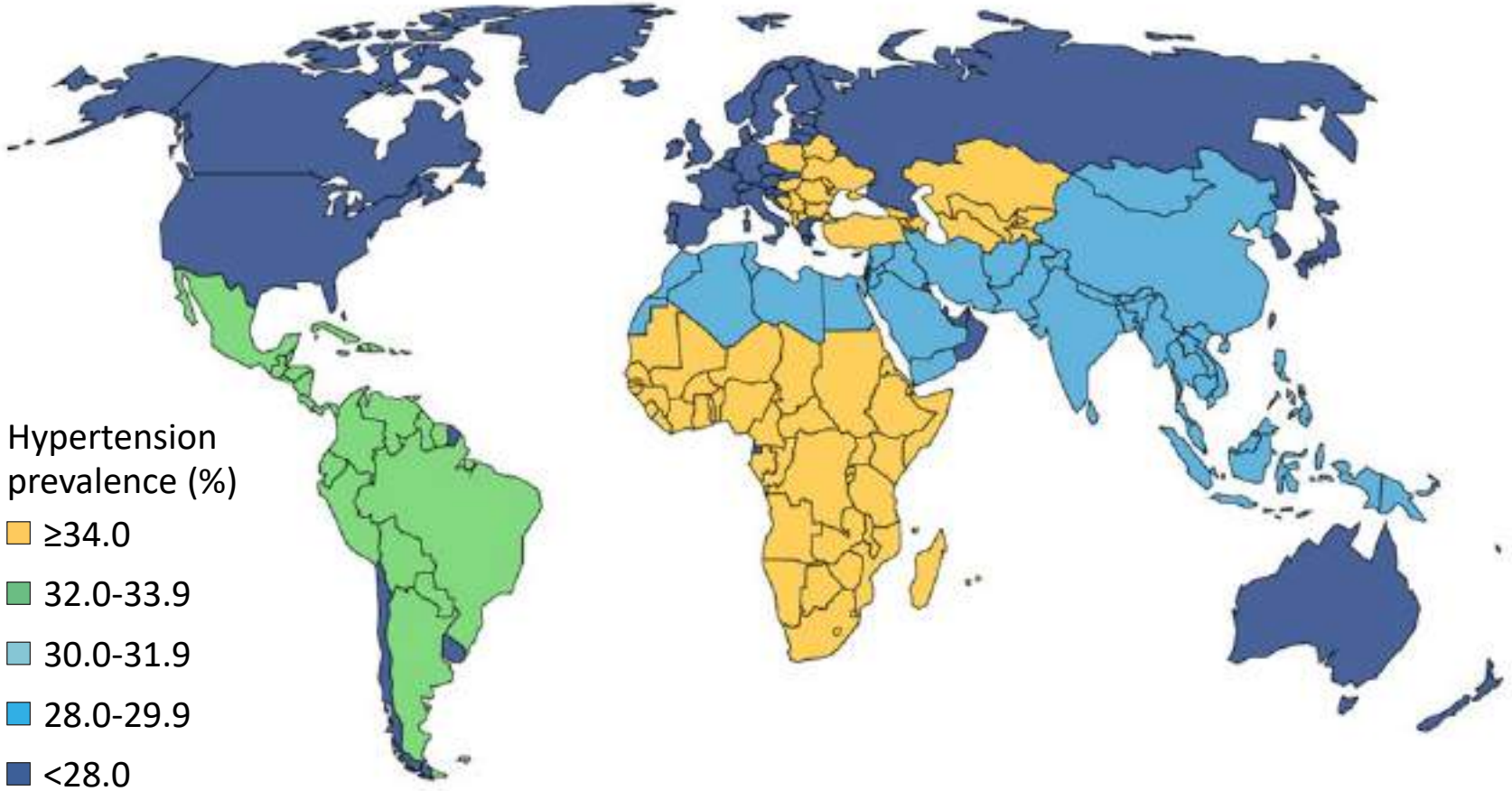
349 million from HIC

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



1.39 billion estimated with hypertension in 2010

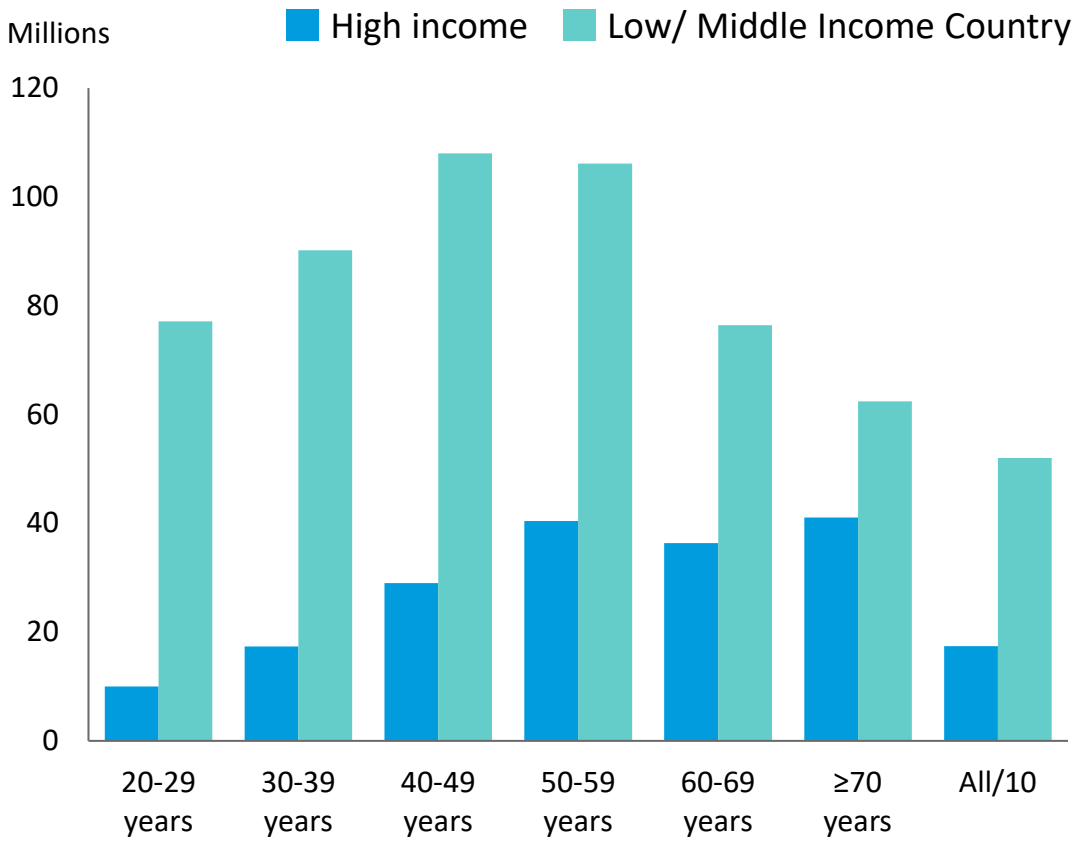
349 million from HIC

1.04 billion from LMIC

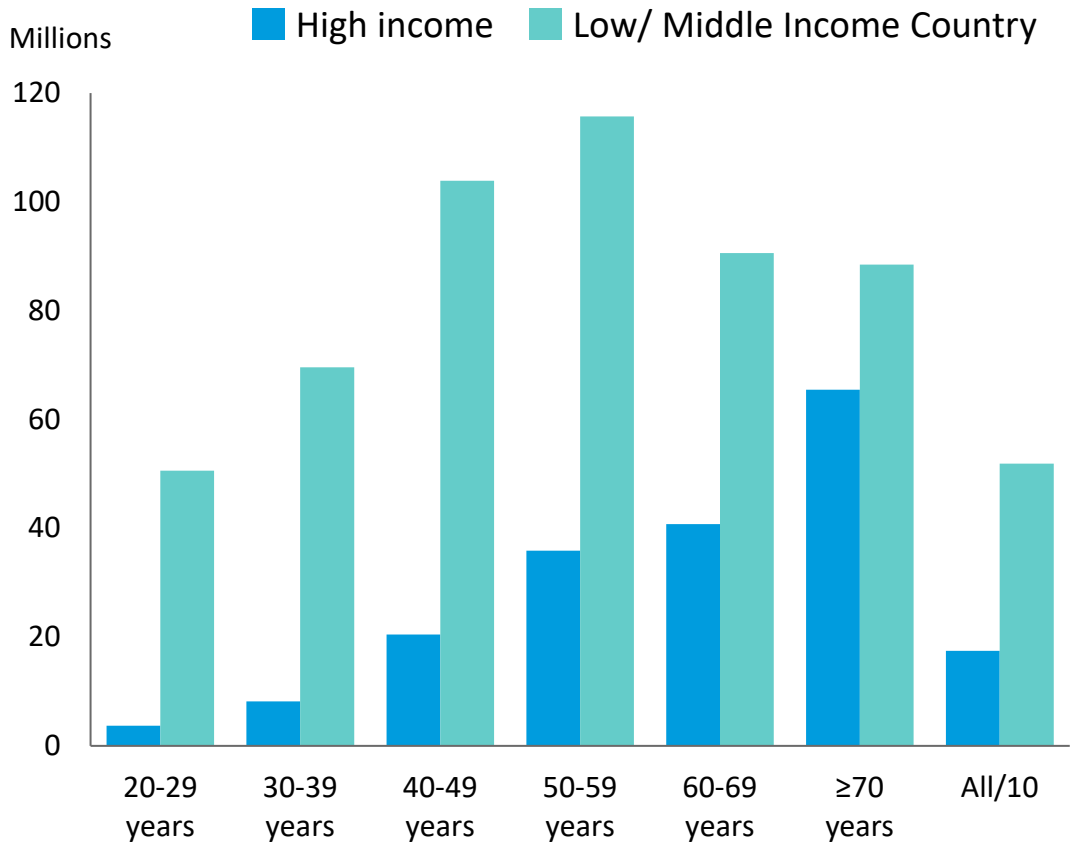
1.Mills Katherine T, Stefanescu Andre and Jiang He. The global epidemiology of hypertension. *Nature Review Nephrology*. 2020 volume 16, Issue 4; 2.Mills Katherine T. Kelly Tanika, *et al.* Global Disparities of Hypertension Prevalence and Control. *Circulation*. 2016;134-441-450

