Abbott

a:care

A:CARE BOOK: CRACKING THE CODE OF MEDICATION NON-ADHERENCE

AND SHIFTING PARADIGM FROM 'TREATING DISEASES' TO 'TREATING PATIENTS

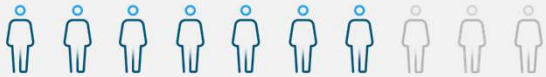
Additional Resources

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

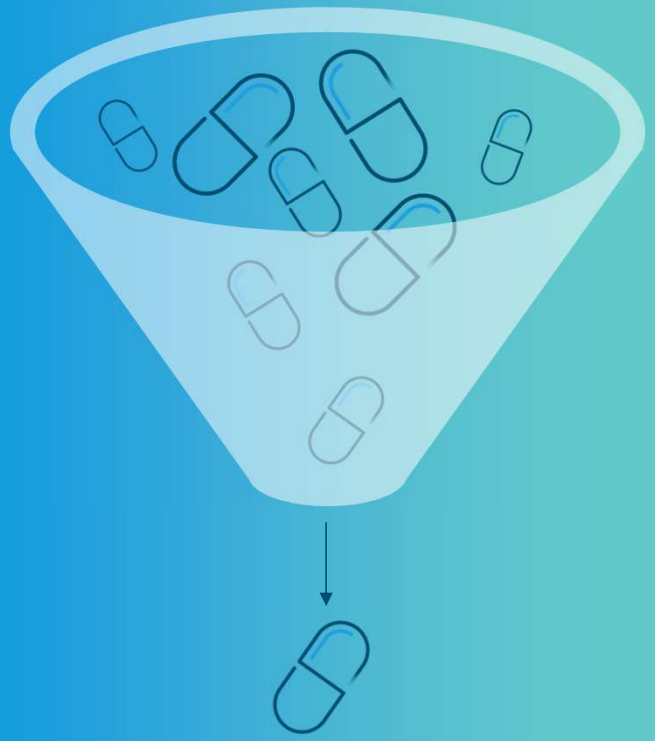
Khan R and Socha-Ditrich K. Investing in medication adherence improves health outcomes and health system efficiency. Adherence to medicines for diabetes, hypertension, and hyperlipidaemia. OECD health working paper No. 105, OECD publishing Paris. 2018.

GLO2329517

What is happening after prescription

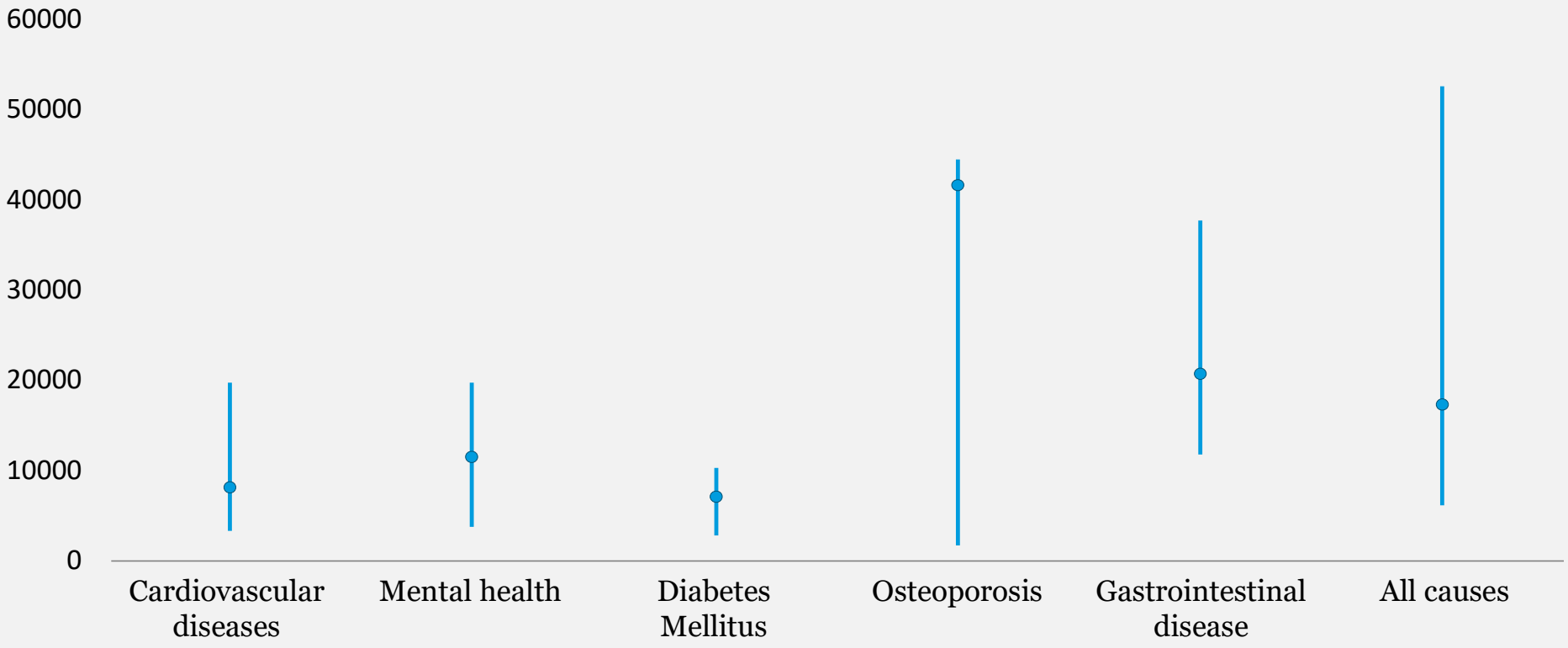
For every 100 prescriptions written

- 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.

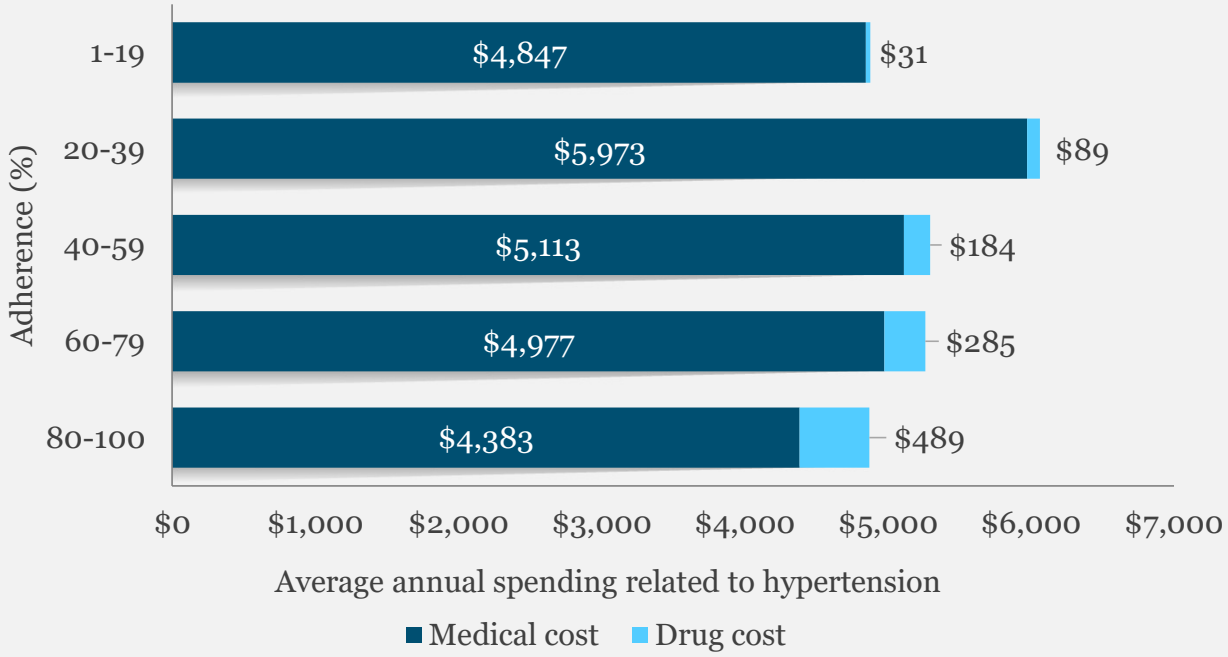
Unadjusted costs of non-adherence



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

Impact of non-adherence on direct costs

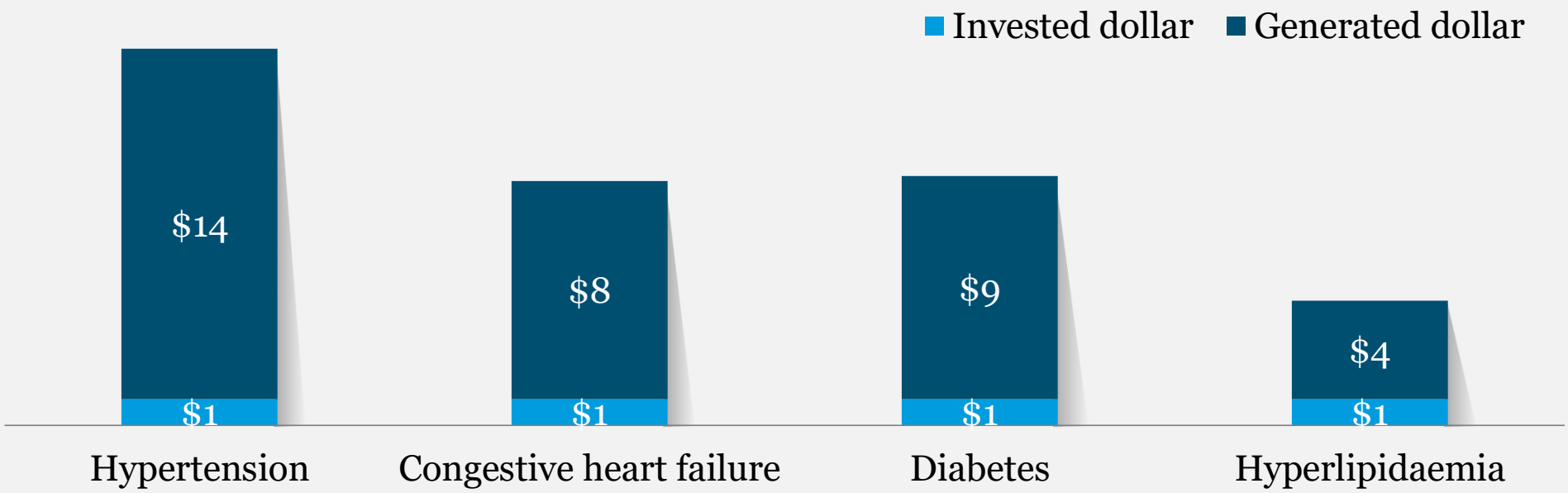
Hypertension average spending by adherence level*



1. 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

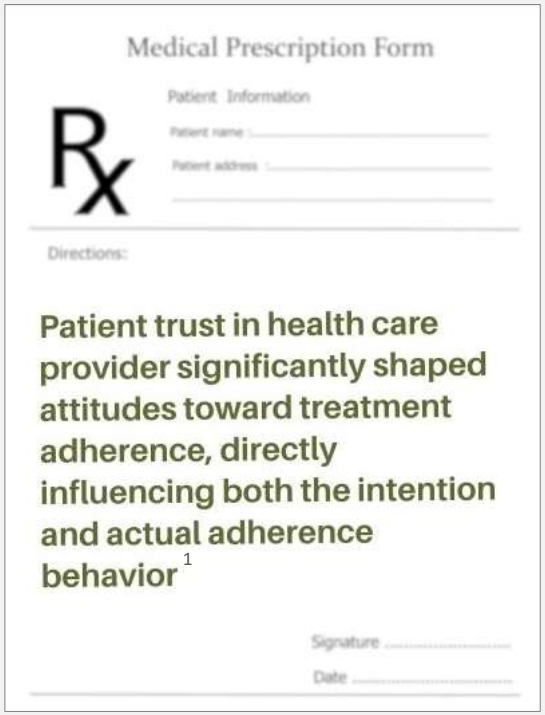
Medication adherence is cost effective

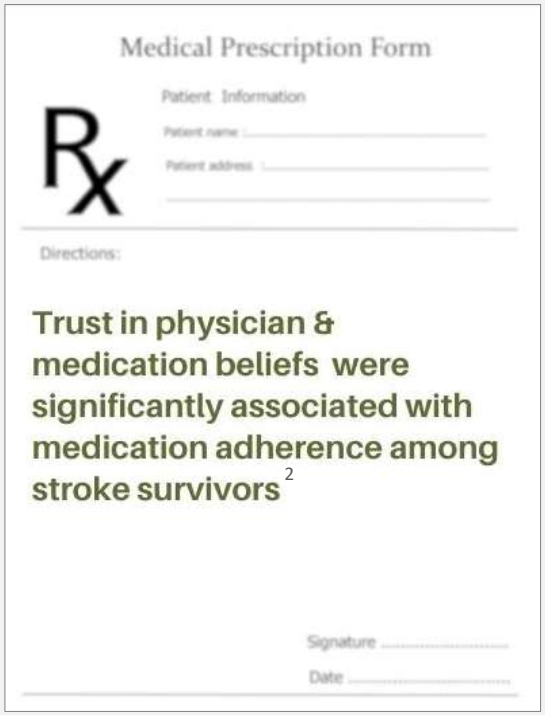
The average cost-benefit ratios from adherence*

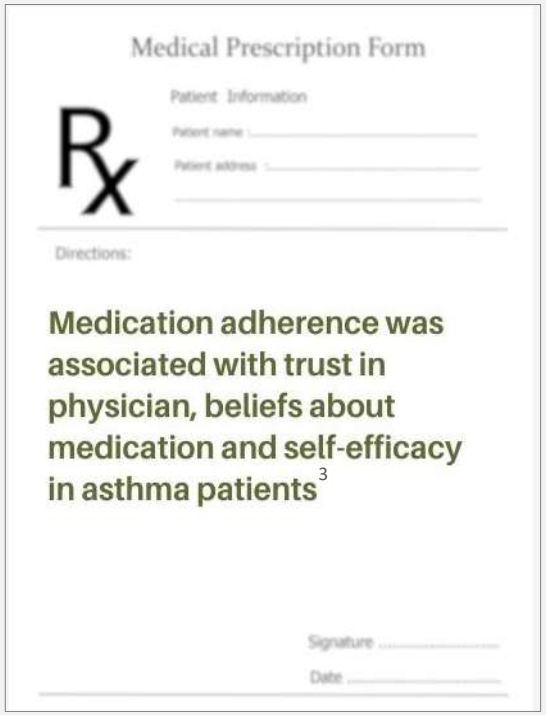


1. Adapted. Rabia Khan and Karolina Socha-Dietrich: Investing in medication adherence improves health outcomes and health system efficiency: Adherence to medicines for diabetes, hypertension, and hyperlipidaemia , OCDE Study, Sep 2018, https://doi.org/10.1787/18152015 [Accessed 29 June 2020], , https://www.oecd-ilibrary.org/social-issues-migration-health/investi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

There is a strong correlation between trust in health care providers and improved medication adherence





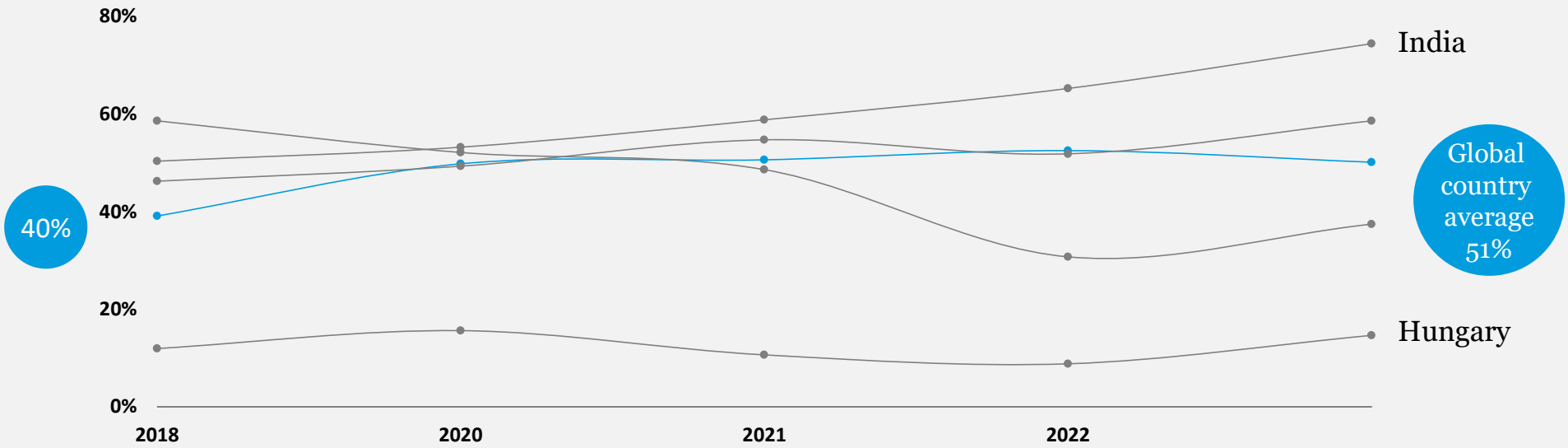


1. Wu D, et al. patient trust in physicians matters-understanding the role of a mobile patient education system and patient-physician communication in improving patient adherence behavior. field study. j med internet res. 2022;24(12). 2. Fan Q, et al. impact of beliefs about medication on the relationship 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

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.

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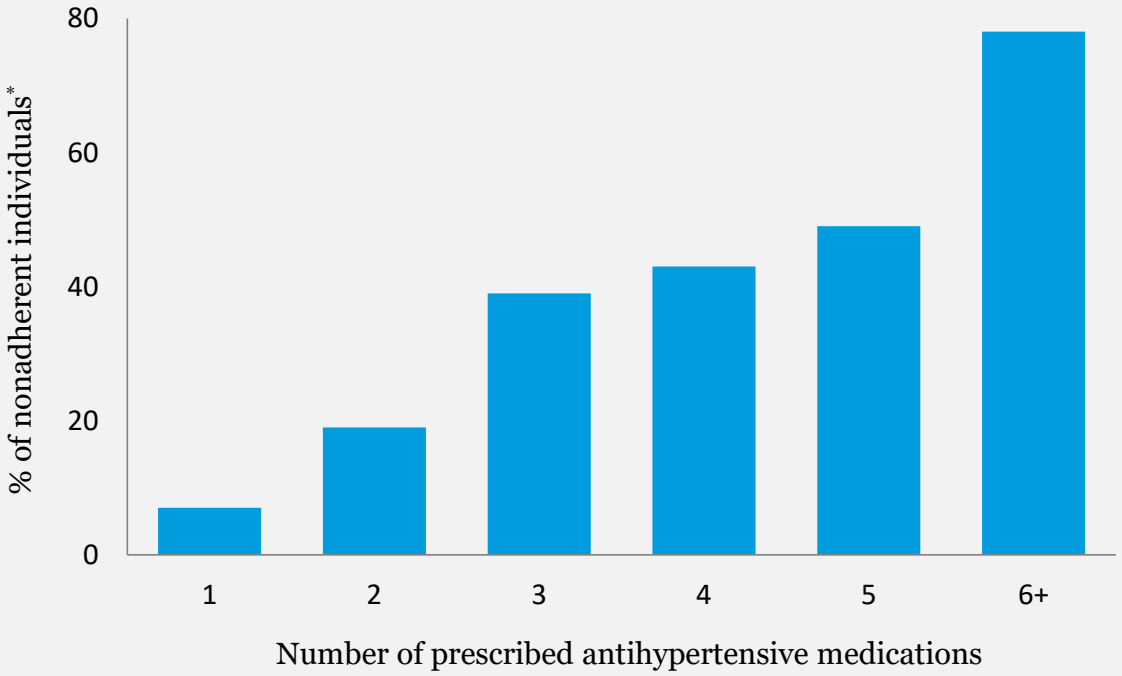
Non-adherence increased with pill burden



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

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

Compliance, adherence and persistence

My personal experience, opinion, recipe and vision

Easy in acute monophasic diseases with acute effects of treatment

Difficult in chronic diseases (progressive/ non-progressive)

More difficult in chronic relapsing (remitting) diseases

Even more difficult in otherwise healthy patients who are at risk of serious or life-threatening disease = silent diseases … **stroke**

Compliance, adherence and persistence

My personal experience, opinion, recipe and vision

Concrete issues in your clinical practice and solutions to be considered and explicitly discussed with patients and caregivers

Delay of onset of positive treatment effects
- Drug, Dosing, Duration

First side-effects or even worsening of symptoms

Why are they not following your advice?
- Effects are not noticed at all by the patient: primary, secondary preventive or disease modifying treatment

Consequences of non-compliance to be explicitly discussed

Delay of re-occurrence of symptoms when treatment is stopped

Best- and worst-case scenario to be discussed

Potential **alternatives** to be discussed

One additional measure to improve CAP

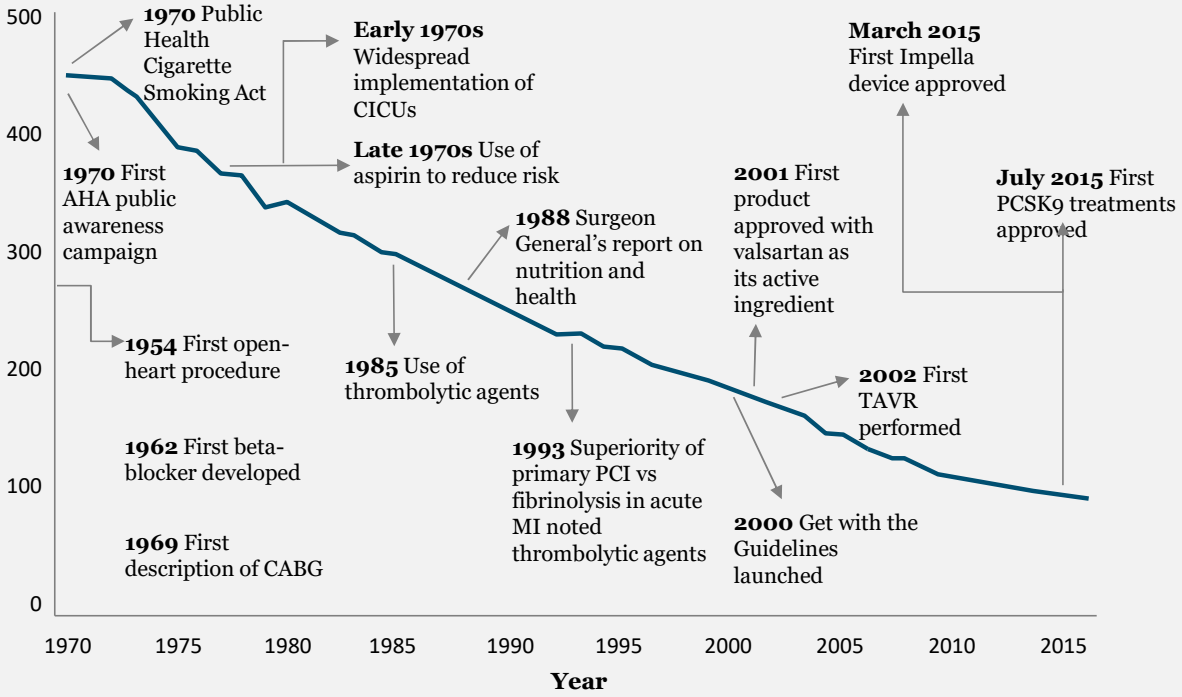
To finish my lecture with positive and optimistic statements

Remote management of your patient!

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

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]

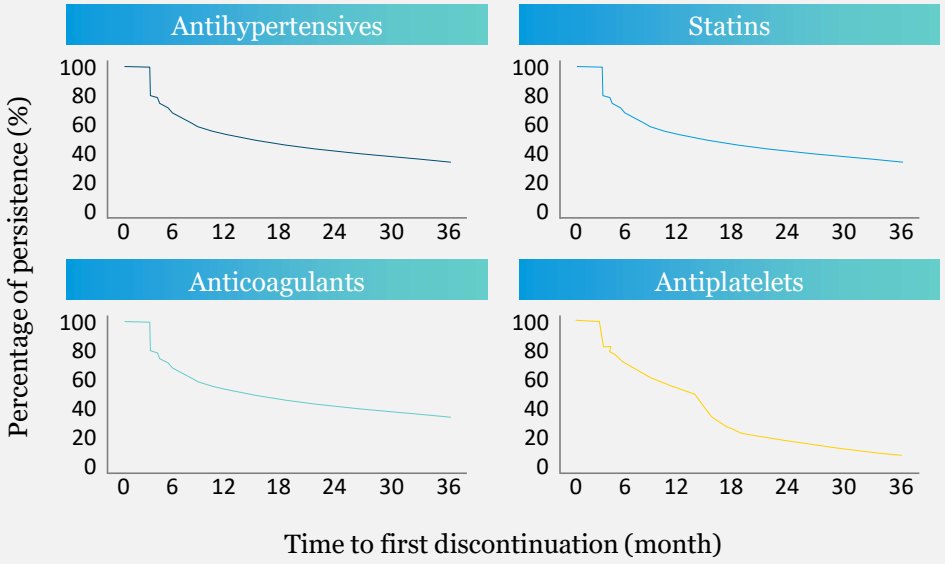
CV= Cardiovascular, CHD= Coronary Heart Disease

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

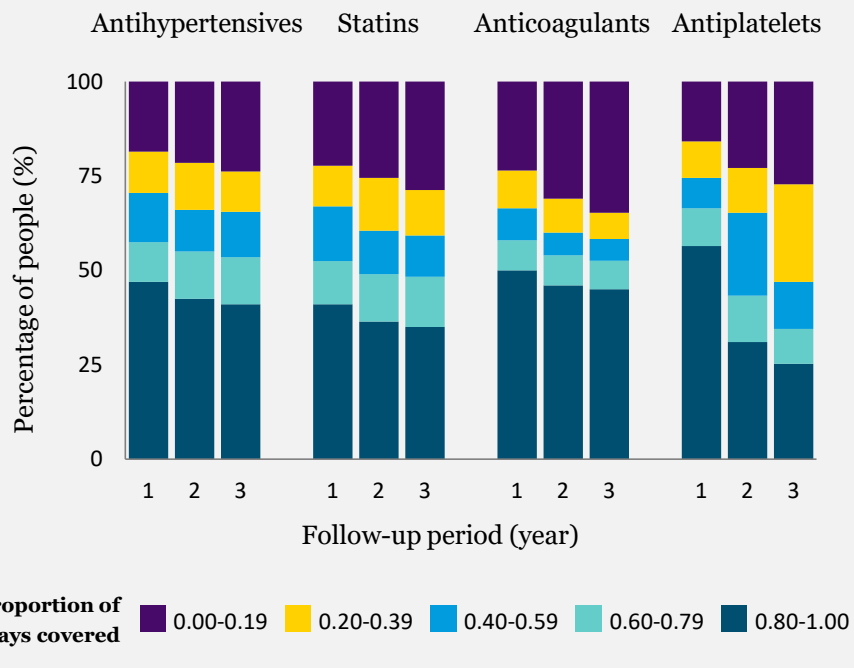
Persistence to cardiovascular medicines significantly declines following initiation

Using Australian national dispensing

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



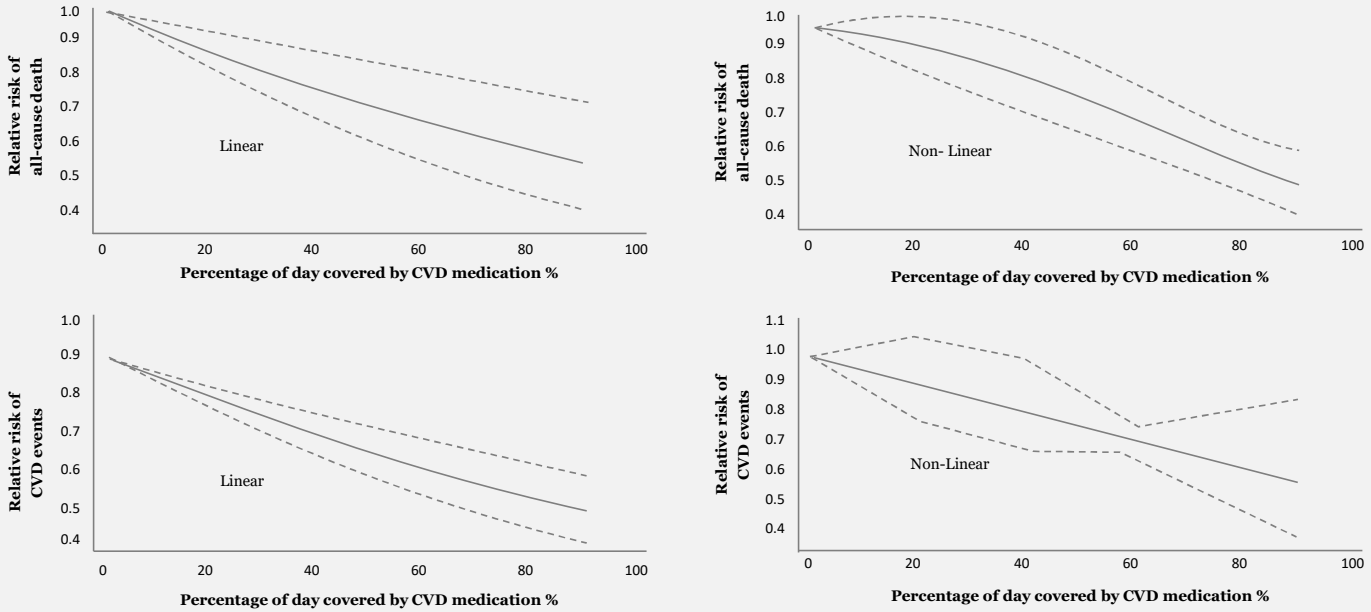
Time to first discontinuation (month) in people initiating 4 different groups of medicines. People were followed up until death, or up to 3 years



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

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



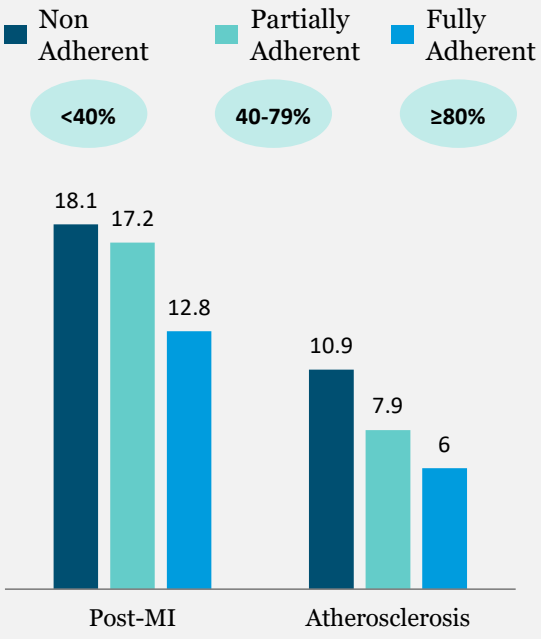
Dose–response relationship (linear and nonlinear) of cardiovascular medication adherence and cardiovascular events. The solid line and the dashed lines represent the estimated relative risk and the 95% confidence interval, respectively

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.

Impact of medication adherence on long term CV outcomes and cost

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

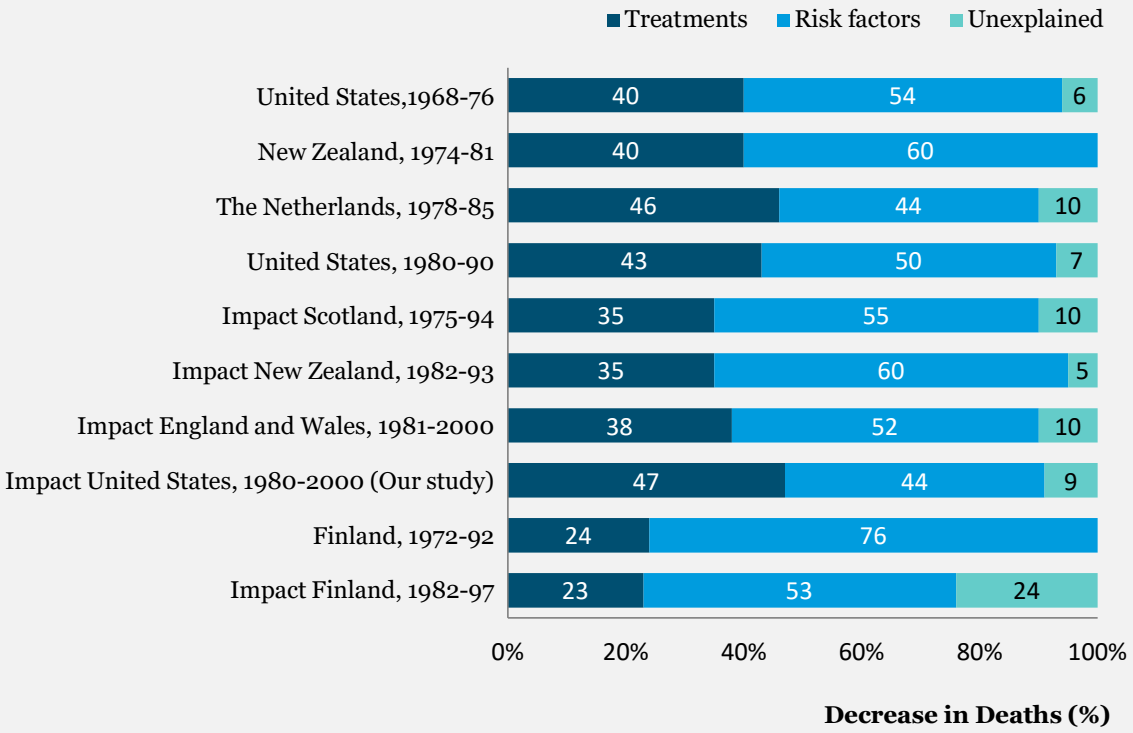


- Database of a large health insurer for patients hospitalized for MI or with atherosclerotic disease in USA
- Proportion of days covered (PDC) for statin and ACE inhibitors
- Outcome: Composite of all-cause death, MI, stroke, or coronary revascularization

	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.

