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a:care

ADHERENCE IS A COMPLEX BEHAVIOR

Non-adherence is the new cardiovascular risk factor

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Past-President, European Atherosclerosis Society
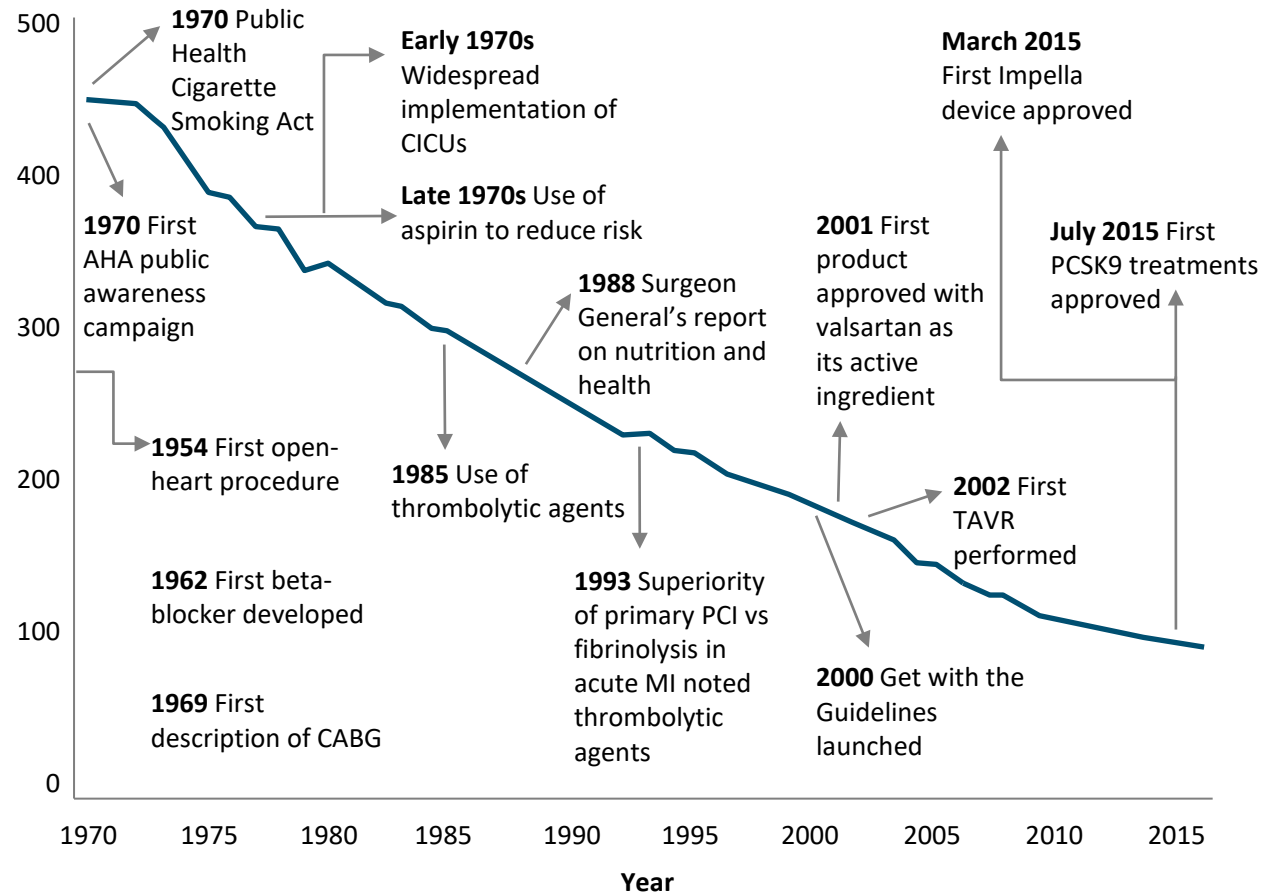Professor of Cardiology
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Ankara, Turkey

Financial disclosure

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

Age-adjusted Mortality

1970 Public Health Cigarette Smoking Act

Early 1970s Widespread implementation of CICUs

Late 1970s Use of aspirin to reduce risk

March 2015 First Impella device approved

2001 First product approved with valsartan as its active ingredient

July 2015 First PCSK9 treatments approved

1970 First AHA public awareness campaign

1988 Surgeon General's report on nutrition and health

1954 First open-heart procedure

1985 Use of thrombolytic agents

2002 First TAVR performed

1962 First beta-blocker developed

1993 Superiority of primary PCI vs fibrinolysis in acute MI noted thrombolytic agents

2000 Get with the Guidelines launched

1969 First description of CABG

Axis values: 0, 100, 200, 300, 400, 500

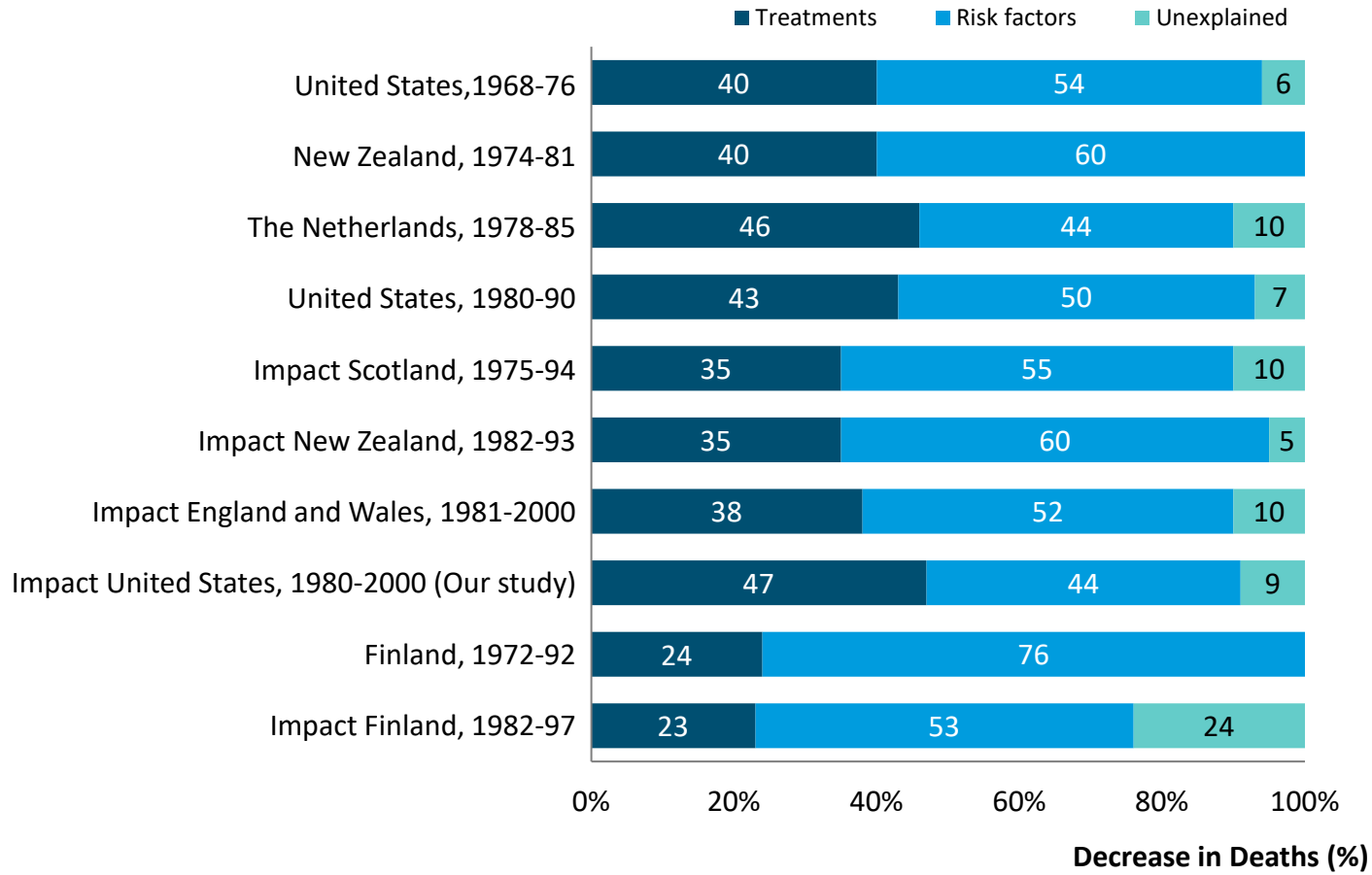Year: 1970, 1975, 1980, 1985, 1990, 1995, 2000, 2005, 2010, 2015

