

Adherence issues

“Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population (and healthcare systems) than any improvement in specific medical treatments”.

Wright B.F.D. et al. Br J Clin Pharmacol.2023;89:1914–1917.

Tamara Krcmar, Medical communication director, Servier International

29/05/2024

- **Why Adherence matters?**
- **Which are the barriers?**
- **How can we act?- 3 examples**

Working with and for patients

Our unwavering commitment for patients stands out as **the meaning behind our vocation.**

Our teams pursue several initiatives to work with patients at every stage of the medicine life cycle.

Collaborations with **14 international patient organizations** in 2022/2023

Ranked 2nd out of 23 companies by oncology patient organizations, according to the **PatientView Report 2022** on the reputation of pharmaceutical companies



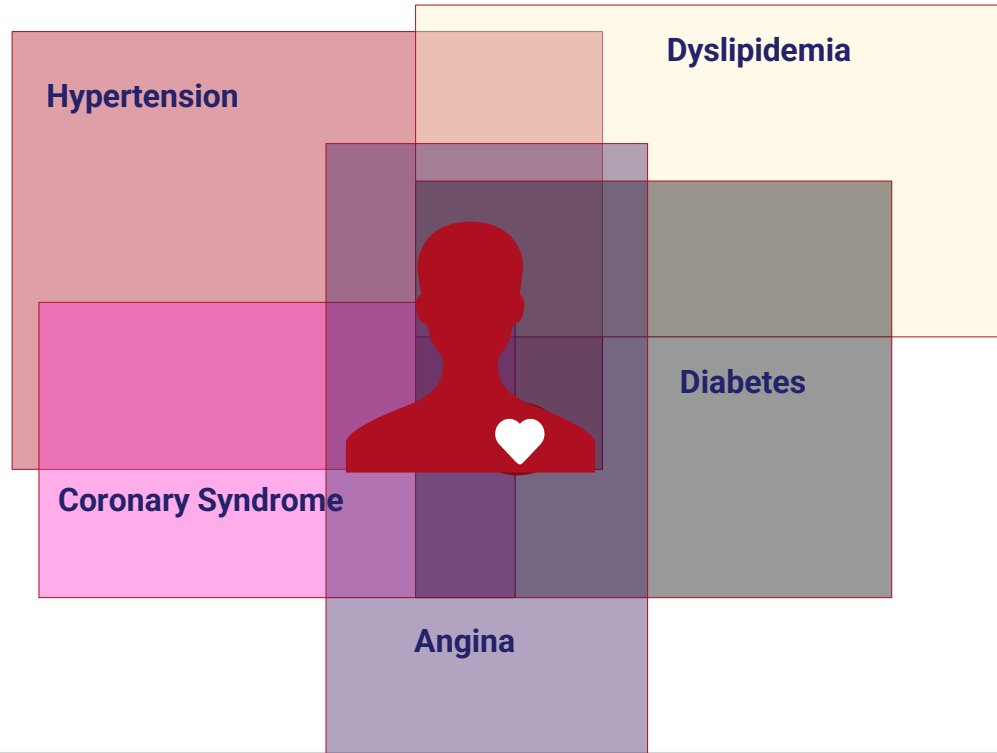
We strongly believe that **working with patients at all stages of the medicine's life cycle** leads to better care and solutions to support them throughout their journey.



Adherence.
The biggest
blockbuster drug
of our generation.



Global ageing and effective drugs allowed patients living longer but with multiple conditions



1 out of 2 patients are NOT ADHERENT, thus NOT CONTROLLED across cardiometabolic diseases



Angina⁽¹⁾



~40%



~50%



Diabetes⁽²⁾

~38%

~51%



Hypertension⁽³⁾

>50%

~48%



Dyslipidemia⁽⁴⁾

~45%

~52%



Heart Failure⁽⁵⁾

~45%

>50%

1. Khatib R. et al. Open Heart. 2019 Jul 3,6(2) e000997



2. Adherence: Khunti K et al. Diabetes Care. 2017;40(11):1588-1596/ Control: DISCOVER: Gomes MB et al. Diabetes Res Clin Pract. 2019; 151:20-32

3. Adherence: Olsen MH et al. Lancet. 2016;388(10060):2665-2712 / Control: Mills KT et al. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation. 2016. 2.