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



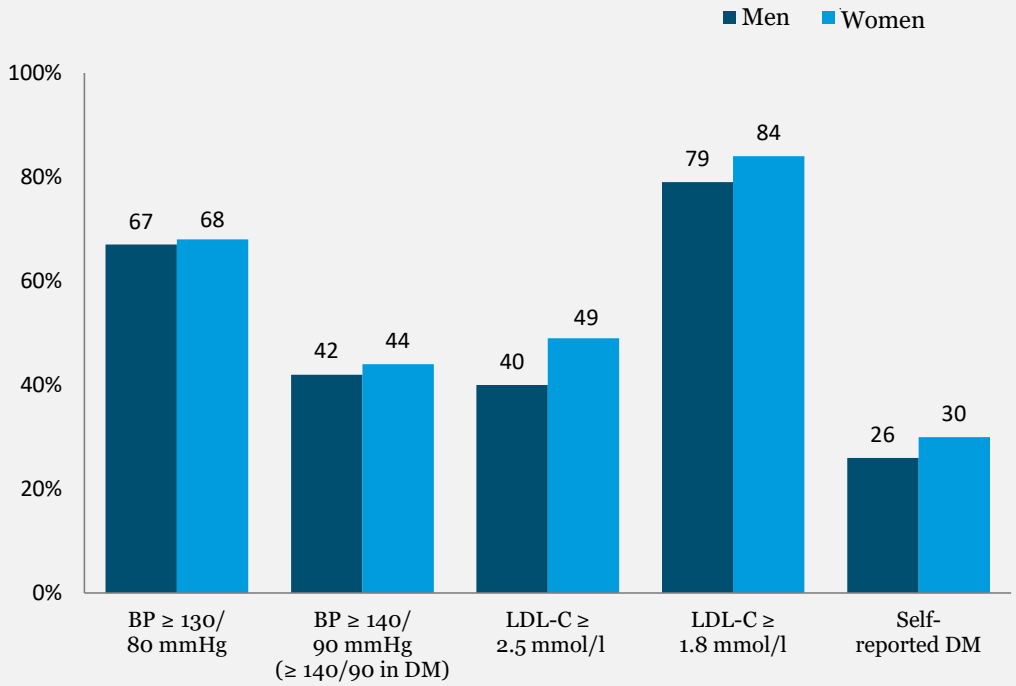
- Adherence to long-term therapy for chronic illnesses averages 50% in developed countries and is lower in developing countries[1]
- In China, the Gambia and the Seychelles, only 43%, 27% and 26% of patients with hypertension adhere to their antihypertensive medication. 80% of noncontrolled HTN are nonadherent[2]
- 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

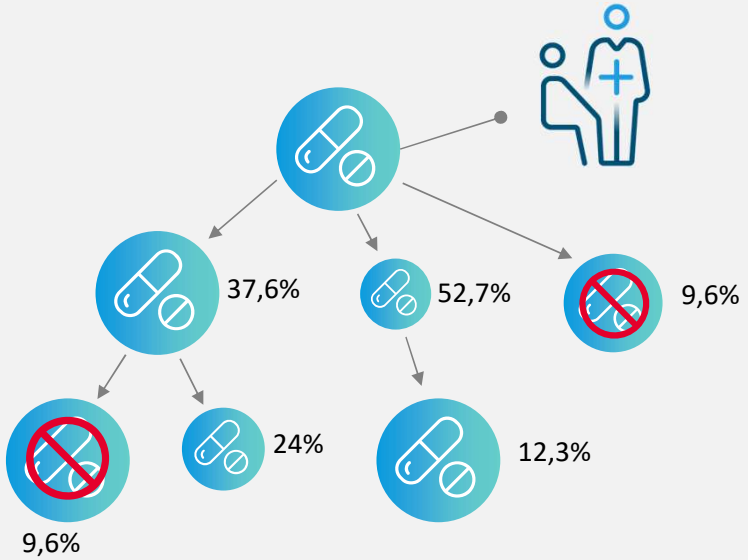
1. Ford ES, Ajani UA, et al. Explaining the decrease in U.S. Deaths from Coronary Disease, 1980-2000. The New england Journal of Medecine. 2007;356:2388-98; 2. World Health Organization. Adhrence to long-term therapies – Evidence for action. 2003; 3. McClellan M, Brown N, et al. Call to action; Urgent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

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]

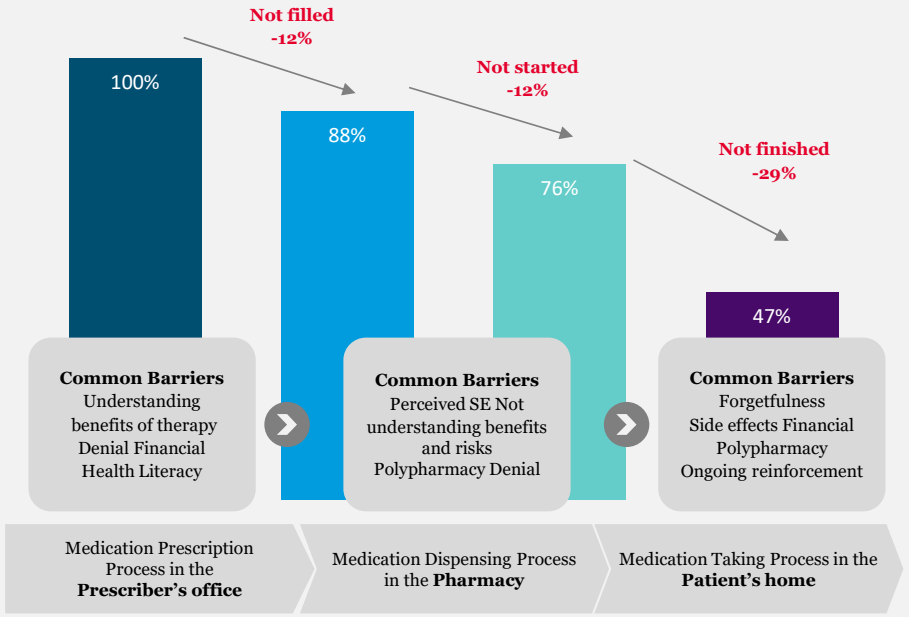


CAD= Coronary Artery Disease, IV= Intravenous, EA= Euroaspire

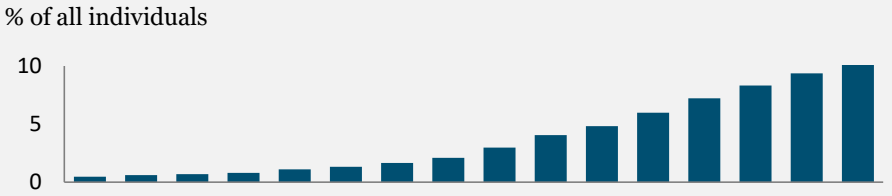
1. Kotseva K, Wood D, De Bacquer D, et al. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. European Journal of Preventive Cardiology. 2016, Val 23(6) 636-648; 2. Reiner Z, De Backer G, Fras 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

Statin compliance and adherence

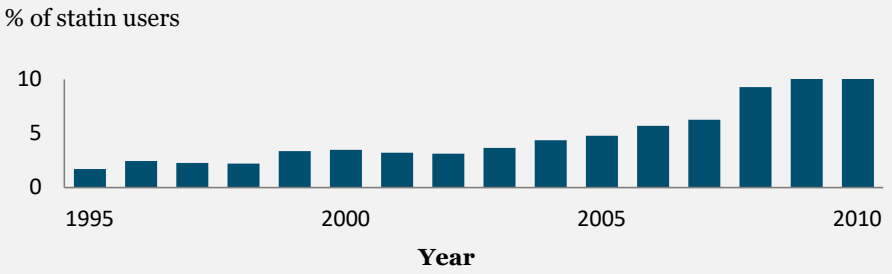
Statin compliance over time[1]



Fraction of individuals ≥40 years of age on statins in denmark[2]



Fraction of statin users with one prescription only[2]

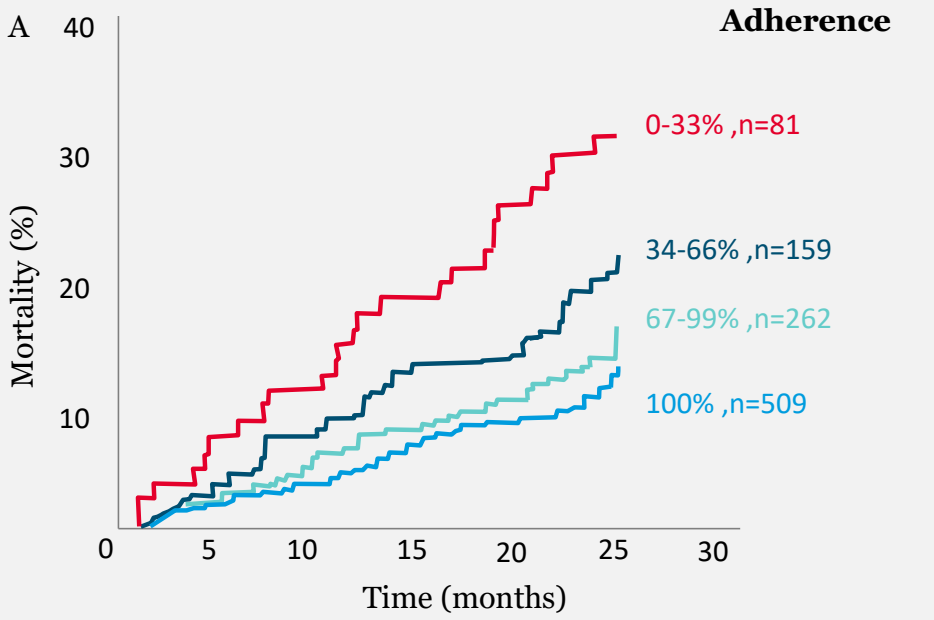


1. Cohen JD, Aspry KE, Brown AS, et al. Use of health information technology to improve statin adherence and low-density lipoprotein cholesterol goal attainment in high-risk patients: Proceedings from a workshop. Journal of Clinical Lipidology. 2013; 7, 573–609; 2. Stroes ES, Thompson PD, Corsini A, 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

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

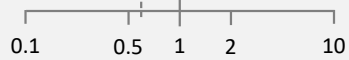
1011 patients with chronic disease on polypharmacy



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 in CAD patients with good vs. poor medication adherence n=106,000

Study	Risk ratio	95%–CI weight
Adherence to multiple agents		
Lenzi J (2015)	0.41 [0.34;0.50]	15.6%
Kumbhani DJ (2013)	0.79 [0.72; 0.88]	17.5%
Kirchmayer U (2013)	0.35 [0.21;0.59]	8.5%
Kuepper-Nybelen J (2012)	0.72 [0.60;0.86]	16.1%
Ho PM (2008)	0.59 [0.52;0.67]	17.0%
Ho PM (2006)	0.52 [0.39;0.69]	13.7%
Subtotal	**0.57 [0.45;0.71]**	**88.4%**
Heterogeneity: I-Squared=89.4%, tau-squared=0.0653, p<0.0001		
Adherence to single agent		
Ko DT (2009)	0.54 [0.33;0.88]	9.1%
Horwitz RI (1990)	0.32 [0.09;1.11]	2.5%
Subtotal	**0.50 [0.32;0.79]**	**11.6%**
Heterogeneity: I-Squared=0%, tau-squared=0, p<0.4476		
Total	0.56 [0.45:0.69]	100%
Heterogeneity: I-Squared=85.7%, tau-squared=0.0627 p<0.0001		



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

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

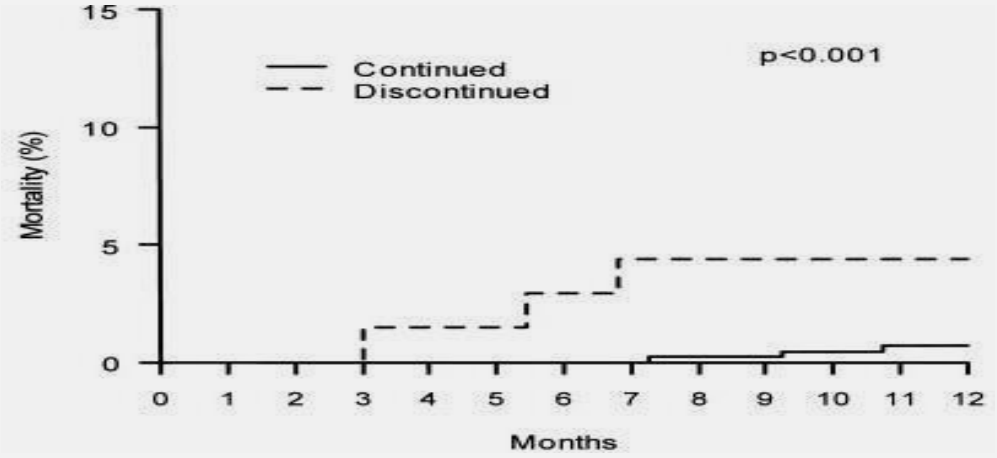
Du L, Cheng Z, Zhang Y, et al. The impact of medication adherence on clinical outcomes of coronary artery disease: A meta-analysis. European Journal of Preventive Cardiology 2017, vol24: 962–970

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

Statin compliance and adherence

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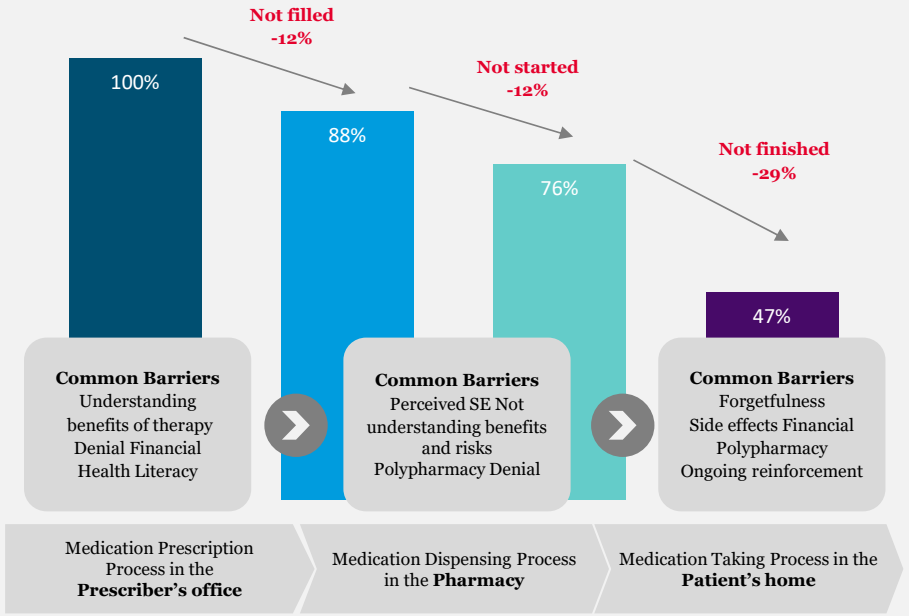

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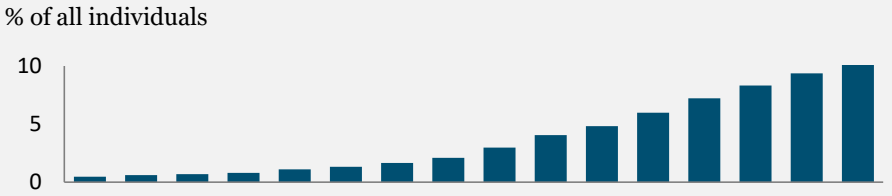
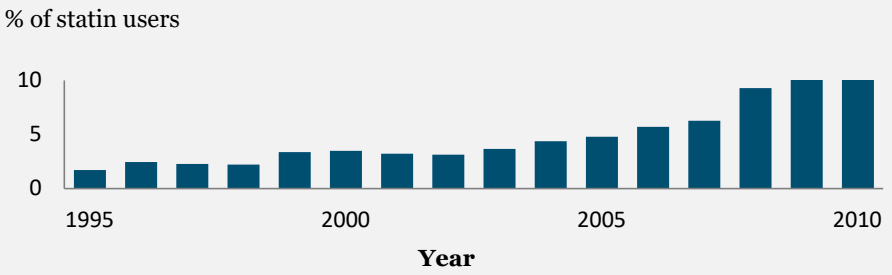


Fraction of statin users with one prescription only[2]



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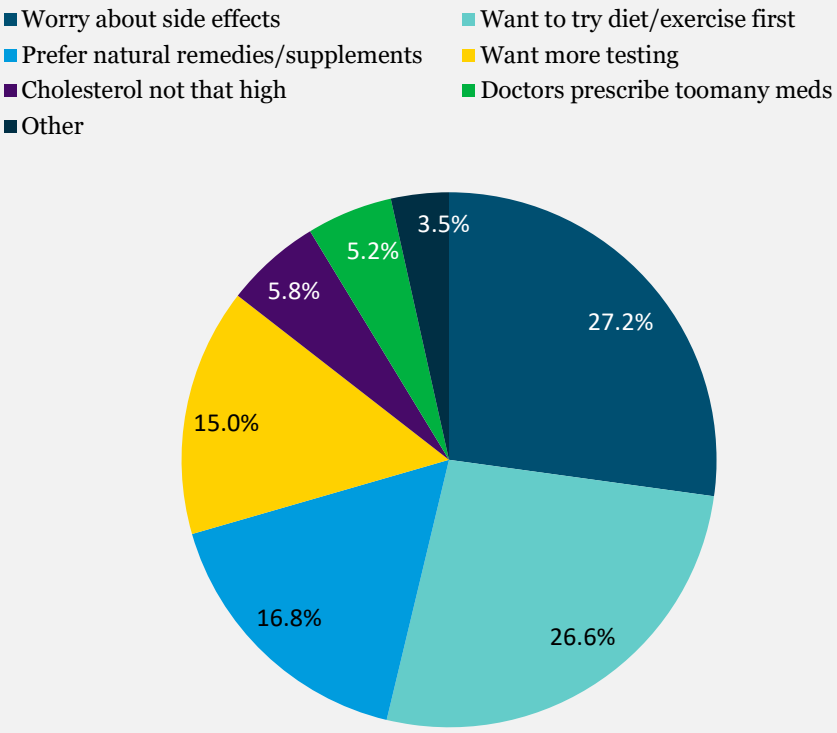
Surveys on patient perspectives[1,2]



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

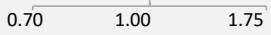
Treatment discontinuation reason	Yes	
	n	%
Negative information about statin treatment	213	40.0
Negative information about statin treatment in TV programs	175	32.9
Patients' lack of sufficient information on high cholesterol and related risks	163	30.6
Negative information about statin treatment heard 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

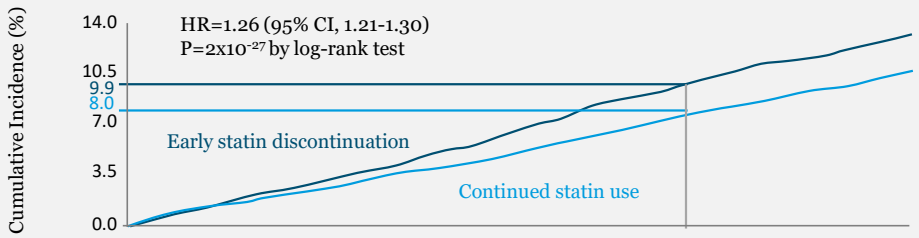
GLO2241819

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

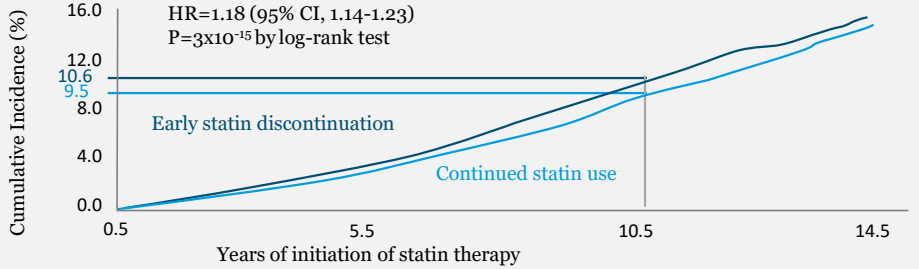
Predictor		P-value
Odds ratio for early statin discontinuation with 95% confidence interval		
Negative nationwide statin-related news story	1.09 (1.06-1.12)	9×10^{-9}
Neutral nationwide statin-related news story	0.98 (0.96-1.01)	0.16
Positive nationwide statin-related news story	0.92 (0.90-0.94)	7×10^{-15}
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



Myocardial infarction



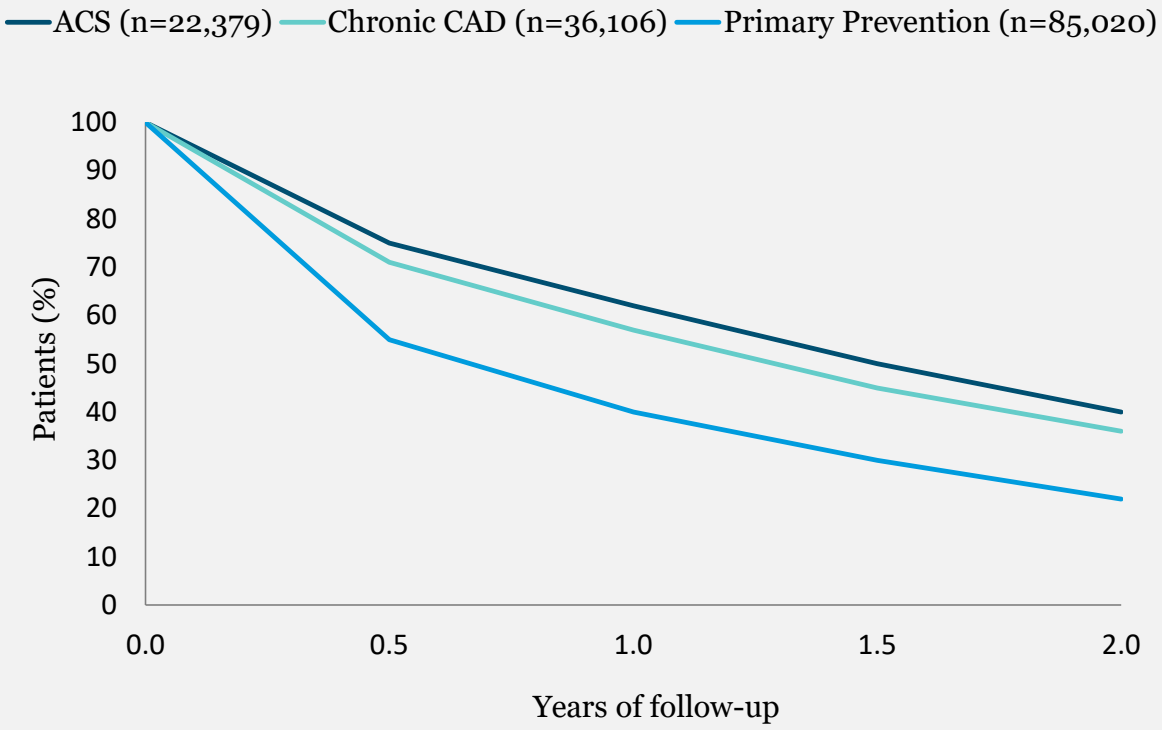
Death from cardiovascular disease



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

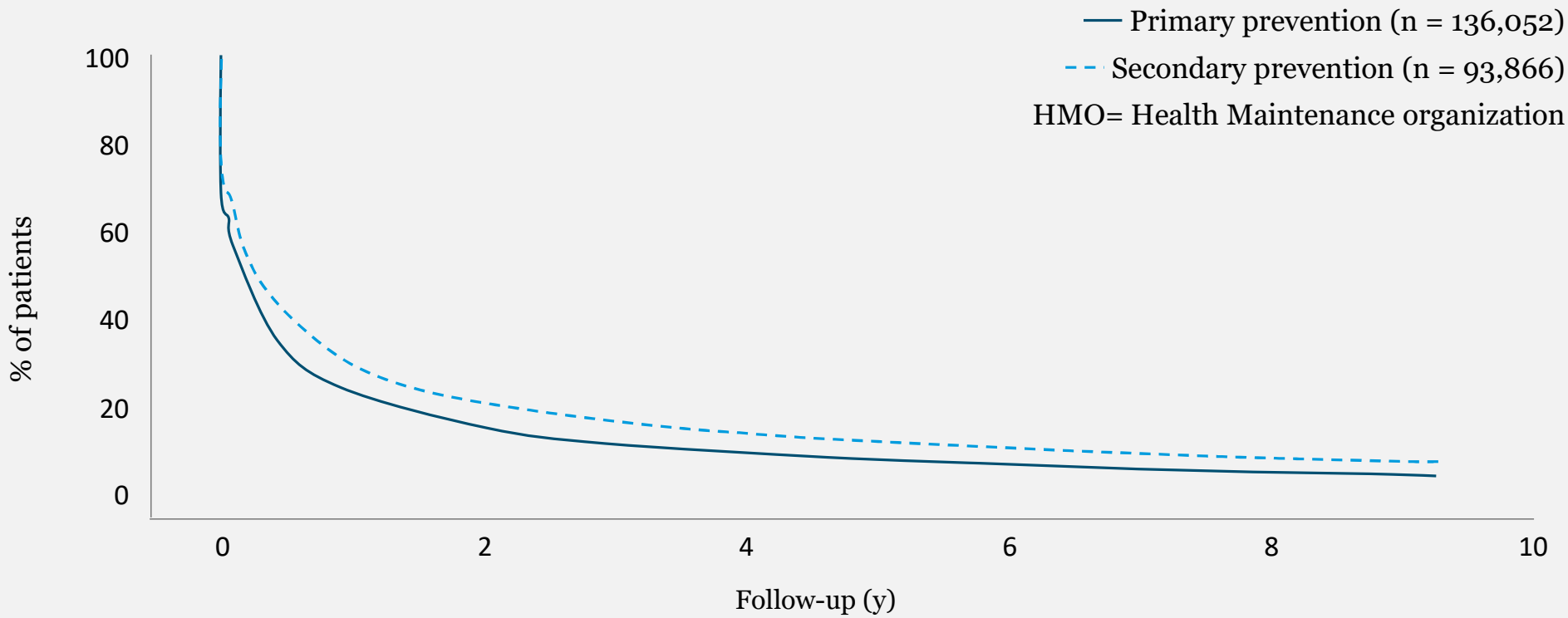
Discontinuation of statin therapy in primary or secondary prevention of CAD[1,2]



- 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.

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

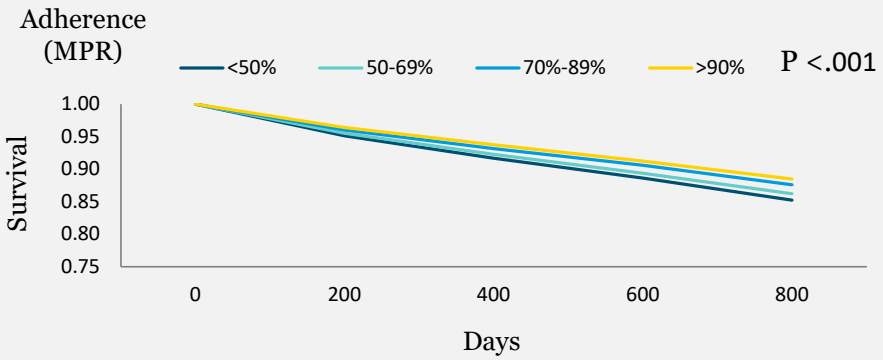


Chodick G, Shavel V, Gerber Y et al. Long-term persistence with Statin Treatment in a Not-for-Profit Health Maintenance Organization: A Population-Based Retrospective Cohort Study in Israel. Clinical Therapeutics. 2008;30:2167-79

Impact of statin adherence on cardiovascular disease (CVD) and mortality outcomes

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

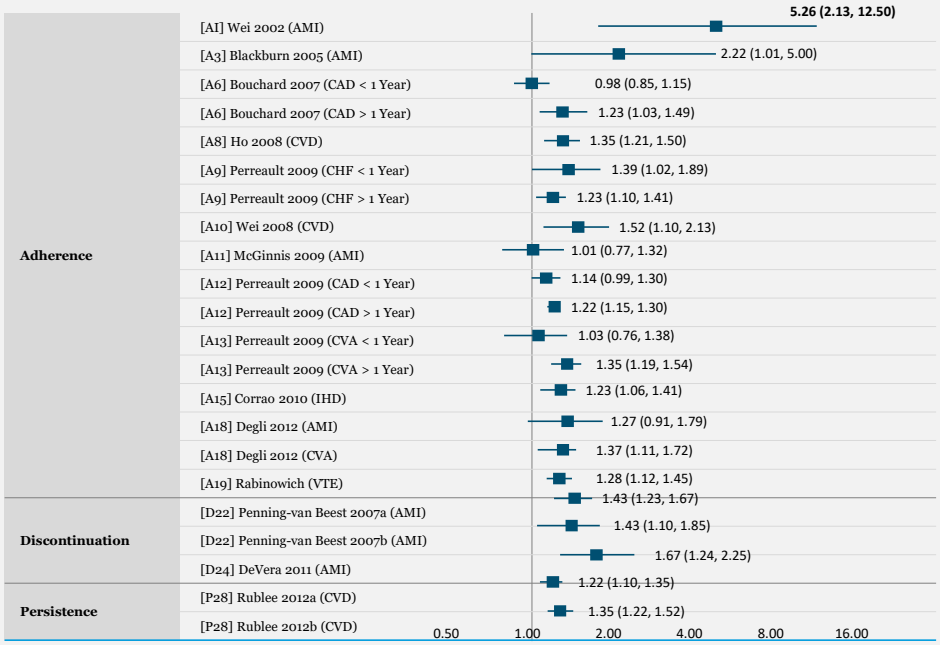
Survival curves by statin adherence level as defined by Medication Possession Ratios (MPRs)



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

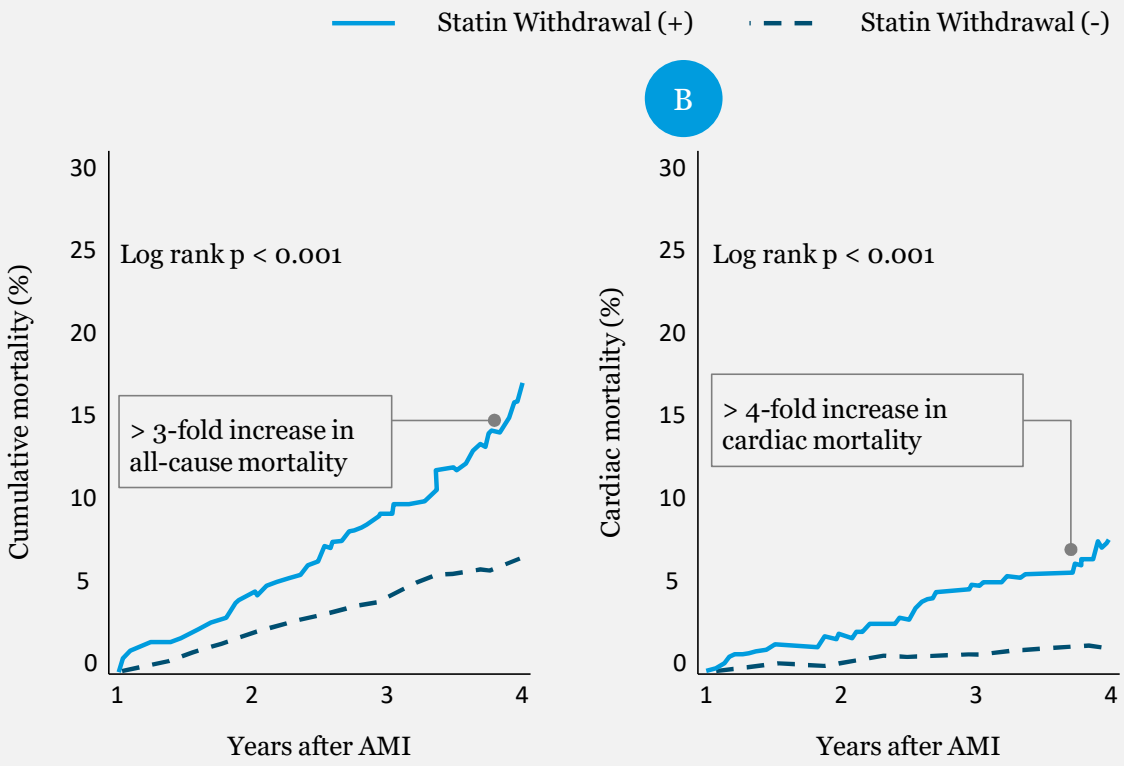
Plotted values include point estimates and 95% confidence intervals. There is a dose-response association between adherence and survival, with the greatest survival among the most adherent patients

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

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

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]

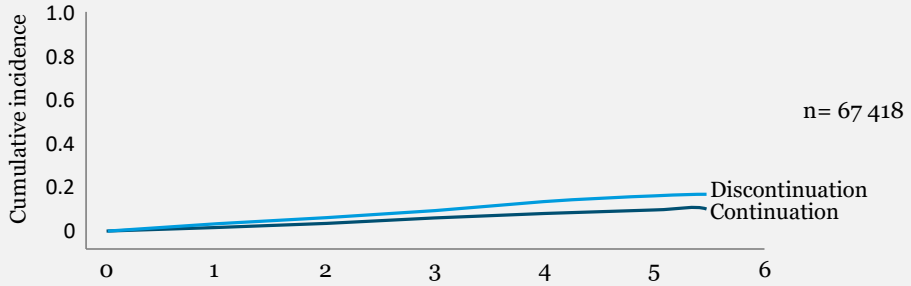
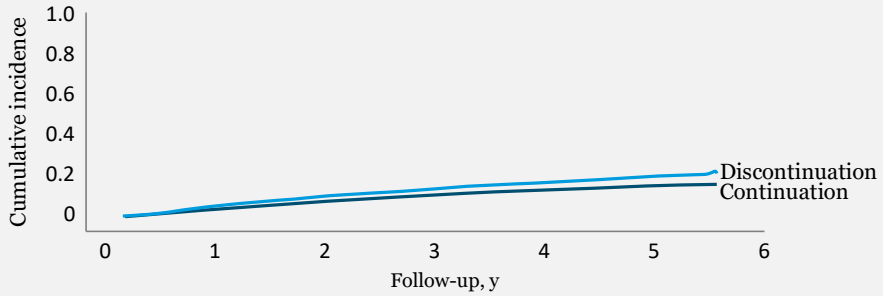
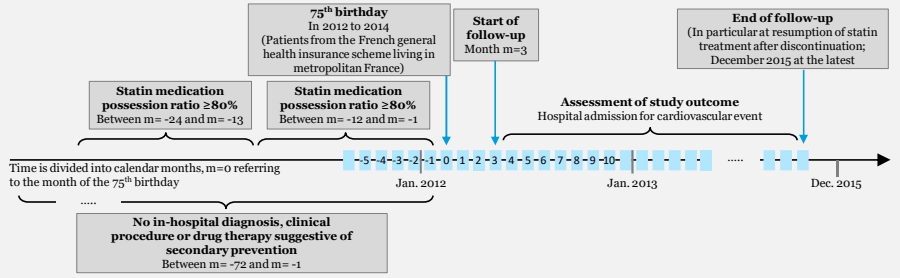


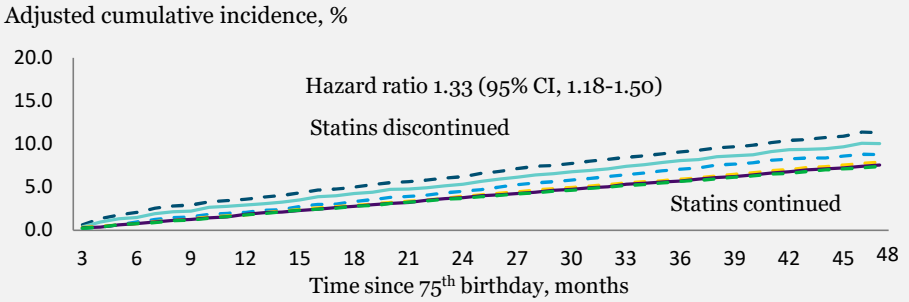
Figure 2. Cumulative incidence curve for the outcome of major adverse cardiovascular events in the secondary prevention cohort[1]



Study design[2]



Principal result[2]

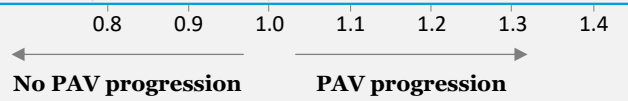


1.Thompson W, Morin L, Jarbol DE, et al. Statin Discontinuation and Cardiovascular Events Among Older People n Denmark. JAMA Network Open. 2021;4(12):e2136802; 2.Giral P, Neumann A, et al. Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide population-based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

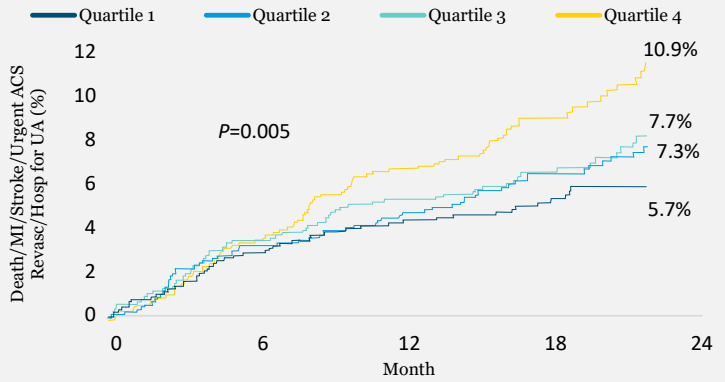
Visit-to-visit cholesterol variability correlates with coronary atheroma progression and clinical outcomes n=4978

Standardized association of variability and average on-treatment cholesterol with coronary atheroma progression

Multivariable Models	OR (95% CI)	p-value
LDL-C		
Standard deviation	1.09 (1.02-1.17)	0.014
Average on-treatment	1.27 (1.17-1.39)	<0.001
Non-HDLC		
Standard deviation	1.10 (1.02-1.18)	0.011
Average on-treatment	1.32 (1.21-1.45)	<0.001
HDL-C		
Standard deviation	1.00 (0.93-1.07)	0.95
Average on-treatment	0.88 (0.79-0.99)	0.034
TC/HDL-C		
Standard deviation	1.14 (1.06-1.24)	0.001
Average on-treatment	1.31 (1.19-1.45)	<0.001
ApoB		
Standard deviation	1.13 (1.03-1.24)	0.010
Average on-treatment	1.20 (1.07-1.35)	0.003



SD of LDL quartile



No. at risk				
Q4: 940	909	881	665	175
Q3: 940	908	893	696	208
Q2: 941	911	902	729	228
Q1: 939	913	901	767	250

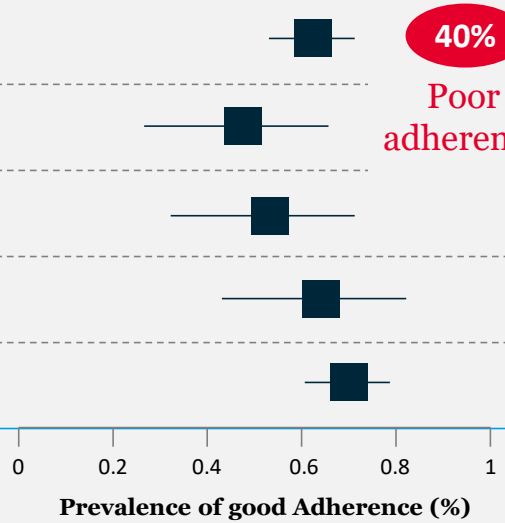
Achieved level more important but variability counted

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.

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

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	Proportion (95% CI)
Adherence to any CVD medication	34	1,230,382	0.60 (0.52, 0.68)
• Adherence to statins	12	771,323	0.54 (0.41, 0.67)
• Adherence to antihypertensives	11	363,819	0.59 (0.42, 0.77)
• Adherence to aspirin	2	11,068	0.70 (0.49, 0.91)
• Adherence to antidiabetics agents	2	1,112	0.69 (0.59, 0.78)

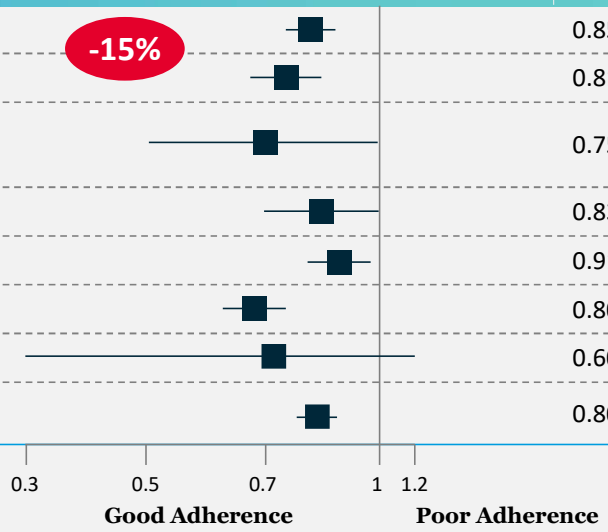


Chowdhury R, Khan H, Heydon E, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. European Heart Journal. 2013;34:2940–48

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

Conclusion

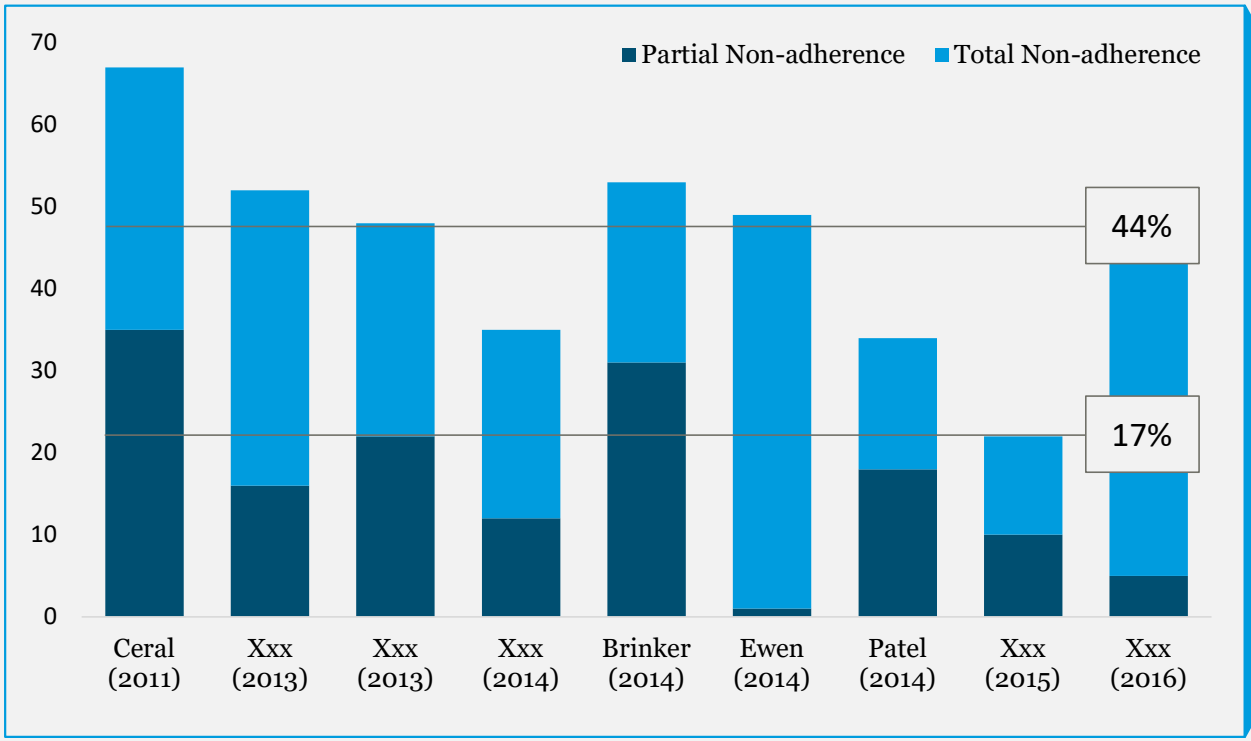
Non-adherence to CV therapies is a preventable risk factor that is often underestimated by clinicians

Non-adherence to statins and antihypertensive drugs are common

The benefits of therapy seen in randomised clinical trials will only be replicated in real life if patients adhere to prescribed treatment regimen, get to goal and stay there!

More health benefits worldwide would result from adherence to existing treatments than from developing new medical treatments!