Global disparities of hypertension prevalence

AGE-SPECIFIC AND AGE-STANDARDIZED ABSOLUTE NUMBERS OF HYPERTENSIVE MEN IN 2010



AGE-SPECIFIC AND AGE-STANDARDIZED ABSOLUTE NUMBERS OF HYPERTENSIVE WOMEN IN 2010



Adapt. Mills Katherine T. Kelly Tanika, *et al*. Global Disparities of Hypertension Prevalence and Control. *Circulation*. 2016;134:441-450

Circulation Research

HYPERTENSION COMPENDIUM

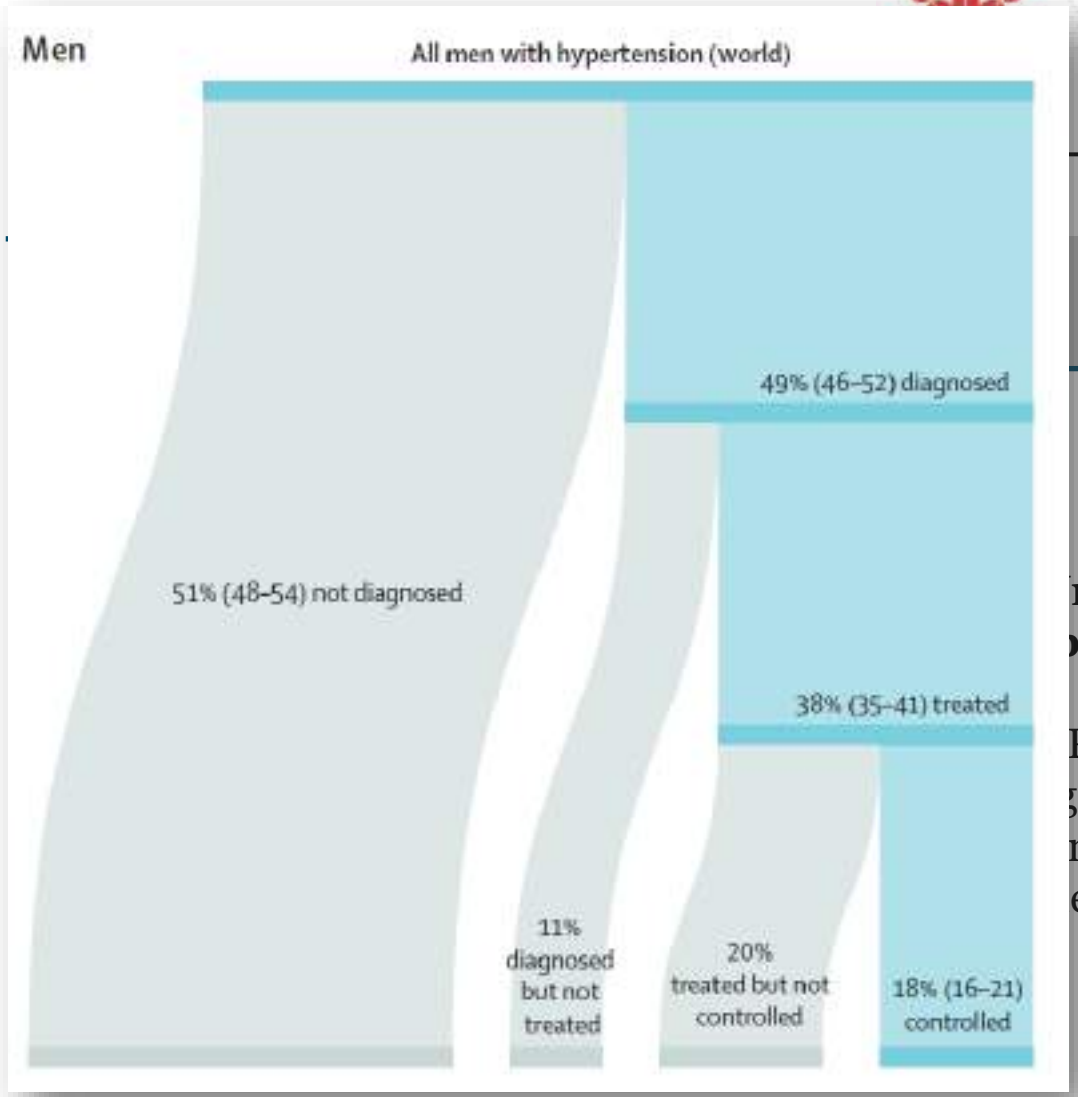
AGE-STANDARDIZED DEATHS (PER 100 000 WITH 95% CIS) DUE TO CVD, HIGH SBP, AND HIGH SODIUM INTAKE ACCORDING TO WORLD BANK INCOME CLASSIFICATION OF COUNTRIES IN 2019