4. Adherence: Chowdhury R, Khan H, Heydon E, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. Eur Heart J. 013;34:2940–8 IQVIA RWD/ Control: Gitt AK et al. Eur J Prev Cardiol. 2012;19:201-208

5. ESC Heart Failure guidelines 2021


3 Key steps of Adherence



FULFILMENT of a treatment means that the patient has received/get the medicines prescribed by the doctor ¹



COMPLIANCE with treatment means that the patient has taken the medicines as prescribed ^{1,2,3}

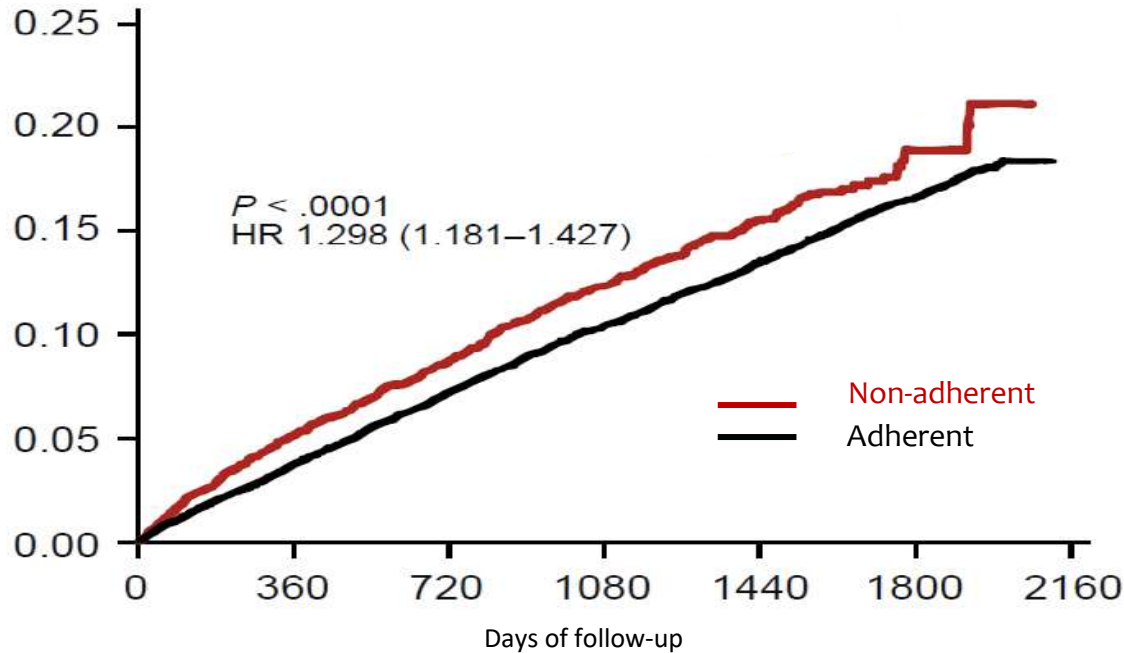


PERSISTENCE of a treatment means that the patient has taken the medicine over the initially intentioned duration ^{1,2,3}

1. Jimmy B, & Jimmy J. Patient medication adherence: Measures in daily practice, Oman Medical Journal, 2011, 26(3): 155-9. 2. Abhijit S. Gadkari & Colleen A. McHorney (2010) Medication nonfulfilment rates and reasons: narrative systematic review, Current Medical Research and Opinion, 26(3), 693-705. 2. Cramer JA, Roy A, Burrell A, et al. Medication compliance and persistence: terminology and definitions. Value Health, 2008, 11(1): 44-47. 3. Vrijens B, De Geest S, Hughes DA, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol, 2012, 73(5): 691-705. doi: 10.1111/j.1365-2125.2012.04167

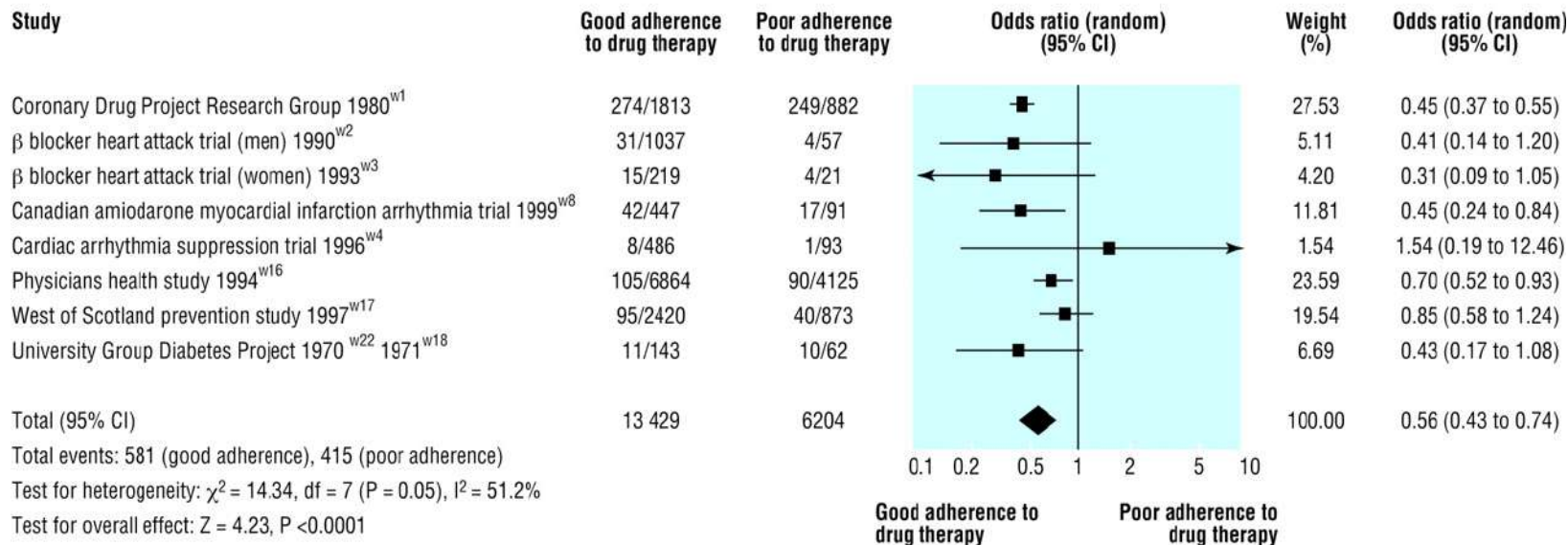
Non-adherence to antihypertensive treatment increases CV events