Non-adherence with prescribed antihypertensive drug in clinical studies



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

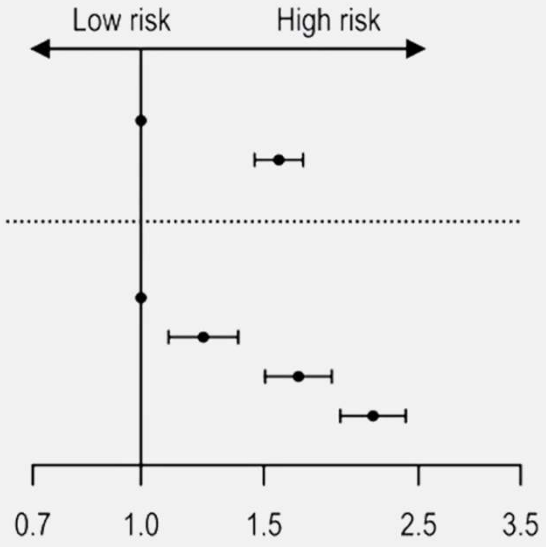
Poor and dynamic adherence introduces variability to trial endpoints

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

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

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

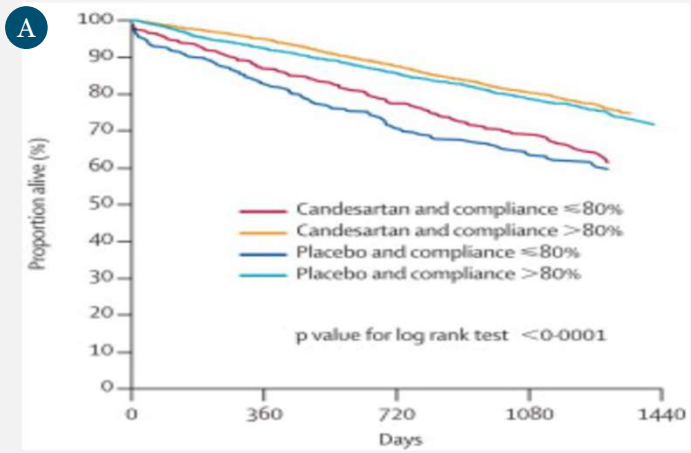
8.2% of adults would give up 2 years of their life to avoid adding 1 daily pill

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

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)

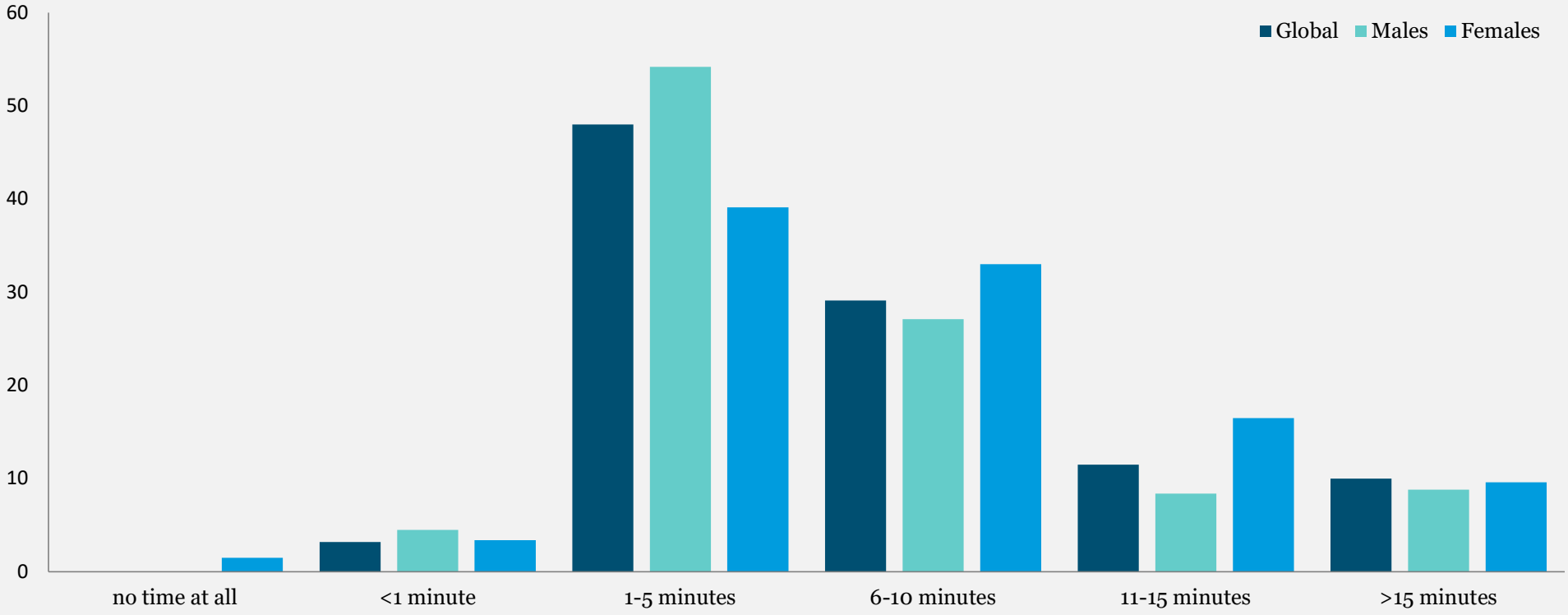
The adjusted HR for good adherence was similar in the candesartan (0·66) and placebo (0·64) groups



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

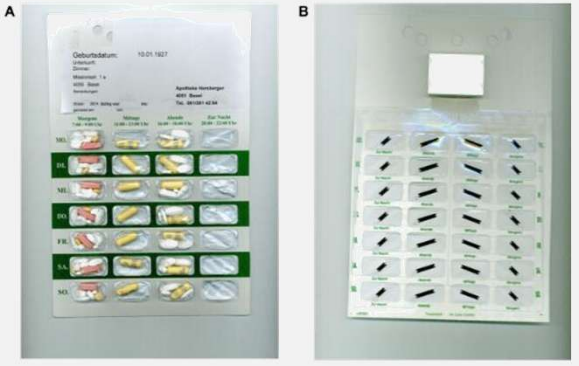
Time spent by physicians talking with patients about their use of medications - a survey of ESH Centers of Excellence

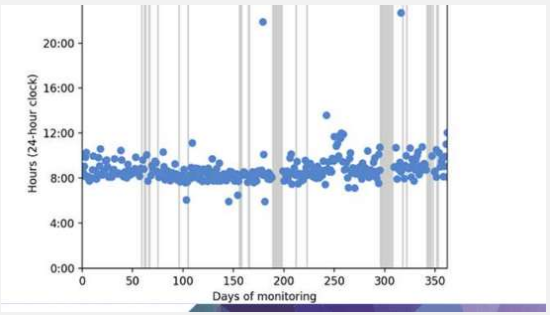


Burnier M, Prejbisz A, Weber T, et al. Hypertension healthcare professional beliefs and behaviour regarding patient medication adherence: a survey conducted among European Society of Hypertension Centres of Excellence. Blood Pressure. 2021 Oct;30(5):282-290.

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.

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 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

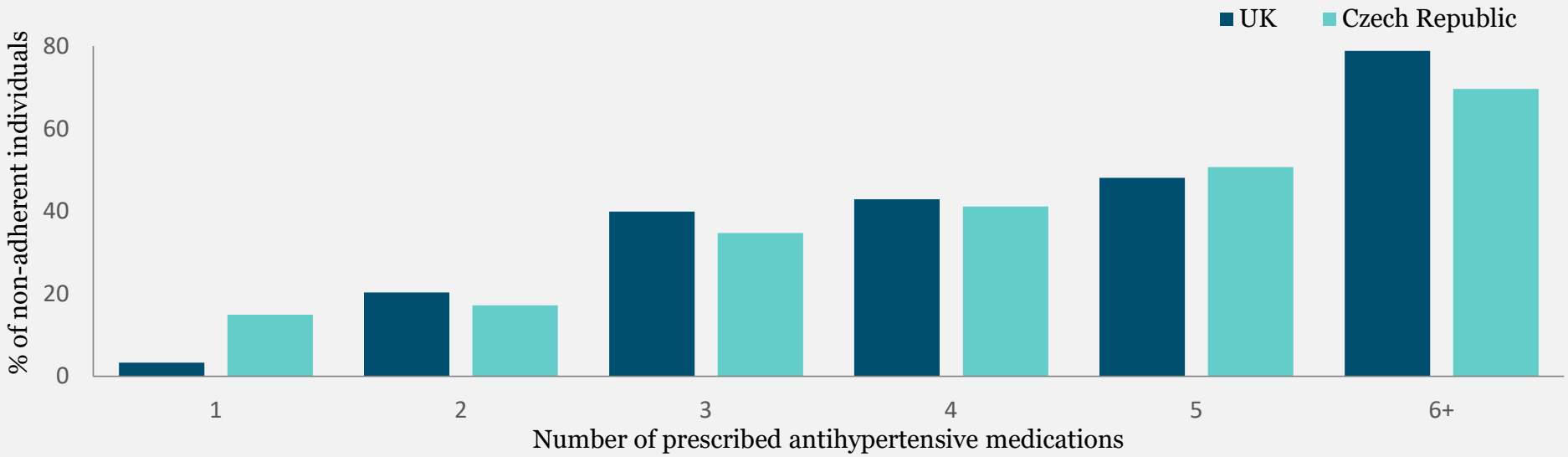
MEMS, medication event monitoring systems

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.

Patients prefer to take less pills

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

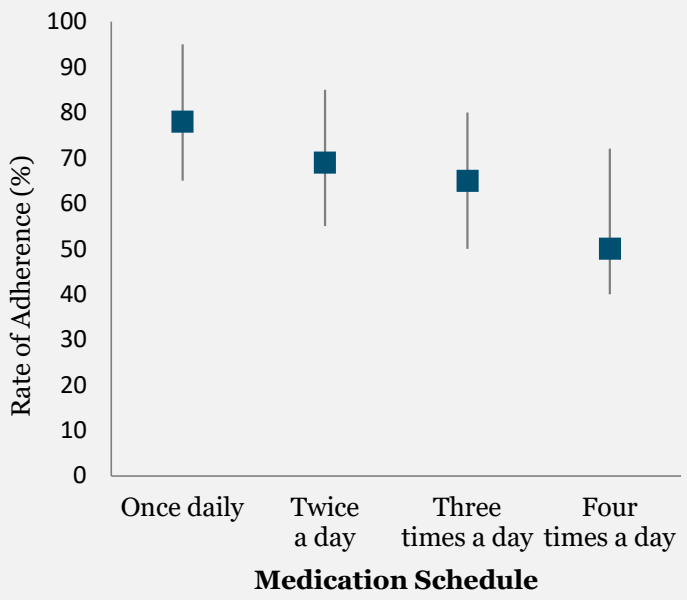
Patients prefer to take 1 PILL



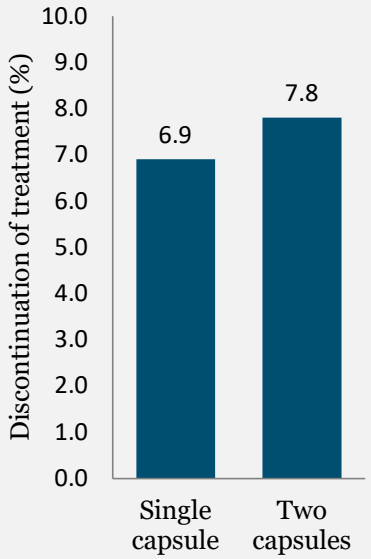
Gupta P, et al. Risk Factors for Nonadherence to Antihypertensive Treatment. Hypertension. 2017 Jun;69(6):1113-1120.

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

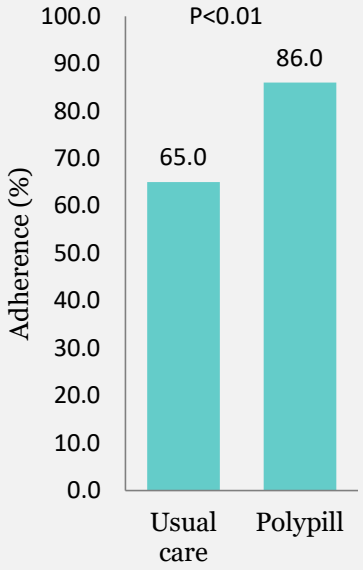
Adherence to medication due to frequency of doses



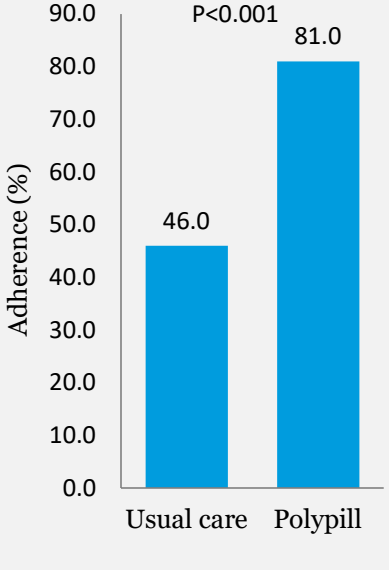
Indian polycap study



Umpire



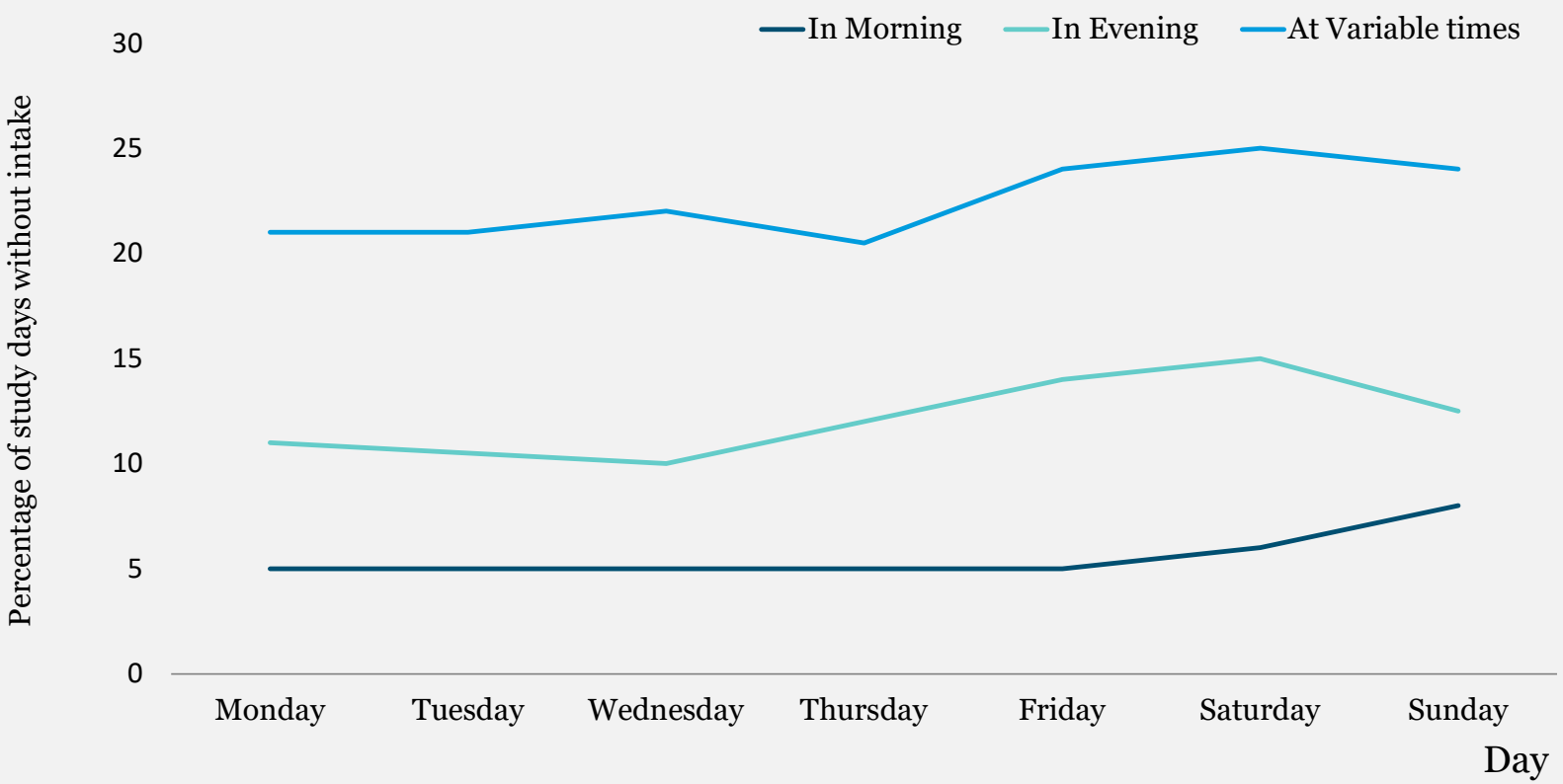
Impact



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.

Relevance of timing of antihypertensive therapy

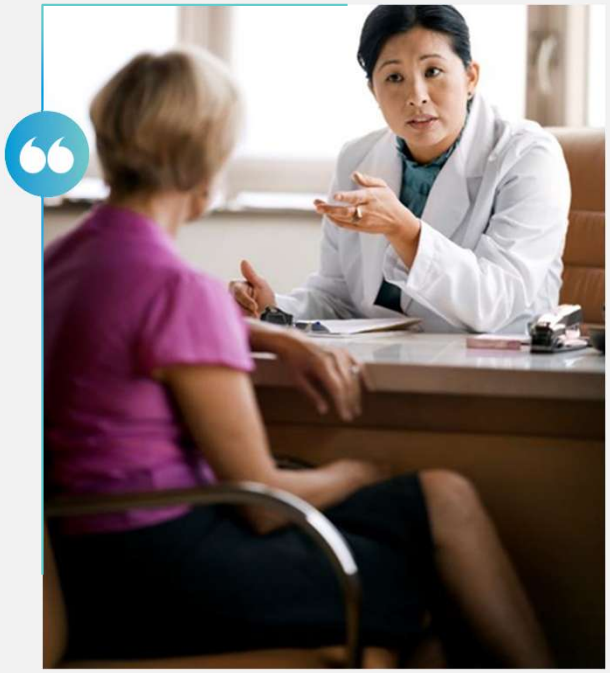
Drug taken



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.

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?

Providers can absolutely influence adherence

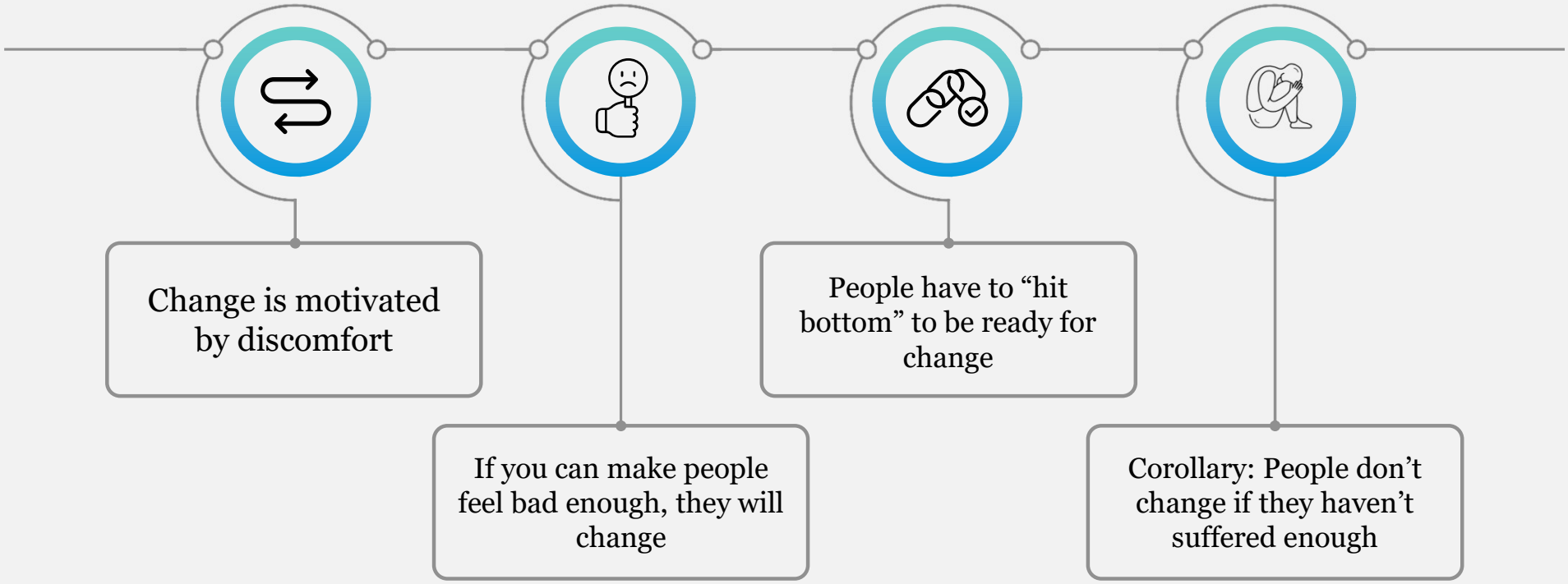
Effective two-way communication is critical

Meet patients “where they are” in terms of what they can achieve

Don’t tell patients what to do

Use patient’s emotions/values to create intrinsic motivation to be healthy and follow your advice

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

Another approach: motivating!

Motivation for change can be fostered by an accepting, empowering, and safe atmosphere

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

What are motivational strategies?

Communication tools and Skills

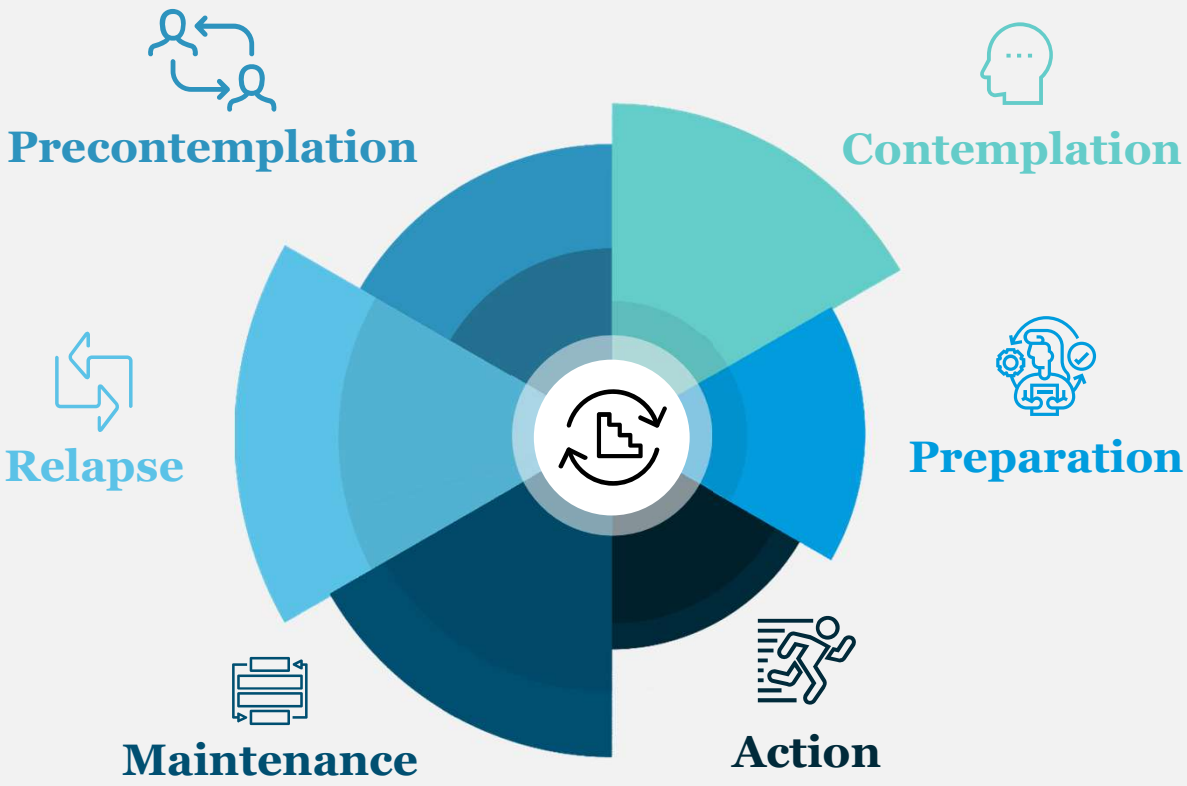
Based on Health Behaviors

A style of talking with patient constructively about reducing their health risks and changing their behavior

Enhance the patient's own motivation to change using strategies that are empathic and non-confrontational

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

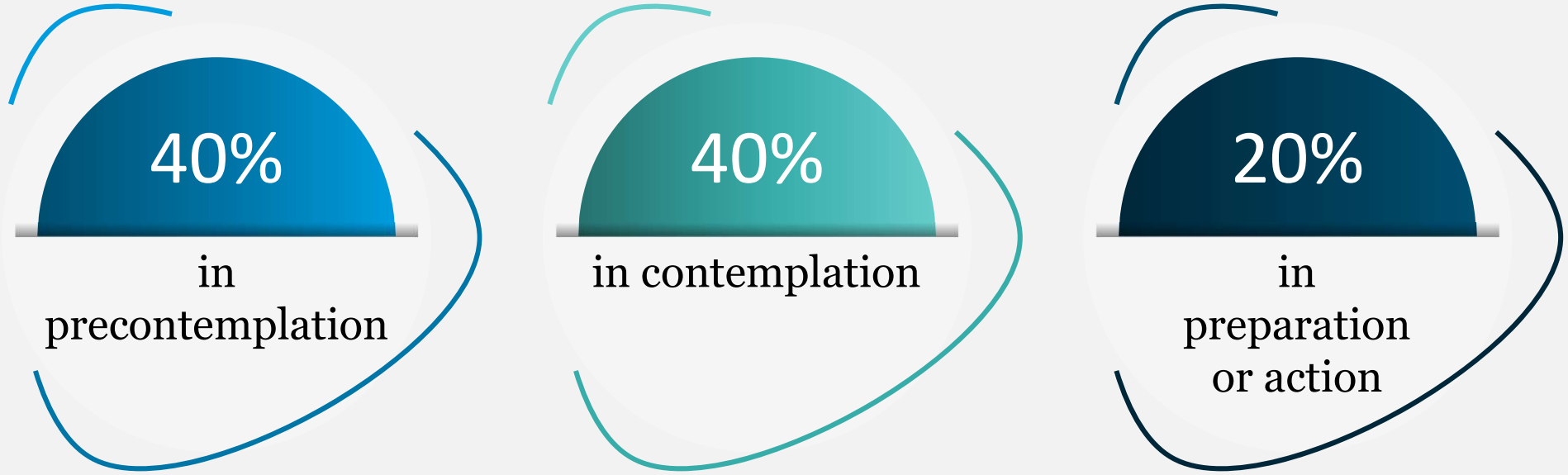
Stages of Change



Prochaska, J. O., & DiClemente, C. C. (1982). Transtheoretical therapy: Toward a more integrative model of change. Psychotherapy: Theory, Research & Practice, 19(3), 276–288.

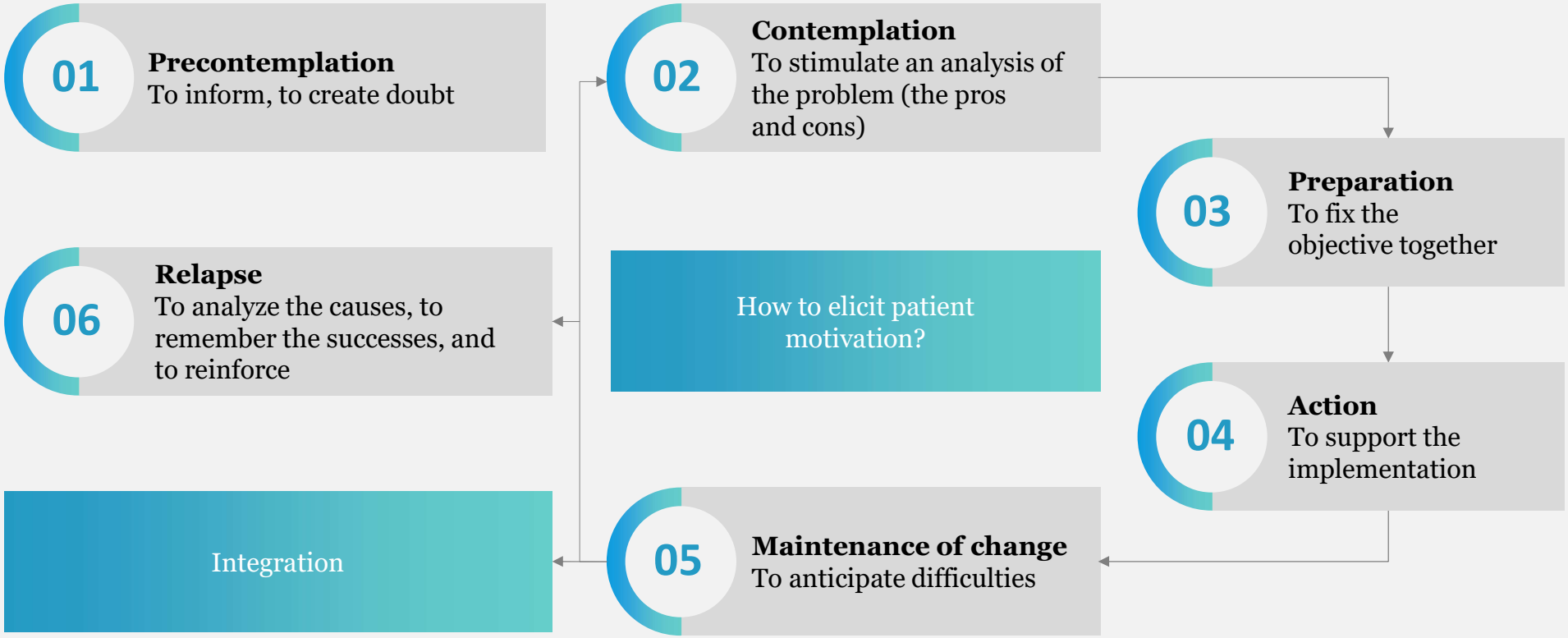
Sources: Slide adapted by Jeanne Obert, 2006, from Miller, W.R., & Rollnick, S. (2002). Motivational Interviewing: Preparing people for change. New York: Guilford Press

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



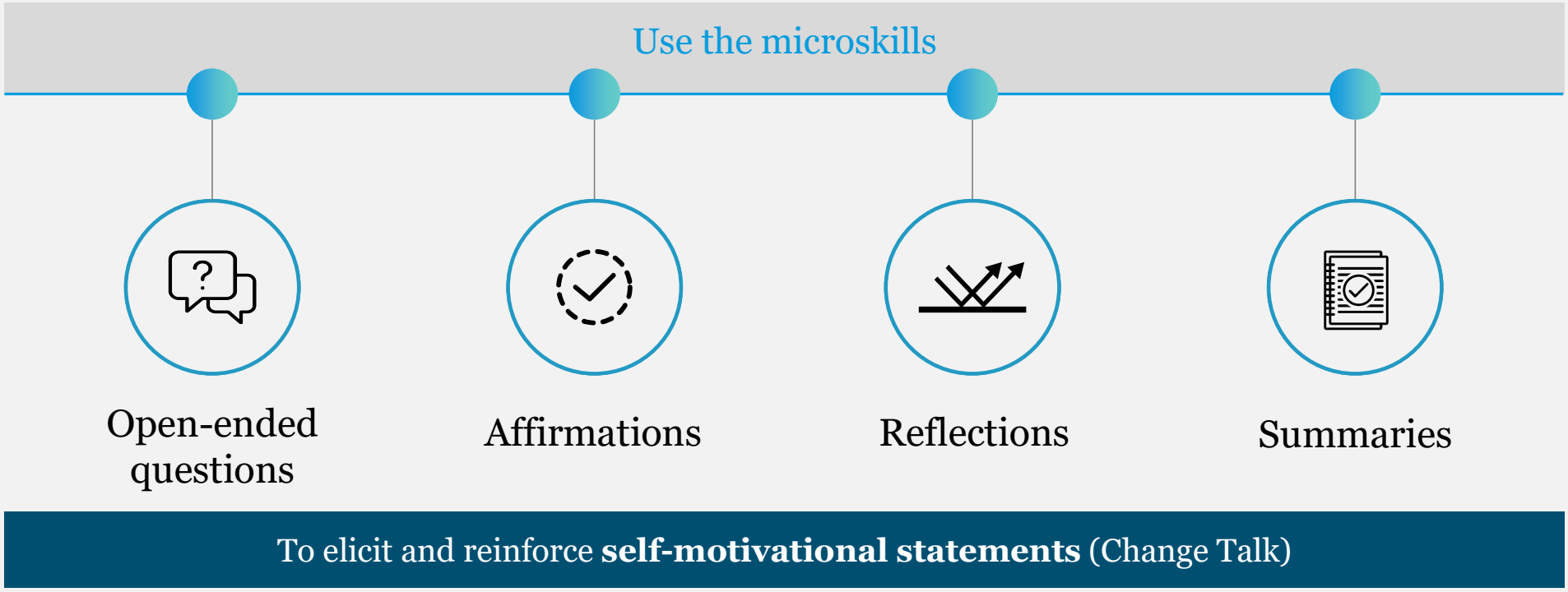
Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot. 1997 Sep-Oct;12(1):38-48.

The stages of motivation



Building motivation using OARS (the microskills)

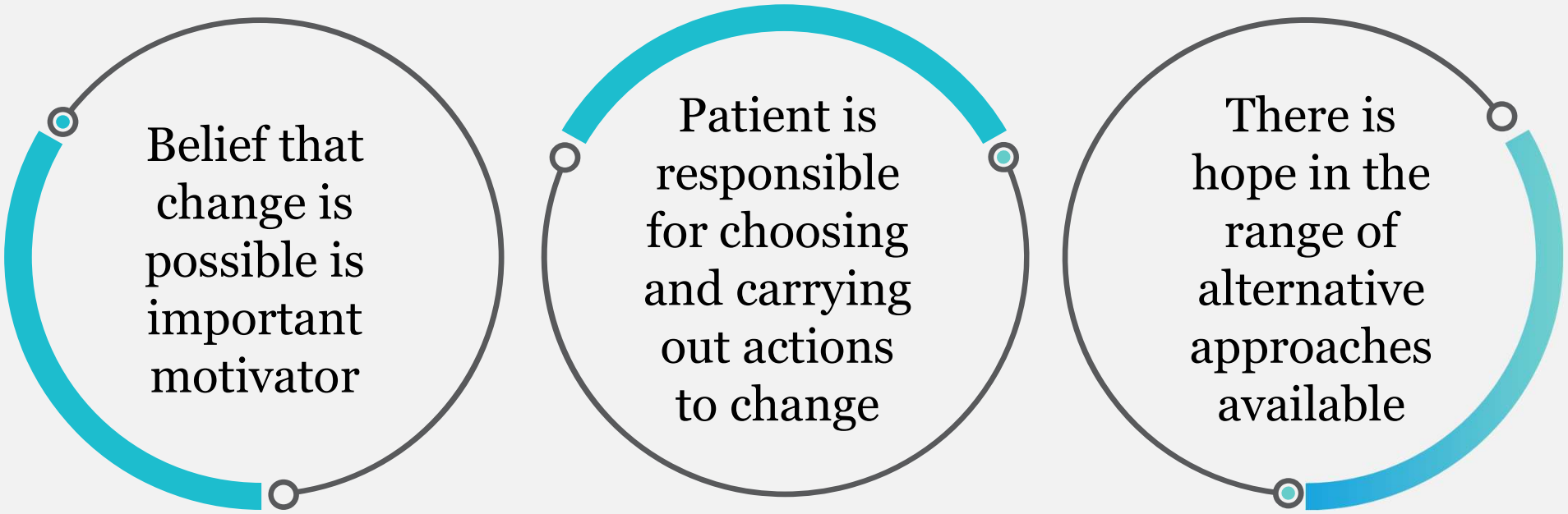
How can I help patients



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

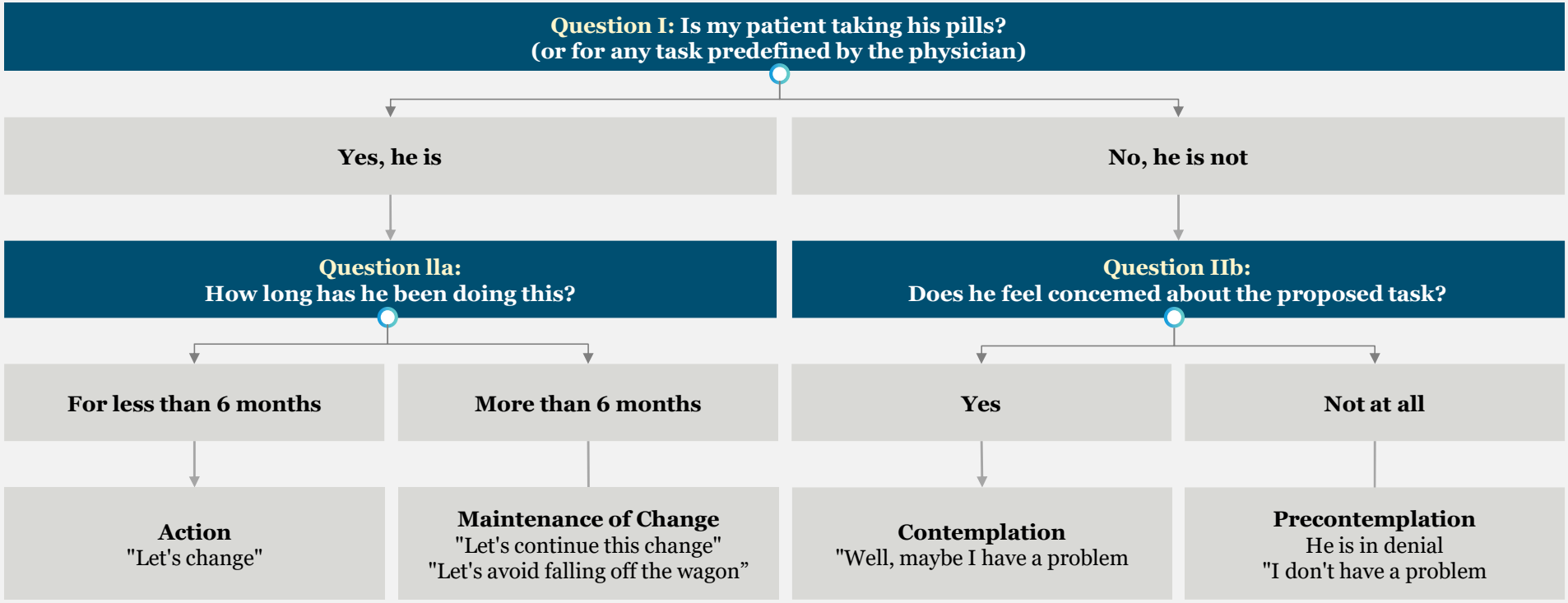
Support Self-Efficacy



GLO2208853

The tool

Motivational stage



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.