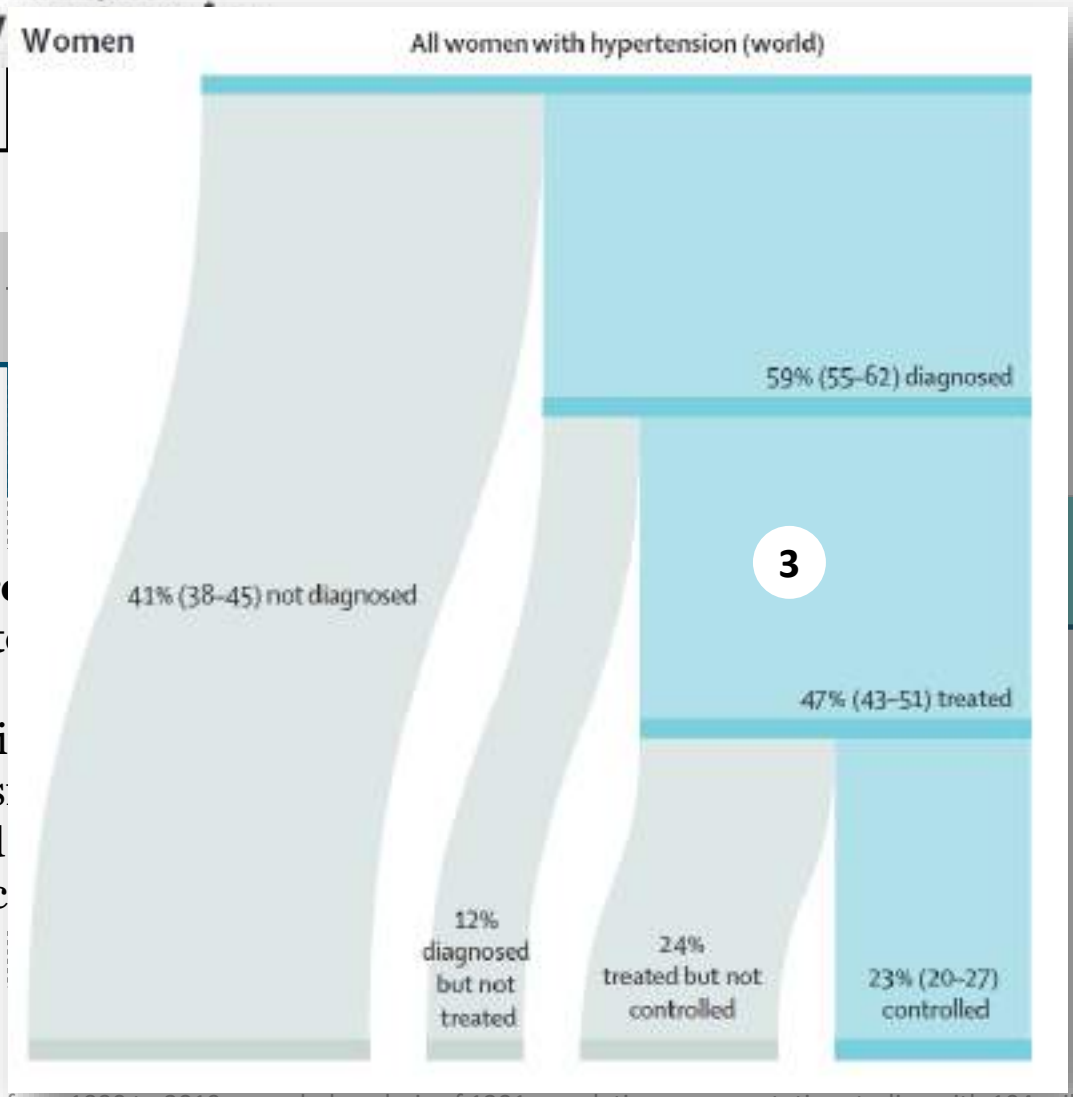
	World Bank income classification of countries			
	High income	Upper middle income	Lower middle income	Low income
Deaths due to CVD	133 (118-142)	267 (24-283)	313 (287-337)	304 (270-340)
CVD deaths due to high SBP	64 (54-74)	143 (121-164)	172 (149-197)	167 (142-192)
Deaths due to high SBP	**72 (61-83)**	**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

