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# **Reducing CVD globally through combination approaches to prevention: the polypill.**

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# Disclosure

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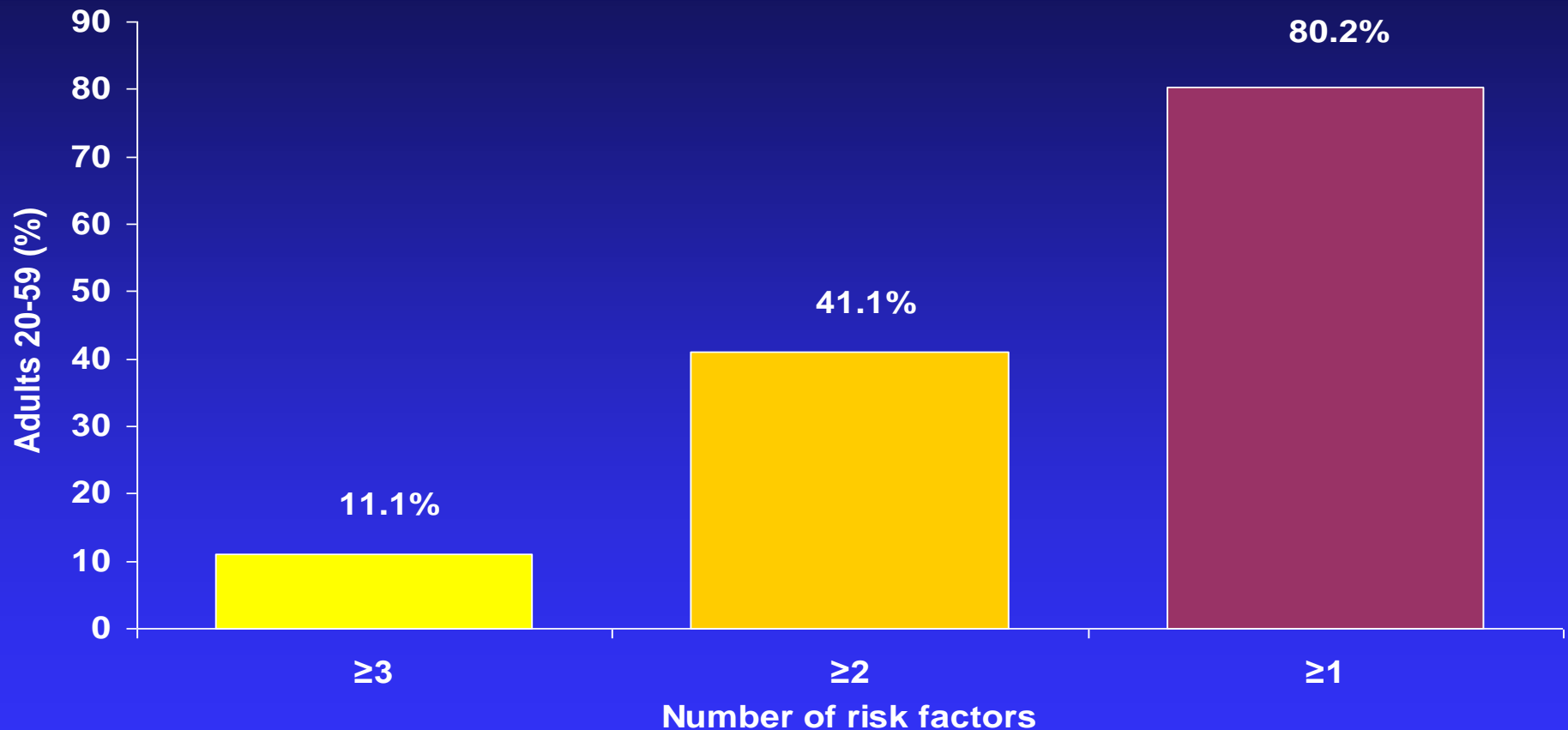
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# Polypill & CVD Prevention

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1. Why do we need a polypill?
2. What components in the polypill?
3. What are the data re polypill?
4. In whom can the polypill be used?
  - now
  - potentially in the future
5. The polypill as part of a strategy for cost efficient prevention & treatment