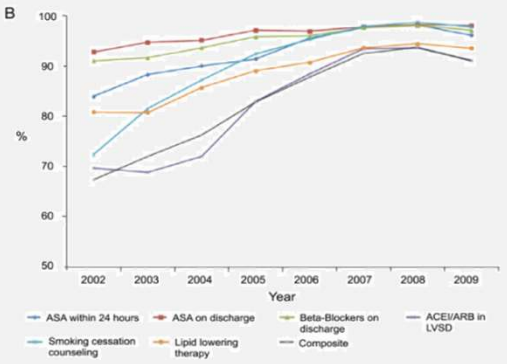
Pharmacy care improves adherence: In FAME, elderly patients with coronary risk factors were randomized to usual care vs. a multi-component program

Fame study

	RUN IN PHASE	PHASE 1 (8 mo)	PHASE 2 (24 mo)	
Usual care	Usual care	Pharmacy care	Usual care	**21.7%** (≥80% adherence to all medications)
Pharmacy care	Usual care	Pharmacy care	Pharmacy care	**97.4%** (≥80% adherence to all medications)
	5% (≥80% adherence to all medications)	98.7% (≥80% adherence to all medications)		

Interventions

- Individualized medication education (using standardized scripts)
- Medications dispensed using an adherence aid (blister packs)
- Regular follow-up with clinical pharmacists every 2 months



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

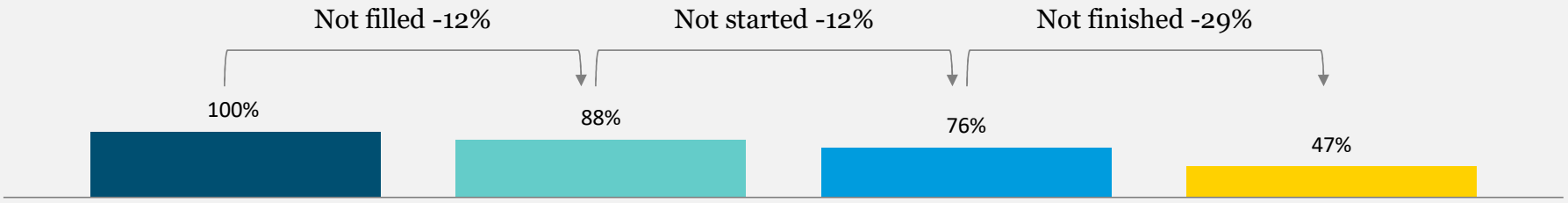
Patient engagement essential even for pharmacy care and for most other methods to work ! (1/2)

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



	Medication Prescription Process In the **Prescriber's Office**	Medication Dispensing Process In the **Pharmacy**	Medication Taking Process In the **Patient's home**
Common barriers	• Understanding benefits of therapy • Denial • Financial • Health literacy	• Perceived SE • Not Understanding benefits and risks • Polypharmacy • Denial	• Forgetfulness • Side effects • Financial • Polypharmacy • Ongoing reinforcement

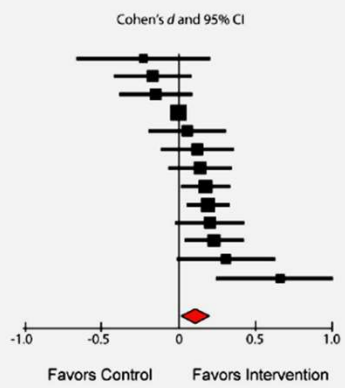
1. Cohen, J.D., Aspry, K., Brown, A.S., Foody, J.A., Furman, R., Jacobson, T.A., Karalis, D.G., Kris-Etherton, P.M., Laforge, R., O'Toole, M.F., Scott, R.D., Underberg, J.A., Valuck, T., Willard, K., Ziajka, P.E., & Ito, M.K. (2013). Use of health information technology (HIT) to improve statin adherence 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.

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

Study name	Cohen's *d*	SE	Lower limit	Upper limit	Z-Value	p-Value	Weight %
Bieber (2006)	-0.23	0.22	-0.67	0.20	-1.05	0.29	3.37
Williams (2001)	-0.17	0.13	-0.42	0.08	-1.35	0.18	6.90
White (2011)	-0.15	0.12	-0.39	0.09	-1.25	0.21	7.31
Sequist (2010)	0.00	0.02	-0.05	0.04	-0.09	0.93	13.80
Kinmonth (1998)	0.06	0.13	-0.19	0.30	0.43	0.66	6.90
Cooper (2001)	0.12	0.12	-0.12	0.36	1.00	0.32	7.31
Girgis (2009)	0.14	0.10	-0.07	0.34	1.33	0.18	8.32
Cleland (2007)	0.17	0.08	0.02	0.33	2.18	0.03	10.03
Chassany (2006)	0.19	0.07	0.05	0.33	2.71	0.01	10.78
Christian (2008)	0.20	0.11	-0.02	0.43	1.77	0.08	7.67
Cals (2009)	0.23	0.10	0.04	0.42	2.37	0.02	8.80
Aiarzaguena (2007)	0.31	0.16	-0.01	0.62	1.90	0.06	5.21
Bolognesi (2006)	0.66	0.21	0.24	1.08	3.11	0.00	3.59
Combined	0.11	0.05	0.02	0.20	2.30	0.02	100.00



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.

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)

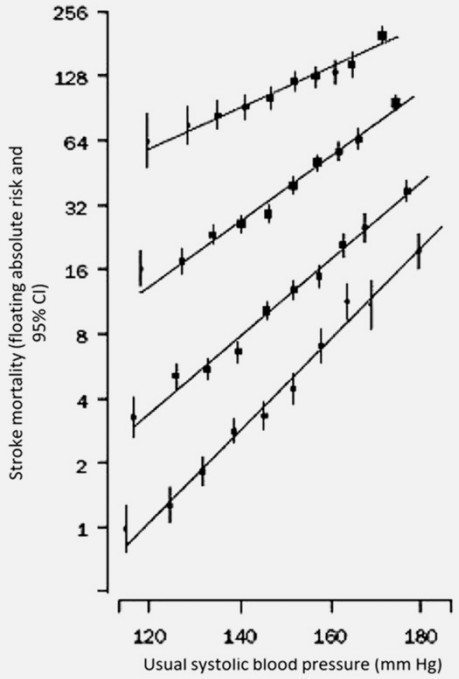
10.8 million deaths/year

= 29,589 DEATHS/DAY

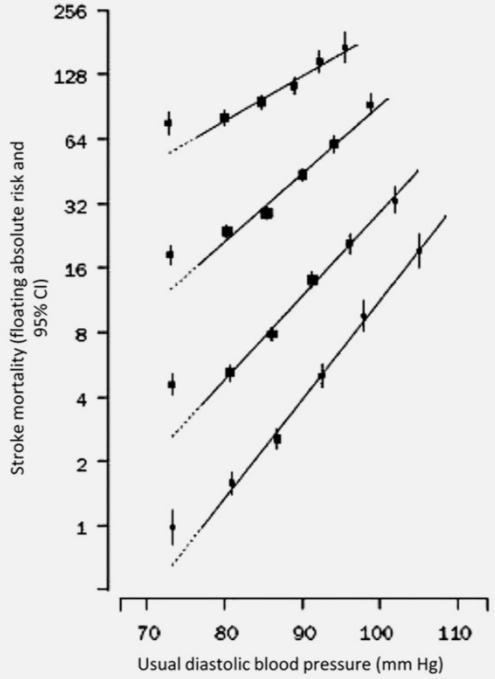
Murray JL, Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396:1223-49

Absolute risk of stroke mortality in relation to blood pressure

A



B



Age (y) at risk

80-89

70-79

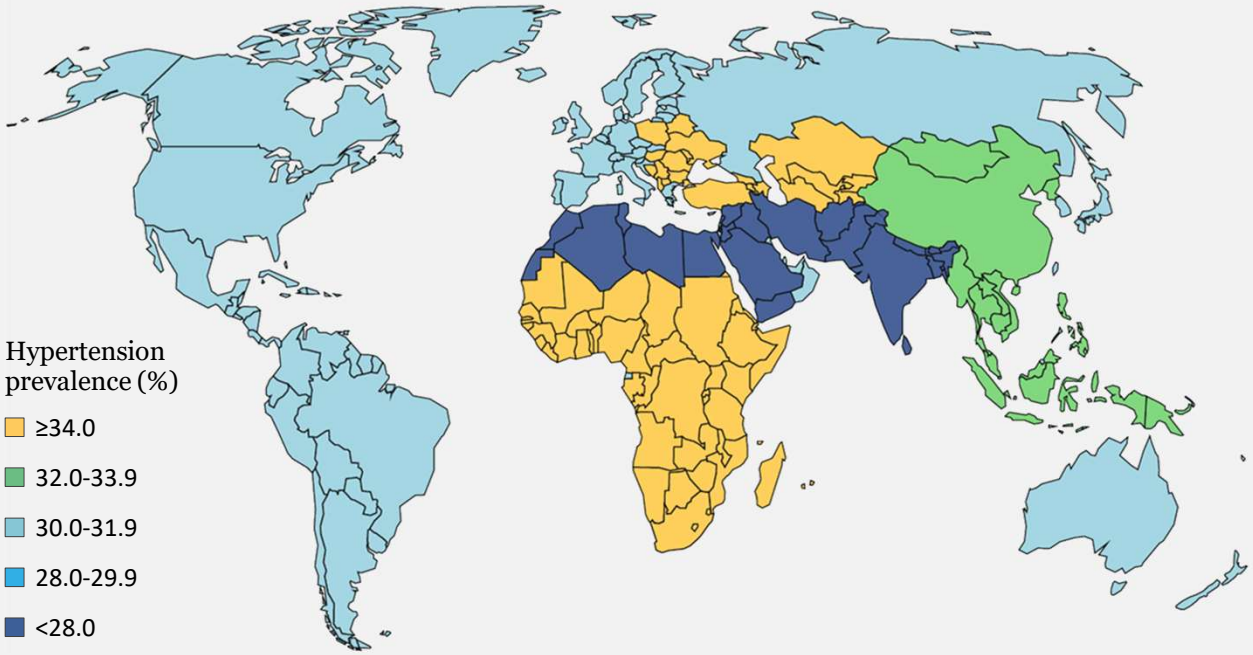
60-69

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

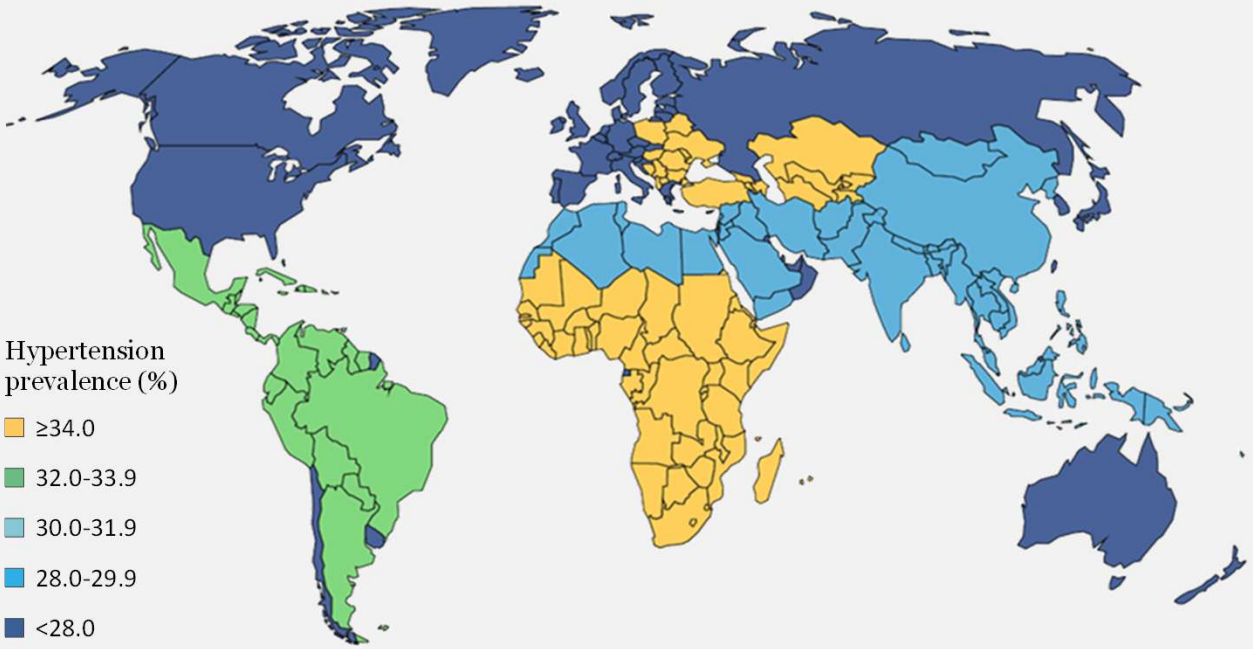
349 million from HIC

1.04 billion from LMIC

1.Mills Katherine T, Stefanescu Andre and Jiang He. The global epidemiology of hypertension. Nature 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

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

B Women



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Circulation Research

Hypertension compendium

Hypertension in Low- and Middle-Income Countries

Aletta E. Schutte, Nikhil Srinivasapura Venkateshmurthy, Sailesh Mohan, Dorairaj Prabhakaran

GLO2246865

Circulation Research

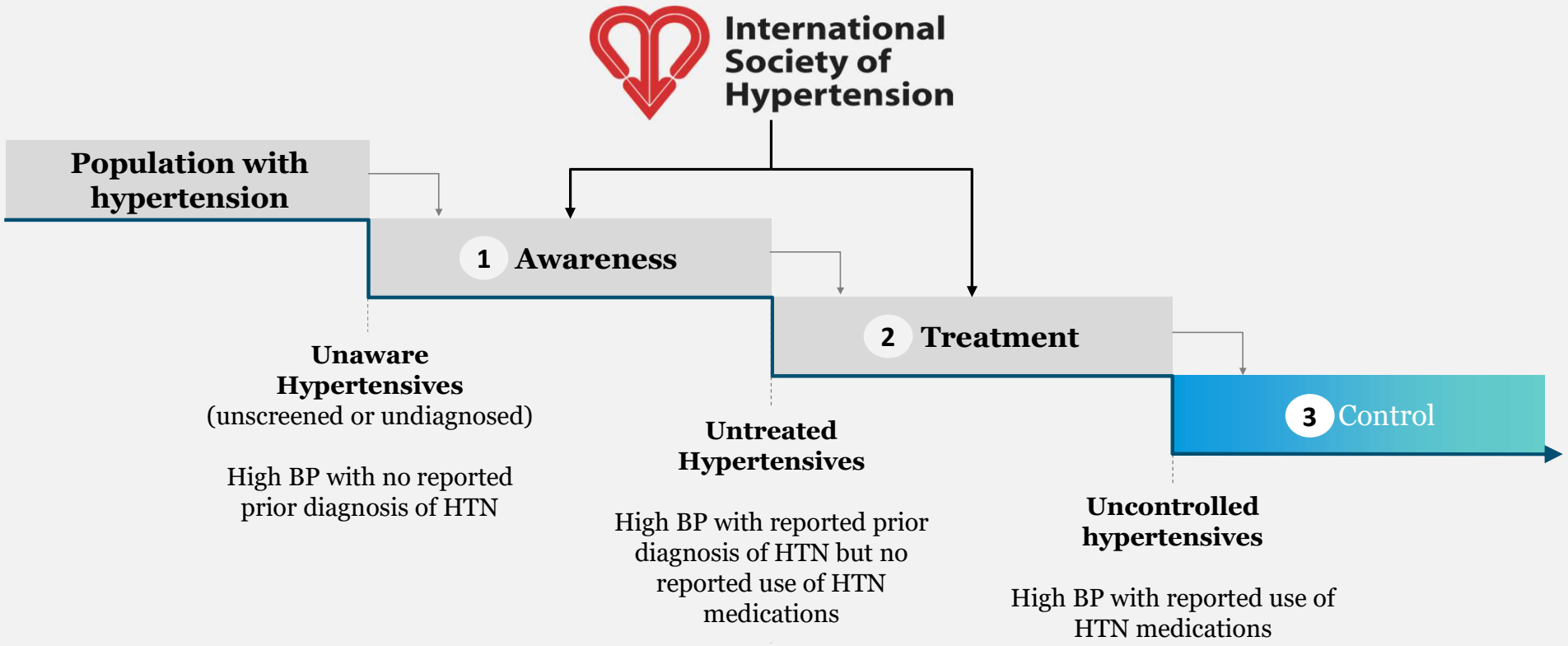
Hypertension compendium

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



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

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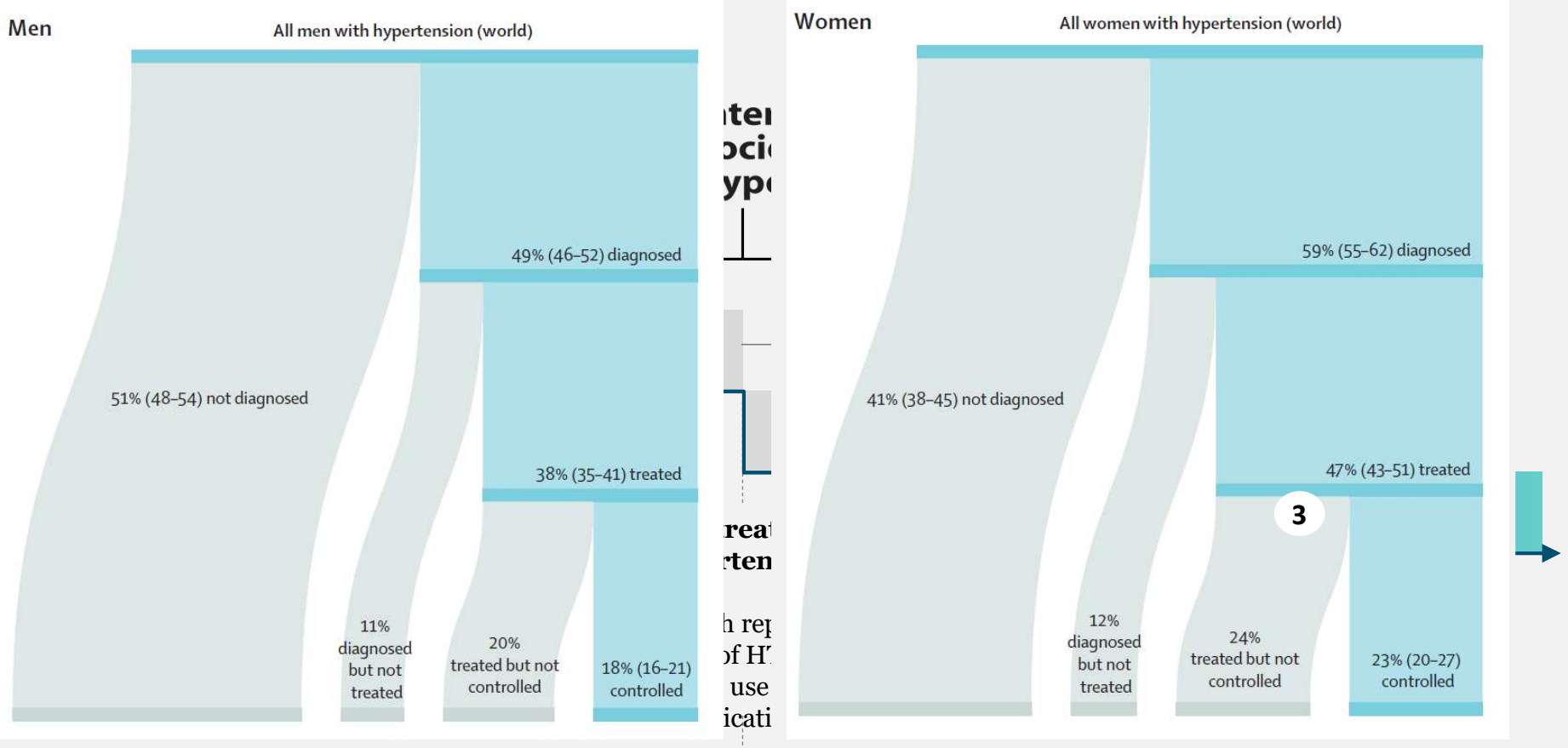


Ezzati Majid. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet 2021;298:957-80

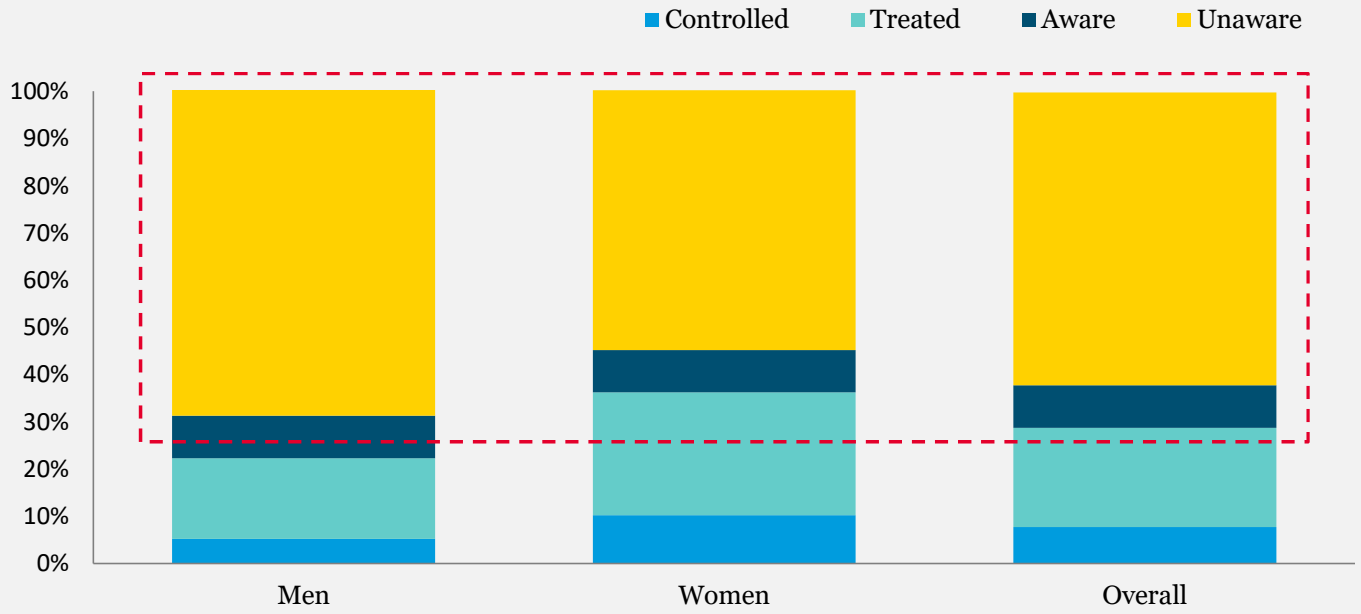
GLO2246865

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

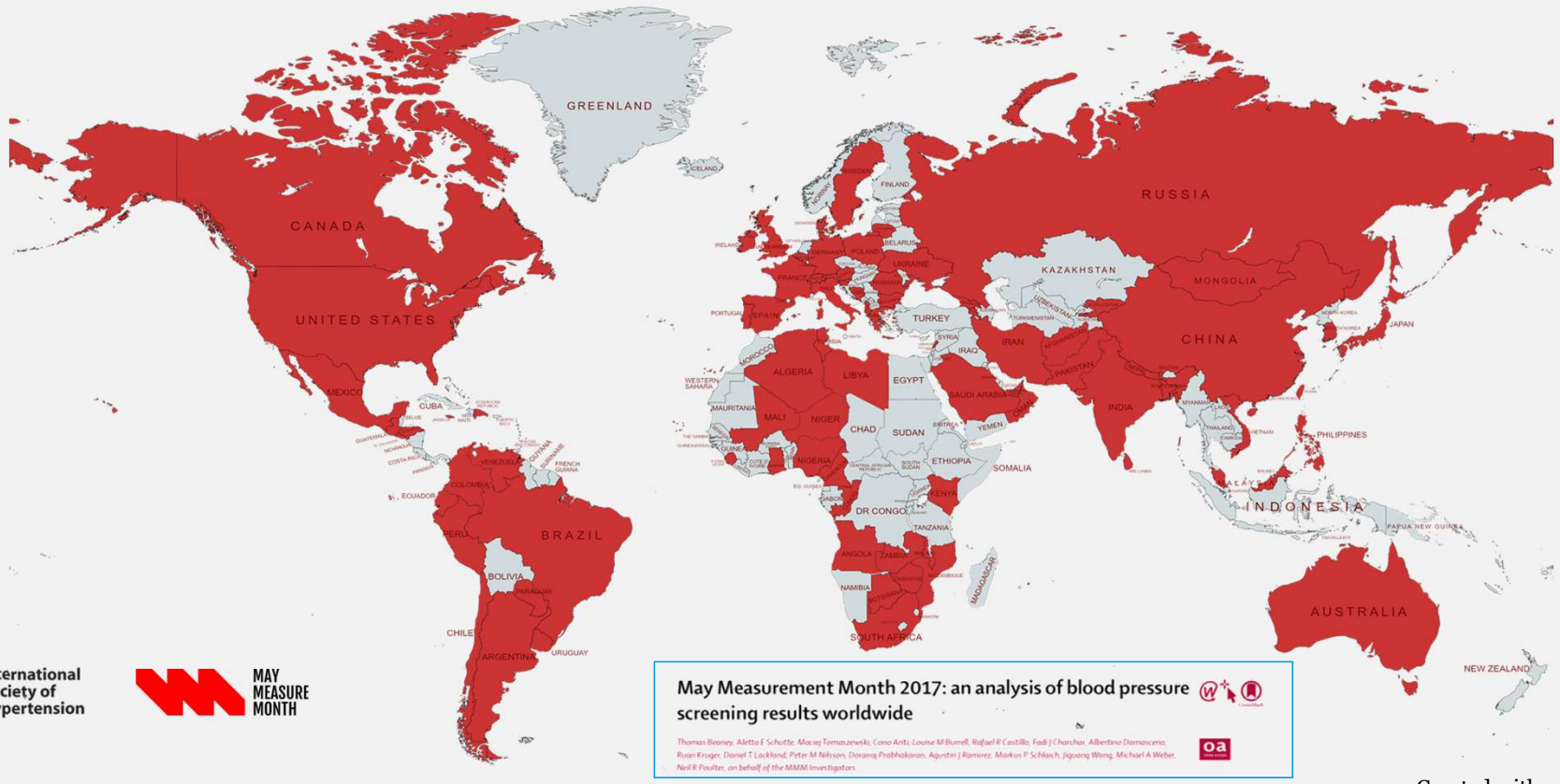
International Society of Hypertension

MAY MEASURE MONTH

Created with mapchart.net

GLO2246865

#SLEEVESUP #GETCHECKED



International Society of Hypertension

MAY MEASURE MONTH

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

GLO2246865

#SLEEVESUP #GETCHECKED

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

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,

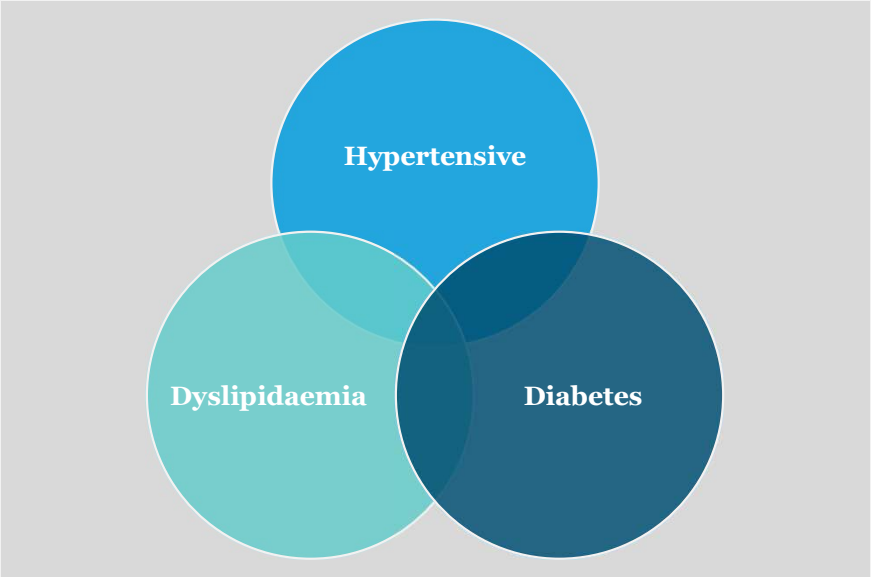
monotherapy is likely to be inadequate therapy in most patients. Indeed, almost all patients in RCTs have required combinations of drugs to control their BP

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)

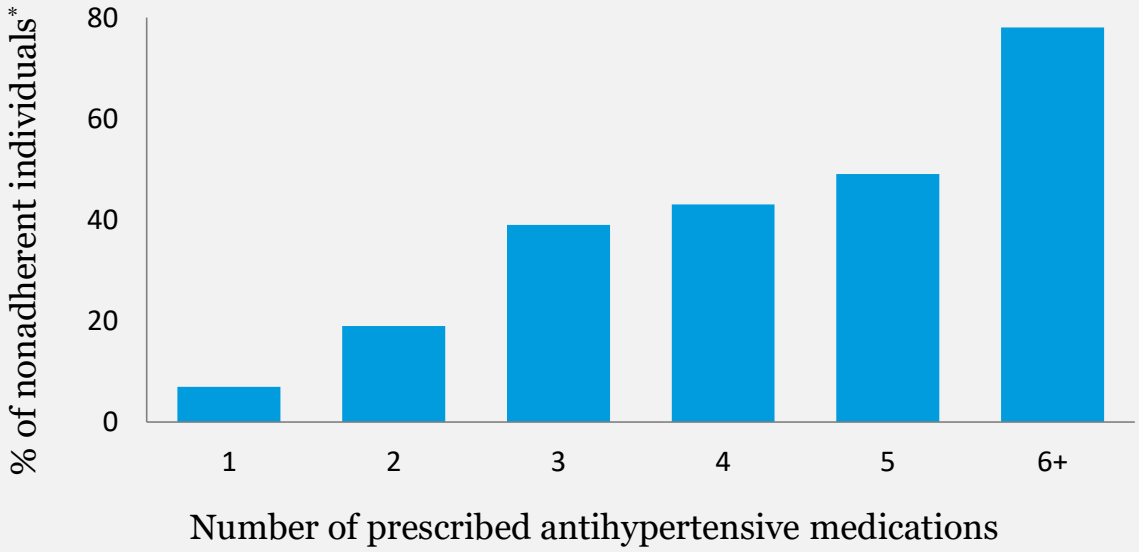
5 Complexity of current treatment strategies

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

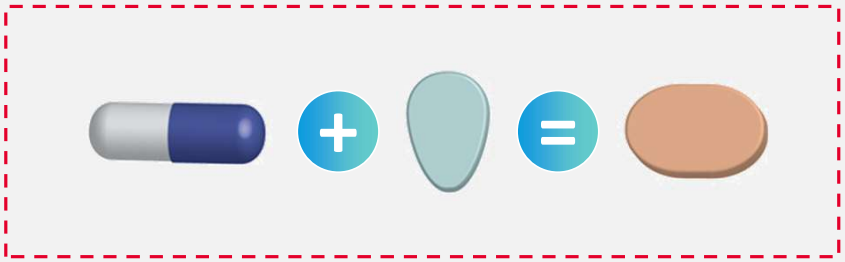
Adapted from Gupta Pankaj, Patel Prashanth, et al. Biochemical Screening for Nonadherence is associated with blood pressure reduction and improvement in adherence. Hypertension. 2017;70:1042-1048

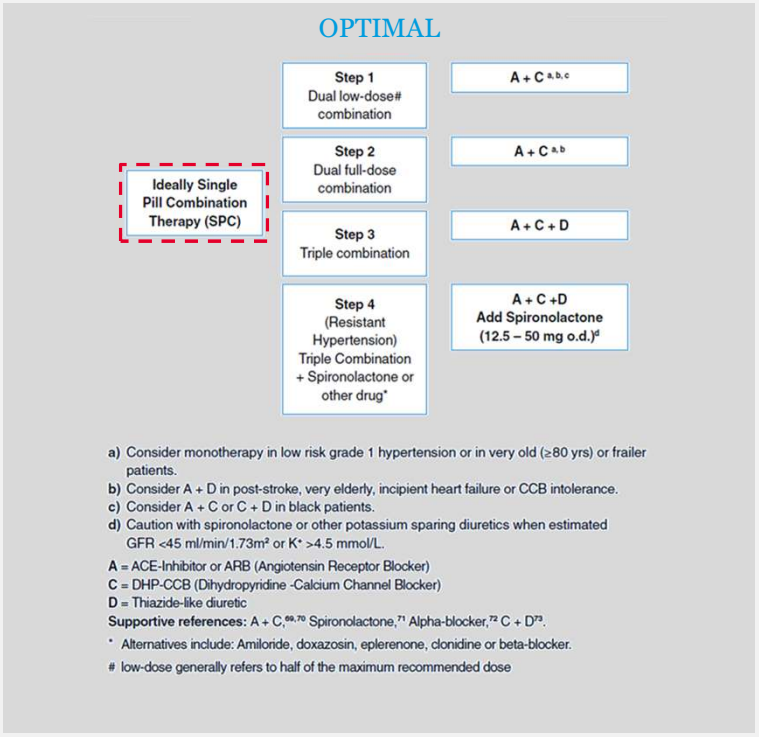
International Society of Hypertension

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]



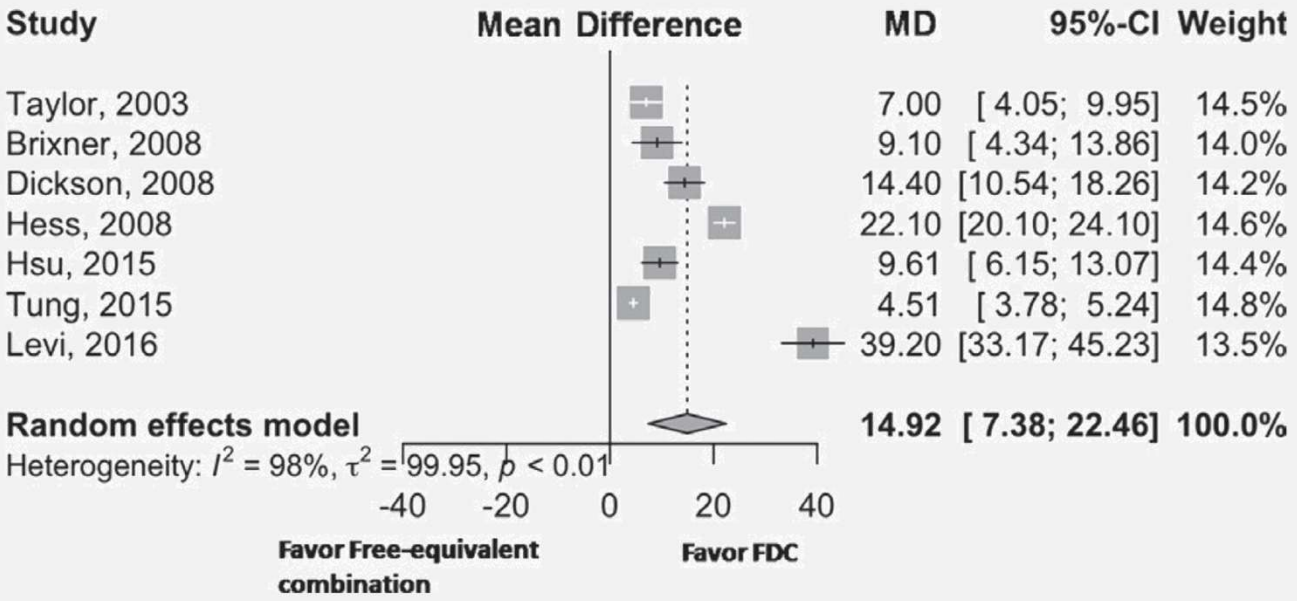


ISH core drug-treatment strategy

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

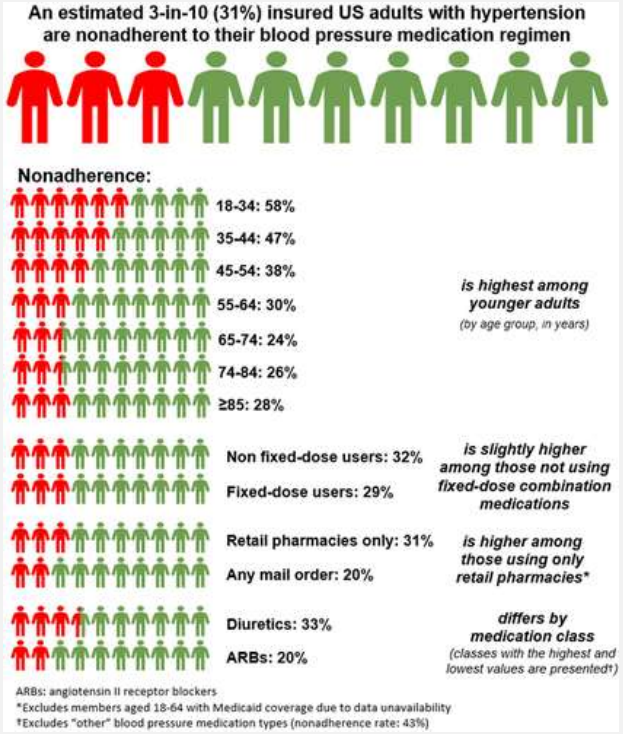
Forest plot for medication adherence. CI, confidence interval; FDC, Fixed-dose combination; MD, mean difference



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

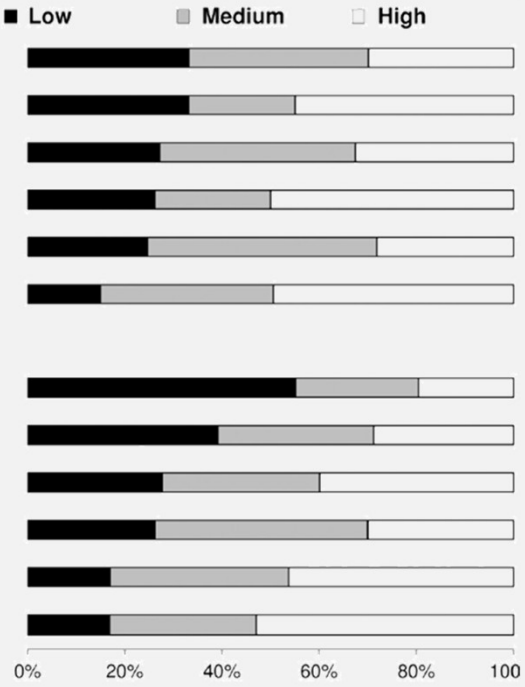
A global phenomenon affecting both high and low income countries



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%)



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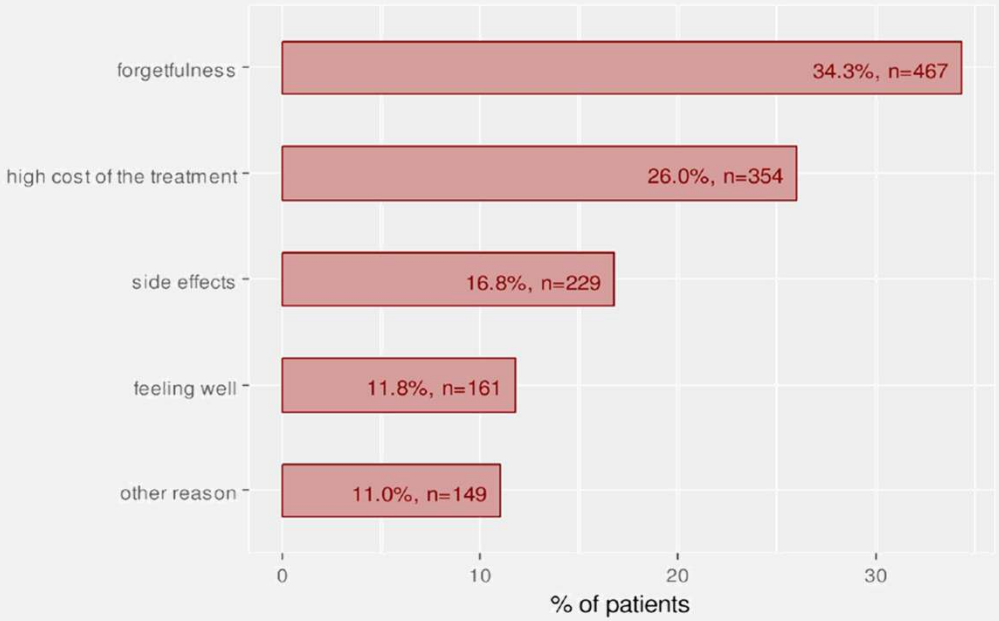
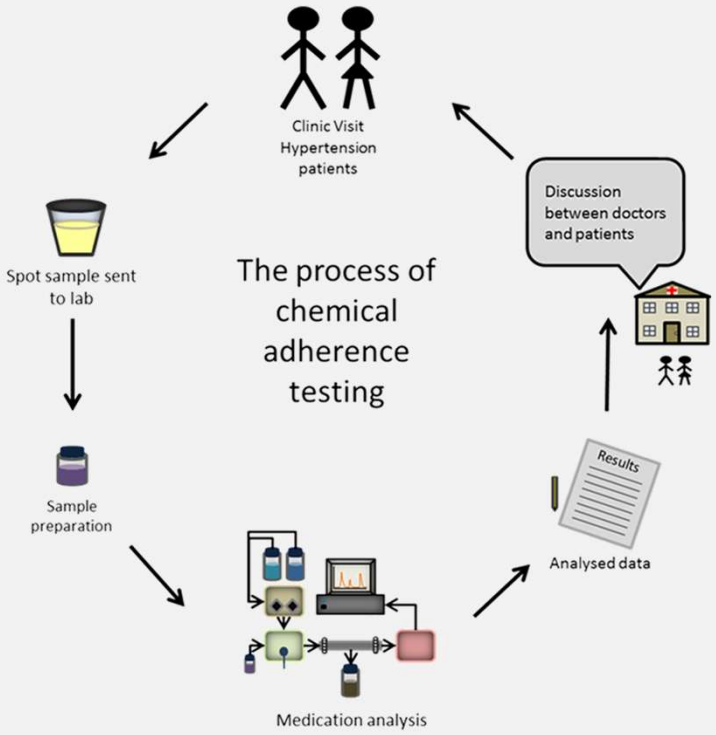
For many years non-adherence was under-recognized in patients with hypertension

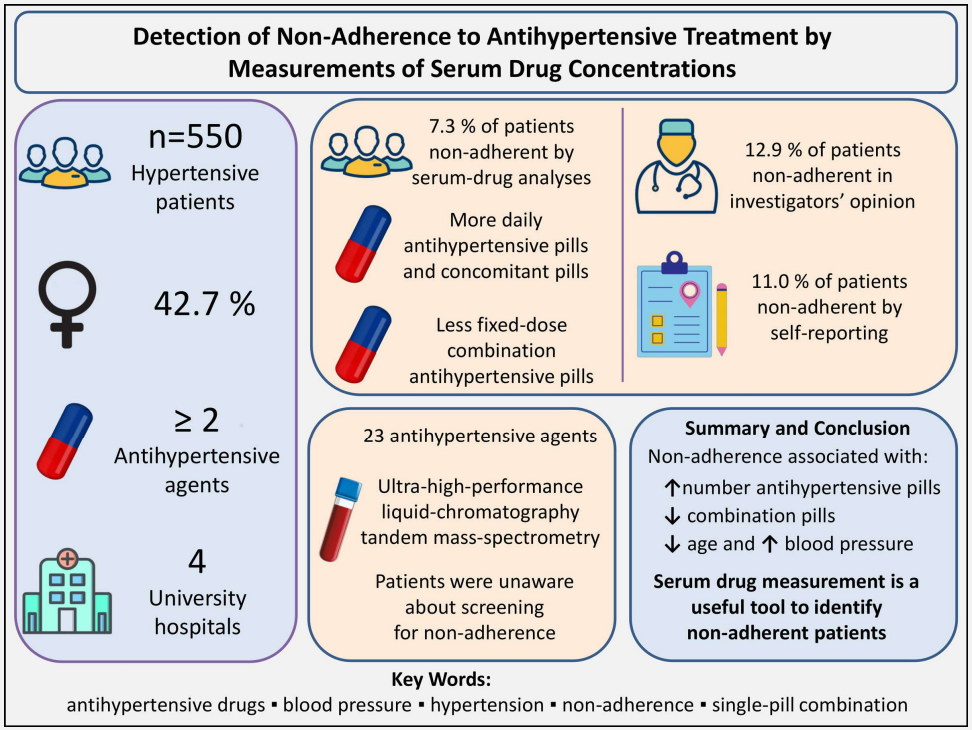
A global phenomenon affecting both high and low income countries

Patients' main reason for not taking their treatment



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***

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

GLO2246865

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.