International Society of Hy





3

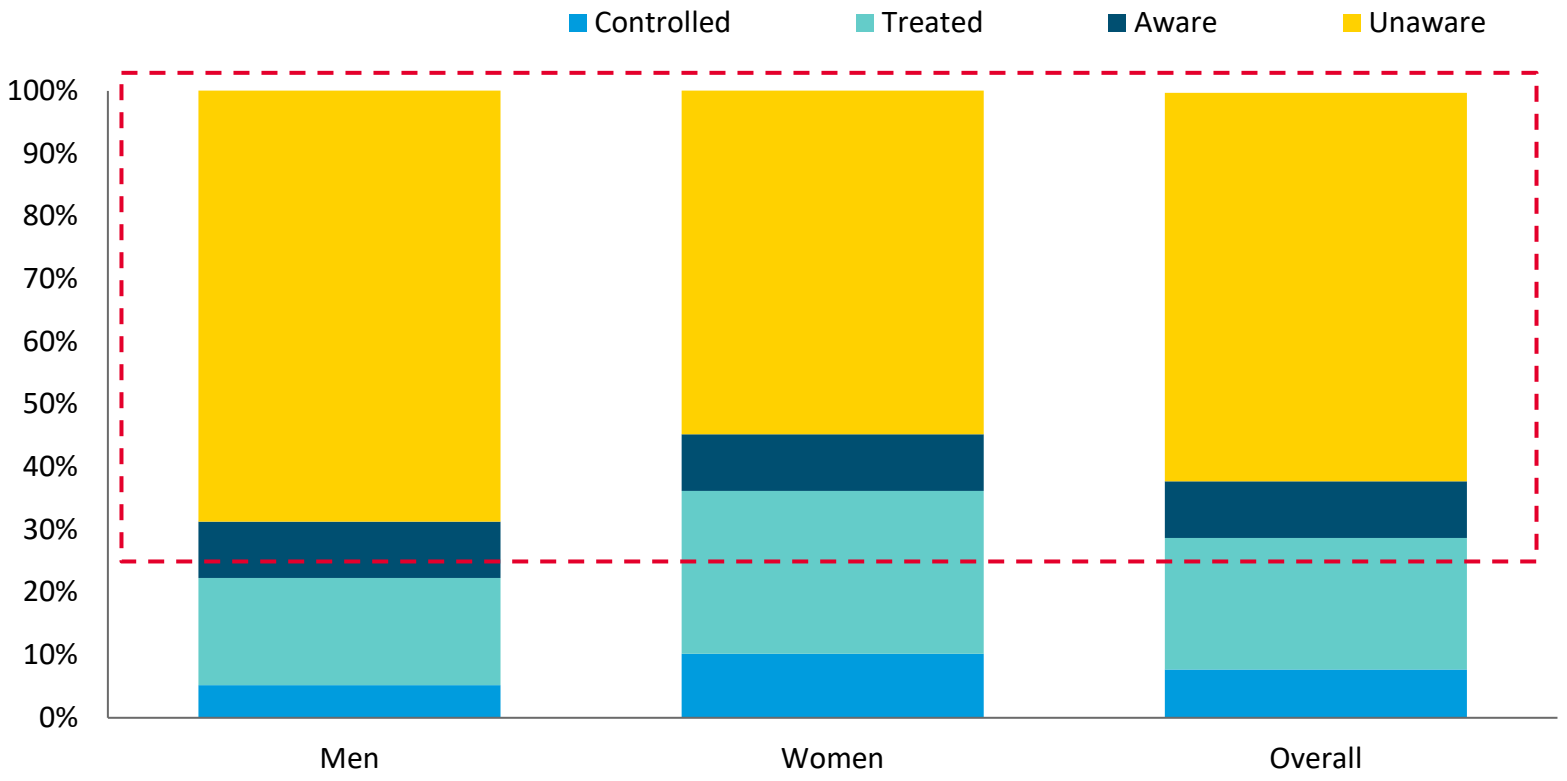
Ezzati Majid. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet* 2021;298:957-80

The Lancet

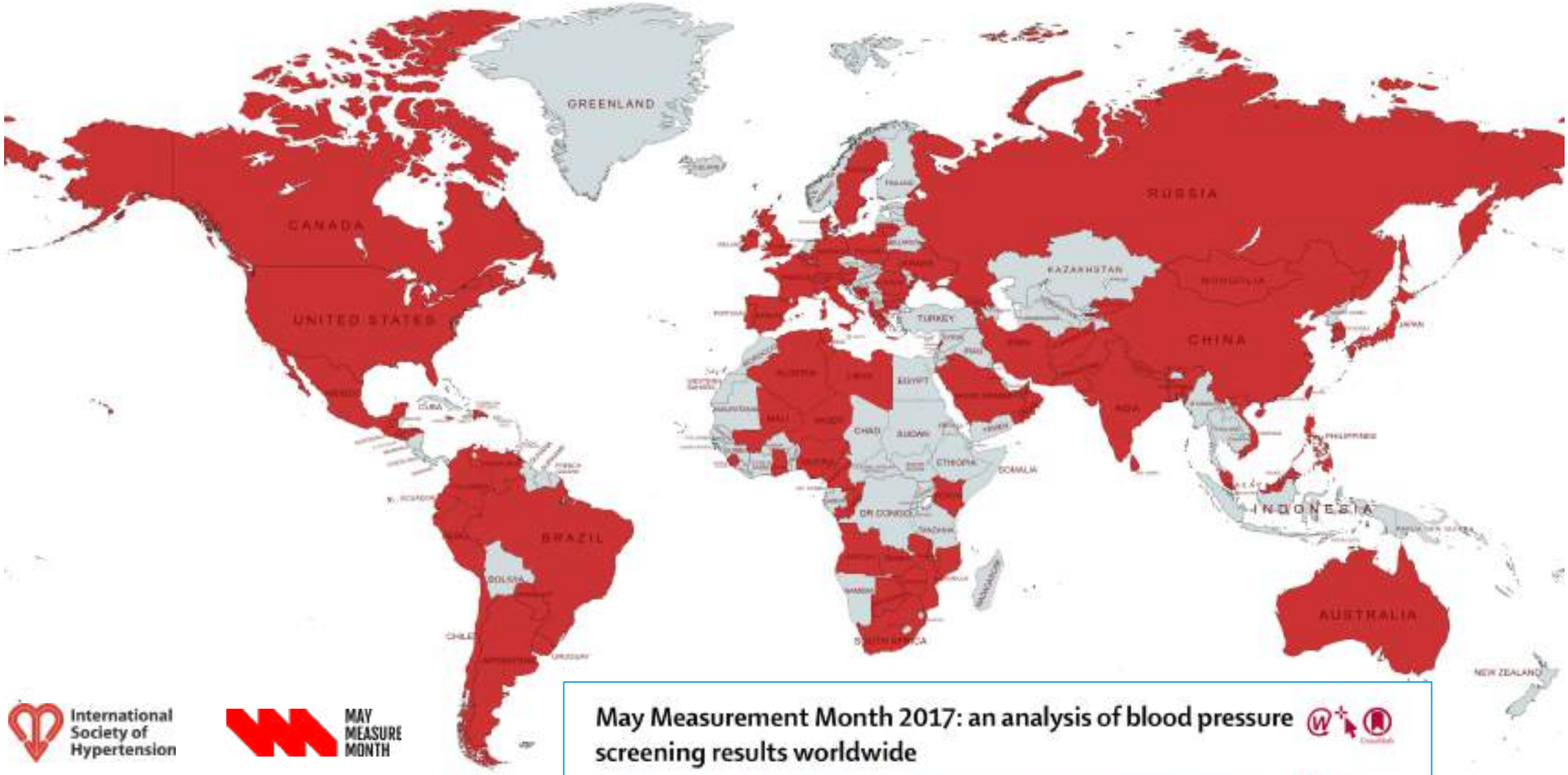
GOALS

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



International Society of Hypertension

MAY MEASURE MONTH

May Measurement Month 2017: an analysis of blood pressure screening results worldwide

Thomas Beaney, Aletta E Schutte, Maciej Tomaszewski, Cono Ariti, Louise M Burrell, Rafael R Castillo, Fadi J Charchar, Albertino Damasceno, Ruan Kruger, Daniel F Lackland, Peter M Nilsson, Dorairaj Prabhakaran, Agustin J Ramirez, Markus P Schlaich, Jiguang Wang, Michael A Weber, Neil R Poulter, on behalf of the MMW Investigators