Proportion of patients with combined endpoint of CV mortality, MI, stroke, CHF hospitalization



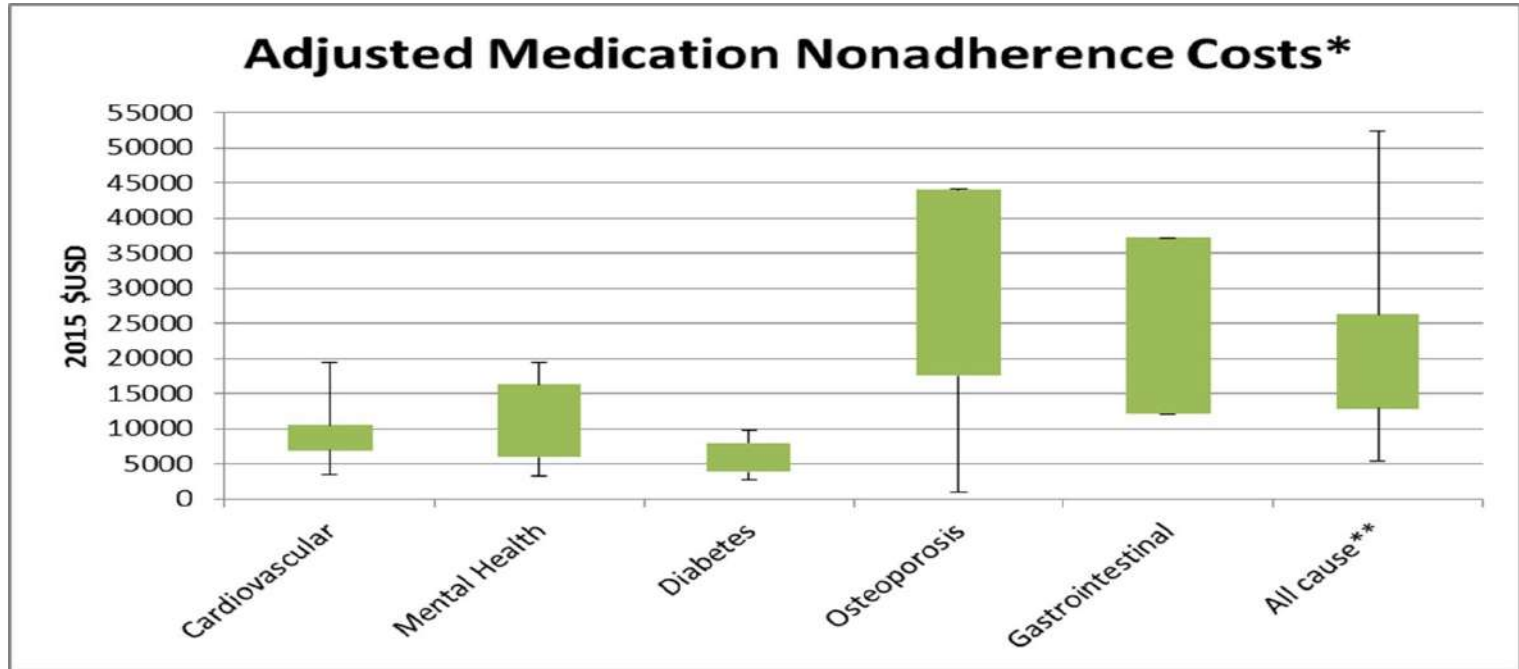
n=25 650, high CV risk patients on an ARB and/or ACE (ONTARGET/HOPE), follow up 5.5 years
Adherent (at least one study drug taken over the full 5.5 years), n=20991
Non-adherent (premature or permanent stopping of both drugs), n=4629