Year

- 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

Attribution of treatment and risk factors changes in deaths from coronary heart disease
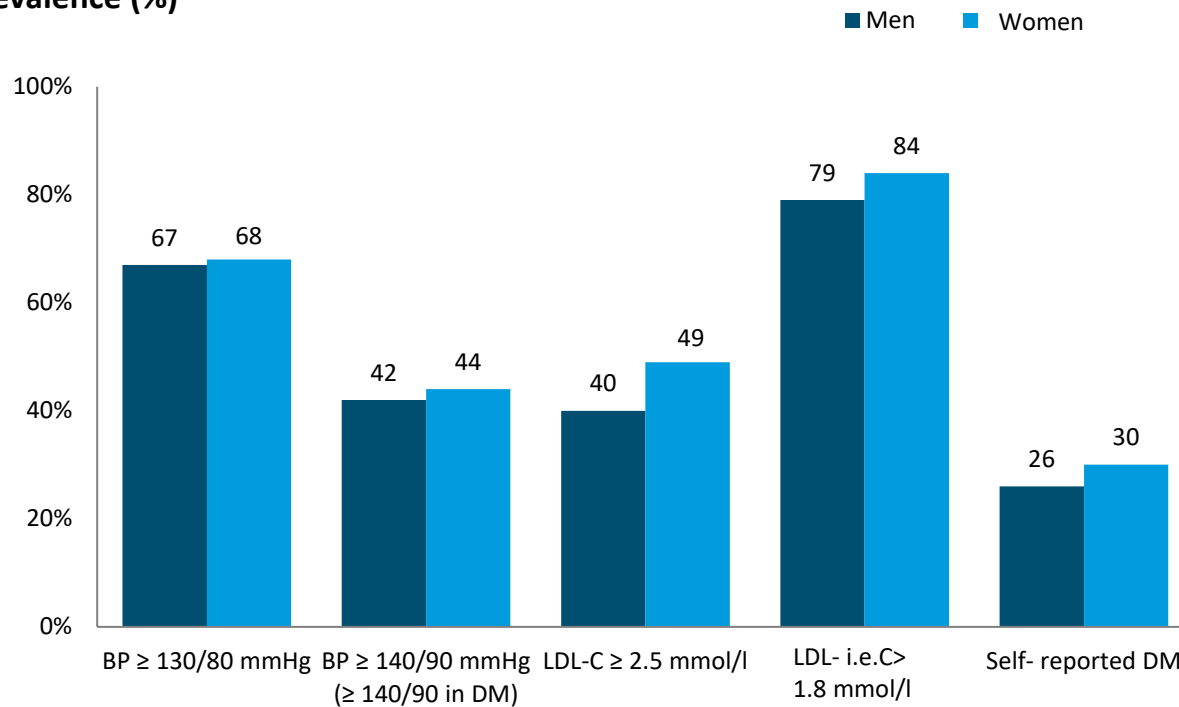
Legend: ■ Treatments ■ Risk factors ■ Unexplained

Country/Study	Treatments	Risk factors	Unexplained
United States, 1968-76	40	54	6
New Zealand, 1974-81	40	60	
The Netherlands, 1978-85	46	44	10
United States, 1980-90	43	50	7
Impact Scotland, 1975-94	35	55	10
Impact New Zealand, 1982-93	35	60	5
Impact England and Wales, 1981-2000	38	52	10
Impact United States, 1980-2000 (Our study)	47	44	9
Finland, 1972-92	24	76	
Impact Finland, 1982-97	23	53	24

X-axis: 0% 20% 40% 60% 80% 100%

Decrease in Deaths (%)

- 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 (%)

■ Men ■ Women

Bar chart values:
- BP ≥ 130/80 mmHg: Men 67, Women 68
- BP ≥ 140/90 mmHg (≥ 140/90 in DM): Men 42, Women 44
- LDL-C ≥ 2.5 mmol/l: Men 40, Women 49
- LDL- i.e.C> 1.8 mmol/l: Men 79, Women 84
- Self- reported DM: Men 26, Women 30

EUROASPIRE IV STATIN THERAPY AT DISCHARGE: INSTEAD OF ESCALATING RX TO GET TO GOAL, DE-ESCALATE AT FU[2]


37,6% — 9,6% — 24%
52,7% — 12,3%
9,6%
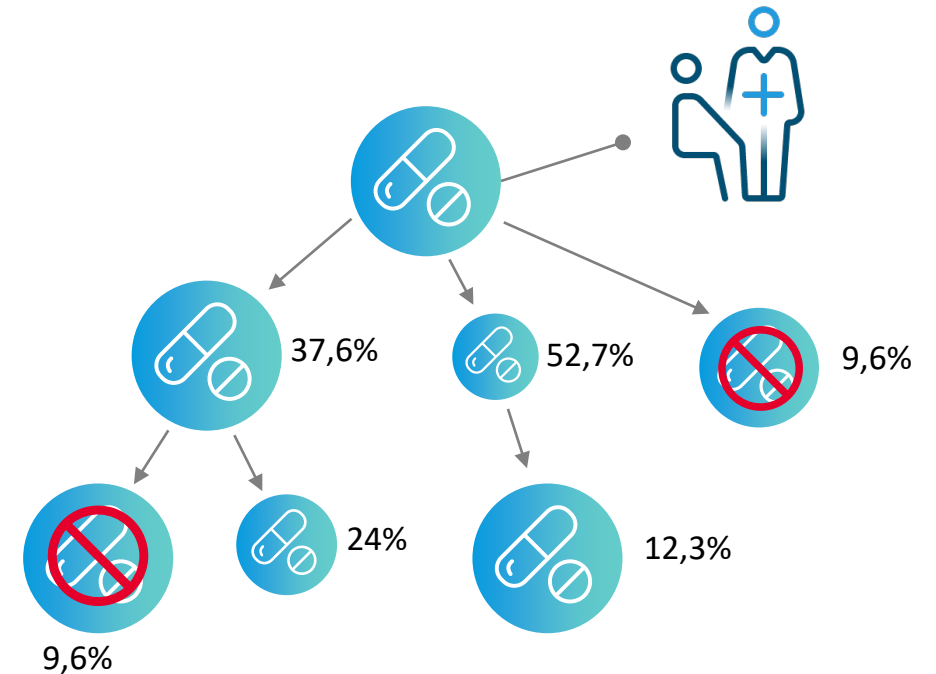
CAD= Coronary Artery Disease, IV= Intravenous, EA= Euroaspire