Medical treatments in oncology

In the past	Currently
Based on IV chemotherapy	Frequent use of oral/subcutaneous drugs
Drug provided by health care facilities	Drug acquisition by the patient
Administered in health care 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

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 health care 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 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 (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

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

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

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

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

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, health care, 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

Toxicity and adherence

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

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

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

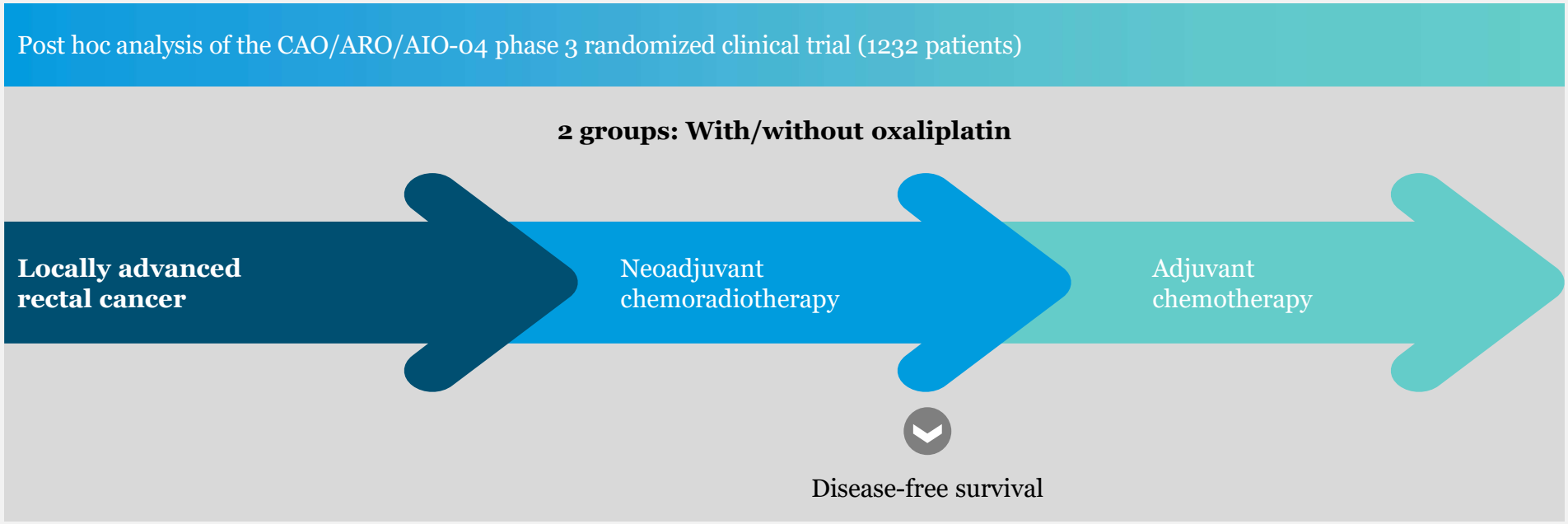
Taking oral chemo every 8h

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

Outcomes and adherence (1/2)

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

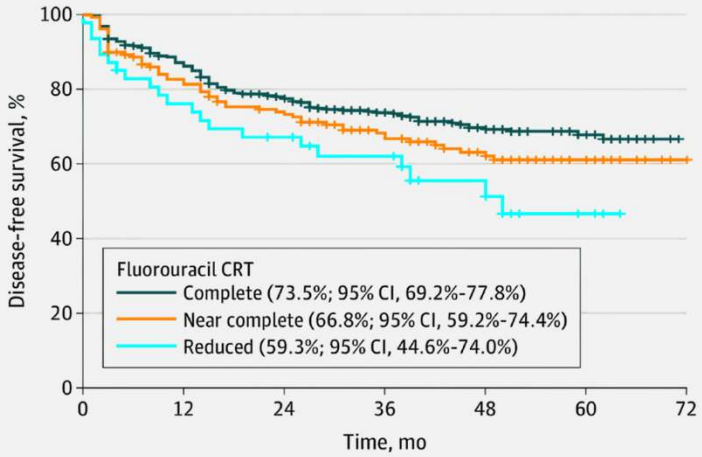


Diefenhardt Markus, Ludmir Athan, et al. Association of Treatment Adherence With Oncologic Outcomes for Patients with Rectal Cancer. JAMA oncology 2020; 6:1416-1421

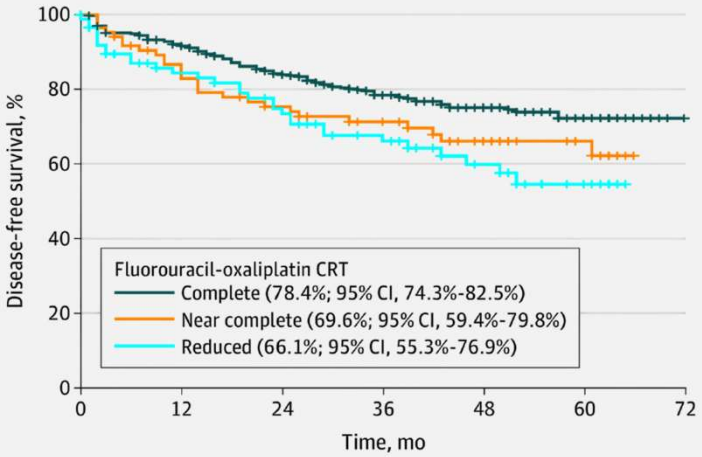
Outcomes and adherence (2/2)

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

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

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

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	Phenytoin: ~20 h	Zonisamide: ~50-70 h
Lamotrigine: 12 h	Phenobarbital: ~ 24 h	Perampanel: 105 h
Carbamazepine: 12-17 h		Cenobamate: 60 h
Valproic acid: 6-17		
Lacosamide 7-9 h		
Oxcarbazepine: 8-11 h		
Topiramate: 7-9 h		
Brivaracetam: 7-9 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

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

Non-adherence: Real life experience

- 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
- 40 YO M, idiopathic generalized epilepsy with bilateral tonic clonic seizures since 10s, normal examination and MRI. Body builder, works as a personal fitness trainer. Meds: levetiracetam, primidone. No side effects. Serial non-compliance because of disease denial and belief in his strength. 1 am had a bilateral tonic clonic seizure while asleep, fell out of bed, broke his spine, had compression of lumbar spinal cord with paraparesis and urinary and fecal incontinence. 4 months in rehabilitation, with residual paraparesis and impotence
- 36 YO M with focal seizures secondary to (resected) meningioma. Seizure free on carbamazepine and lamotrigine, with mild fatigue. He was religious, did not want to take medications, and believed that “God will take care of me”. Had a tonic clonic seizure while crossing a road, was hit by a car, had traumatic brain injury, memory loss

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

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

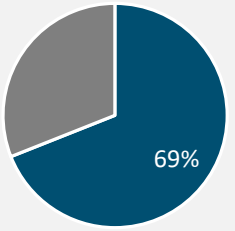
Brodtkorb E, Samsonsen C, Sund JK, Bråthen G, Helde G, Reimers A. Treatment non-adherence in pseudo-refractory epilepsy. Epilepsy Res. 2016;122:1-6

Non-adherence

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

Children and adolescents <16 years

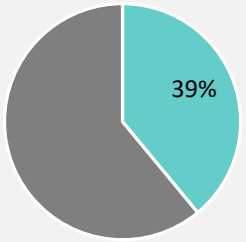
- Population-based study of patients aged <16 years with a diagnosis of epilepsy and receiving AEDs from the Tayside Children's Epilepsy Database in Scotland
- Adherence to AEDs was calculated based on medication dispensing data



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]

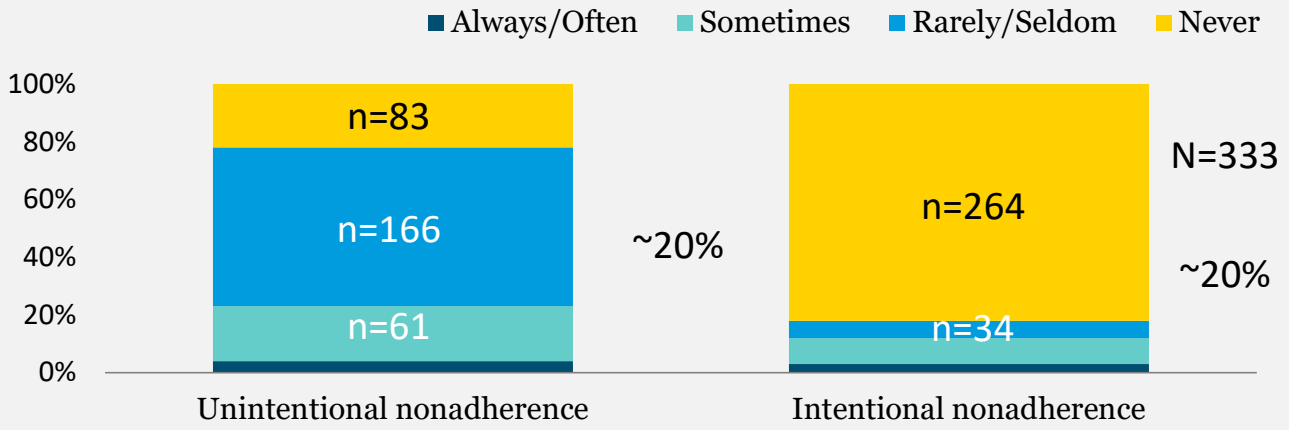
1. Shetty J., Greene SA., et al. Adherence to antiepileptic drugs in children with epilepsy in a Scottish population cohort. Child Neurol. 2016;58:469-474, 2. Davis KL., Candrilli SD., et al. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. Epilepsia. 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

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-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

Risks for non-adherence

Patient related

- Young age
- Depression
- Male
- Dementia
- Poor medication self-administration management
- Disease denial

Medication-related

- Side effects
- Dosing regimen: > 2x/day
- Mono vs polytherapy: > 3 ASMs
- Lack of efficacy

Socioeconomic

- Drug cost
- Drug availability
- Low socioeconomic status
- Living alone

Support

- Healthcare provider/relationship
- Personal/home

Other

- Personal beliefs
- Alternative medicine
- Circumstances: Travel, illness
- Forgetting
- Stigmatization

May differ in different countries/societies/ages **Commonest cause: Simple forgetting**

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

Risks for non-adherence: Ethiopia

N=292

65.4% of epilepsy patients were nonadherent

The commonest cause of nonadherence was forgetfulness (49%), followed by inability to get medicine (29%) and safety concern (24%)

The majority (78%) of the patients had high belief in medication necessity while 44% had high concern about the potential side effects of their medications

39% of the patients had a negative belief toward their medications

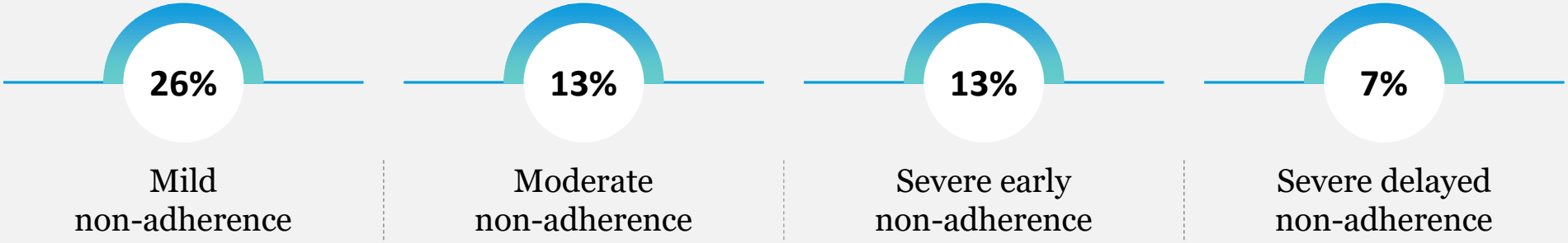
Comorbidity, seizure in the last 3 months, low medication necessity, high medication concern belief, and negative medication belief were predictors of medication non-adherence

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

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



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.

Consequence of ASM non-adherence

Seizures!

N=661, postal survey

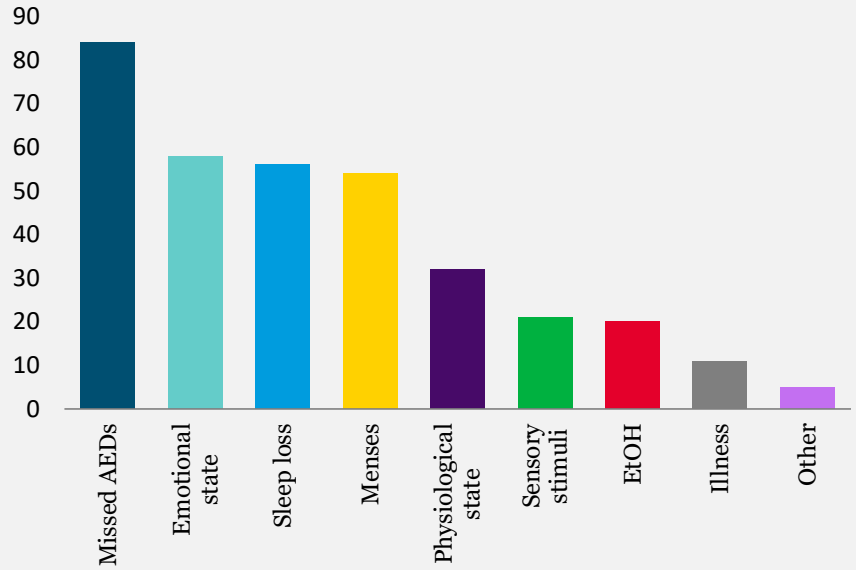
Dose omissions were reported by 71%

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

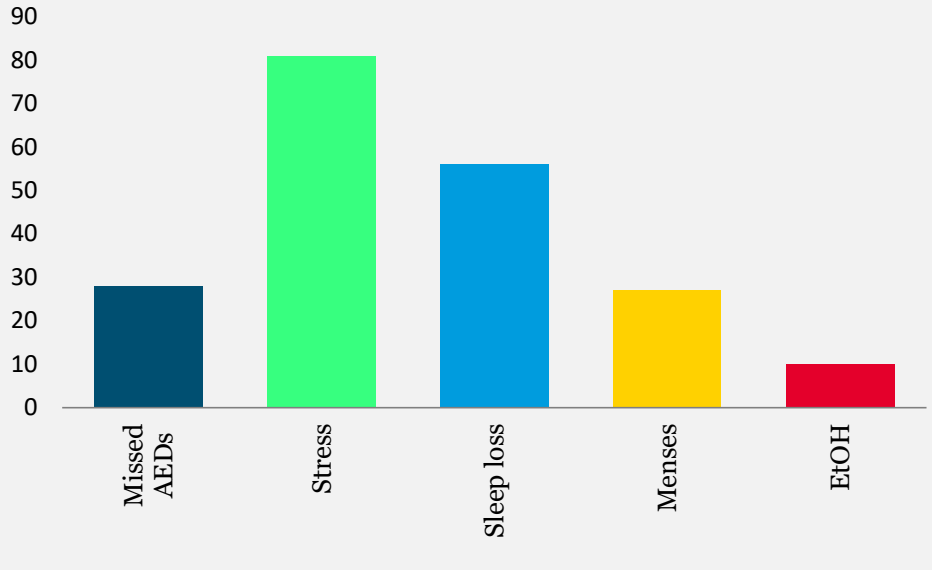
Cramer JA, Glassman M, Rienzi V. The relationship between poor medication compliance and seizures. Epilepsy Behav EB. 2002;3(4):338-342.

Non-compliance is a common trigger of seizures in epilepsy

82% of all seizures



28% of all seizures



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

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)

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

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)

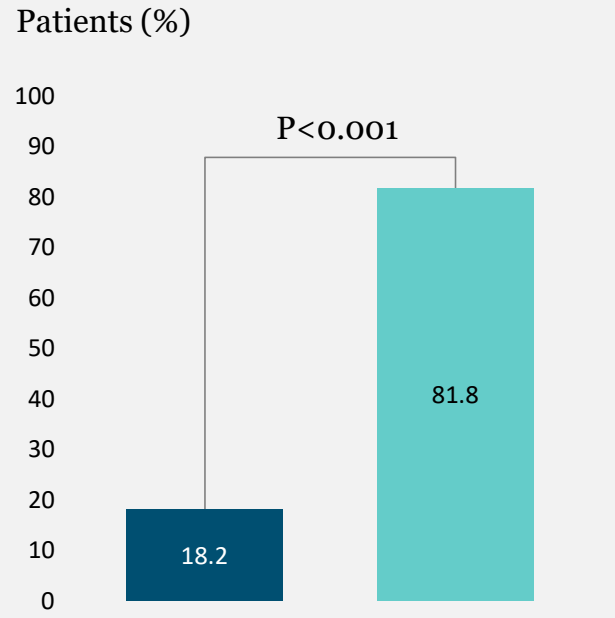
The rate during periods of nonadherence was 39% higher for hospitalizations, 76% higher for inpatient days, and 16% higher for ED visits relative to periods of adherence

	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

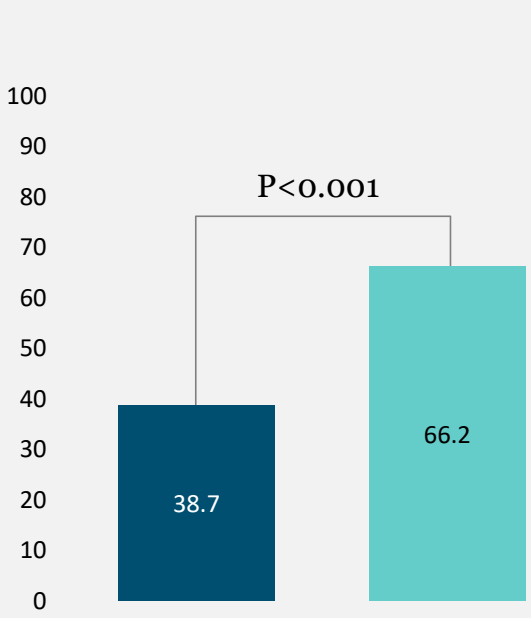
Faught RE, Weiner JR, Guérin A, Cunnington MC, Duh MS. Impact of nonadherence to antiepileptic drugs on health care utilization and costs: findings from the RANSOM study. Epilepsia. 2009;50(3):501-509.

Seizures reduce the quality of life

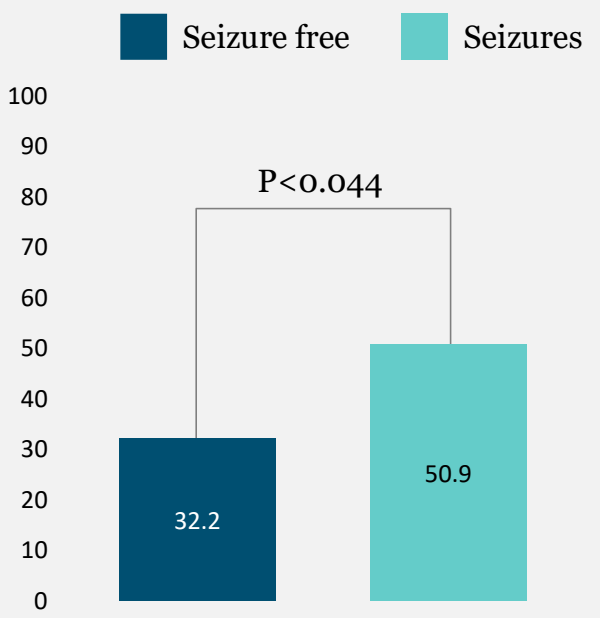
Prevention from driving



Limitations in employment*



Limitations in education received*



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.

Mitigating against non-adherence

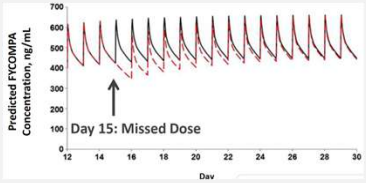
1. Adjust treatment to minimize patient burden

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

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

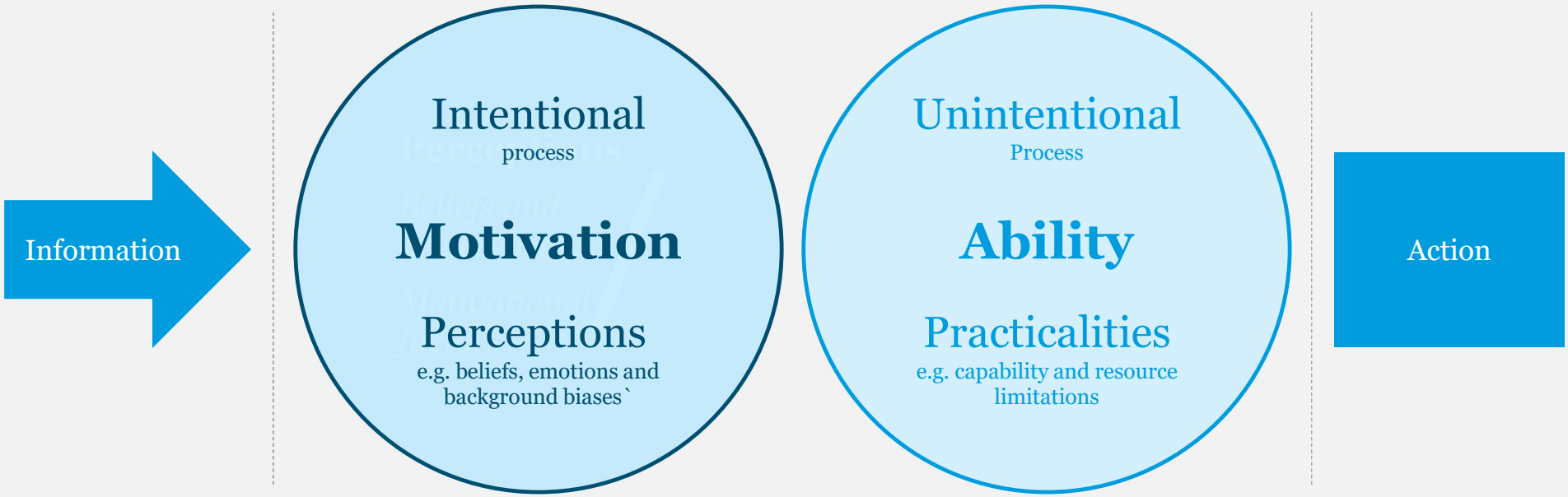
Management	Change of levetiracetam from 1000 mg bid to Extended Release 2000 mg qhs	Suggested routine: take meds at night when brushing teeth	Smart phone reminder – just before bedtime	Addition of zonisamide to levetiracetam (long half life)

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 health care 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

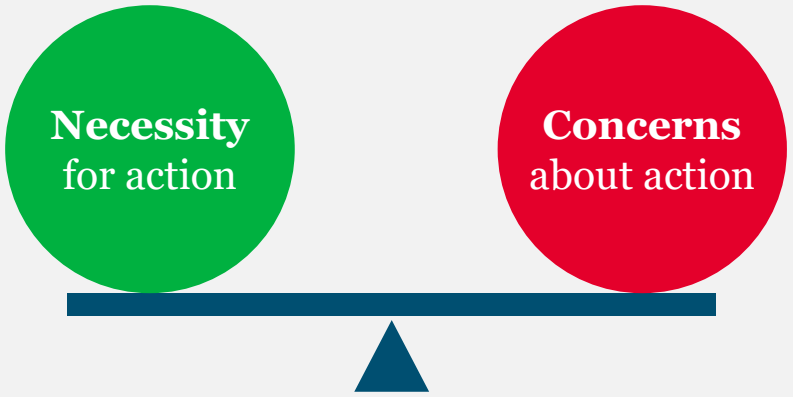
The Perceptions & Practicalities Approach (PaPA)[1-2]

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

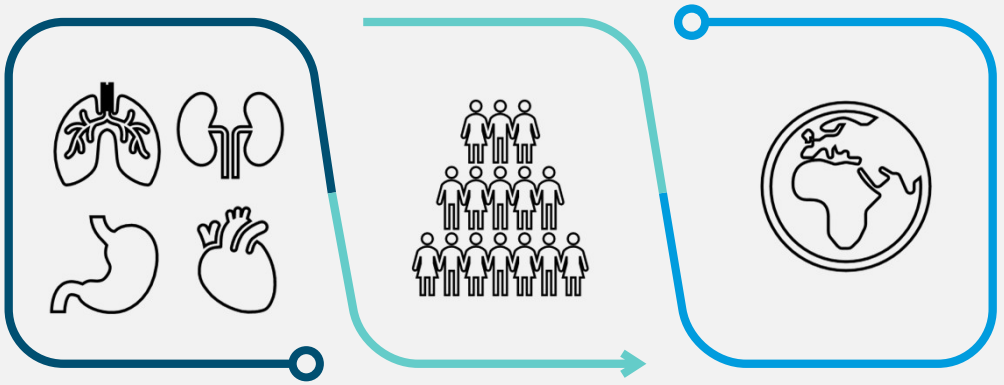


1. Horne R. In Pharmacy Practice, 2001. Ed. by KMG Taylor & G Harding. London: Taylor & Francis [Accessed October 2021]; 2. Horne, R., Cooper, V., Wileman, V., & Chan, A. (2019). Supporting adherence to medicines for long-term conditions: A perceptions and practicalities approach based on an extended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

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



Disease-agnostic framework



> 23 different therapy areas

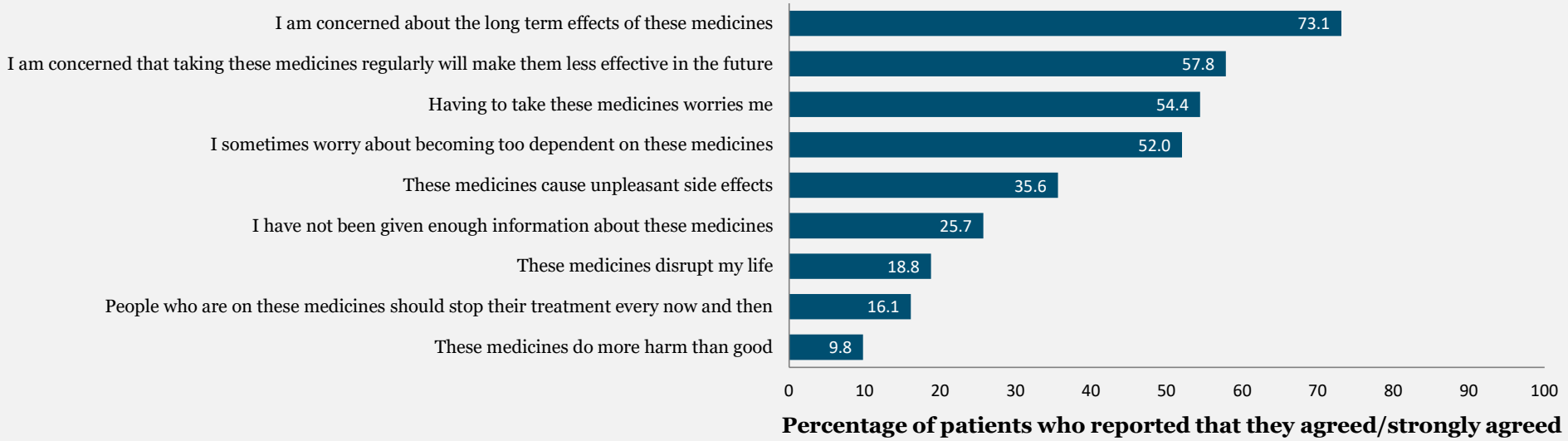
> 27,000 patients

>18 countries & healthcare systems

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 meta-analytic review of the Necessity-Concerns Framework. PLoS One. 2013;8(12): e80633

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 Inflamm Bowel 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.

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]

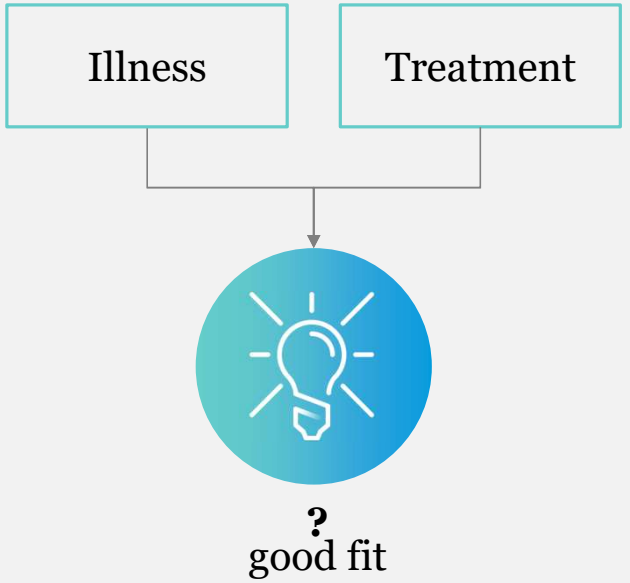
1. Sun CC, Bodurka DC, Weaver CB, Rasu R, Wolf JK, Bevers MW, Smith JA, Wharton JT, Rubenstein EB. Rankings and symptom assessments of side effects from chemotherapy: insights from experienced patients with ovarian cancer. Support Care Cancer. 2005 Apr;13(4):219-27; 2. Bernard M, Brignone M, Adehossi 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

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]

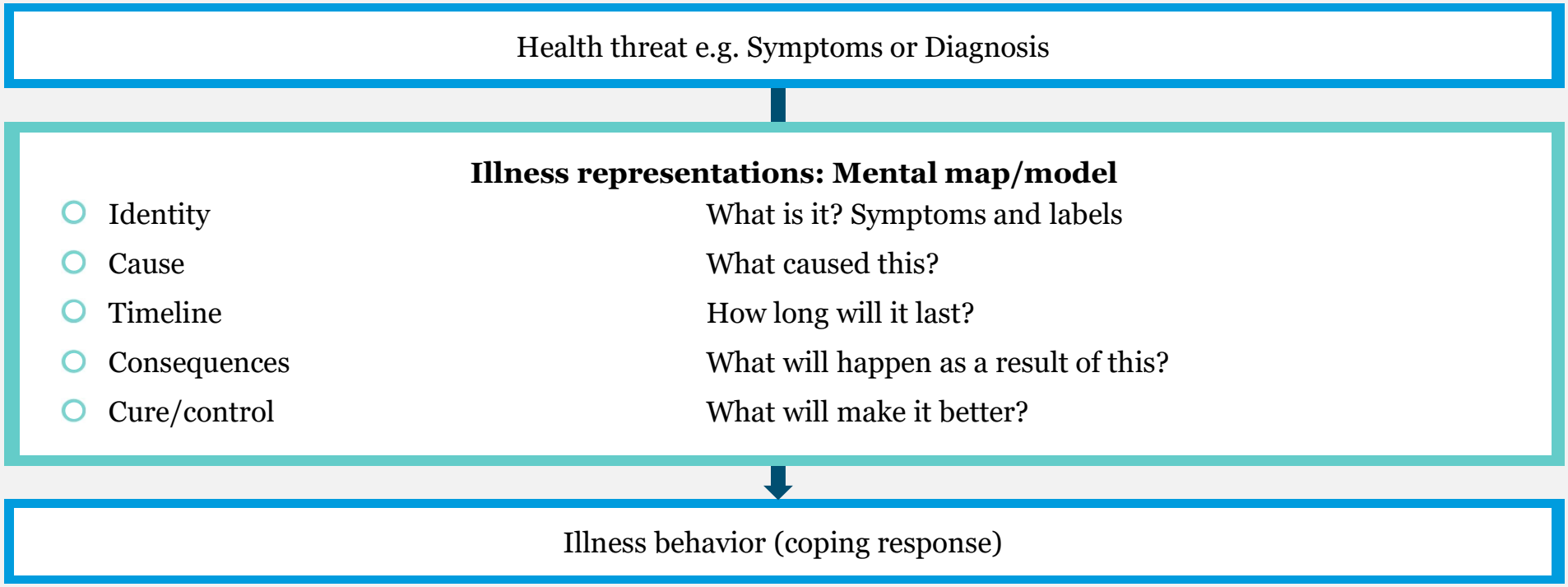
For many patients that fit is not clear

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



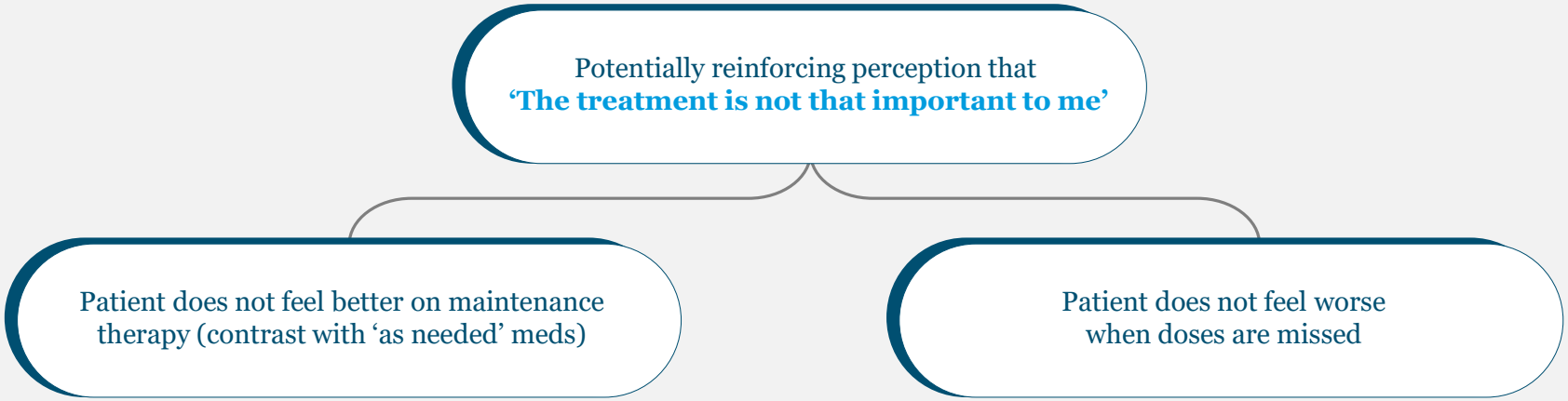
1. Horne, R., & Weinman, J. (2002). Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. Psychology & Health, 17(1), 17–32. 2. Halm EA, Mora P, Leventhal H. No symptoms, no asthma: the acute 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.