Non-Adherence & mortality: a clear association in cardiometabolic patients

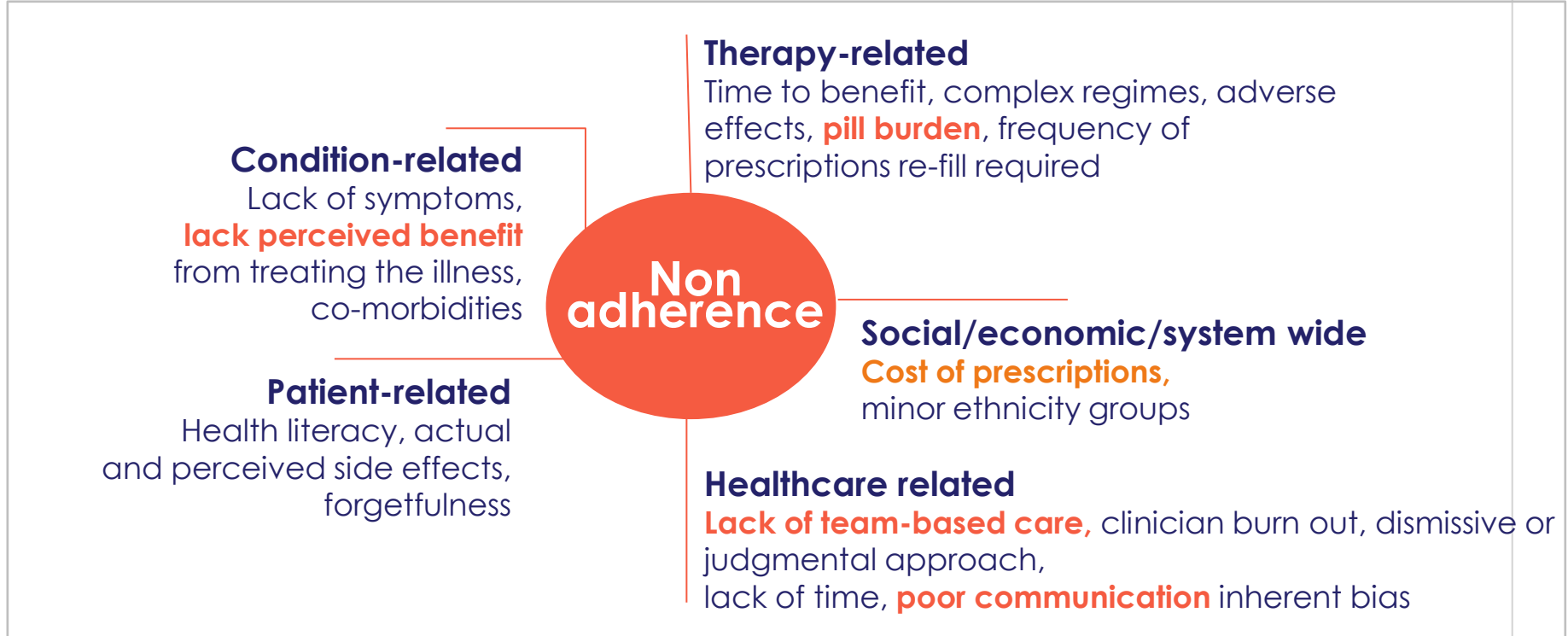


Simpson SH, Eurich DT, et al. *A meta-analysis of the association between adherence to drug therapy and mortality.* BMJ. 2006 Jul 1;333(7557):15.