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

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

A

Adherence

0-33% ,n=81

34-66% ,n=159

67-99% ,n=262

100% ,n=509

Mortality (%)

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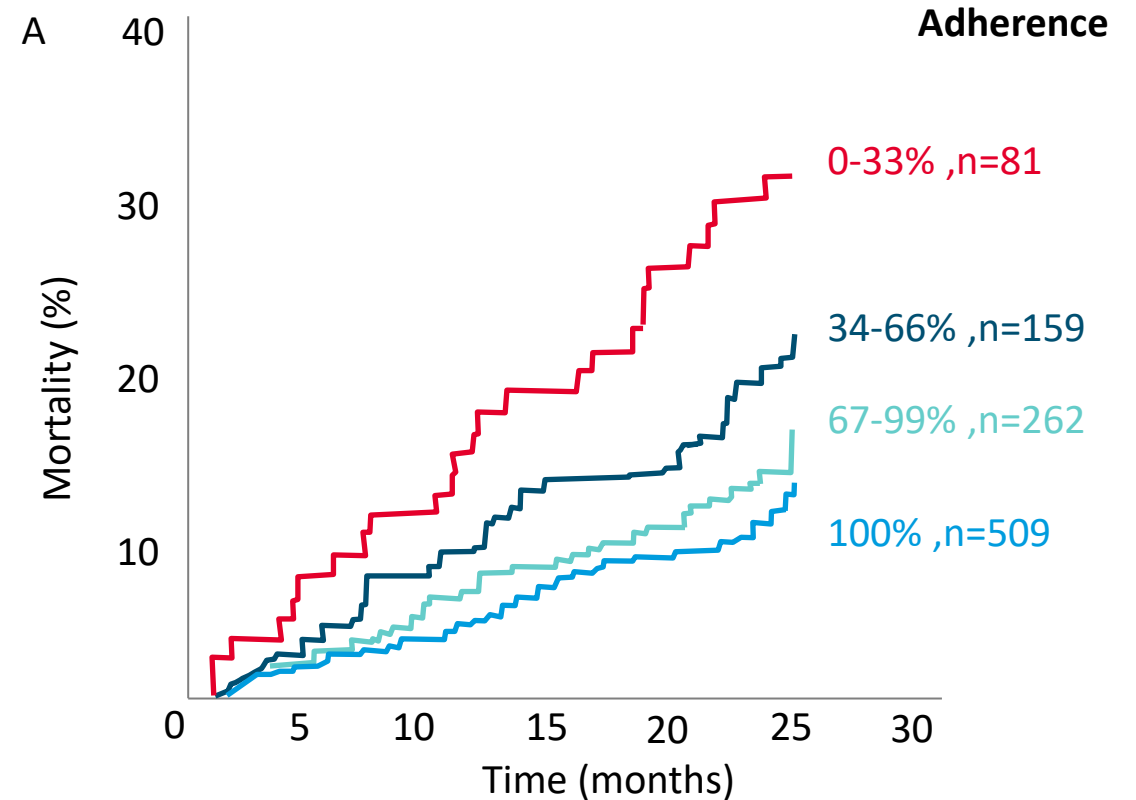
Wu JYF, Leung WYS, Chang S, *et al*. Effectiveness of telephone counselling by pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial. *BMJ*. 2006 Sep 9;333(7567):522

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

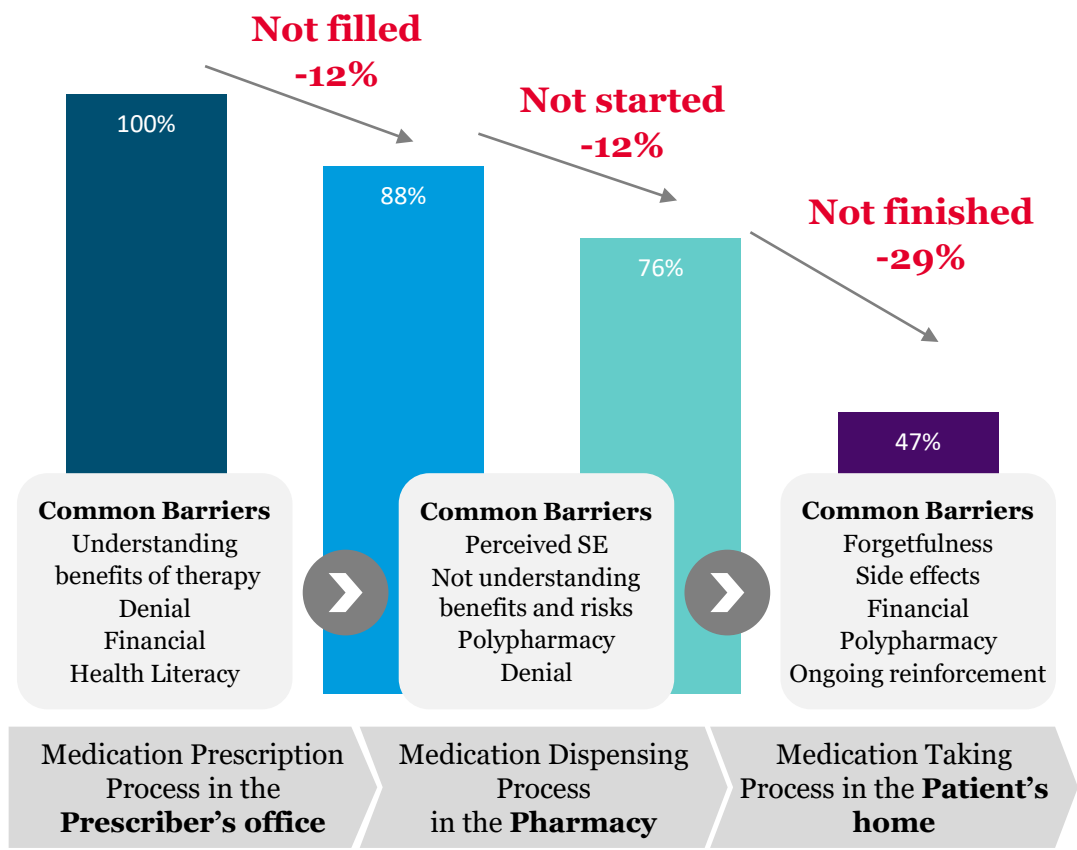| STUDY	RISK RATIO	RISK RATIO	95%–CI Weight
Adherence to multiple agents			
Lenzi J (2015)		0.41 [0.34;0.50]	15.6%
Kumbhani DJ (2013)		0.79 [0.72; 0.88]	17.5%
Kirchmayer U (2013)		0.35 [0.21;0.59]	8.5%
Kuepper-Nybelen J (2012)		0.72 [0.60;0.86]	16.1%
Ho PM (2008)		0.59 [0.52;0.67]	17.0%
Ho PM (2006)		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			