# High Prevalence of Multiple Risk Factors Among Canadian Adults

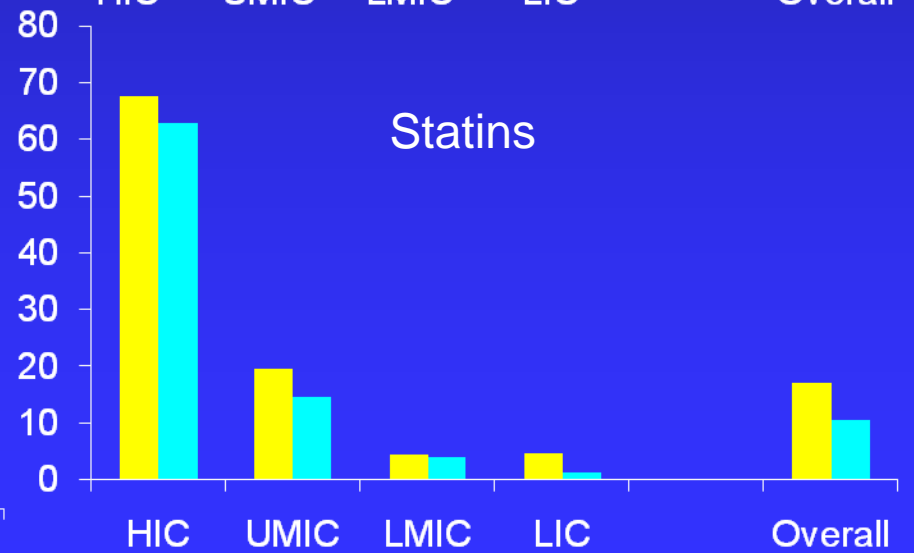