Economic Impact of Medication Nonadherence

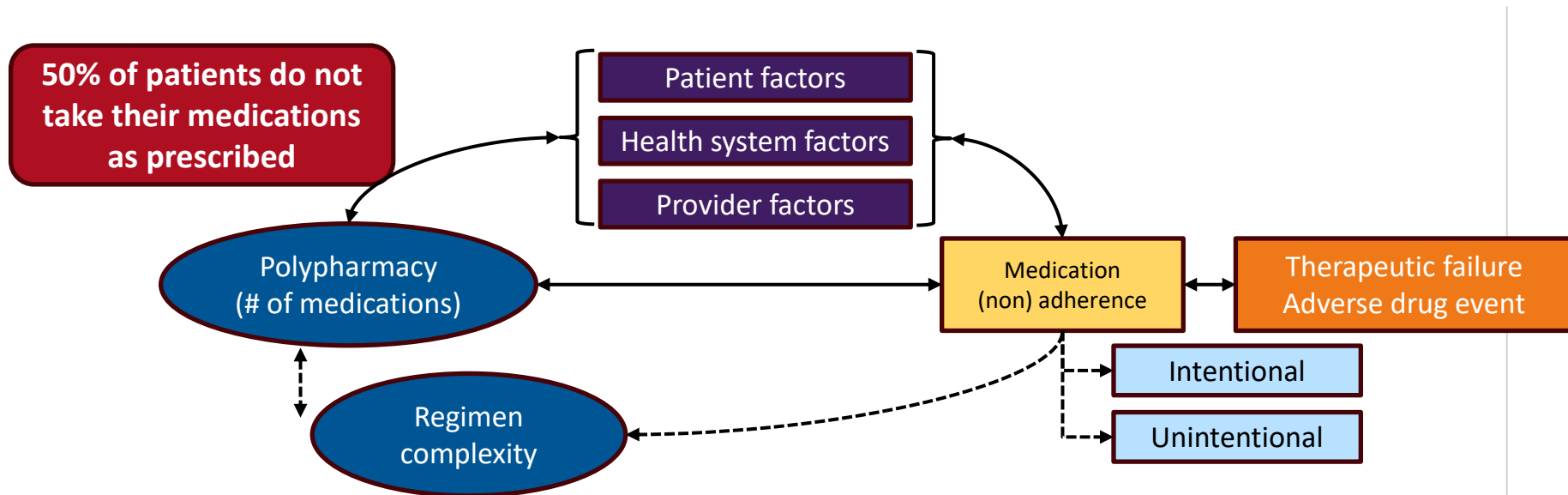


The annual cost of non-adherence is estimated to exceed £930 million in England and between \$100 and \$300 billion in the USA



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Polypharmacy Can Lead to Adherence Issues



Patient factors

- Demographics
- Illness representation
- Cognitive function
- Medication side effects
- Self-administration of medications

Health system factors

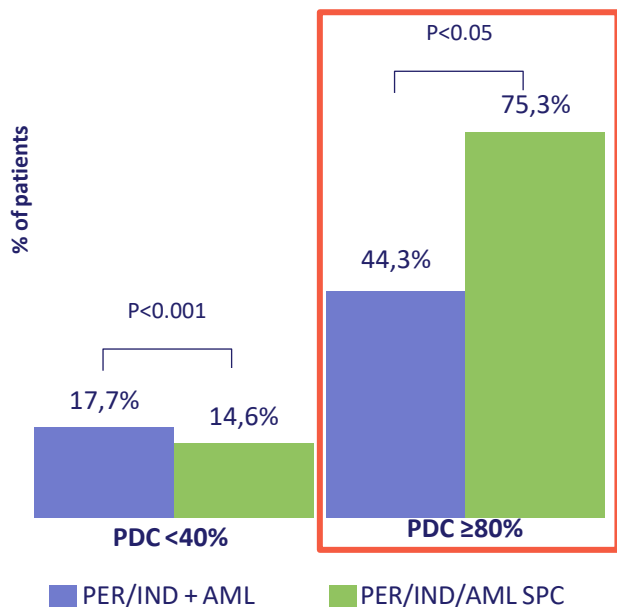
- Multiple pharmacies
- Formularies
- Prior authorization, step therapy, benefit cap
- Fragmentation of care
- Access to care, transportation
- Time/reimbursement

Provider factors

- Multiple prescribers
- Not discussing side effects, cost, and/or importance of medication
- Patient-provider trust
- Prescribing complex regimens