Risk ratio axis: 0.1 0.5 1 2 10

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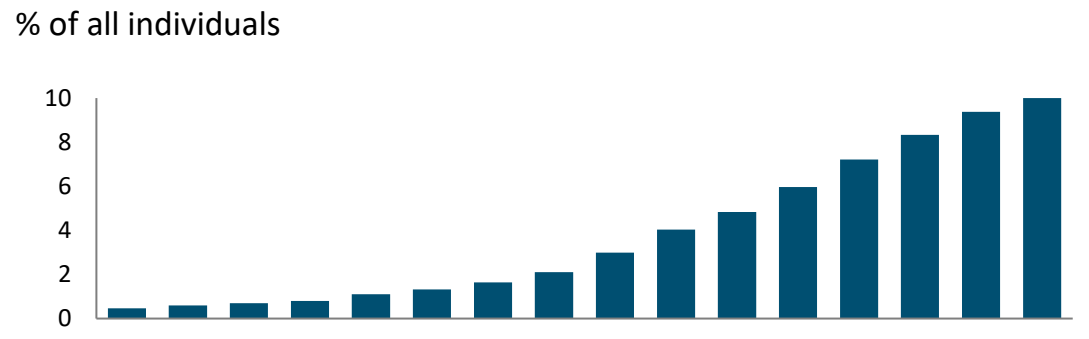
Du L, Cheng Z, Zhang Y, *et al*. The impact of medication adherence on clinical outcomes of coronary artery disease: A meta-analysis. *European Journal of Preventive Cardiology* 2017, vol24: 962–970

Statin compliance and adherence

STATIN COMPLIANCE OVER TIME[1]

Not filled -12%

Not started -12%

Not finished -29%

100%

88%

76%

47%

Common Barriers
Understanding benefits of therapy
Denial
Financial
Health Literacy

Common Barriers
Perceived SE
Not understanding benefits and risks
Polypharmacy
Denial

Common Barriers
Forgetfulness
Side effects
Financial
Polypharmacy
Ongoing reinforcement

Medication Prescription Process in the **Prescriber's office**

Medication Dispensing Process in the **Pharmacy**

Medication Taking Process in the **Patient's home**

FRACTION OF INDIVIDUALS ≥40 YEARS OF AGE ON STATINS IN DENMARK[2]

% of all individuals

FRACTION OF STATIN USERS WITH ONE PRESCRIPTION ONLY[2]

% of statin users

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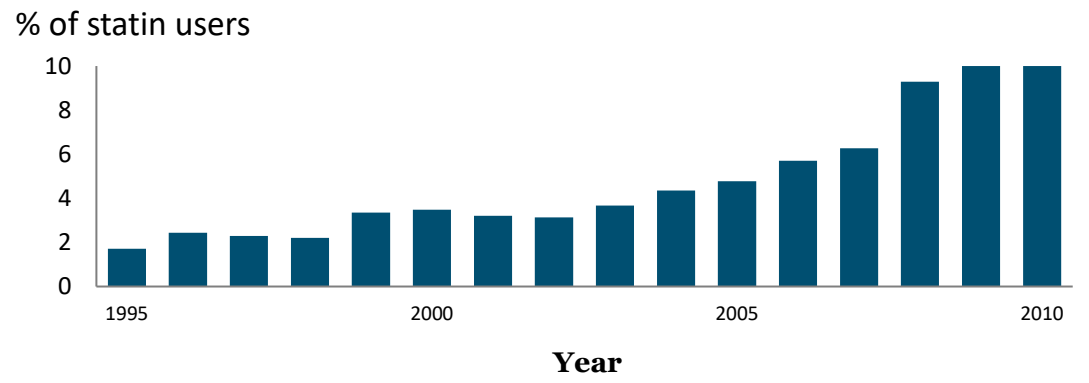
1. Cohen JD, Aspry KE, Brown AS, *et al.* Use of health information technology to improve statin adherence and low-density lipoprotein cholesterol goal attainment in high-risk patients: Proceedings from a workshop. *Journal of Clinical Lipidology*. 2013; 7, 573–609; 2. Stroes ES, Thompson PD, Corsini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

Surveys on patient perspectives[1,2]

Legend:
- Worry about side effects
- Prefer natural remedies/supplements
- Cholesterol not that high
- Other
- Want to try diet/exercise first
- Want more testing
- Doctors prescribe toomany meds

Pie chart values:
- 27.2%
- 26.6%
- 16.8%
- 15.0%
- 5.8%
- 5.2%
- 3.5%
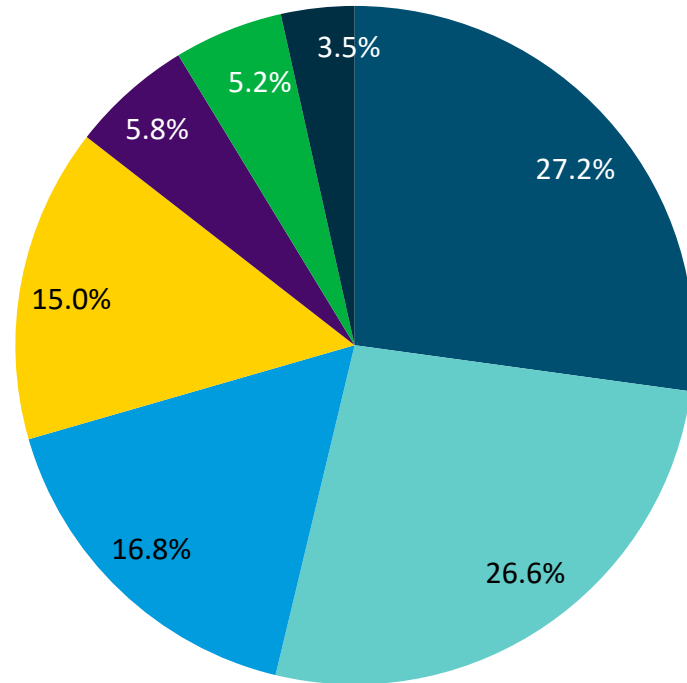
FACTORS CONTRIBUTING TO THE DECISION OF STATIN TREATMENT DISCONTINUATION (N = 532) [2]		
TREATMENT DISCONTINUATION REASON	**Yes**	
	n	**%**
Negative information about statin treatment	213	40.0
Negative information about statin treatment in TV programs	175	32.9
Patients' lack of sufficient information on high cholesterol and related risks	163	30.6
Negative information about statin treatment heard from the relatives of the patient relatives of the patient	155	29.1
Completion of the treatment as considered by the patient	149	28.0
Switching to non-drug alternatives	139	26.1
Negative information about statin treatment in newspapers	117	22.0
Disbelief in long-term treatment	87	16.4
Not considering high cholesterol as a disease that needs treatment	78	14.7
Considering treatment to be inefficient	74	13.9
Chronically forgetting to take the medicine	61	11.5
Patient copayment contribution	30	5.6
Lack of complete reimbursement by Social Security Institute	14	2.6
High drug costs	13	2.4
Difficulty in payment	13	2.4