Created with mapchart.net

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

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

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

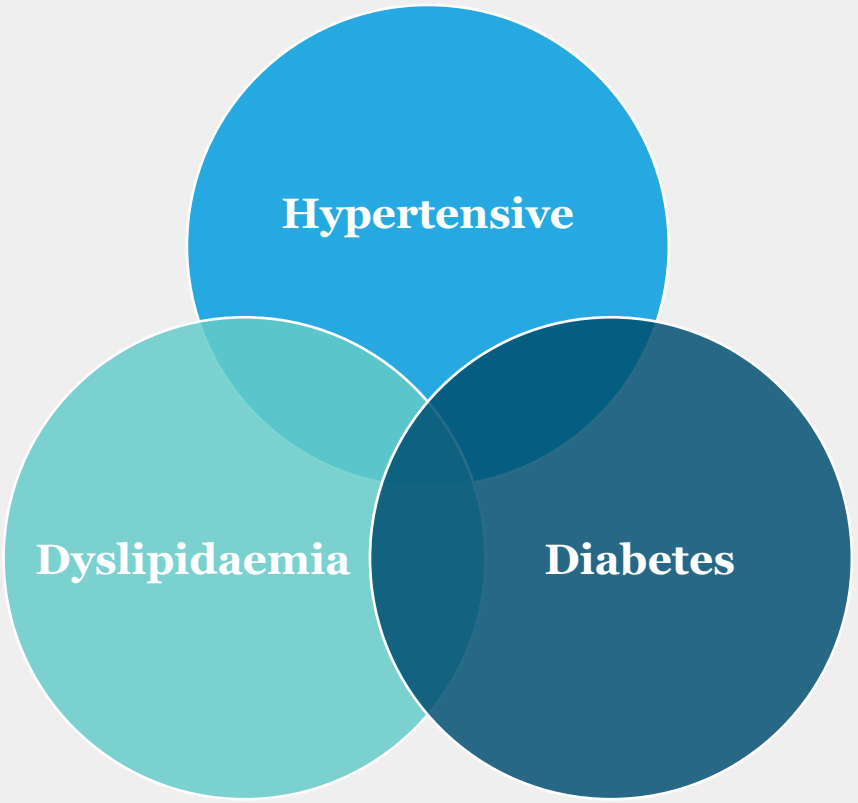
BP is a multiregulated variable depending on many compensating pathways. Consequently, combinations of drugs, working through different mechanisms, are required to reduce BP in most people with hypertension. Thus, monotherapy is likely to be inadequate therapy in most patients. Indeed, almost all patients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

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

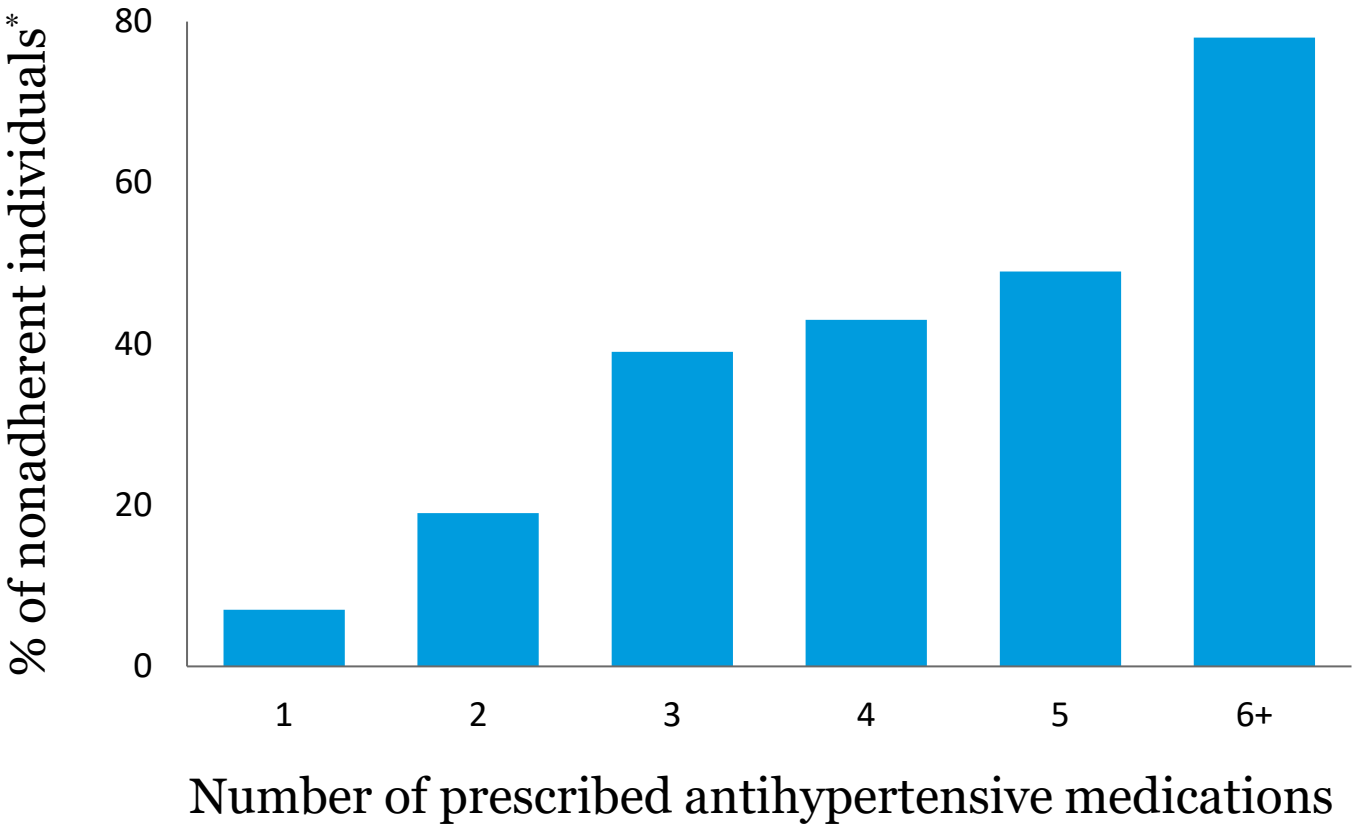
5 COMPLEXITY OF CURRENT TREATMENT STRATEGIES

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

Non-adherence increased with pill burden



Going from 2 to 3 medications doubled non-adherence

Patients on 5 medications are nearly 50% non-adherent

Majority of patients prescribed 6+ medications were non-adherent

*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 nonadherent.