The example of RWE showing the impact of FDCs on Adherence

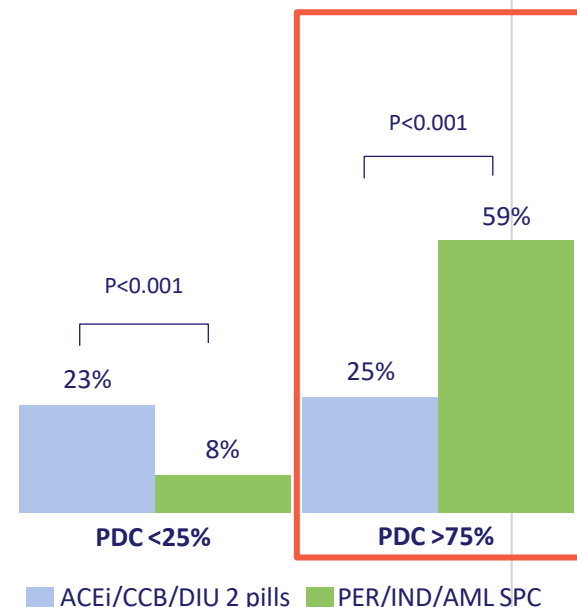
Switch from FREE COMB. to FDCs



FREE COMB. Free Vs FDCs



FDCs vs ACEi/CCB/DIU as 2 pills

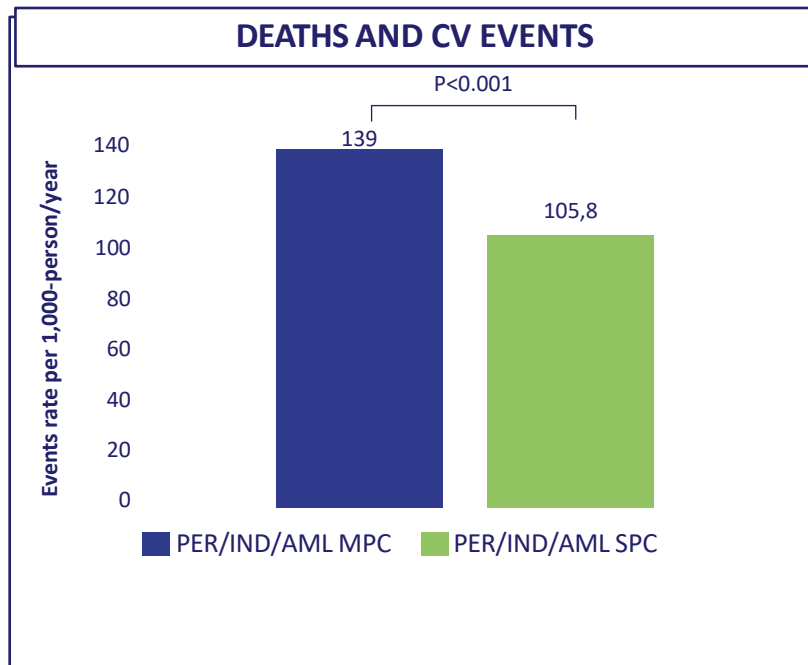


1. Borghi et al. *Adv Ther.* 2023. N=158 patients who switched from PER/IND+AML to PER/IND/AML SPC. 2. Snyman et al. *J Hypert.* 2023. N=12150 patients in the SPC cohort and N=6105 in the MPC cohort. 3. Rea et al. *J Hypert.* 2023. N=28210 patients/ group.

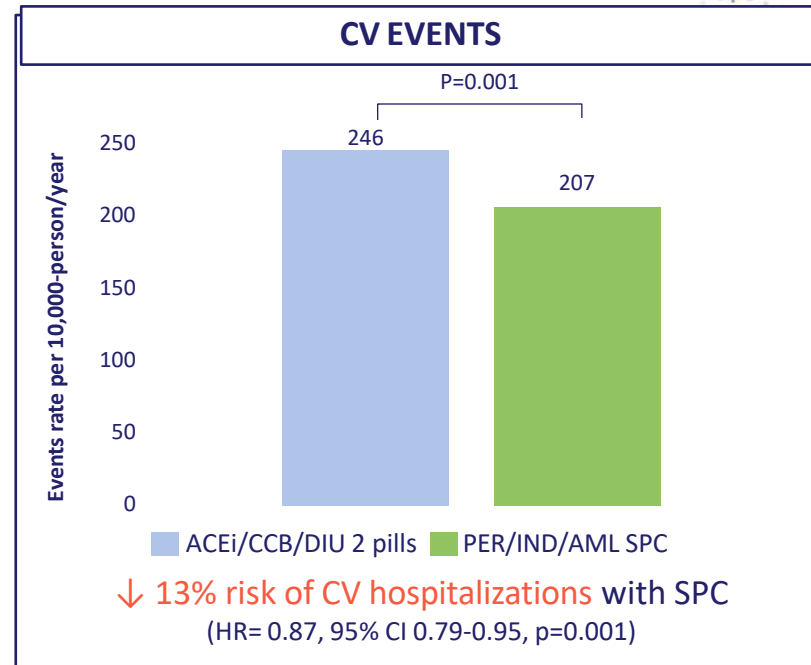
ACEi, angiotensin-converting enzyme inhibitor ; AML, amlodipine; CCB, calcium channel blocker; DIU, diuretic; IND, indapamide; MPC, multiple-pill days; PDC, proportion of days covered; PER, perindopril; SPC, single-pill combination

Lower incidence of death and CV events in patients treated with SPC vs multiple pills