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

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

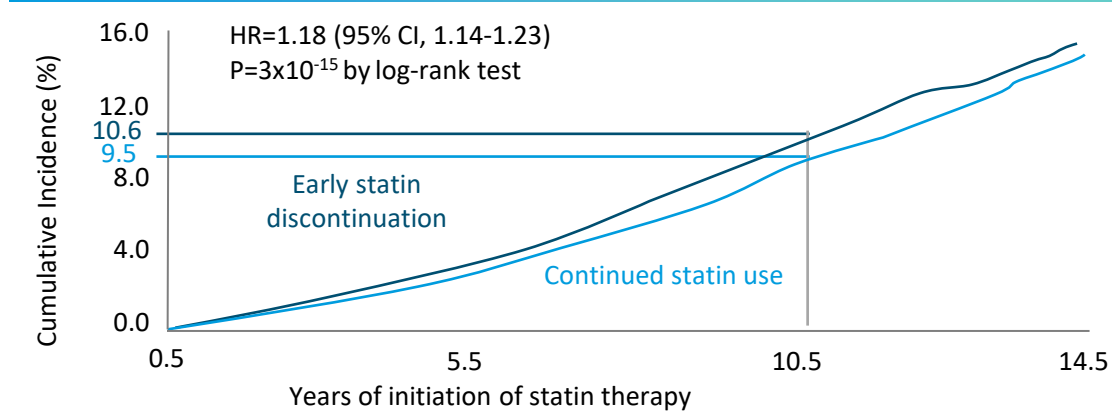| PREDICTOR			P-value
Odds ratio for early statin discontinuation with 95% confidence interval			
Negative nationwide statin-related news story	1.09 (1.06-1.12)		9×10^{-9}
Neutral nationwide statin-related news story	0.98 (0.96-1.01)		0.16
Positive nationwide statin-related news story	0.92 (0.90-0.94)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

0.70　1.00　1.75

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

MYOCARDIAL INFARCTION

HR=1.26 (95% CI, 1.21-1.30)
P=2×10^{-27} by log-rank test

Cumulative Incidence (%): 14.0, 10.5, 9.9, 8.0, 7.0, 3.5, 0.0

Early statin discontinuation

Continued statin use
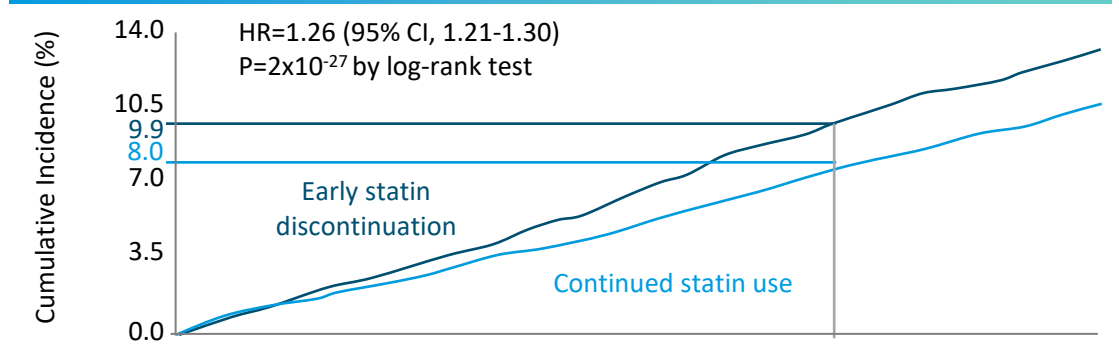
DEATH FROM CARDIOVASCULAR DISEASE

HR=1.18 (95% CI, 1.14-1.23)
P=3×10^{-15} by log-rank test

Cumulative Incidence (%): 16.0, 12.0, 10.6, 9.5, 8.0, 4.0, 0.0

Early statin discontinuation

Continued statin use

Years of initiation of statin therapy: 0.5　5.5　10.5　14.5

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

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

ACS (n=22,379) — **Chronic CAD (n=36,106)** — **Primary Prevention (n=85,020)**

Patients (%)

100 90 80 70 60 50 40 30 20 10 0

0.0   0.5   1.0   1.5   2.0

Years of follow-up
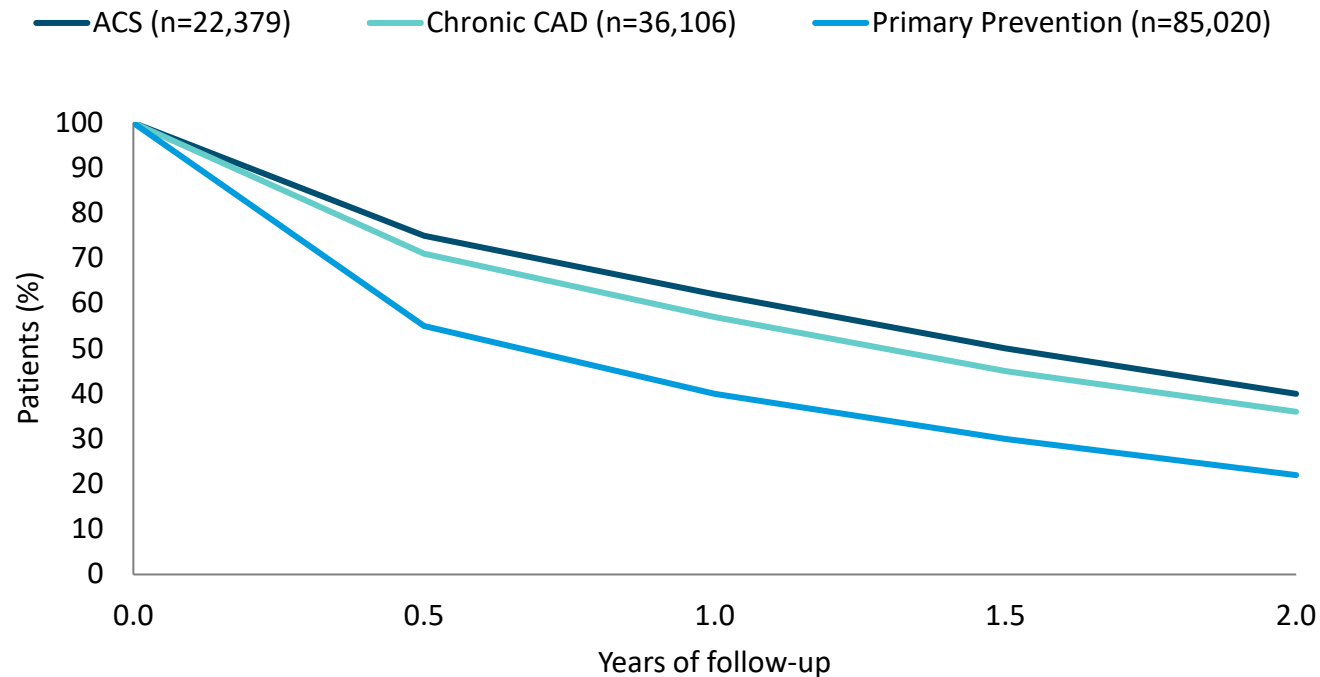
○ **Independent predictors of statin therapy discontinuation[2]**