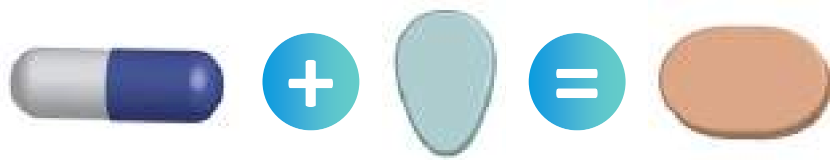
Adapted from Gupta Pankaj, Patel Prashanth, *et al*. Biochemical Screening for Nonadherence is associated with blood pressure reduction and improvement in adherence. *Hypertension*. 2017;70:1042-1048

International Society of Hypertension

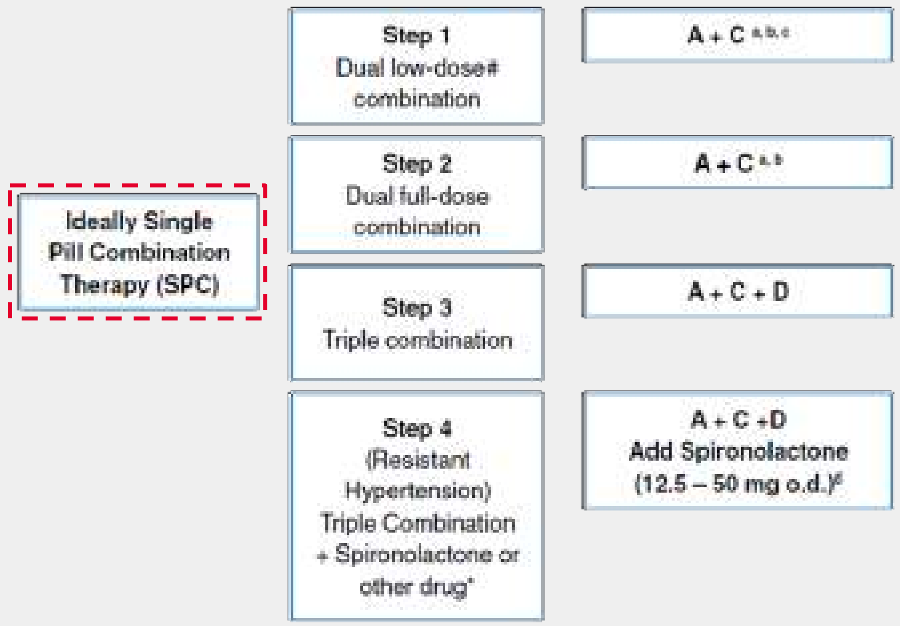
GUIDELINES

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]



OPTIMAL



a) Consider monotherapy in low risk grade 1 hypertension or in very old (≥80 yrs) or frailer patients.
b) Consider A + D in post-stroke, very elderly, incipient heart failure or CCB intolerance.
c) Consider A + C or C + D in black patients.
d) Caution with spironolactone or other potassium sparing diuretics when estimated GFR <45 ml/min/1.73m² or K⁺ >4.5 mmol/L.

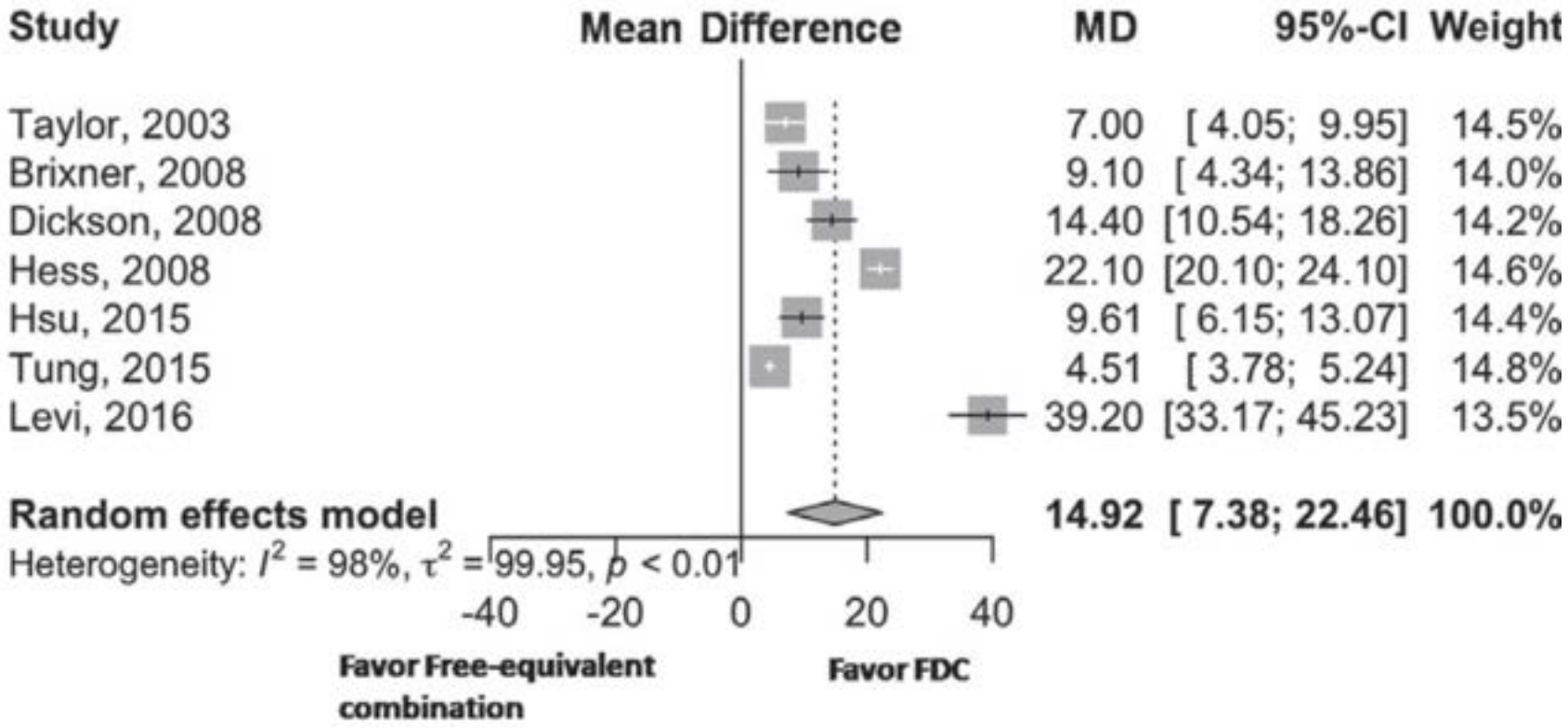
A = ACE-Inhibitor or ARB (Angiotensin Receptor Blocker)
C = DHP-CCB (Dihydropyridine-Calcium Channel Blocker)
D = Thiazide-like diuretic
Supportive references: A + C;[68-70] Spironolactone,[71] Alpha-blocker,[72] C + D[73].
* Alternatives include: Amiloride, doxazosin, eplerenone, clonidine or beta-blocker.
\# low-dose generally refers to half of the maximum recommended dose

ISH core drug-treatment strategy.