Free Vs FDCs

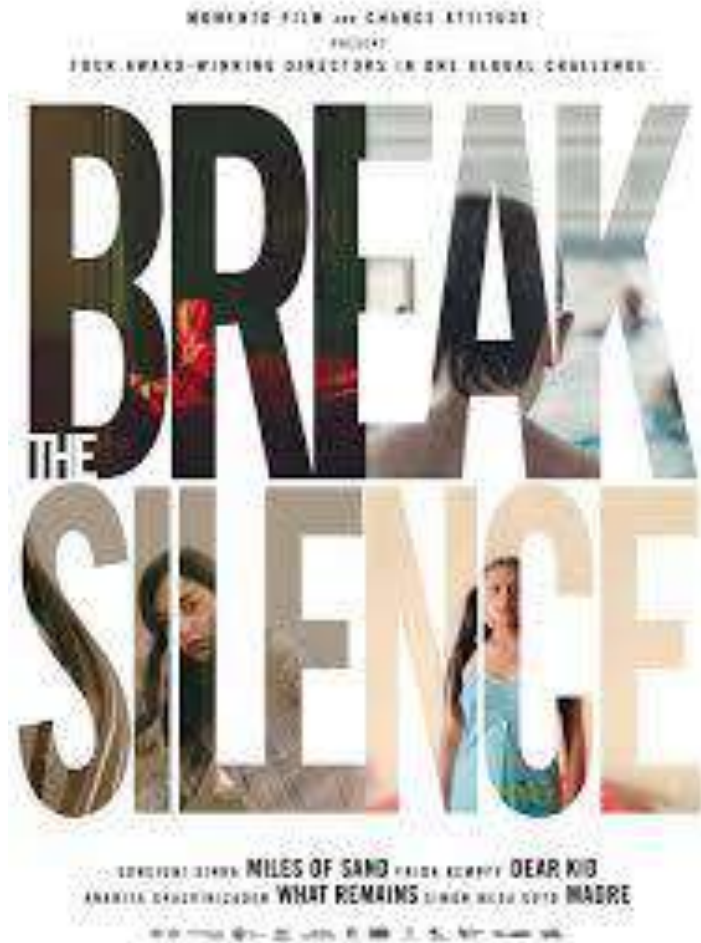


FDCs vs ACEi/CCB/DIU as 2 pills

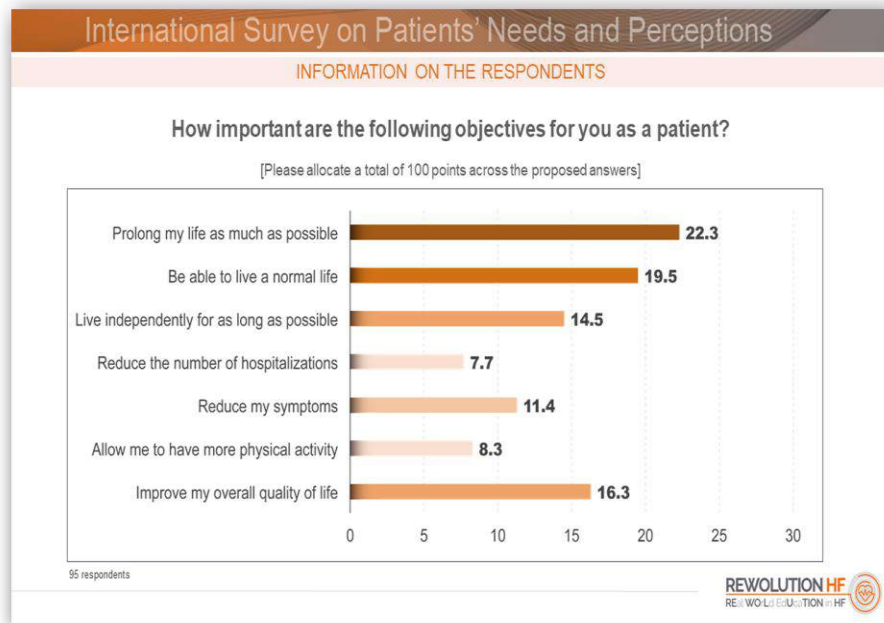


1. Snyman et al. *J Hypert.* 2023. N=12150 in the SPC cohort and N=6105 in the MPC cohort. CV events: ischemic heart disease, heart failure, cerebrovascular diseases, peripheral vascular diseases after the first year and up to the end of the follow-up 2. Rea et al. *J Hypert.* 2023. N=28210 patients/ group. CV events: hospitalization for stroke, myocardial infarction and/or heart failure listed as the primary diagnosis over the follow-up period from 1 year after the index date until censoring.

ACEi, angiotensin-converting enzyme inhibitor ; AML, amlodipine; CCB, calcium channel blocker; CV, cardiovascular; DIU, diuretic; IND, indapamide; MPC, multiple-pill days; PDC, proportion of days covered; PER, perindopril; SPC, single-pill combination



Example of collaborative survey and publications with HCPs and Patients on patients and HCPs expectations