- 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

Legend:
- Primary prevention (n = 136,052)
- Secondary prevention (n = 93,866)
- HMO= Health Maintenance organization

Y-axis: % of patients
X-axis: Follow-up (y)
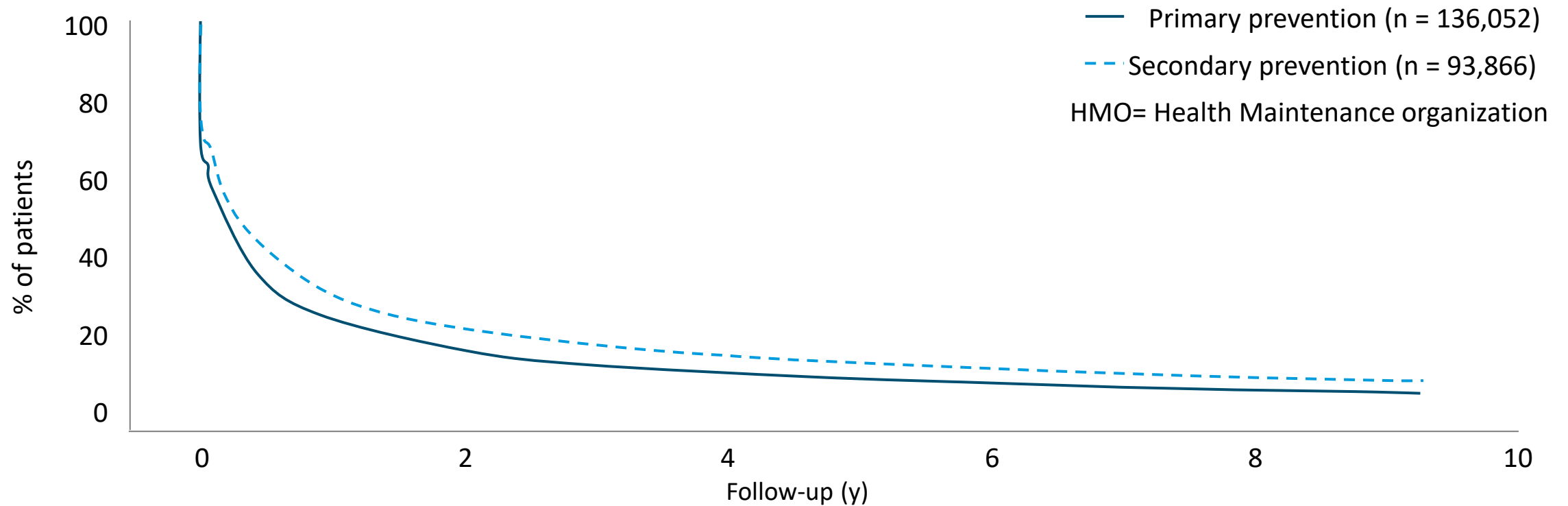
Chodick G, Shavel V, Gerber Y *et al.* Long-term persistence with Statin Treatment in a Not-for-Profit Health Maintenance Organization: A Population-Based Retrospective Cohort Study in Israel. *Clinical Therapeutics*. 2008;30:2167-79

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

ASCVD PTS ON STATIN N=3,47,104[1]

IN META-ANALYSIS RR 1.22 TO 5.26 FOR CVD AND 1.25 TO 2.54 FOR DEATH[2]

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

Adherence (MPR)   <50%   50-69%   70%-89%   >90%   P <.001

Survival

| 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.

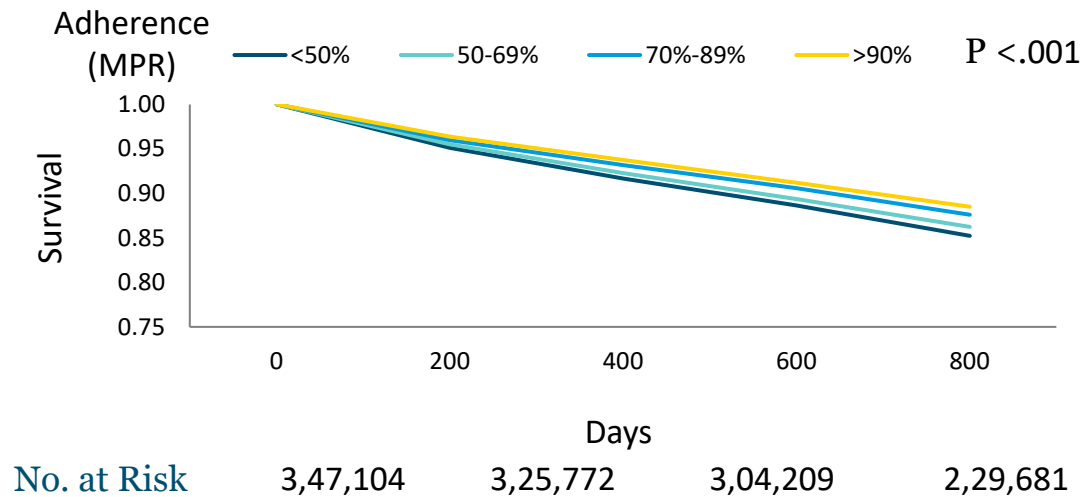|	Study	RR (95% CI)
Adherence	[A1] Wei 2002 (AMI)	5.26 (2.13, 12.50)
	[A3] Blackburn 2005 (AMI)	2.22 (1.01, 5.00)
	[A6] Bouchard 2007 (CAD < 1 Year)	0.98 (0.85, 1.15)
	[A6] Bouchard 2007 (CAD > 1 Year)	1.23 (1.03, 1.49)
	[A8] Ho 2008 (CVD)	1.35 (1.21, 1.50)
	[A9] Perreault 2009 (CHF < 1 Year)	1.39 (1.02, 1.89)
	[A9] Perreault 2009 (CHF > 1 Year)	1.23 (1.10, 1.41)
	[A10] Wei 2008 (CVD)	1.52 (1.10, 2.13)
	[A11] McGinnis 2009 (AMI)	1.01 (0.77, 1.32)
	[A12] Perreault 2009 (CAD < 1 Year)	1.14 (0.99, 1.30)
	[A12] Perreault 2009 (CAD > 1 Year)	1.22 (1.15, 1.30)
	[A13] Perreault 2009 (CVA < 1 Year)	1.03 (0.76, 1.38)
	[A13] Perreault 2009 (CVA > 1 Year)	1.35 (1.19, 1.54)
	[A15] Corrao 2010 (IHD)	1.23 (1.06, 1.41)
	[A18] Degli 2012 (AMI)	1.27 (0.91, 1.79)
	[A18] Degli 2012 (CVA)	1.37 (1.11, 1.72)
	[A19] Rabinowich (VTE)	1.28 (1.12, 1.45)
Discontinuation	[D22] Penning-van Beest 2007a (AMI)	1.43 (1.23, 1.67)
	[D22] Penning-van Beest 2007b (AMI)	1.43 (1.10, 1.85)
	[D24] DeVera 2011 (AMI)	1.67 (1.24, 2.25)
Persistence	[P28] Rublee 2012a (CVD)	1.22 (1.10, 1.35)
	[P28] Rublee 2012b (CVD)	1.35 (1.22, 1.52)