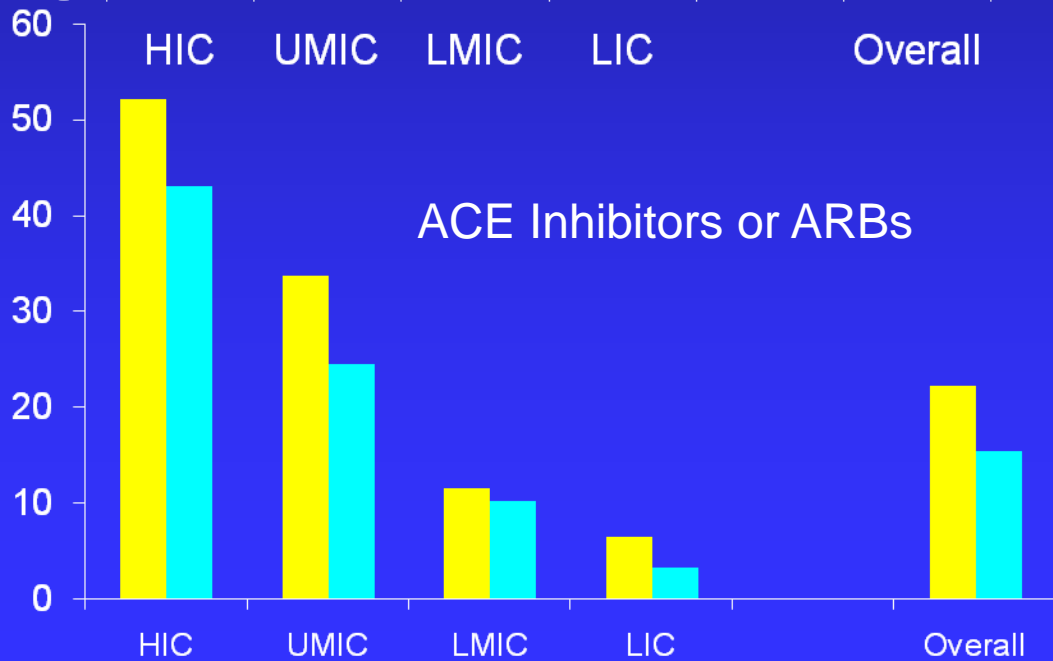
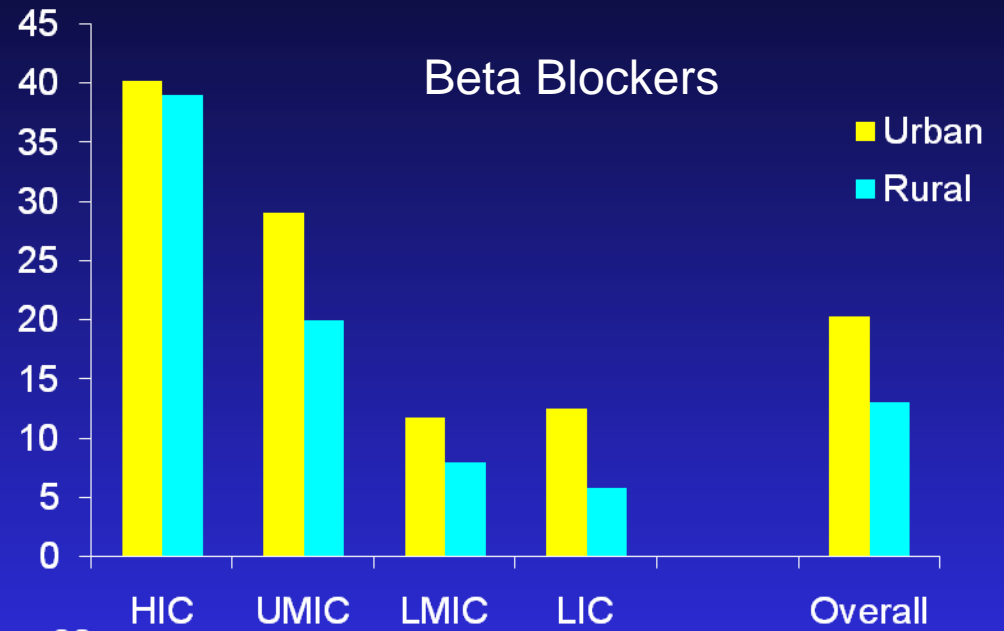
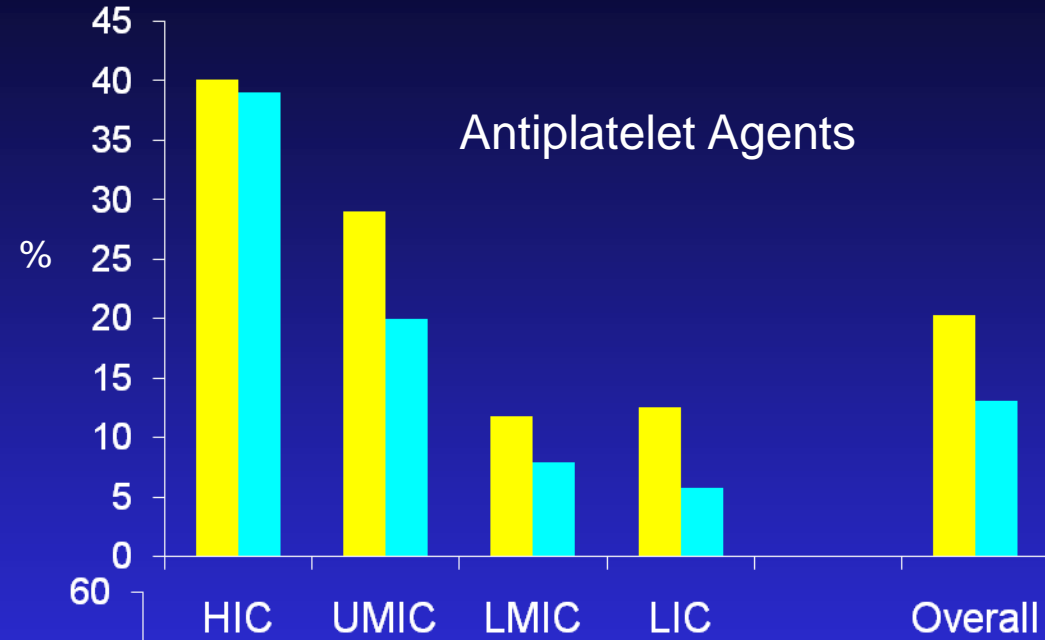