Collaboration with INOCA patients' organization on Angina Management

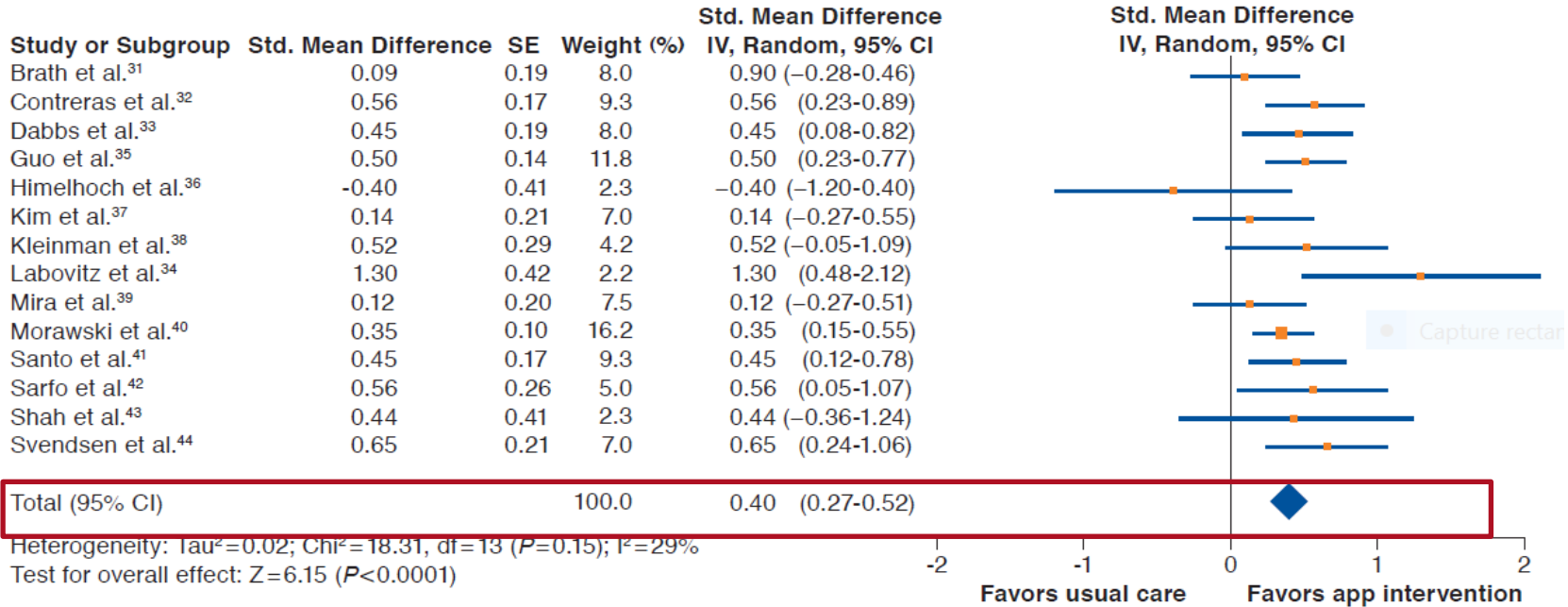
Rank	Method to improve angina management	Cumulative score
1	Have a better follow-up of my symptoms	1565
2	Receive practical and easy to understand information	1413
3	Be involved in shared decision making	844
4	Lifestyle changes counseling (e.g., professional psychological / dietician / cardiac physiotherapist training support)	733
5	Support in taking treatment – discussions about how I follow my treatment	435
6	Use combination pills to reduce the number of pills taken daily	320

The cumulative score was calculated by assigning 3 points to each “rank 1” response, 2 points to each “rank 2” response, and 1 point to each “rank 3” response.

914 respondents

Potential of digital solutions to improve Adherence

FIGURE 2 Meta-analysis of the Effect of Mobile Apps Intervention on Medication Adherence



CI= confidence interval; df= degrees of freedom; I^2 = Higgins I^2 statistic; IV= inverse variance method; SE= standard error; Std= standardized; Z= test statistic resulting from the statistical test used to derive the P value.

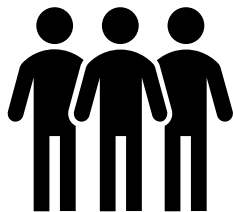
Elfie App Randomized Clinical Trial



N= 866 Participants
Brazil & Vietnam

INCLUSION CRITERIA

Age ≥ 18 years and ≤ 75 years with HTN
Uncontrolled BP (systolic BP ≥ 140 mmHg)
Use of at least 1 anti-hypertensive medication
Ability to use a mobile phone app



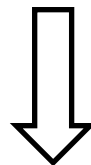
Usual care
(according to local practice)

Randomization 1:1



Solution

ITT analysis



6 months follow-up

Primary Outcome: Office systolic BP

Clinicaltrials.gov NCT06242483

Key takeaways

- Adherence to treatment is a key issue in the management of cardiometabolic patients with heavy impact on control and mortality
- There should be a call to action from all stakeholders in order to improve this burden in CV diseases
- Communication with patients, simplified treatments (FDCs), multidisciplinary approach and digital solutions should all be considered.

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Thank you!