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

Statin Withdrawal (+) —— Statin Withdrawal (-) – – –

B

Log rank p < 0.001

> 3-fold increase in all-cause mortality

Cumulative mortality (%)

Years after AMI

Log rank p < 0.001

> 4-fold increase in cardiac mortality

Cardiac mortality (%)

Years after AMI
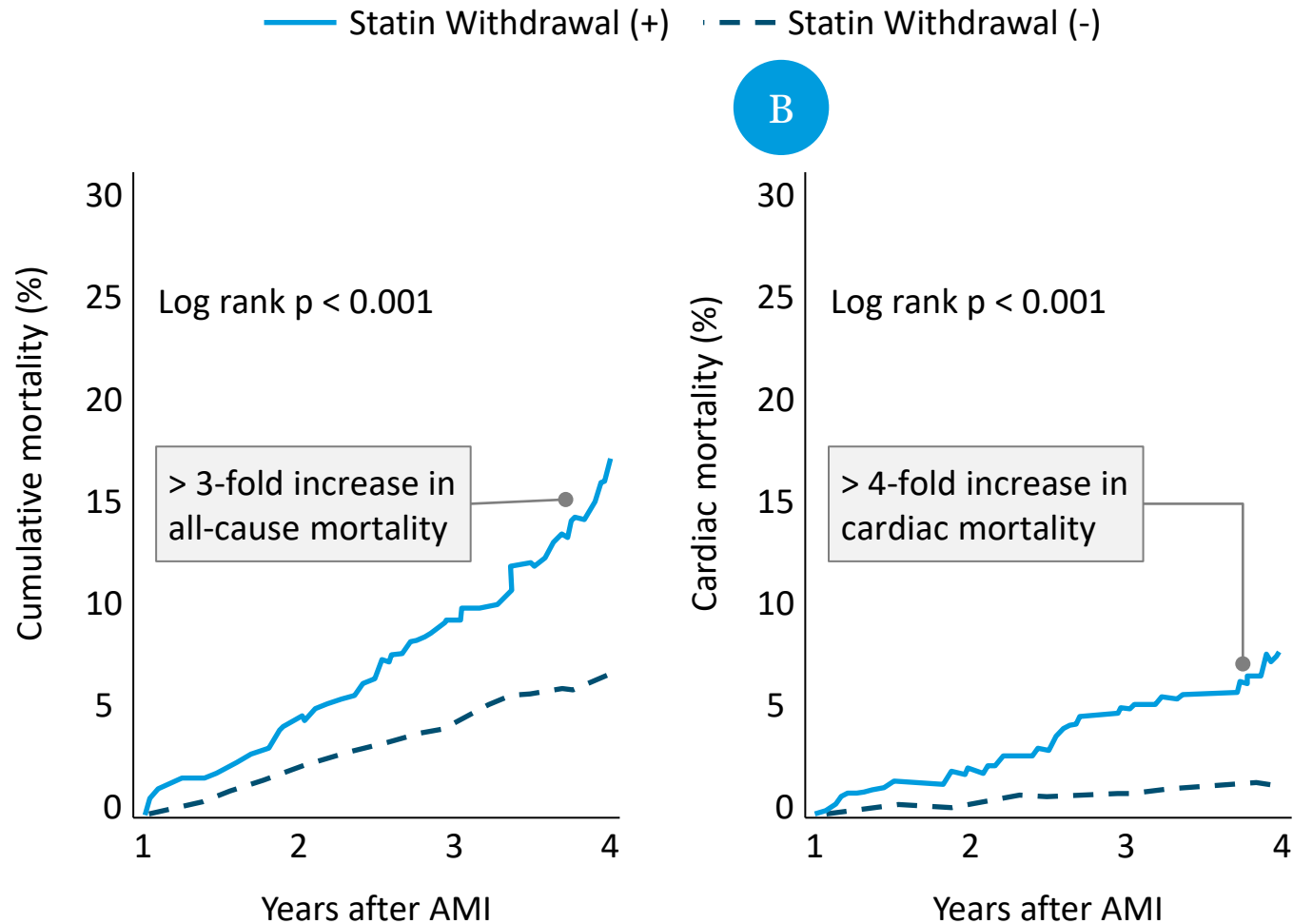
- 3,807 patients in the Korean multicenter registry

- 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]

n= 67 418

Discontinuation
Continuation

STUDY DESIGN[2]

75th birthday
In 2012 to 2014
(Patients from the French general health insurance scheme living in metropolitan France)

Start of follow-up
Month m=3

End of follow-up
(In particular at resumption of statin treatment after discontinuation; December 2015 at the latest

Statin medication possession ratio ≥80%
Between m= -24 and m= -13

Statin medication possession ratio ≥80%
Between m= -12 and m= -1

Assessment of study outcome
Hospital admission for cardiovascular event

Time is divided into calendar months, m=0 referring to the month of the 75th birthday

-5 -4 -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 ......

Jan. 2012   Jan. 2013   Dec. 2015

No in-hospital diagnosis, clinical procedure or drug therapy suggestive of secondary prevention
Between m= -72 and m= -1

FIGURE 2. CUMULATIVE INCIDENCE CURVE FOR THE OUTCOME OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN THE SECONDARY PREVENTION COHORT[1]

Discontinuation
Continuation

Follow-up, y

PRINCIPAL RESULT[2]

Adjusted cumulative incidence, %

Hazard ratio 1.33 (95% CI, 1.18-1.50)