Leventhal's common-sense model: Illness perceptions



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; 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

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



Many patients are not convinced of personal need for daily medication treatment … 'no symptoms, no problem'

Expectations of treatment linked to symptom experiences, e.g. 'I feel better now, I don't need it' OR 'I still feel ill; it's not working'

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

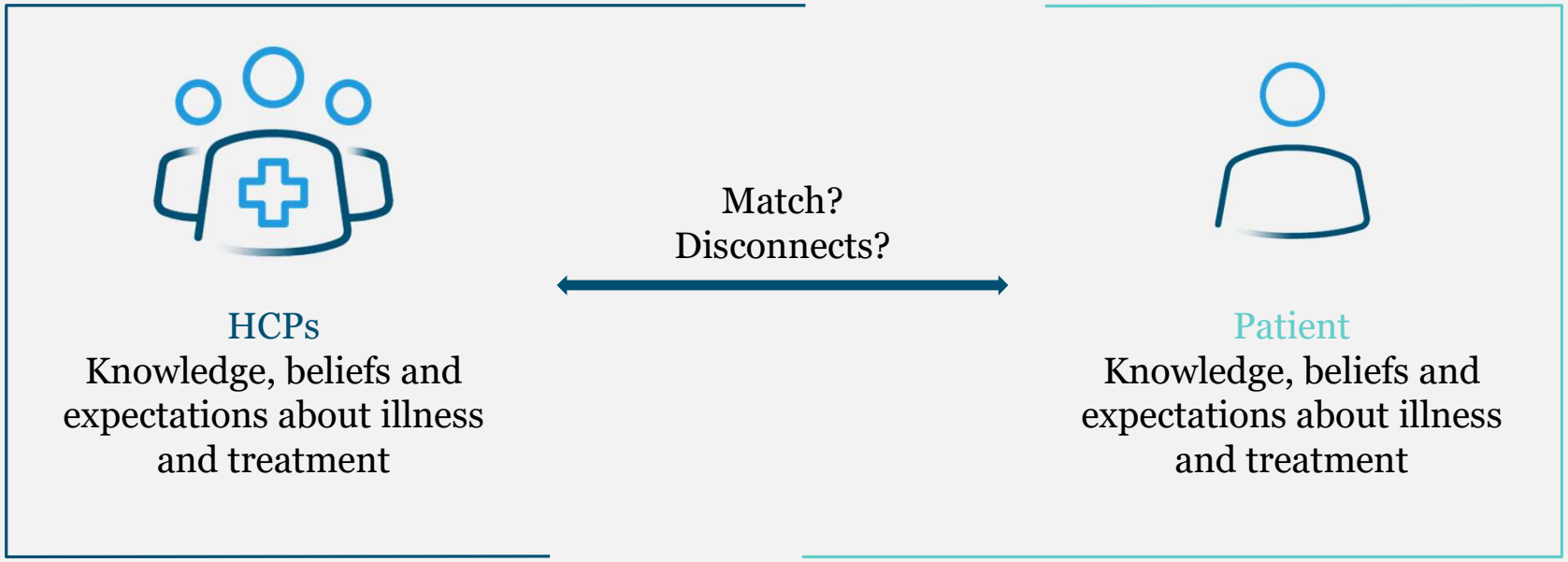
Other common – sense defaults

- 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-use-evidence [Accessed October 2021]

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.

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

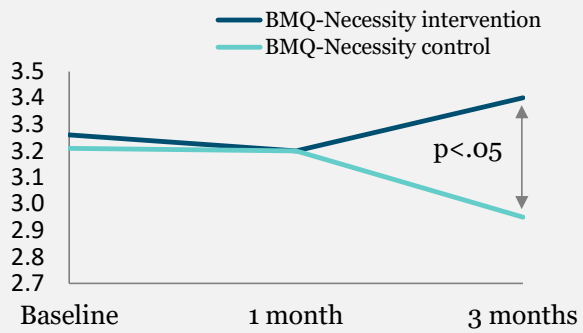
1. Horne, R., Cooper, V., Wileman, V., & Chan, A. (2019). Supporting adherence to medicines for long-term conditions: A perceptions and practicalities approach based on an extended common-sense model. European Psychologist, 24(1), 82–96

Changing necessity beliefs and concerns

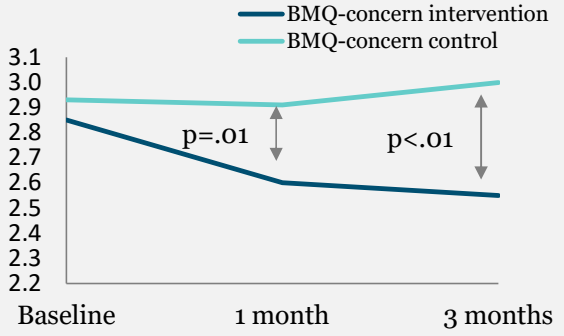
Tailoring support to address the patient's belief barriers can improve adherence[1]

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

GLO2248421

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

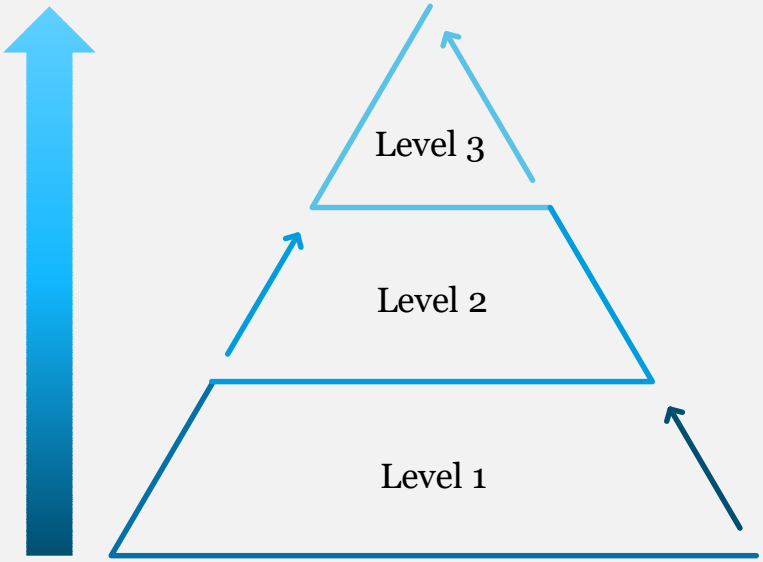
Lack of social support

- 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

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

Increasing programme 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

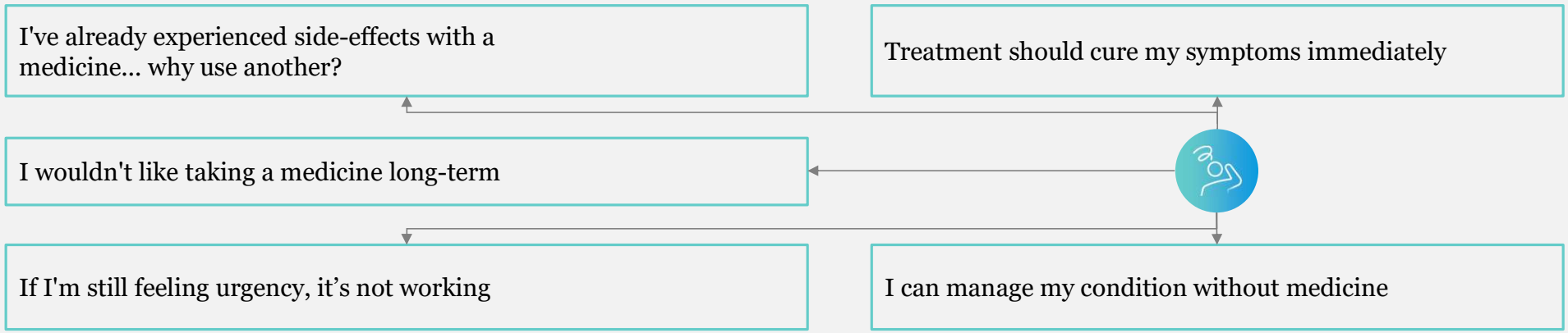
Text reminders

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

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



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 – 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.

Do reminders work?

JAMA Internal Medicine | Original investigation

Effect of reminder devices on medication adherence

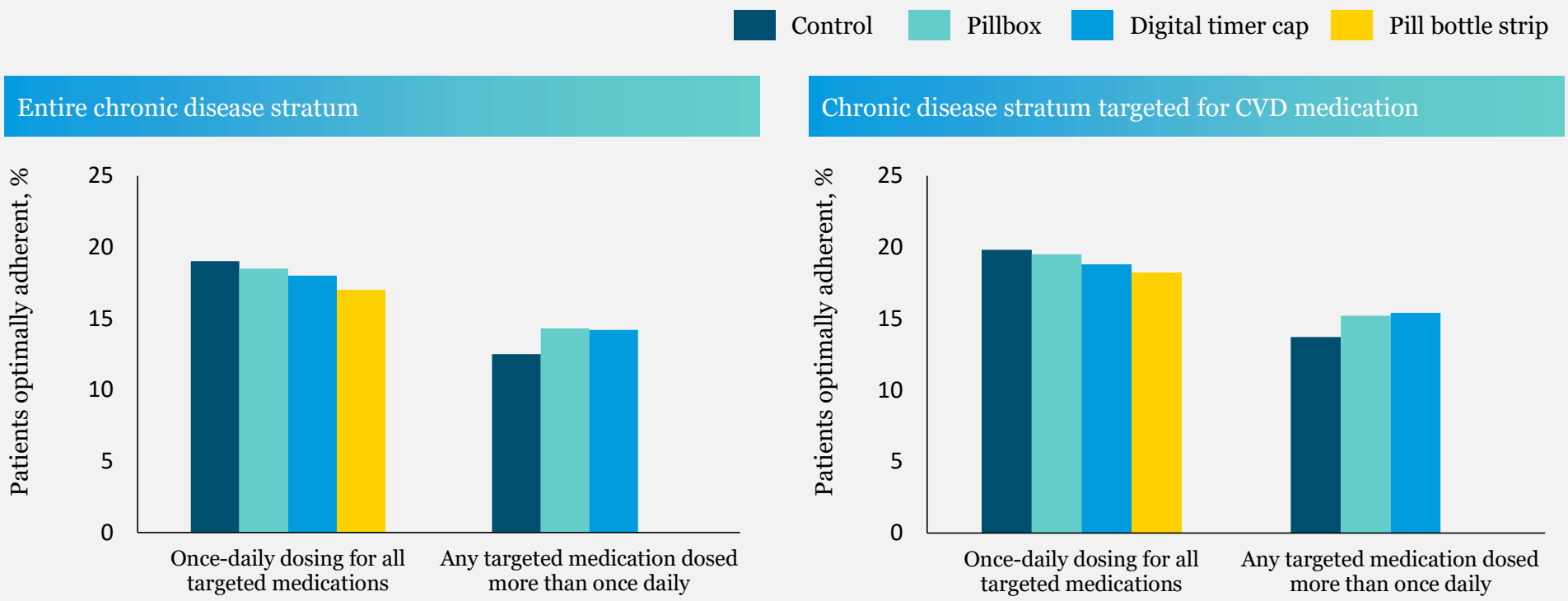
The REMIND randomized clinical trial

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.

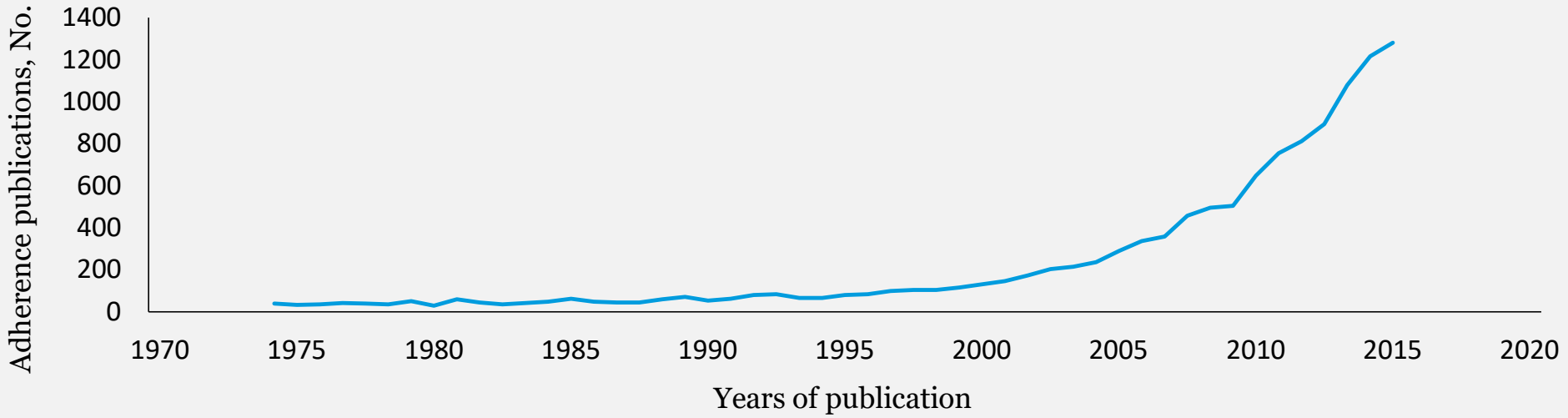
Remind trial: Results (Optimal adherence at 12 months)



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

Adherence research over the years

Forty years of medication adherence research



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

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.

COM-B factors related to non-adherence

Capability

- Forgetting
- Planning/organizing
- Strength/dexterity

Motivation

- Treatment beliefs (necessity/concerns)
- Illness perceptions
- Emotional wellbeing (depression/anxiety)
- Self-efficacy (treatment)

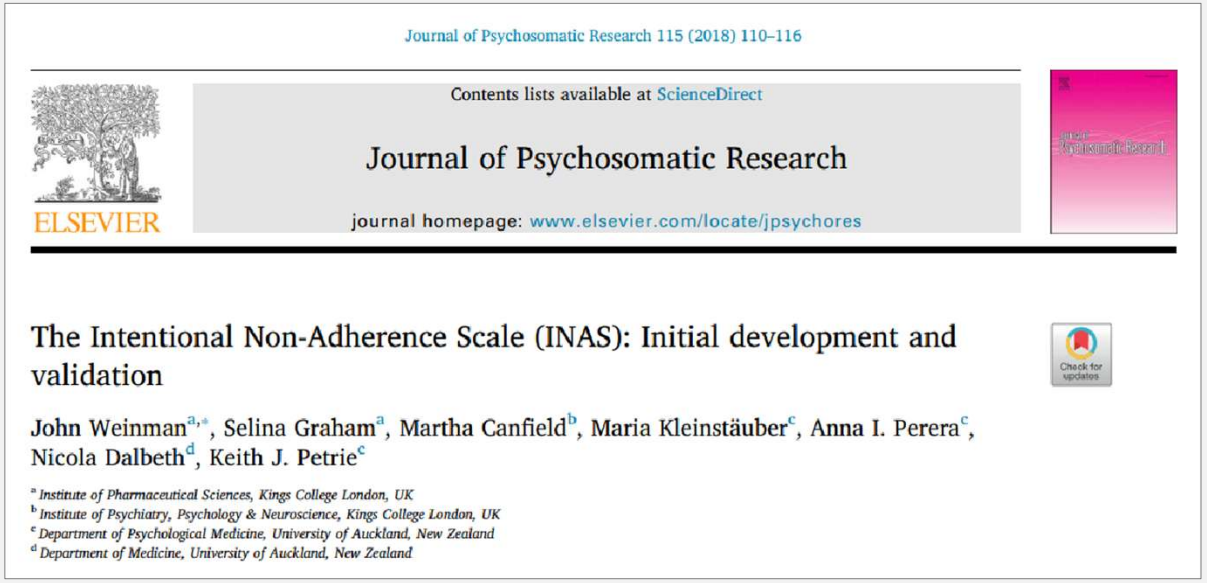
Opportunity

- Relationship with HCP
- Social support
- Finance
- Access to healthcare

Adherence

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.

Self identity & treatment adherence



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journal homepage: www.elsevier.com/locate/jpsychores

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

John Weinman[a,*], Selina Graham[a], Martha Canfield[b], Maria Kleinstäuber[c], Anna I. Perera[c], Nicola Dalbeth[d], Keith J. Petrie[c]

[a] Institute of Pharmaceutical Sciences, Kings College London, UK
[b] Institute of Psychiatry, Psychology & Neuroscience, Kings College London, UK
[c] Department of Psychological Medicine, University of Auckland, New Zealand
[d] Department of Medicine, University of Auckland, New Zealand

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

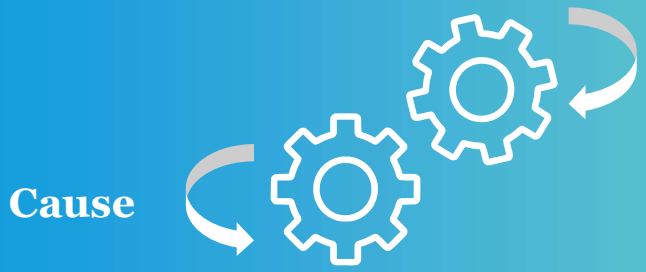
Weinman J, et al. The Intentional Non-Adherence Scale (INAS): Initial development and validation. J Psychosom Res. 2018 Dec;115:110-116

Importance of understanding causes of non-adherence

Adherence is a behavior

To change a behavior:

- Need to know its cause(s)
- Need to use Behavior Change Techniques (BCTs), which target the cause of the behavior



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

Examples of targeted BCTs for non-adherence

Cause	BCT/intervention
Forgetting	Reminders/action plans
Low Necessity Beliefs	Information about consequences non-adherence
High treatment concerns	Pros and Cons
Resisting illness	Acceptance based intervention

Speaker input.

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 & patient

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"

Patient barriers to managing non-adherence in routine care

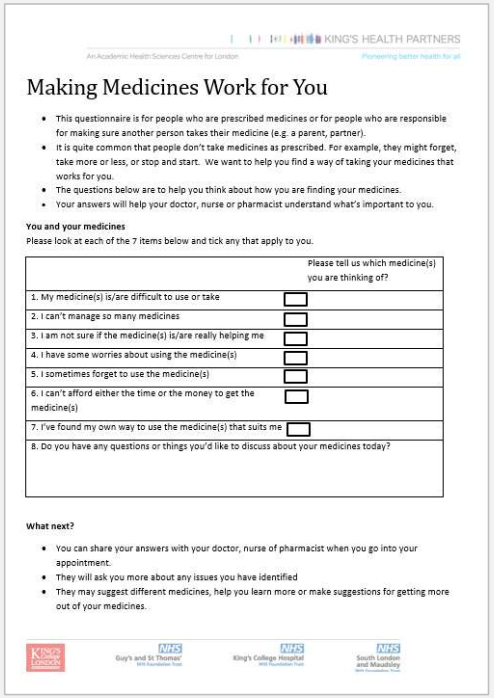
- Hiding non-adherence from the clinician
- Not wishing to disappoint or get “told-off”
- Defensive - in response to direct questioning re adherence
- Motivational and opportunity factors rarely addressed

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]



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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.

King's College London

NHS Guy's and St Thomas' NHS Foundation Trust

NHS King's College Hospital NHS Foundation Trust

NHS South London and Maudsley NHS Foundation Trust

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.

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.)

Adherence support in the consultation: Basic steps

Check patient's understanding of treatment and, if necessary

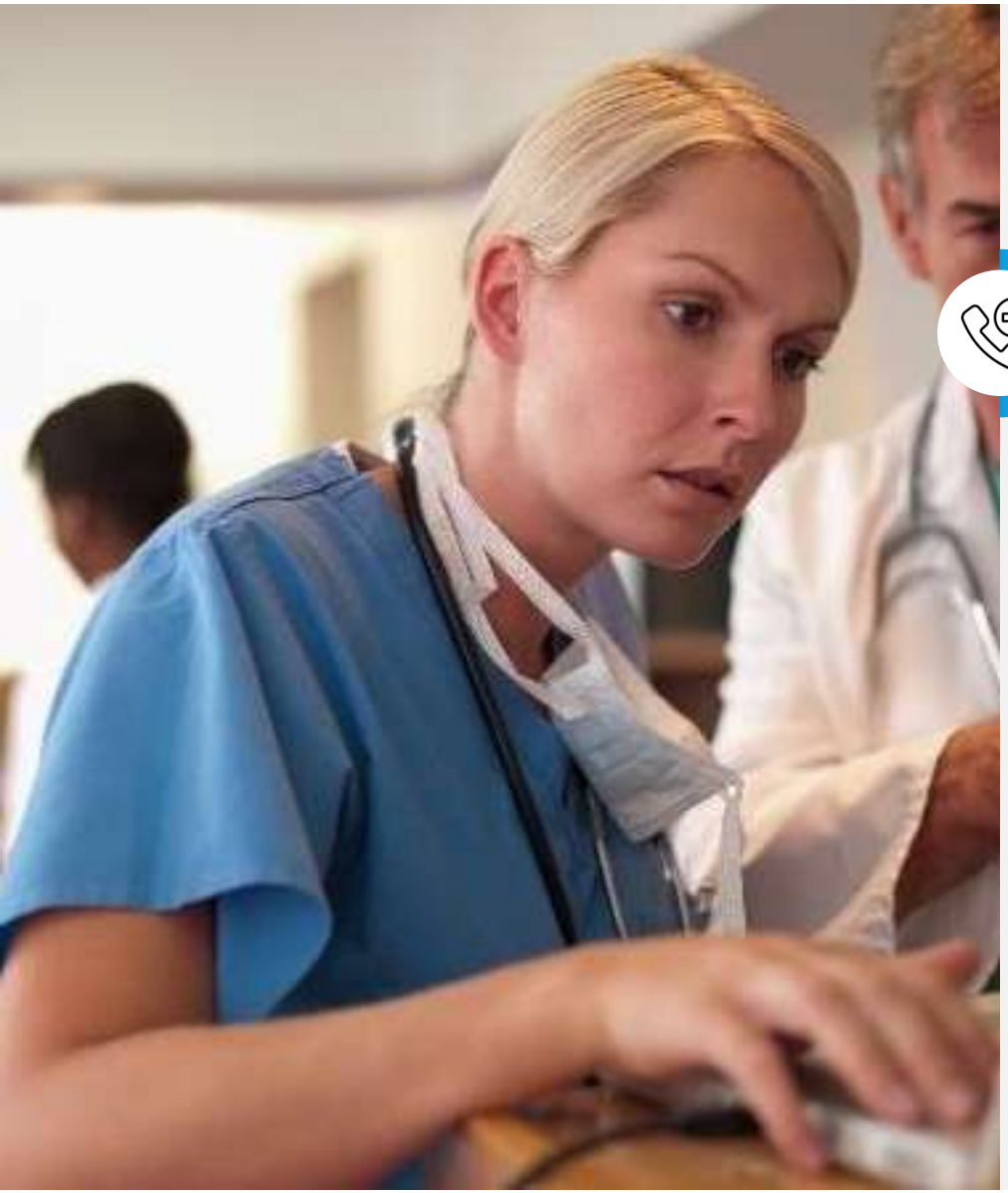
Provide clear rationale for **necessity** of treatment

Elicit and address **concerns**

Agree practical plan for how, where and when to take treatment

Identify any possible barriers & problem solve these collaboratively

Follow up to assess outcome



Adherence often goes unrecognized

Most providers think patients follow our excellent healthcare advice, but they don't!

Why we think our patients adhere:

- Optimistic bias[1]
- Patients tend to exaggerate and want to please us[2]
- We think we can predict who will adhere[3]

1. 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; 2. Rand. C , Wise. R et al: Metered-Dose Inhaler Adherence in a Clinical Trial. American Review of Respiratory Disease, December 1992; 3. 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

Adherence must be addressed

"Increasing the effectiveness of adherence interventions may have far greater impact on health than any improvements in specific medical treatments"[1]

How can we do better with the medications we have?

Is medical care more than writing a prescription?

1. Adherence to long-term therapies: Evidence for action, WHO study, 2003, [Accessed October 2021], https://www.who.int/chp/knowledge/publications/adherence_report/en/

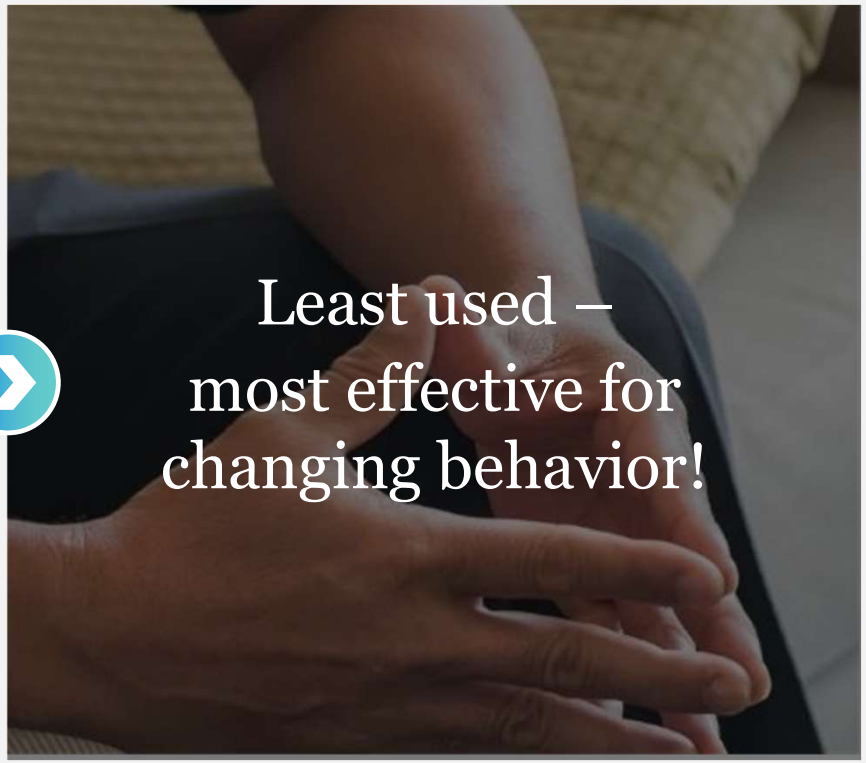
Common communication strategies to influence others

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

Uncommon communication strategies to influence others

- Curious
- Nonjudgmental
- Other-focused
- Empathic
- Collaborative



Three steps to integrate effective communication strategies

1

Strategic, open-ended questions to assess adherence

(curious, nonjudgmental, patient-focused)

2

Empathic response

"You must be feeling _____"

(empathy)

3

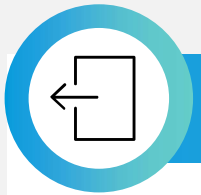
Promise of provider-patient partnership

"We can work together on this"

(collaborative)

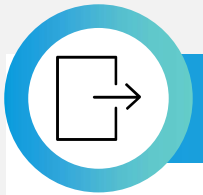
Step 1: Assess adherence with open-ended questions

Examples of what to say



Open

"Some of my patients have difficulties taking the medications as they are supposed to be taken. Over the past 2 weeks, how many days do you think you missed a dose of your medication?"



Closed

"You are taking your medications, right?"

"Are you still taking the medicine I prescribed for you?"

Step 2: Provide empathic responses

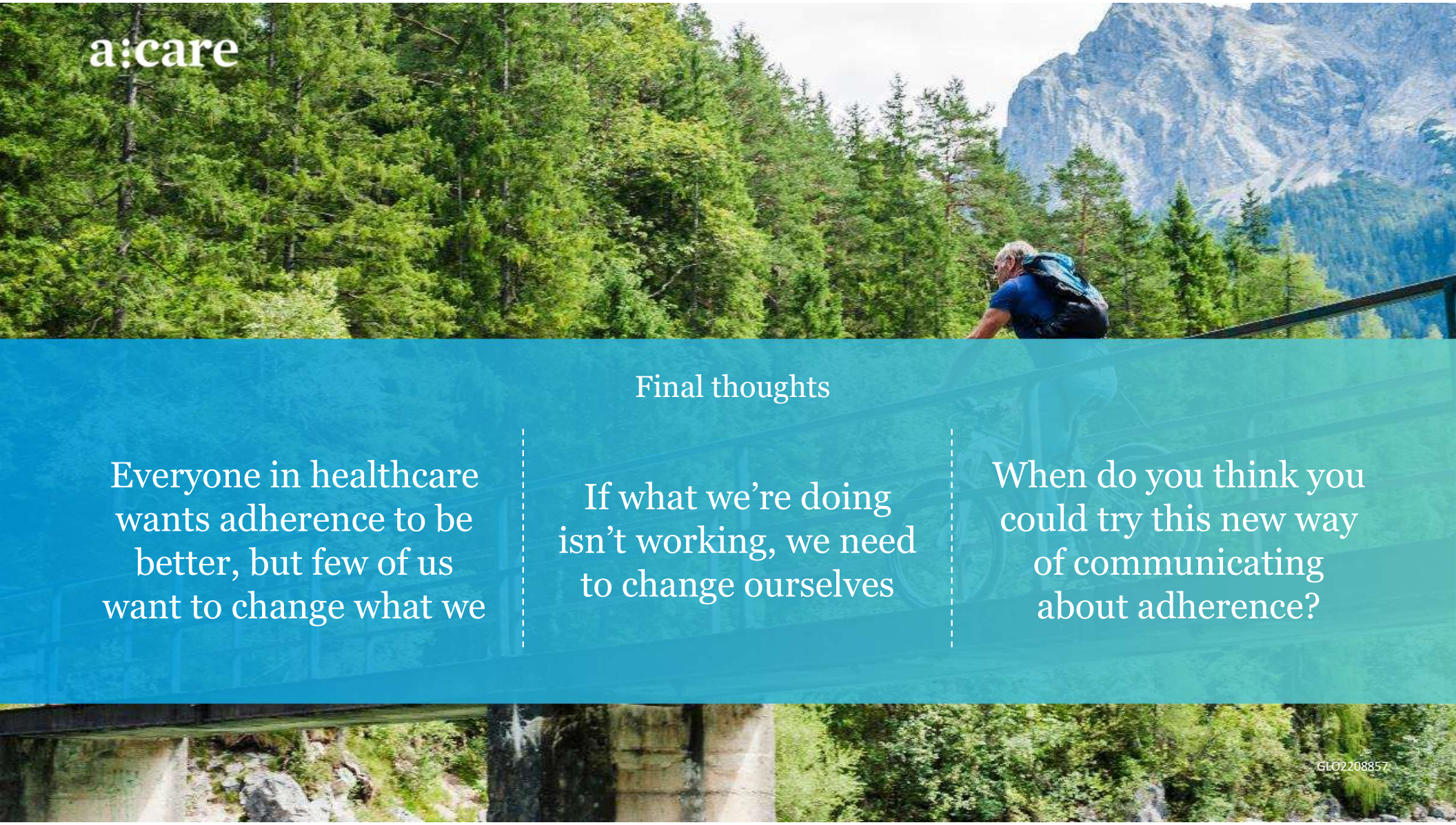
Examples of what to say

- 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 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

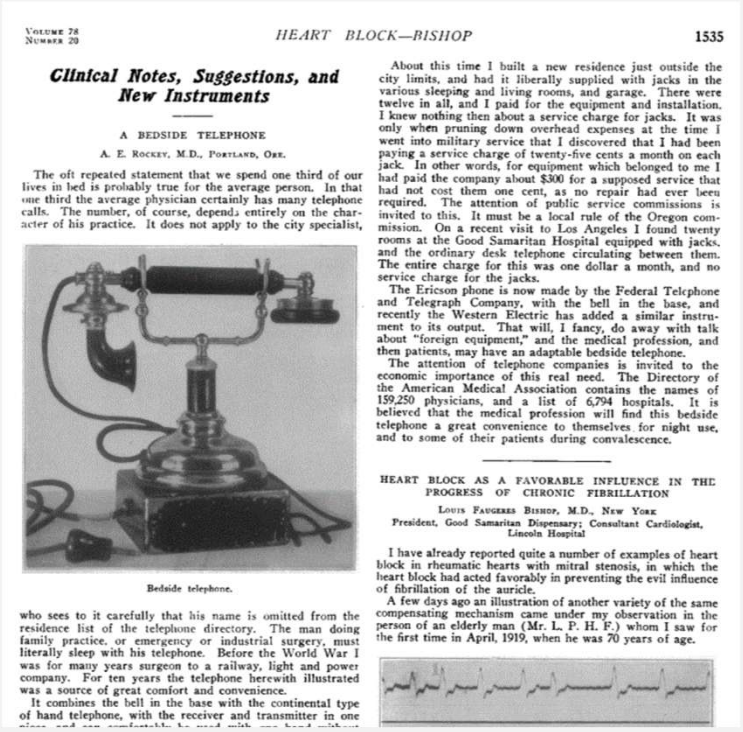


Final thoughts

Everyone in healthcare wants adherence to be better, but few of us want to change what we

If what we're doing isn't working, we need to change ourselves

When do you think you could try this new way of communicating about adherence?



VOLUME 78
NUMBER 20

HEART BLOCK—BISHOP 1535

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 herewith 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

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 $300 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 159,250 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.

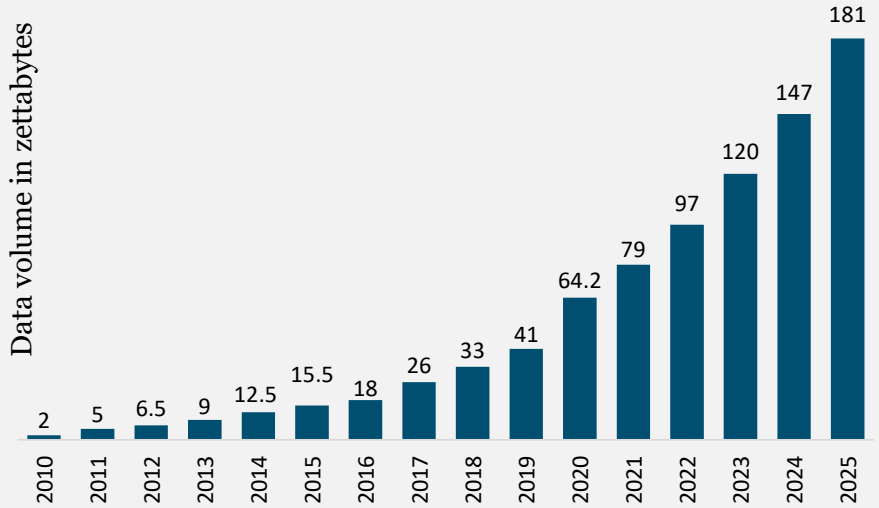
A few days ago an illustration of another variety of the same compensating mechanism came under my observation in the person of an elderly man (Mr. L. P. H. F.) whom I saw for the first time in April, 1919, when he was 70 years of age.

"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"

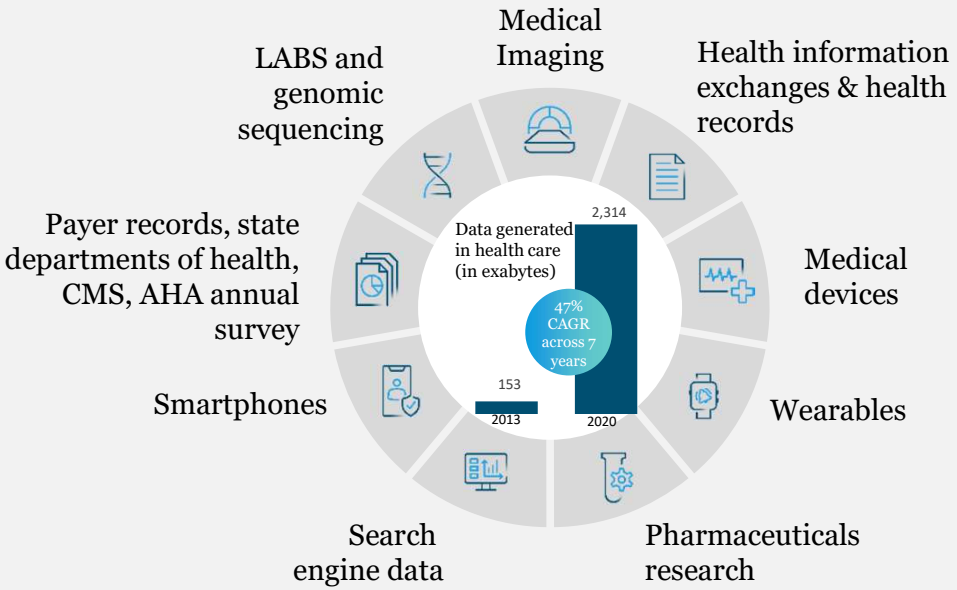
Rockey AE. Clinical Notes, Suggestions, and New Instruments. A bedside telephone. JAMA. 1922;78(20)1535.

So much DATA!

Between the years 2010-2025, it is estimated that the total amount of data created in a 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 Health Care Revolution. Infographic based on the Health Trends Reports Stanford Medicine 2017 « Harnessing the Power of Data in Health » Stanford Medicine 2017.

Transforming Cardiovascular Care With Artificial Intelligence: From Discovery to Practice

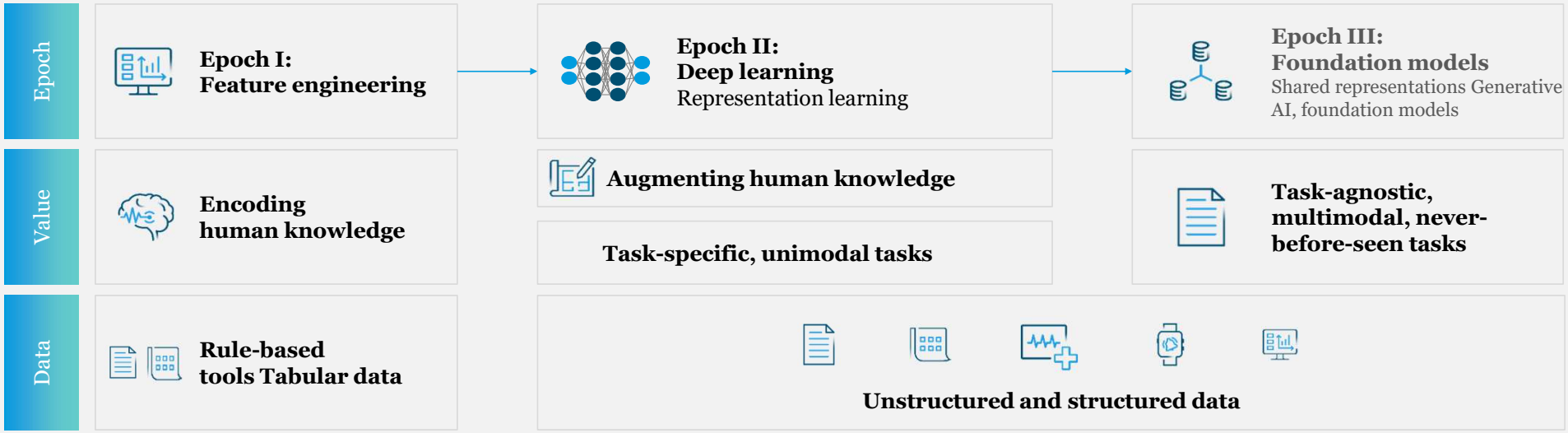
JACC State-of-the-Art Review

Rohan Khera, MD, MS,[a,b,c,d] Evangelos K. Oikonomou, MD, DPhil,[a] Girish N. Nadkarni, MD, MPH,[e,f] Jessica R. Morley, PhD,[g] Jenna Wiens, PhD,[h] Atul J. Butte, MD, PhD,[i,j] Eric J. Topol, MD[k]

JAMA | Special Communication | AI IN MEDICINE

Three Epochs of Artificial Intelligence in Health Care

Michael D. Howell, MD, MPH; Greg S. Corrado, PhD; Karen B. DeSalvo, MD, MPH, MSc



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 Health Care. JAMA. 2024;331(3):242-4.