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

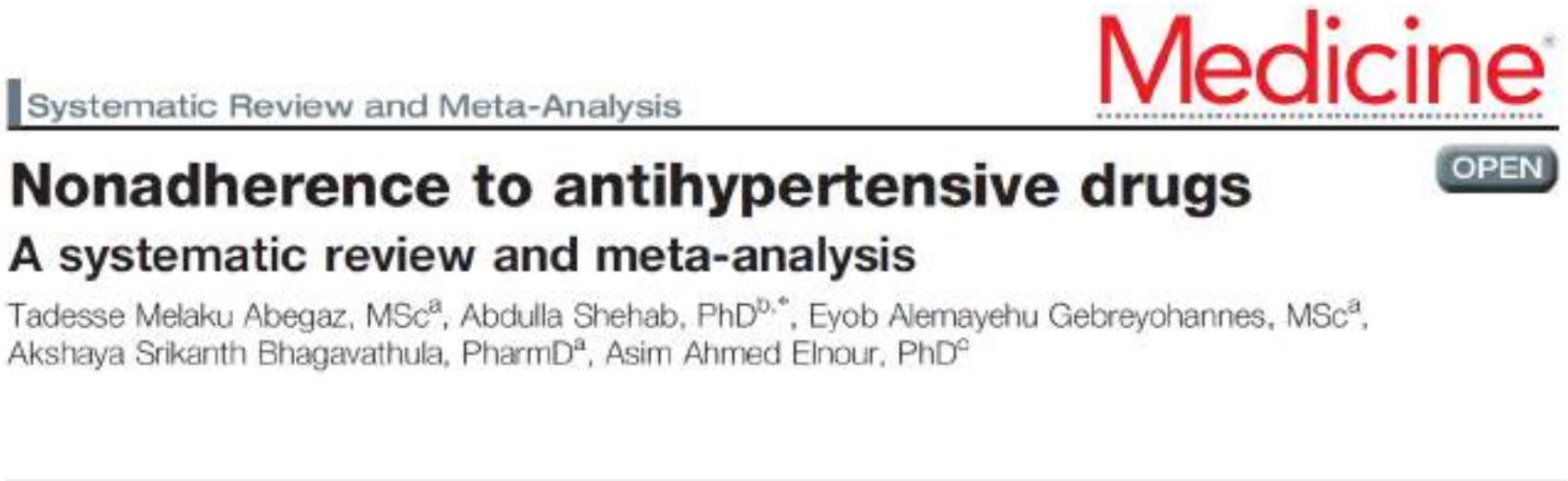
Single-pill combination is one approach to improve medication adherence

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

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



Systematic Review and Meta-Analysis

Medicine

OPEN

Nonadherence to antihypertensive drugs

A systematic review and meta-analysis

Tadesse Melaku Abegaz, MSc[a], Abdulla Shehab, PhD[b,*], Eyob Alemayehu Gebreyohannes, MSc[a], Akshaya Srikanth Bhagavathula, PharmD[a], Asim Ahmed Elnour, PhD[c]

This comprehensive meta-analysis of nonadherence to antihypertensive medication documented a significantly higher proportion (45.2%) of medication non-adherence was noticed among hypertensive patients, particularly uncontrolled BP patients (83.7%).

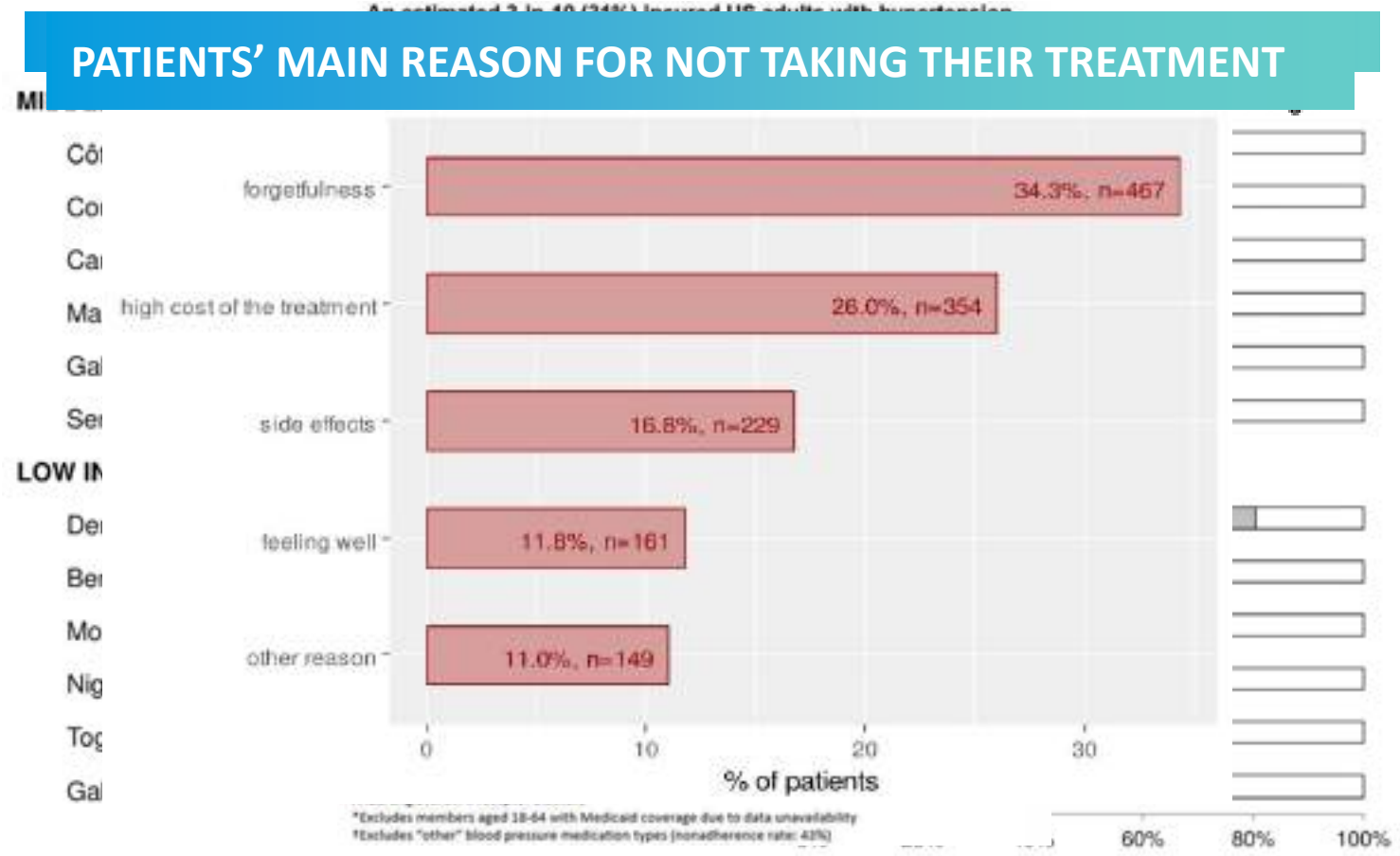
RESULTS

A total of 28 studies from 15 countries were identified, in total comprising of 13,688 hypertensive patients, were reviewed.