Statins discontinued

Statins continued

Time since 75th birthday, months
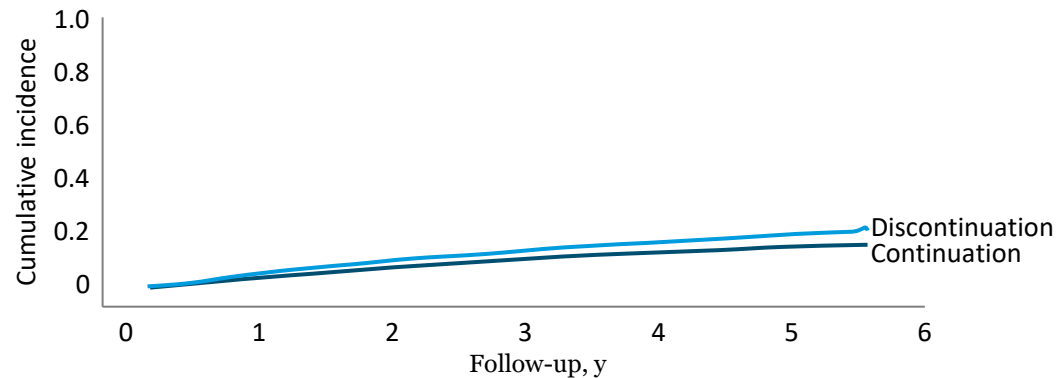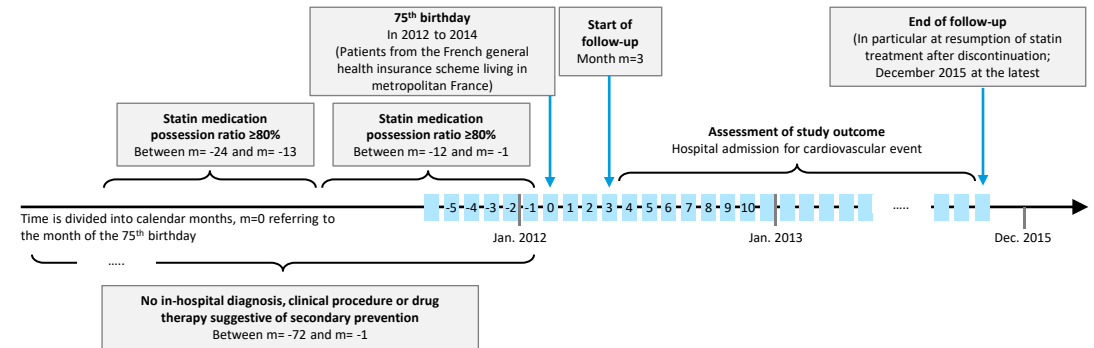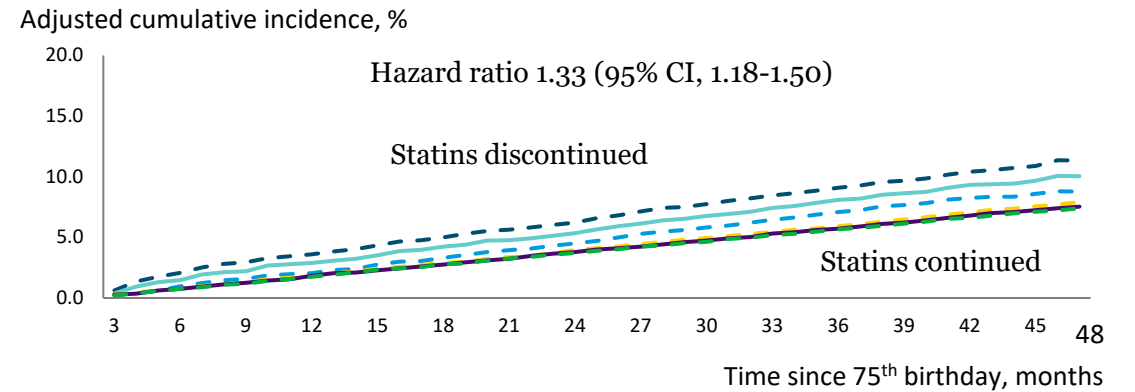
1.Thompson W, Morin L, Jarbol DE, *et al*. Statin Discontinuation and Cardiovascular Events Among Older People n Denmark. *JAMA Network Open*. 2021;4(12):e2136802; 2.Giral P, Neumann A, *et al*. Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide 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

No PAV progression ← → PAV progression

SD OF LDL QUARTILE

Quartile 1, Quartile 2, Quartile 3, Quartile 4

Death/MI/Stroke/Urgent ACS Revasc/Hosp for UA (%)

P=0.005

10.9%
7.7%
7.3%
5.7%

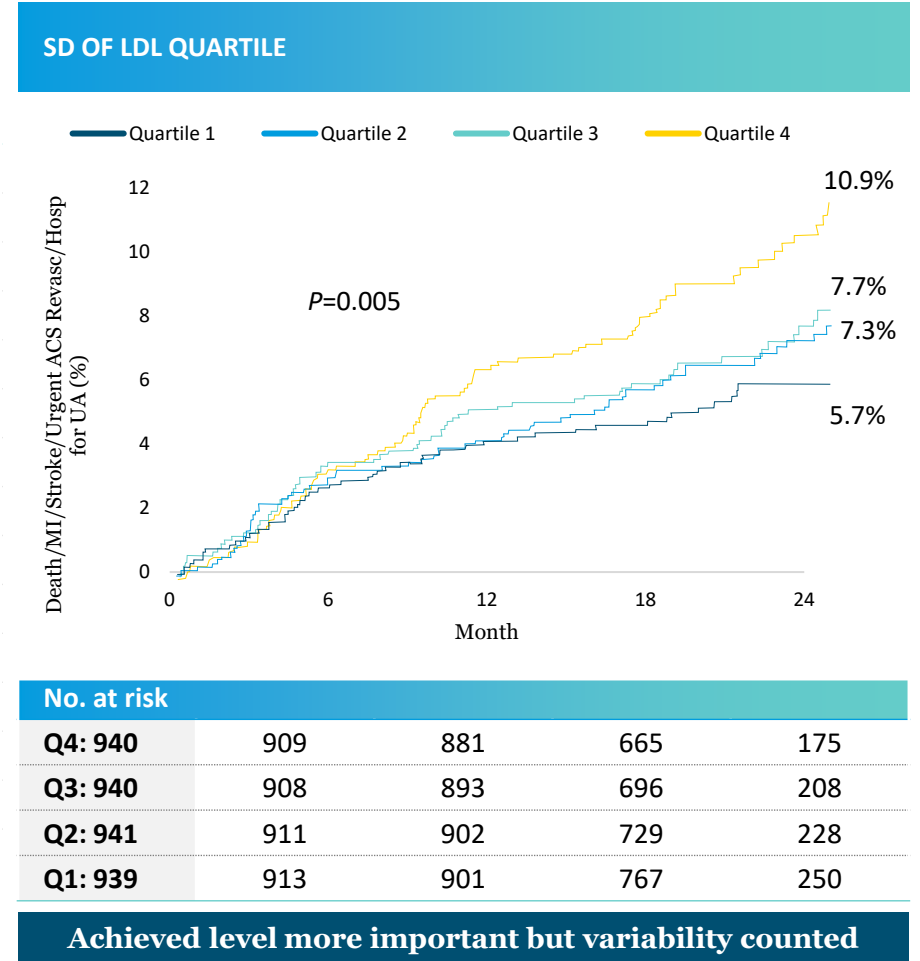Month

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)

40%

Poor adherence

0   0.2   0.4   0.6   0.8   1

Prevalence of good Adherence (%)

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	**-15%**	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)

0.3 0.5 0.7 1 1.2

Good Adherence   **Poor Adherence**

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!