The San Diego Union-Tribune

Can chatbots handle medical questions better than doctors? UCSD study says yes

John W. Ayers, a UC San Diego computational epidemiologist, led a team that explored using a chatbot to answer routine medical questions. (John Gibbins)

ChatGPT often answered routine questions on Reddit with more empathy than busy human doctors

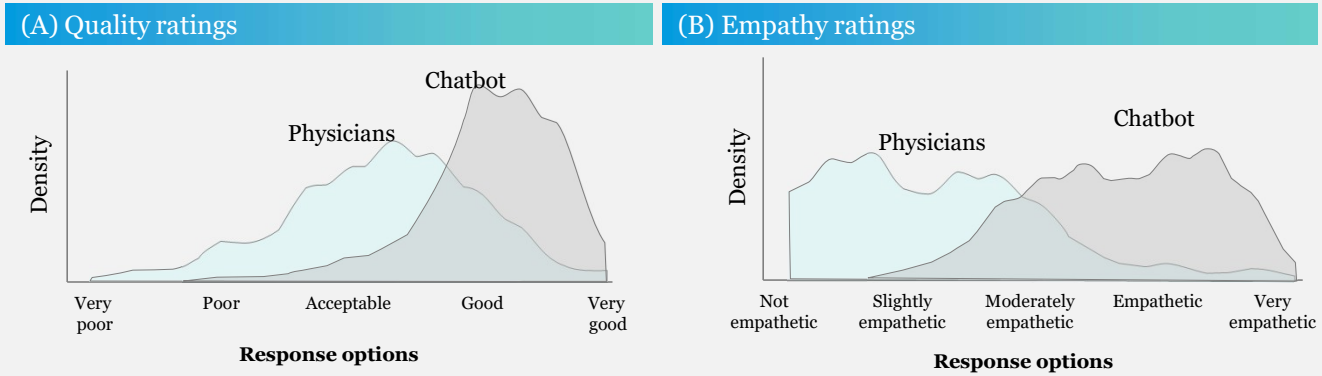
BY PAUL SISSON

APRIL 28, 2023 9:58 AM PT

JAMA Internal Medicine | Original Investigation

Comparing Physician and Artificial Intelligence Chatbot Responses to Patient Questions Posted to a Public Social Media Forum

John W. Ayers, PhD, MA; Adam Poliak, PhD; Mark Dredze, PhD; Eric C. Leas, PhD, MPH; Zechariah Zhu, BS; Jessica B. Kelley, MSN; Dennis J. Faix, MD; Aaron M. Goodman, MD; Christopher A. Longhurst, MD, MS; Michael Hogarth, MD; Davey M. Smith, MD, MAS



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-medical-questions-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.

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: 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.

What are the perceived shortcomings of AI?

Physician

- Fear of alienation and reduced interaction between patients and physicians
- De-skill in observations and recognizing emotions in humans

Patient

- AI cannot provide emotional support or empathy to them
- 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.

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

GLO2329521

Sparrow R and Hatherley J. High hopes for "deep medicine"? AI, economics, and the future of care. Hastings Cetn Rep 2020; 50: 14–17

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 healthcare providers. 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.

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.

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.

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)

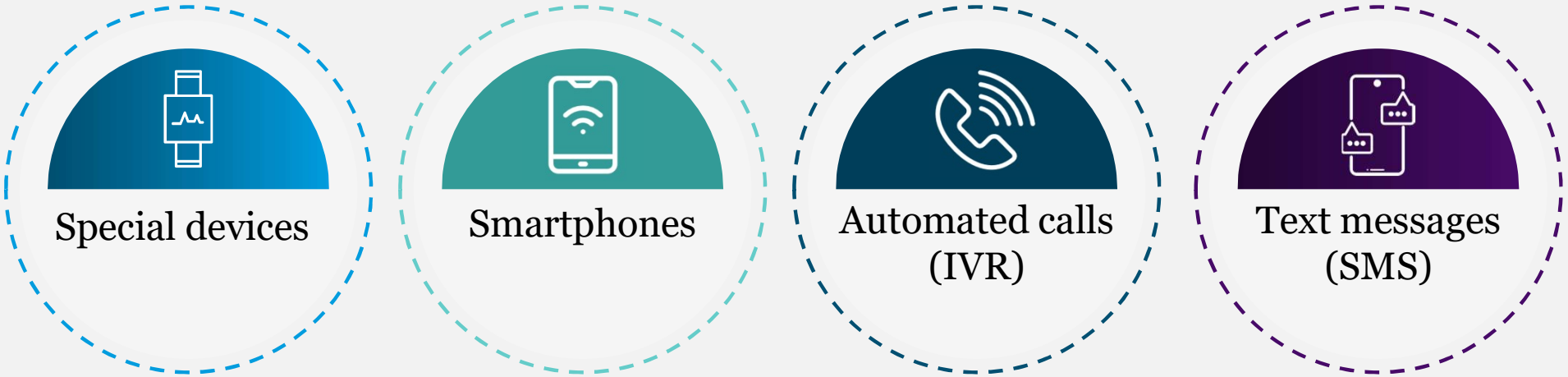
A digital solutions can be defined along three dimensions

Sociodemographic population served

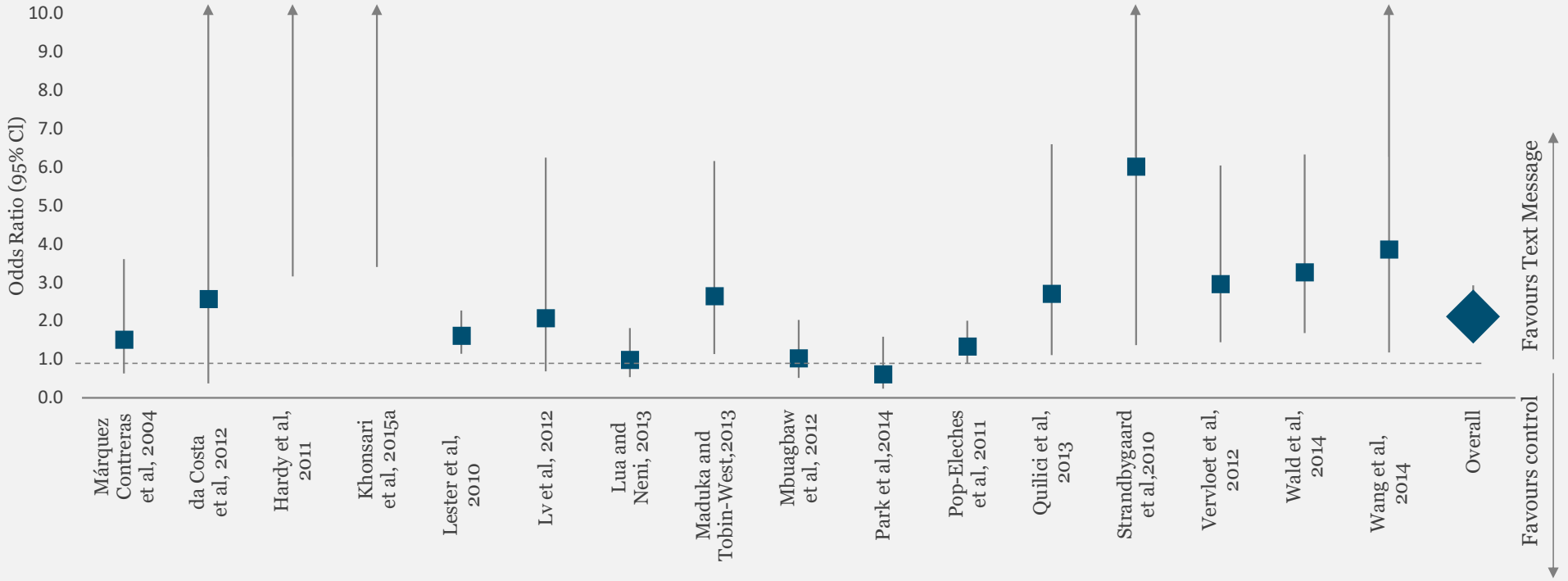
Mobile technologies and communication channels

Program goals and functions

Mobile technologies for improving self-care support



Mobile telephone text messaging for medication adherence in chronic disease a meta-analysis[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%200f%2017.8%25.

Text Messaging for Disease Monitoring in Childhood Nephrotic Syndrome

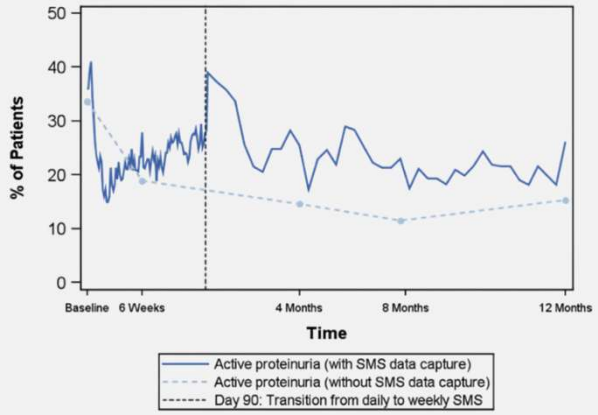


Figure 4: Percentage of patients with nephrotic range proteinuria as captured by short message service (SMS) reporting versus in-person clinic visits

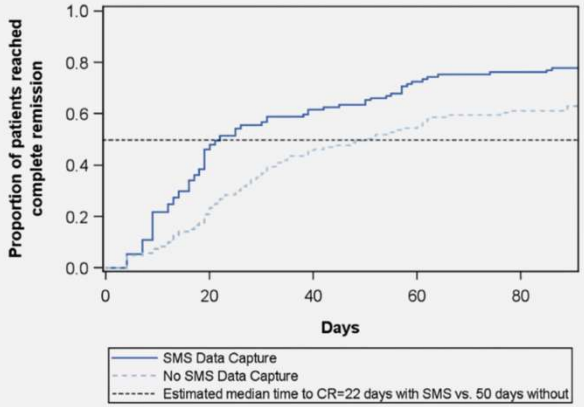


Figure 5: Time to remission after study enrolment by short message service (SMS)- captured urine protein results versus participant reporting during in-person study visits. CR, complete remission

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

GLO2208858

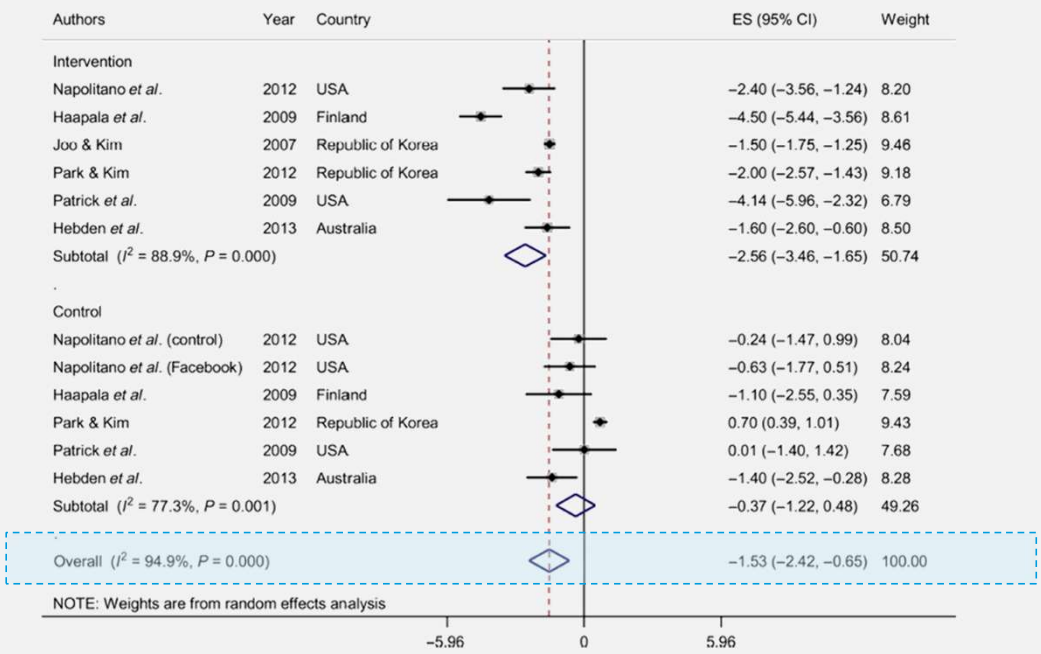
Interventions for weight management using text messaging

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

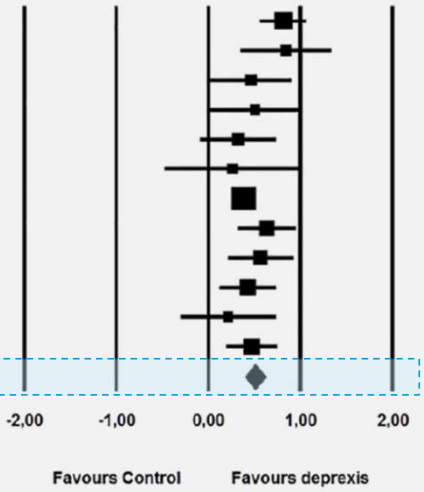
Tailored integrative Internet intervention for depression

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]

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)	0,46	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



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

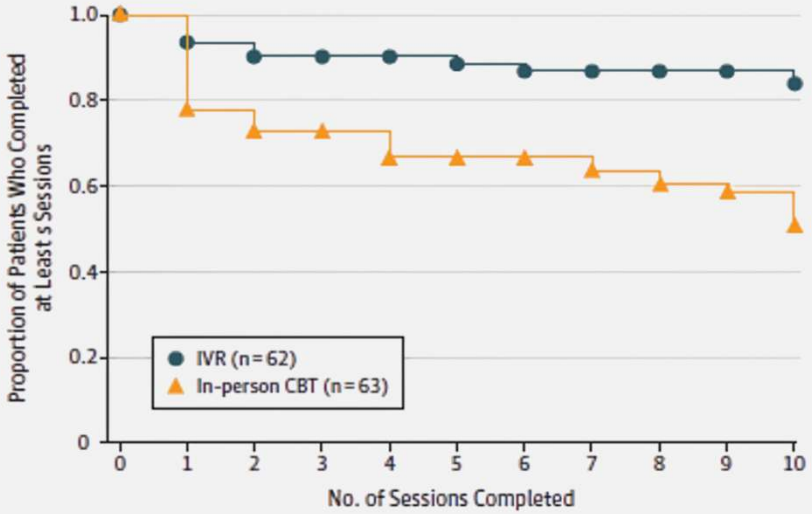
GLO2208858

JAMA Internal Medicine | Original investigation

Interactive Voice Response-Based Self-management for Chronic Back Pain

The COPES Noninferiority Randomized Trial

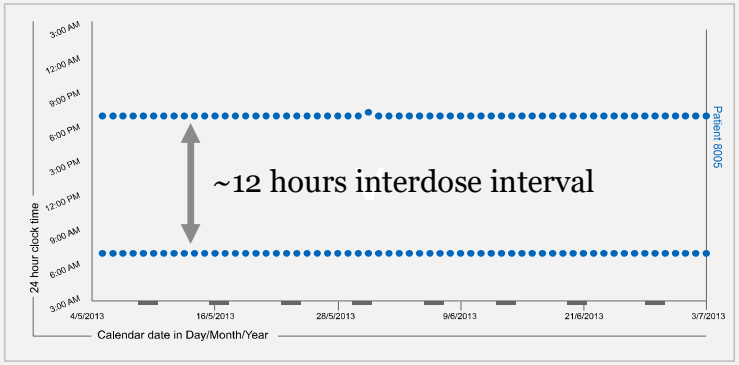
Number of treatment weeks by condition



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.

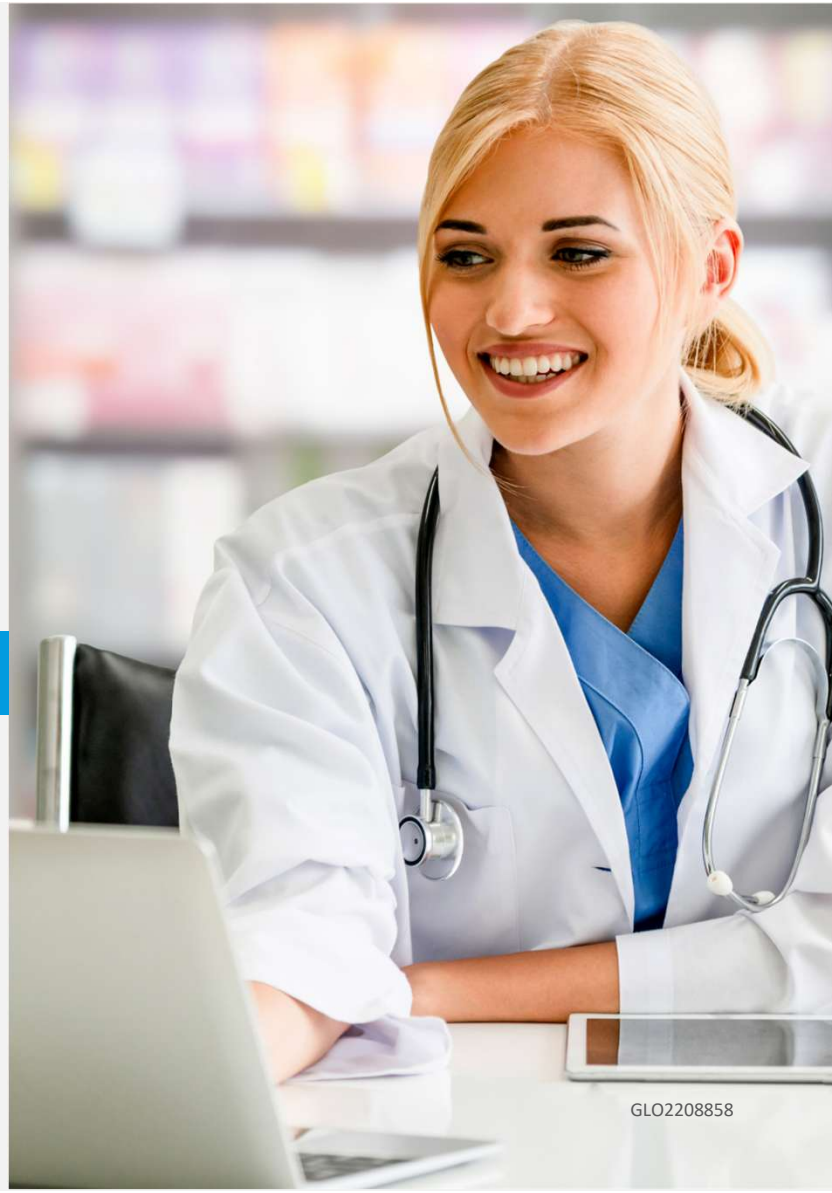
Medication Intake Behavior



You can't manage what you don't measure

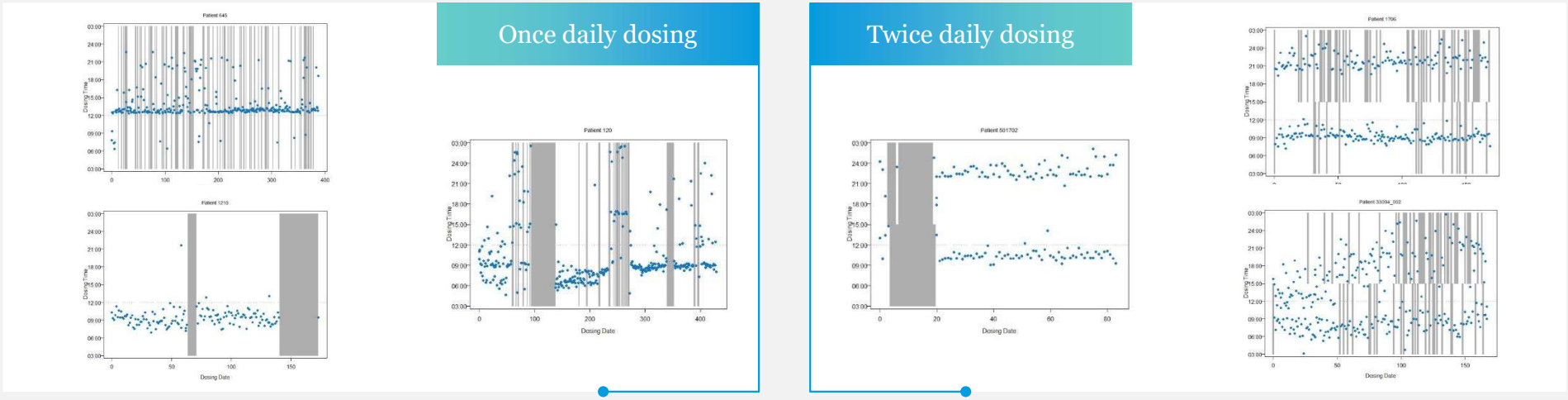
Measure

Manage



The Unfortunate 80% Rule!

Each of these 6 patients took the same percentage (81%) of prescribed doses, which sounds good, but look

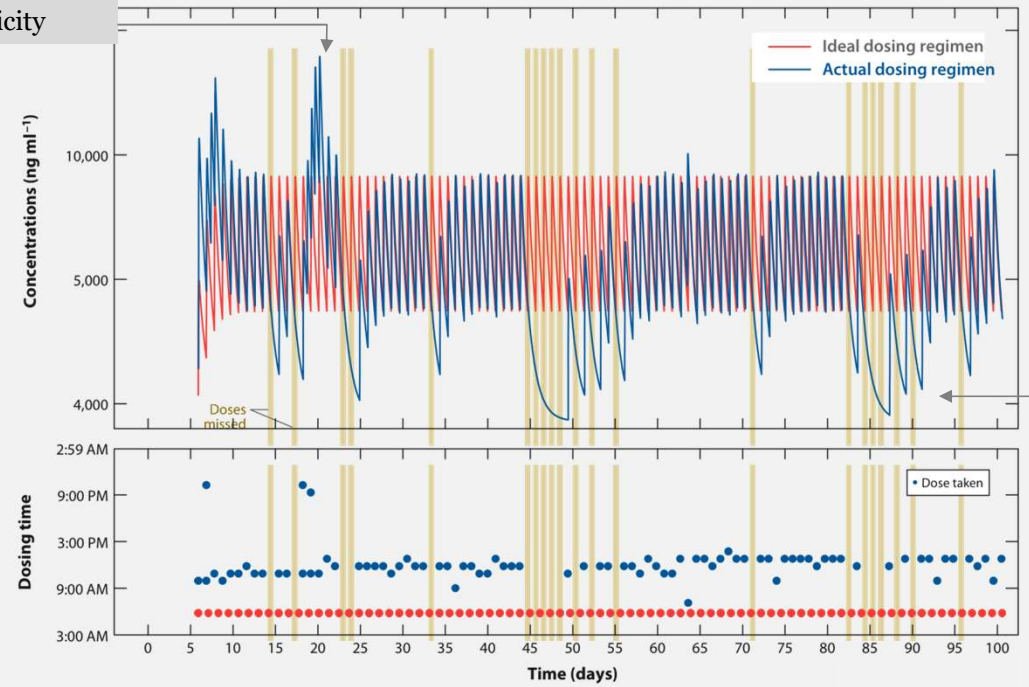


The variability in all these cases poses a significant risk to clinical success

Vrijens B et al., Assessment of medication adherence in field research, First Edition, John Wiley & Sons, Ltd., 2016

Variable adherence creates drug-specific issues of efficacy, safety & drug resistance

Occasional toxicity



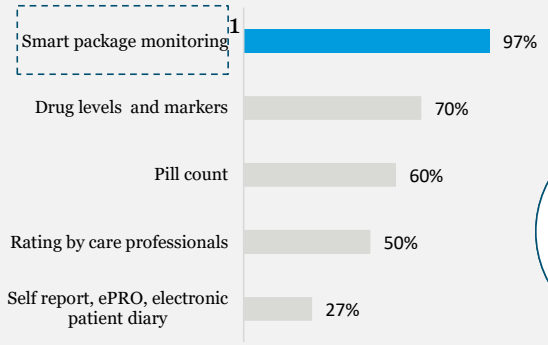
Periodic loss of effectiveness & emergence of drug resistance

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.

The Scientific Evidence

Measure

Accuracy of the measurement methods



- Accurate & continuous measure
- No burden for the patients
- Available for all patients included

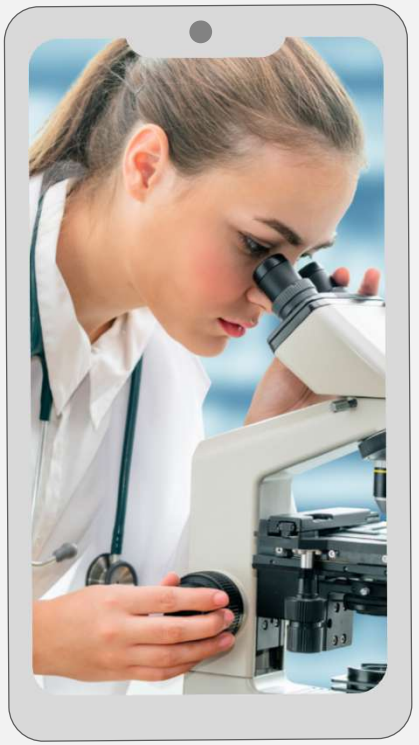
&

Manage

↑20%

Up to ↑ 50%

Data-driven adherence feedback is the most effective means to empower patients and improve adherence



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 meta-analysis. Drugs. 2013 May;73(6):545-62.

Empower Patients and Providers

- 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 providers' time)

Digitally-Enabled Integrated Person-Centred Care[1]

Benefits for all stakeholders – time is ripe for a change!

Patients

- Improves quality, safety, and effectiveness of medications
- Greater patient awareness and participation in care

Providers

- Better use of time allocation
- Emergence of new forms of collaboration and multidisciplinary approaches

Payers

- Decrease healthcare expenditures on chronic therapies
- Improve return on Rx spend by improving outcomes and reducing wastage

Industry

- Maximise value of the molecule to sustain high growth
- Improve image, retain patients

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.

The pandemic of unintended pregnancies

Unintended pregnancy and abortion are experiences shared by people around the world[1]

These reproductive health outcomes occur irrespective of country income level, region or the legal status of abortion

Roughly 121 million unintended pregnancies occurred each year between 2015 and 2019[2]

Of these unintended pregnancies, 61% ended in abortion. This translates to 73 million abortions per year[2]

- Unintended pregnancies have a higher risk of obstetrical complications[3]
- Negative psychosocial consequences for the woman and the newborn especially in adolescents[3]

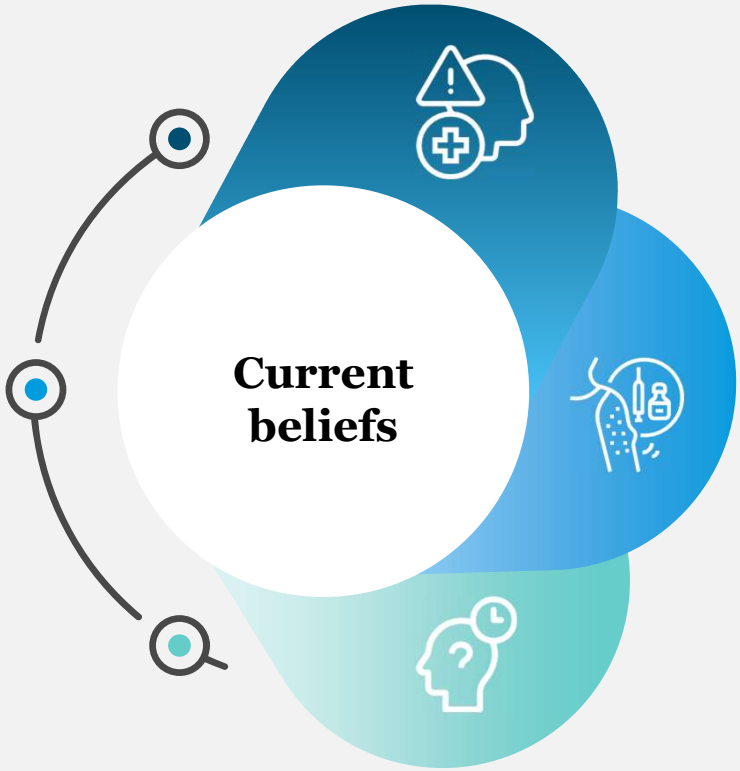
1.RCOG and FSRH key messages on safe abortion. https://www.rcog.org.uk/globalassets/documents/global-network/projects-and-partnerships/making-abortion-safe/rcog-and-fsrh-key-messages-on-safe-abortion.pdf [Accessed October 2021]; 2. Bearak J et al, Unintended pregnancy and abortion by income, region, 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.

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

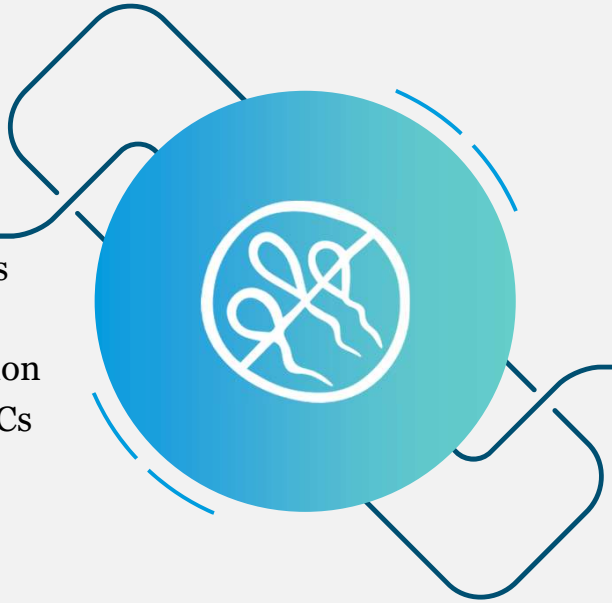


How to improve adherence in Contraception

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.

The right method

Combined oral contraceptives

EE dose
15 µg
20 µg
25 µg
30 µg
35 µg
≥ 50 µg

Progestogen type
Norethisterone
Levonorgestrel
Gestodene
Chlormadinonacetate
Desogestrel
Drospirenone
Cyproterone acetate
Dienogest
NOMAC

Regimen
21/7
24/4 or 26/2
Continuous

Estradiol 1.5
E2V 2,0

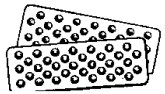
Mono, Bi, Triphasic

Long acting reversible contraceptives

Hormonal contraceptives

Non-daily (non-oral) Contraceptives

Progesterone only pills



Progestogen type
Norethisterone
Ethynodiol diacetate
Levonorgestrel
Desogestrel

Nonhormonal contraceptives

Clinician dependent

Not clinician dependent

The right woman

GLO2208860

What do doctors want, what do women want?

The health care professional

Maximize efficacy

Realize additional health benefits | **Medical Counselling** | **Optimize tolerability**

Minimize health risks

Cost effectiveness

The patient, client, user

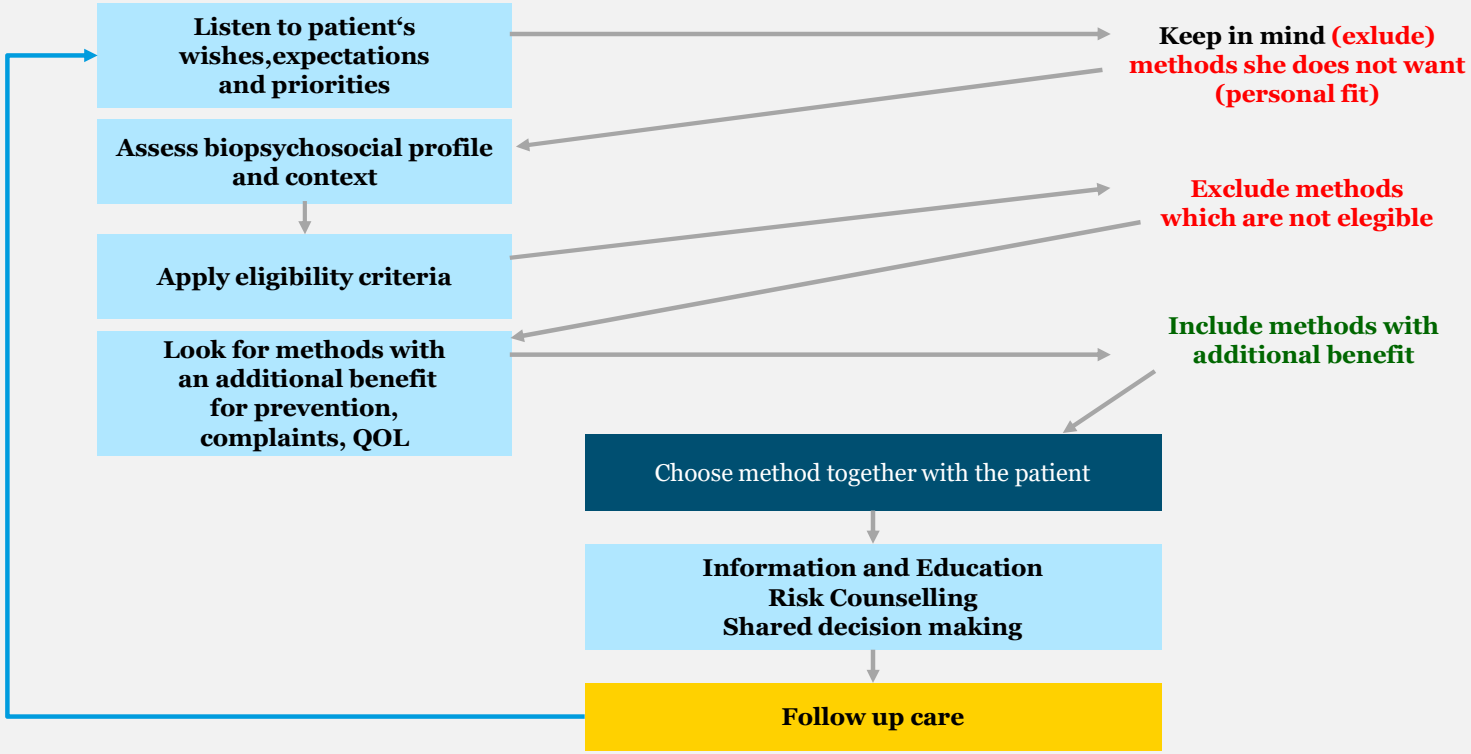
Maximal efficacy

Independent of partner		Easy to use
Under the control of the woman		Linked/ not linked to sexual activity
Additional health benefits	**Individualized Counselling**	**Optimal tolerability**
Discrete		On demand
Low Cost		Forgettable

Minimal health risks

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 Health Care. 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 Health Care. 2021 Aug;26(4):326-333.