Abegaz Tadasse Melaku, Shehab Abdulla, *et al*. Nonadherence to antihypertensive drugs. *Medicine*. 2017;96:4

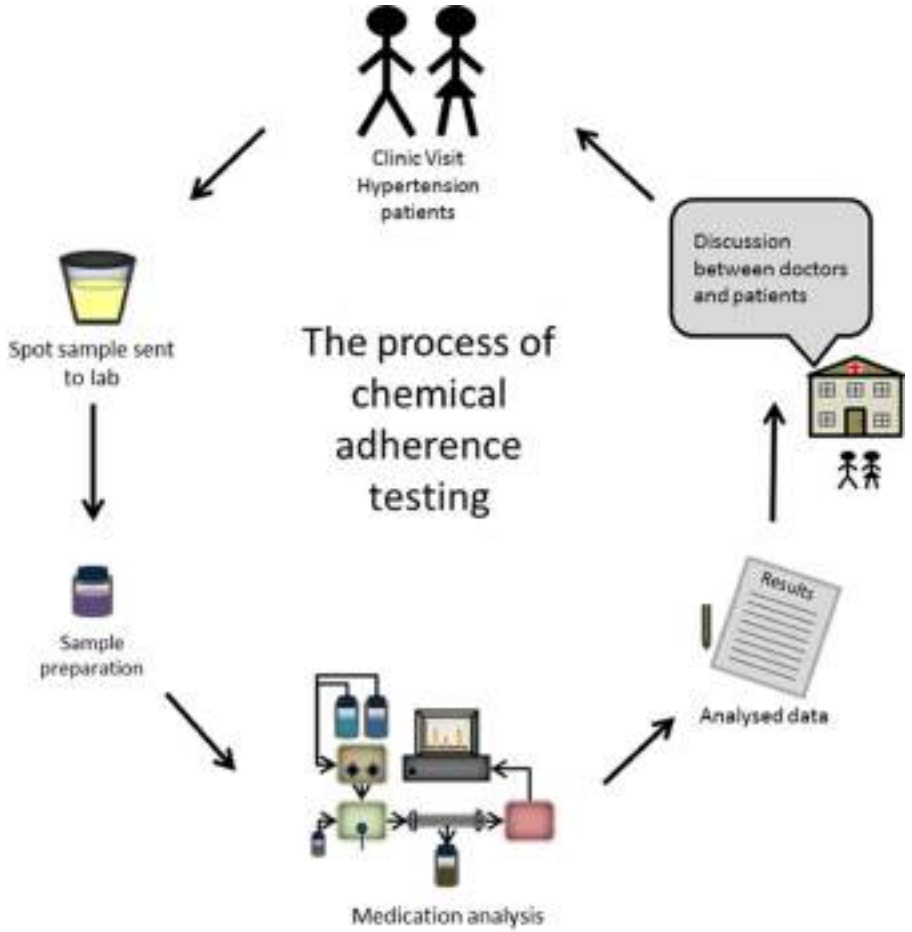
For many years non-adherence was under-recognized in patients with hypertension

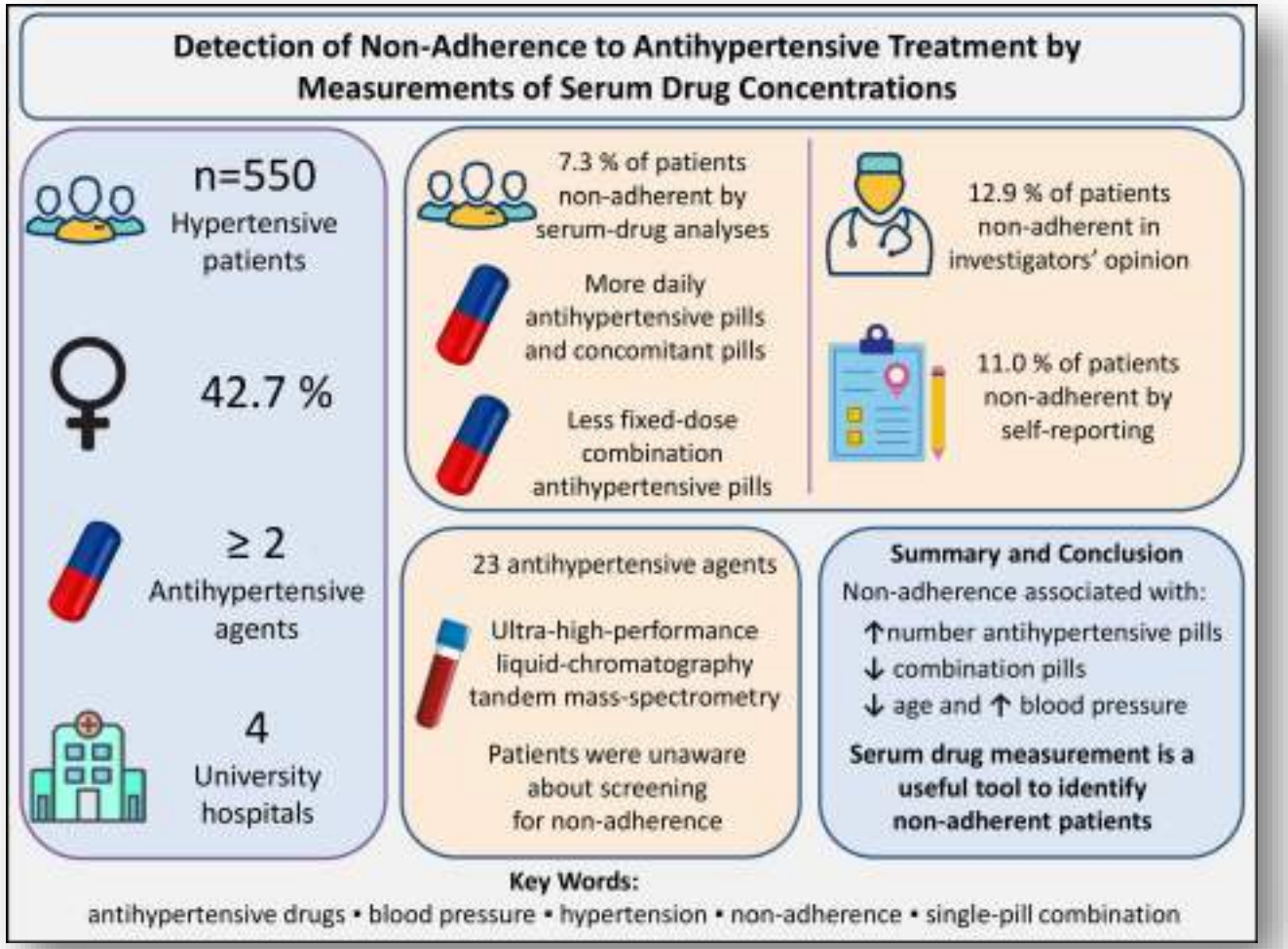
A global phenomenon affecting both high and low income countries



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





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

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.