The Contraceptive Dialogue



Step 1
Exclusion based on the patients, preferences

Step 2
Exclusion based on Medical Eligibility Criteria

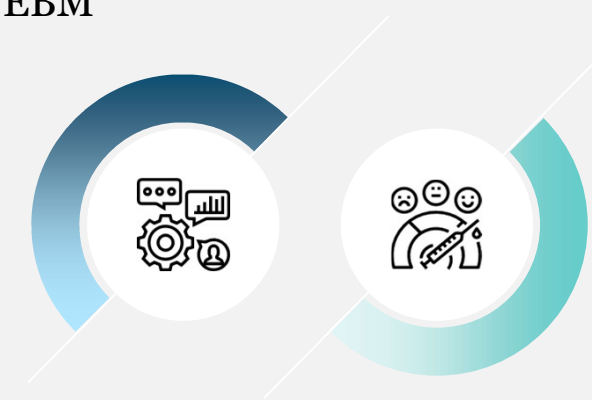
Step 3
Among the methods left look for additional benefits

Step 4
Informed Consent and Shared decision making

Step 5
Follow-up visits: satisfaction, proper use, QoL

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

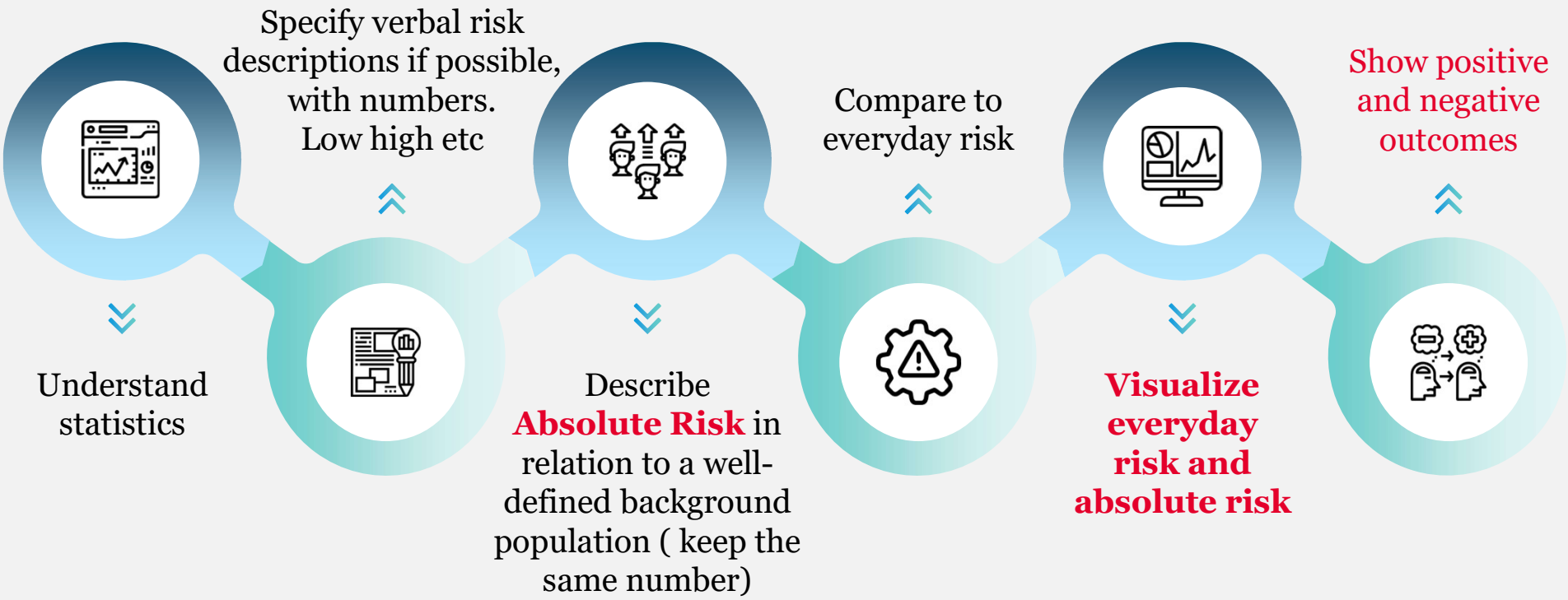
Elicit
- Needs, knowledge, expectations, experience

Provide
- Small units of
- information, Structurizing,
- Summarizing

Elicit
- Understaning, Interpretation

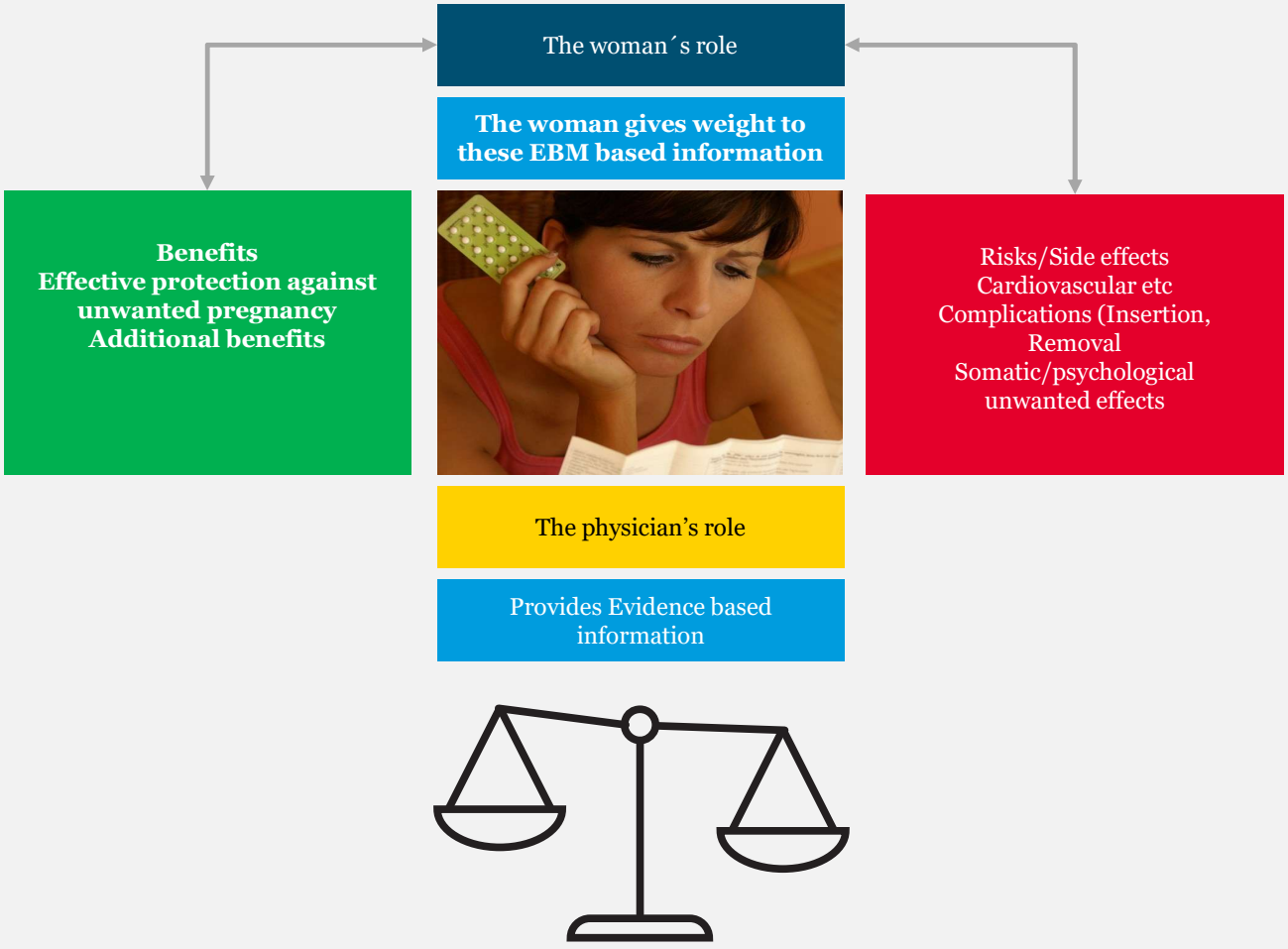
Bitzer J, Marin V, Lira J. Contraceptive counselling and care: a personalized interactive approach. Eur J Contracept Reprod Health Care. 2017 Dec;22(6):418-423

Recommendations and guidelines for risk counselling



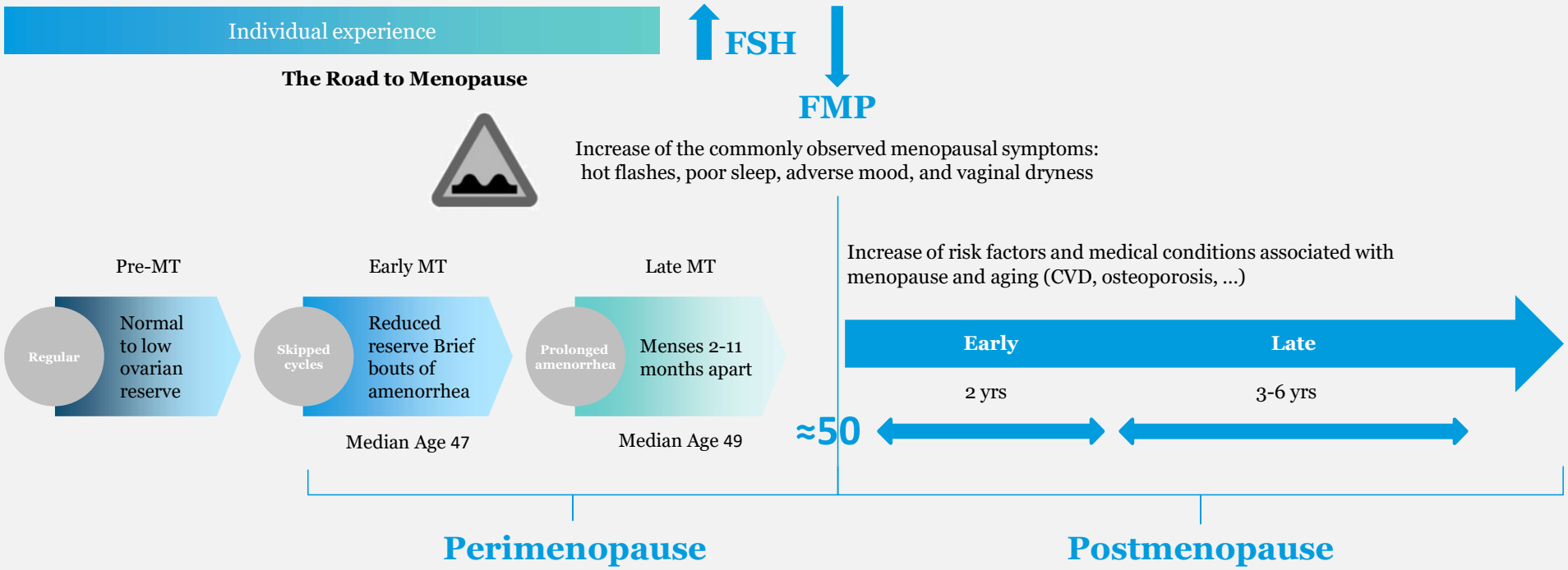
Bitzer J, Marin V, Lira J. Contraceptive counselling and care: a personalized interactive approach. Eur J Contracept Reprod Health Care. 2017 Dec;22(6):418-423

Contraceptive counselling and care is a continuous benefit/ risk evaluation-trade off



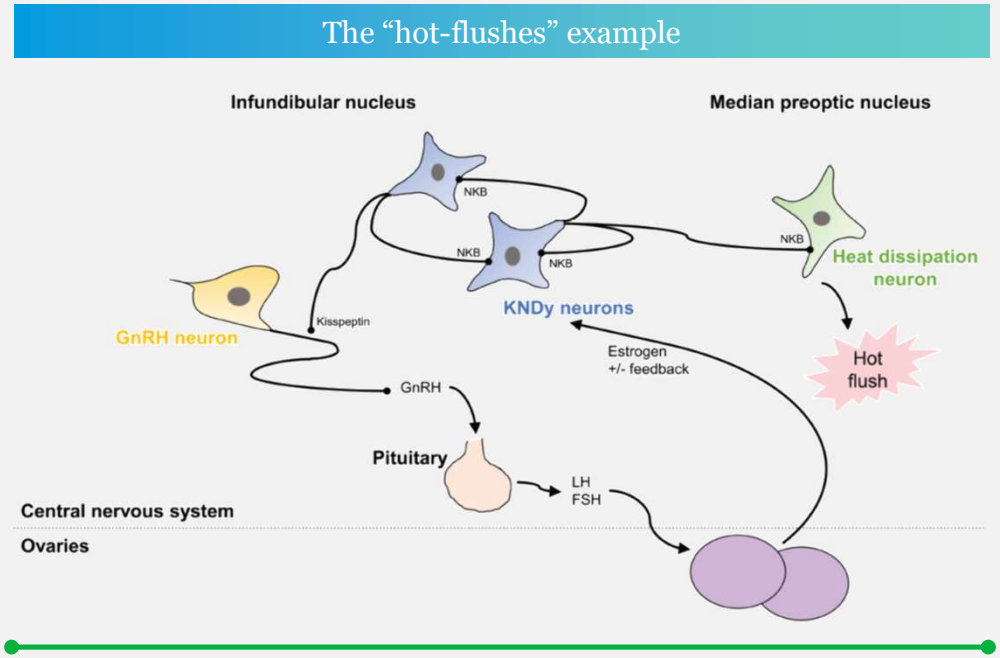
Bitzer J, Marin V, Lira J. Contraceptive counselling and care: a personalized interactive approach. Eur J Contracept Reprod Health Care. 2017 Dec;22(6):418-423

Menopause is a long journey

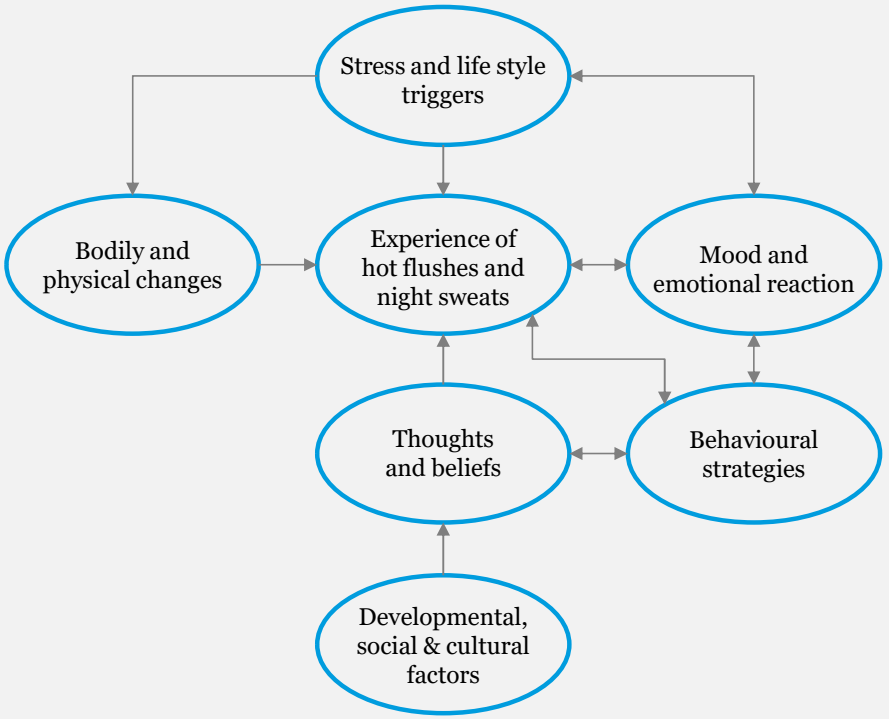


Santoro N. Perimenopause: From Research to Practice. J Womens Health (Larchmt). 2016 Apr;25(4):332-9. Epub 2015 Dec 10.; Harlow Sd et al.; STRAW 10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. Menopause. 2012 Apr;19(4):387-95; The NAMS. Keeping your heart healthy at menopause https://www.menopause.org/for-women/menopauseflashes/bone-health-and-heart-health/keeping-your-heart-healthy-at-menopause [Accessed October2021]

Menopause is a bio-psycho-socio-cultural process

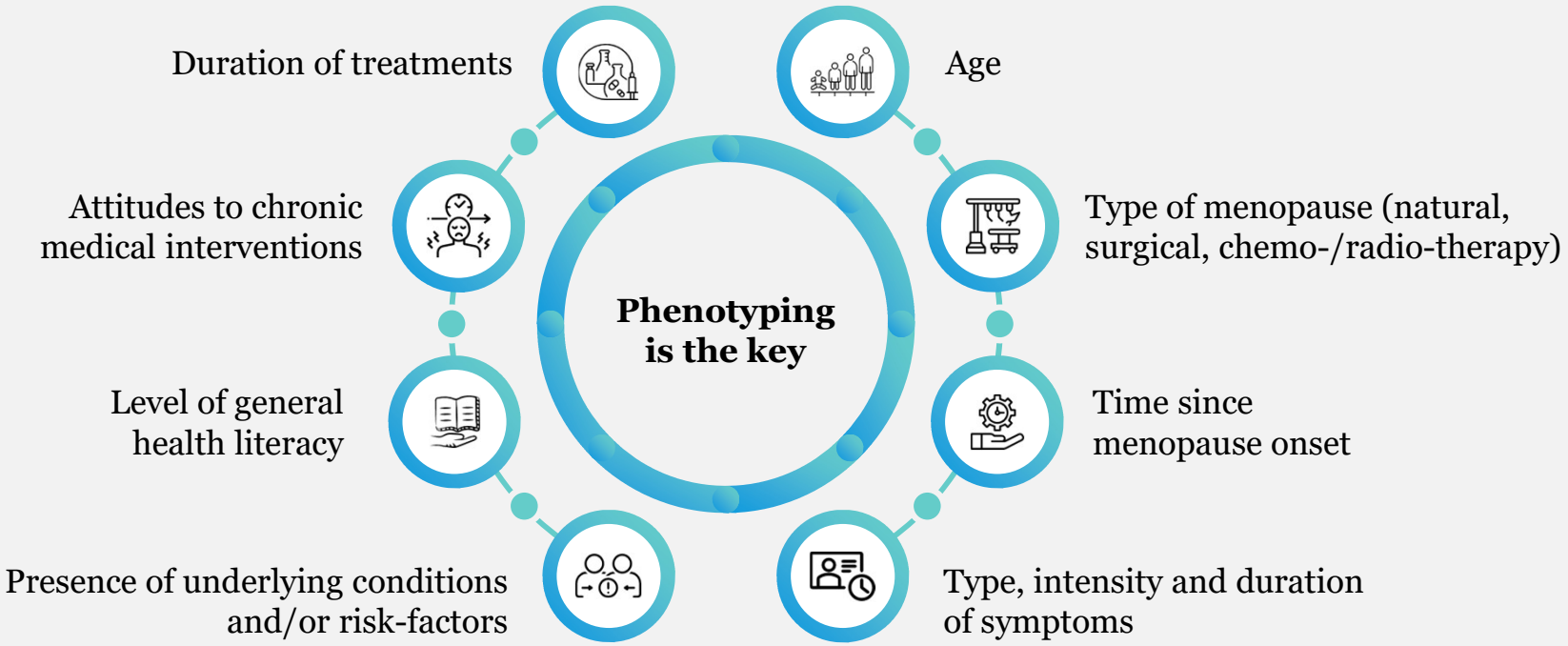


Neuroendocrine mechanisms interact with other dimensions



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.

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.

Specific challenges at menopause

Menopause should be treated like any other medical condition, especially if distressing symptoms and/or specific risk factors are present

- Collect history
- Share information
- Take decisions
- Make appropriate follow-up

Benefit-risk evaluation may be difficult

- Lack of awareness
- Sensitive topics
- Goals and Concerns
- Complex data environment

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.

Successful communication at menopause

OARS

Open questions that encourage further elaboration and consideration	Affirmations that foster positive feelings during the consultation	Reflections that indicate the clinician has heard and accurately understood the patient	Summaries that extend the basic reflections to include additional information
O **Open questions**	**A** **Affirmations**	**R** **Reflections**	**S** **Summaries**
"What do you know about the symptoms of menopause?" "What do you know about taking hormones at the time of menopause?"	"Those hot flushes must be very uncomfortable"	"I understand that you would like to consider treatment options for your symptoms but have some questions"	"Every woman's experience with menopause is her own. We can tailor HT to your specific needs and work to maximize the potential benefits and minimize the potential risks"

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.

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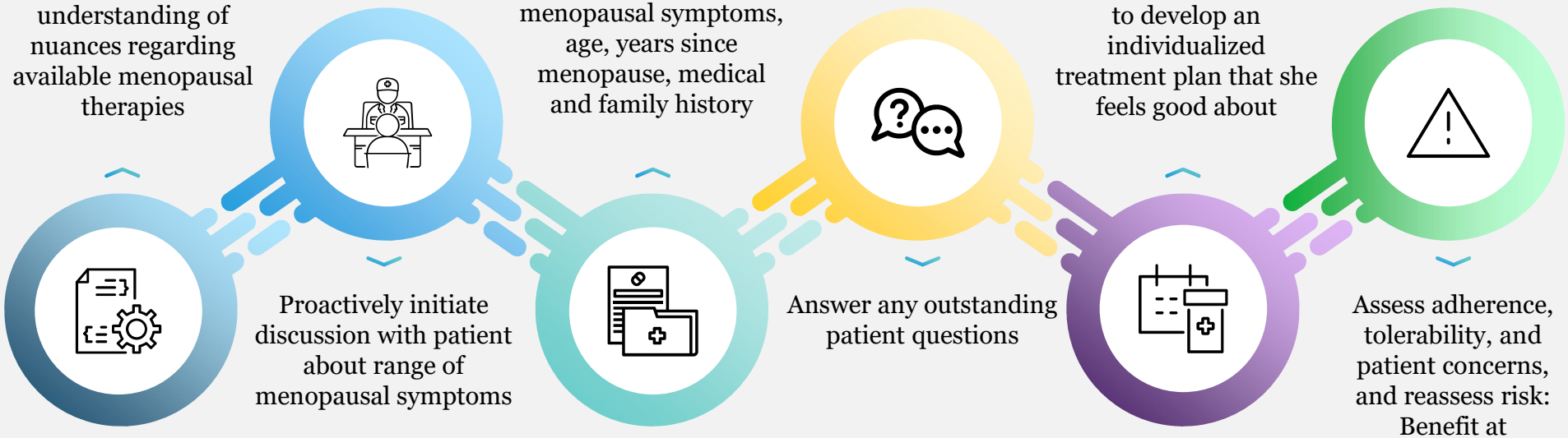
Individualizing discussions with women about treatment of menopausal symptoms



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

Method

Overview | **Health economic model simulation** to estimate benefit of improving adherence during **lifetime** time horizon

Optimal adherence scenario

- Expected outcomes of lipid-lowering agents from **model simulation** using input from **meta-analysis of RCTs and retrospective studies**[1,2]

Status quo scenario

- Current level of adherence

Mexico[3]	Thailand[4]	China[2]
50%	53%	19%

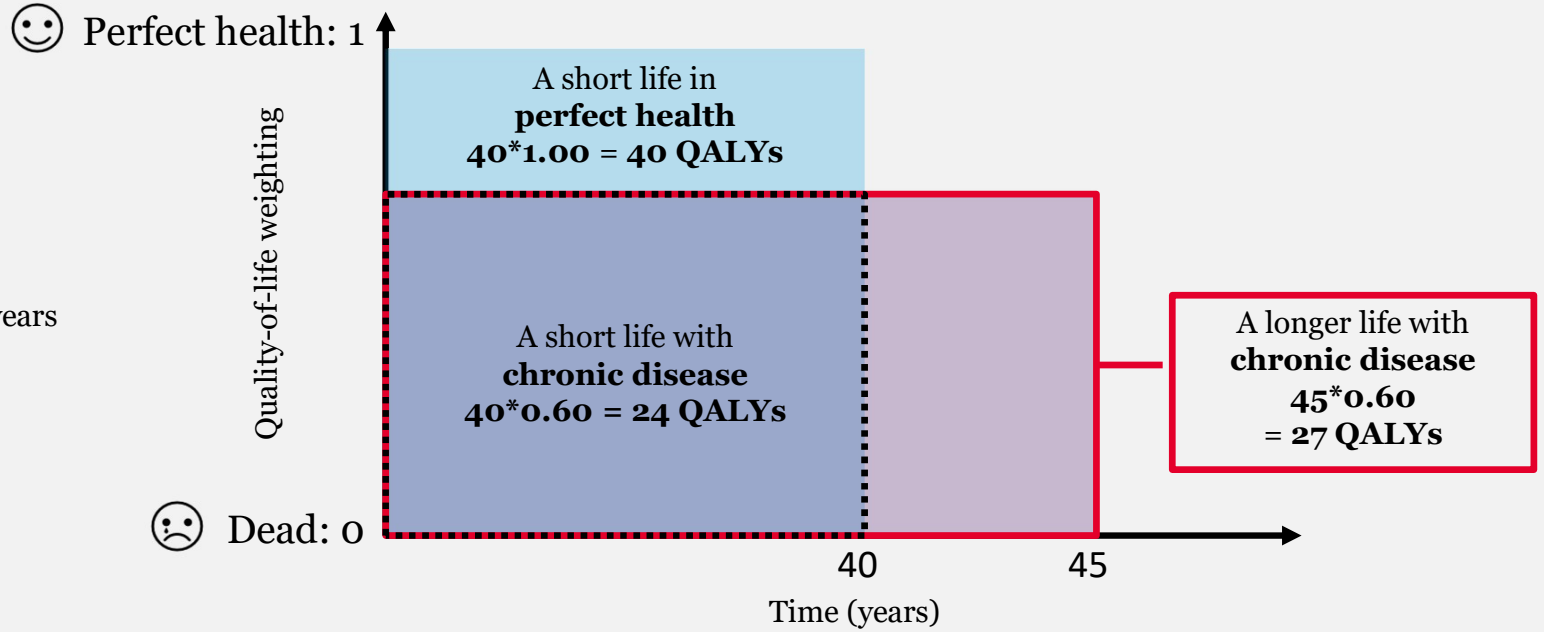
RCT: Randomized controlled trial;

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.

Method

Outcomes

- Number of cardiovascular events
- Life year
- Quality adjusted life years
- Medical costs



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.

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

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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

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

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 quality-adjusted life years** 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

Cardiovascular diseases

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 & 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/indicator-metadata-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 lipid-lowering 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

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

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 providers. **IC** -Public information/education campaigns targeting patients **DTI -** Data & technology infrastructure.

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.

Current spend of health & 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

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 health care problem. Acta méd. Grupo Ángeles. 2018;16(3):226-232.

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 providers

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

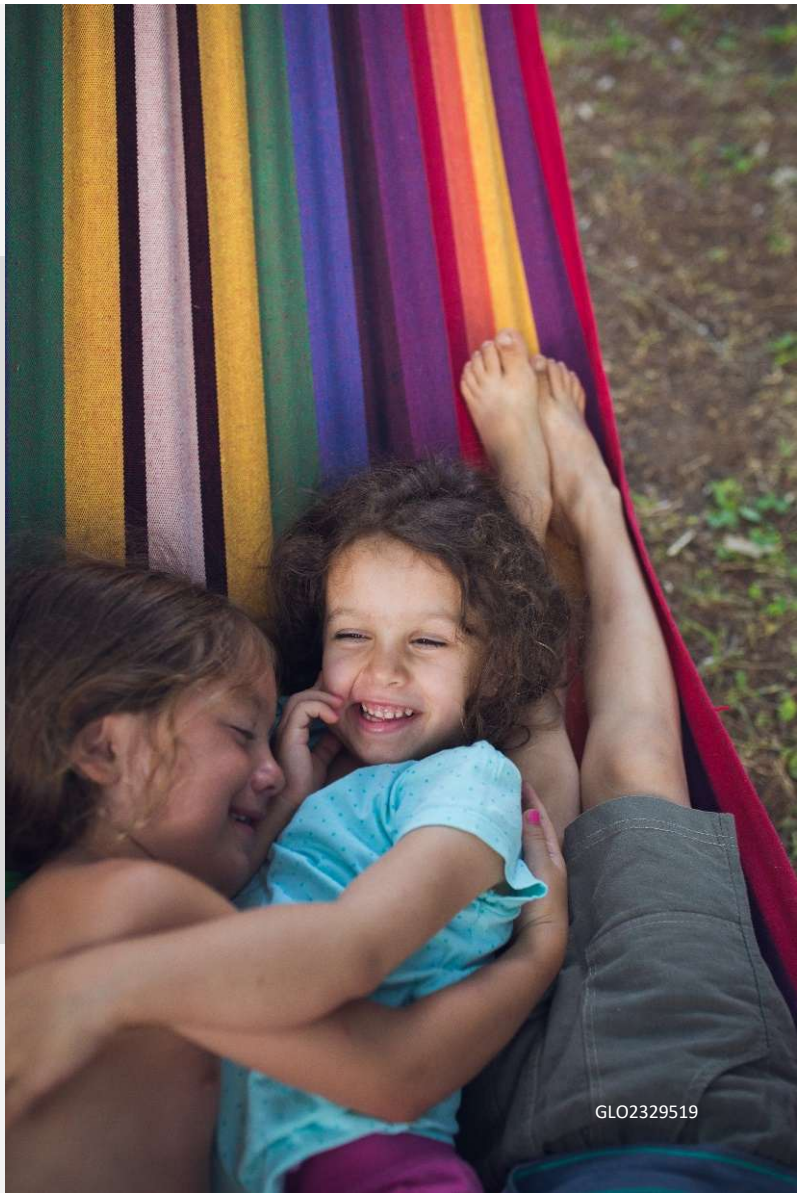
Kardas P. From non-adherence to adherence: Can innovative solutions resolve a longstanding problem?, European Journal of Internal Medicine. 2024;119:6-12.

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 Health Care Professionals: Uses and Benefits. P&T. 2014;39(5):357-364

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

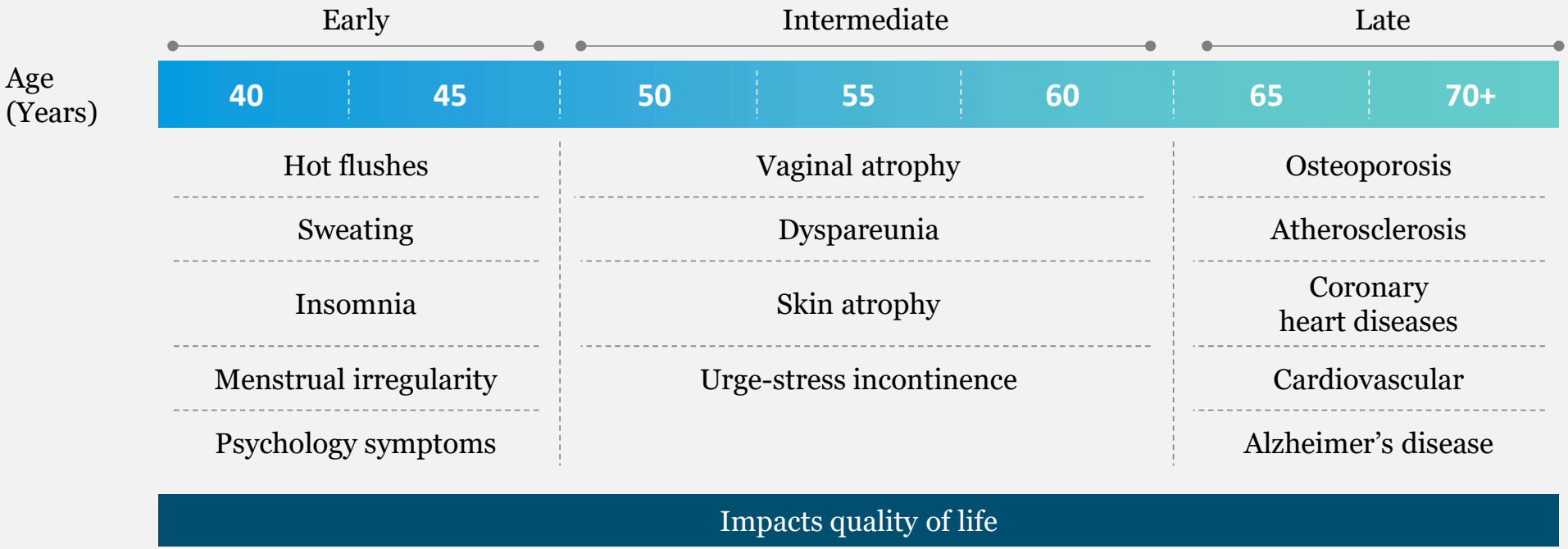
5

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**

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.

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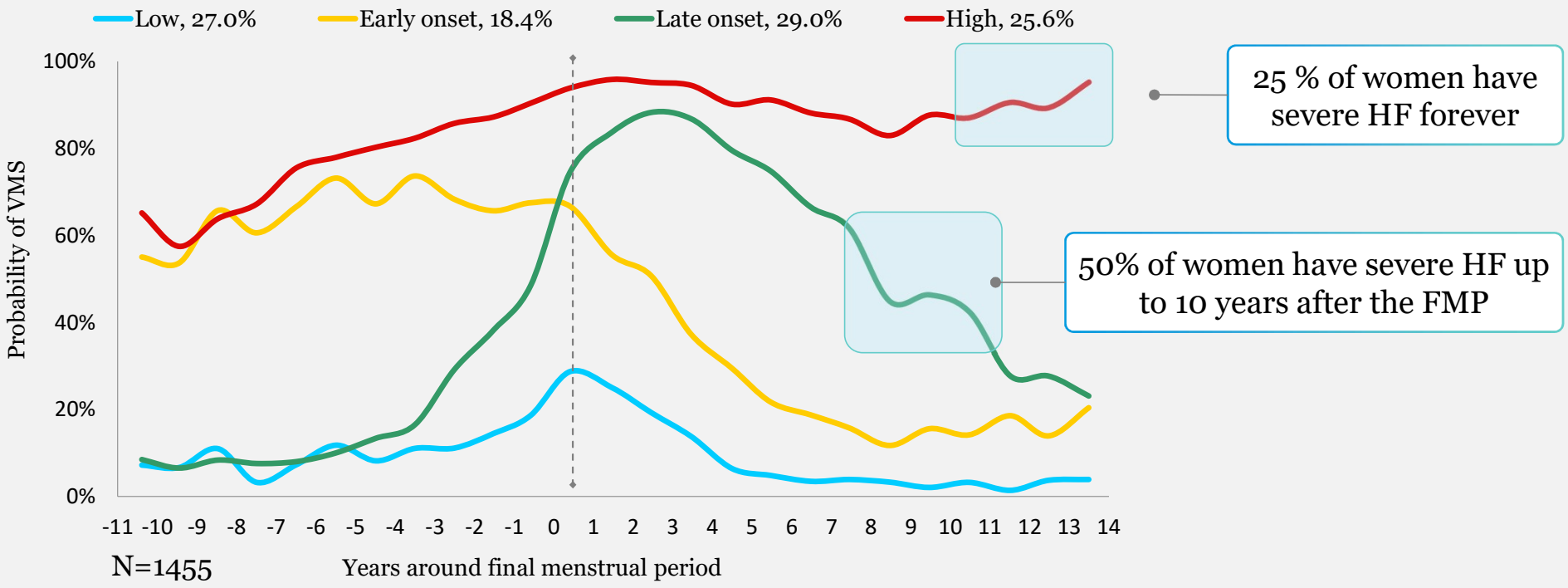
Hot flashes are long lasting



Tepper PG, Brooks MM, et al. Characterizing the trajectories of vasomotor symptoms across the menopausal transition. Menopause. 2016;23(10):1067-74.

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.

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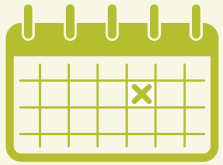
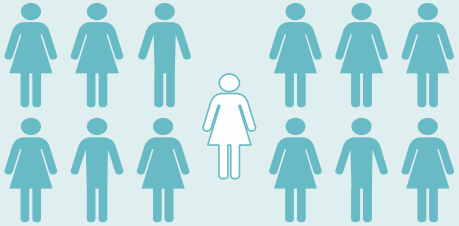
Working can be a struggle

45%
of women say they feel their menopause symptoms have had a negative impact on their work



47%
who have needed to take a day off work due to menopause symptoms say they wouldn't tell their employer the real reason

Social lives can take a back seat



Over **33%** of women feel less outgoing in social situations

32% of women feel they are no longer good company

23% of women feel more isolated

Sexual life can be an issue

51% of women say that their menopause had affected their sex lives

42% of women also say they just didn't feel as sexy since experiencing the menopause

adapted from the British Menopause Society: thebms.org.uk

Women worry about menopause

- A time of transition towards ageing
- 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

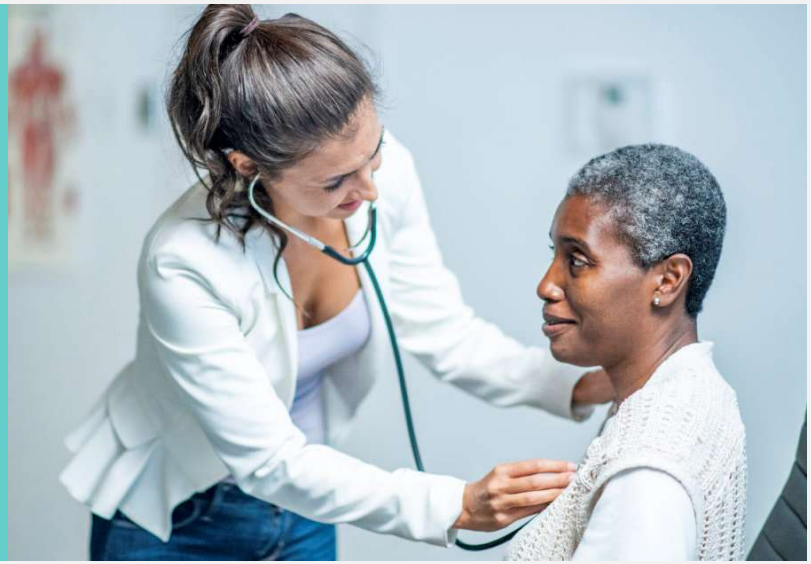
Do women get the support they need?

- 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]
- One 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.

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

How should we discuss about menopause with patients

Make the woman's worries and doubts about menopause emerge

Go beyond medical implications and explore how menopause is changing a woman's life

Right communication skills to touch upon sensitive areas such as sexuality, self image, self esteem, personal and professional role, social relationships..

Go beyond medical treatment and talk about lifestyle, dietary and social interventions trying to comply with the values and attitudes of the woman

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

Comprehensive menopause management

Explain hormonal changes

–

Medical implications and therapeutic options

Break communication barriers

–

Understand individual impact on life

Personalized goals, long-lasting alliance

–

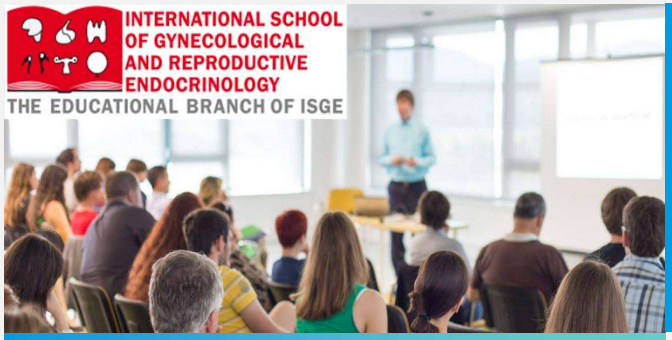
Promote adherence to interventions

Scientific societies: Promoting education

ISGE
INTERNATIONAL SOCIETY OF GYNECOLOGICAL ENDOCRINOLOGY

International IMS Menopause Society

INTERNATIONAL SCHOOL OF GYNECOLOGICAL AND REPRODUCTIVE ENDOCRINOLOGY
THE EDUCATIONAL BRANCH OF ISGE



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

World Menopause & Work Day

EMAS

Raising awareness

GLO2250022

Scientific societies: International networking

Council of Affiliated Menopause Societies (CAMS)

The Council of Affiliated Menopause Societies (CAMS) is comprised of representatives of each of the national/regional societies associated with the IMS.

The purpose of CAMS is to:

- Establish connectivity between the IMS and the national/regional society; and
- Advise and work in partnership with the IMS to deliver its mission and vision.

One representative from each society is nominated to serve on the Council, with equal membership and voting rights for all, irrespective of size or number of members of the national/regional society.

CAMS has an elected Chair, Secretary and Treasurer. The Council meets in person at least once every 2 years, at the IMS World Congress on the Menopause.

CAMS Executive

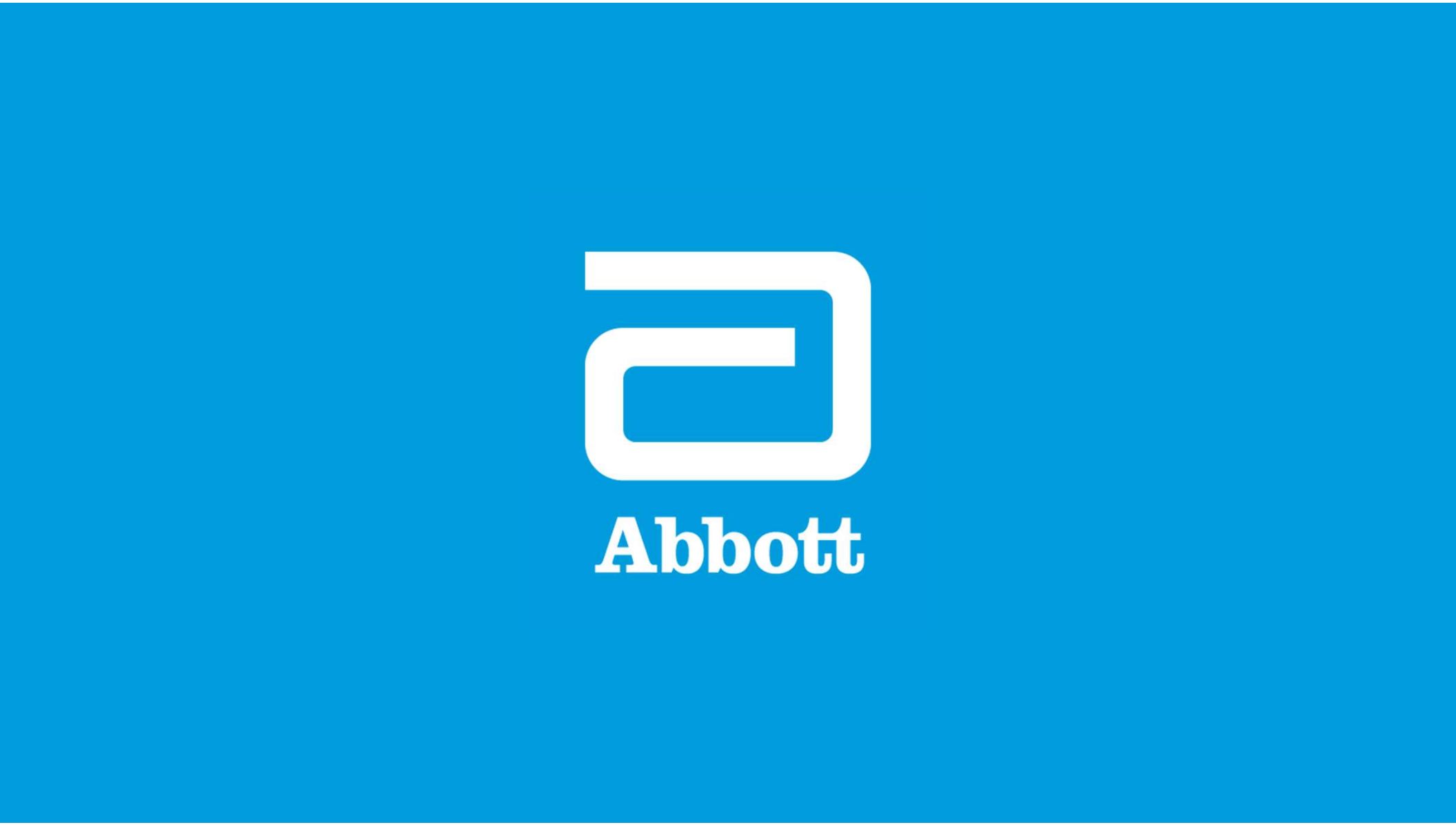
Tommaso Simoncini

CAMS Chair

International IMS Menopause Society

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, healthcare professionals, 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


Abbott