Includes smoking, physical inactivity, overweight, high BP, diabetes

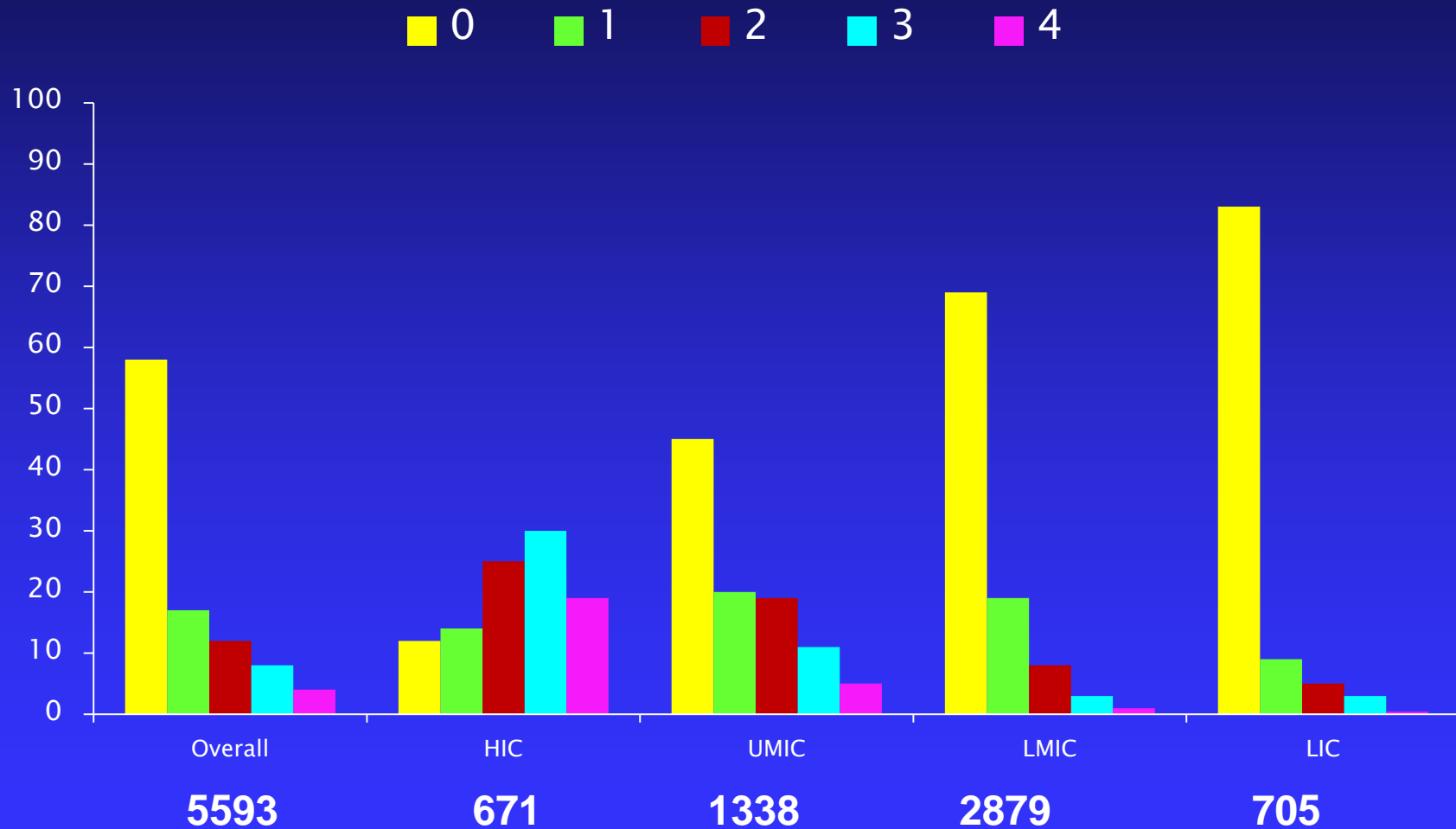
# Risk of AMI associated with Risk Factors in the Overall Population

Risk factor	% Cont	% Cases	PAR 1 (99% CI)
ApoB/ApoA-1(5 v 1)	20.0	33.5	54.1 (49.6, 58.6)
Curr smoking	26.8	45.2	36.4(33.9,39.0)
Diabetes	7.5	18.5	12.3 (11.2, 13.5)
Hypertension	21.9	39.0	23.4 (21.7, 25.1)
Abd Obesity (3 v 1)	33.3	46.3	33.7 (30.2, 37.4)
Psychosocial	-	-	28.8 (22.6, 35.8)
Veg & fruits daily	42.4	35.8	12.9 (10.0, 16.6)
Exercise	19.3	14.3	25.5 (20.1, 31.8)
Alcohol	24.5	24.0	13.9 (9.3, 20.2)
Combined	-	-	<b>90.4 (88.1, 92.4)</b>

# Drugs



# % receiving proven medications in CAD (154,000 people from 17 countries:PURE)

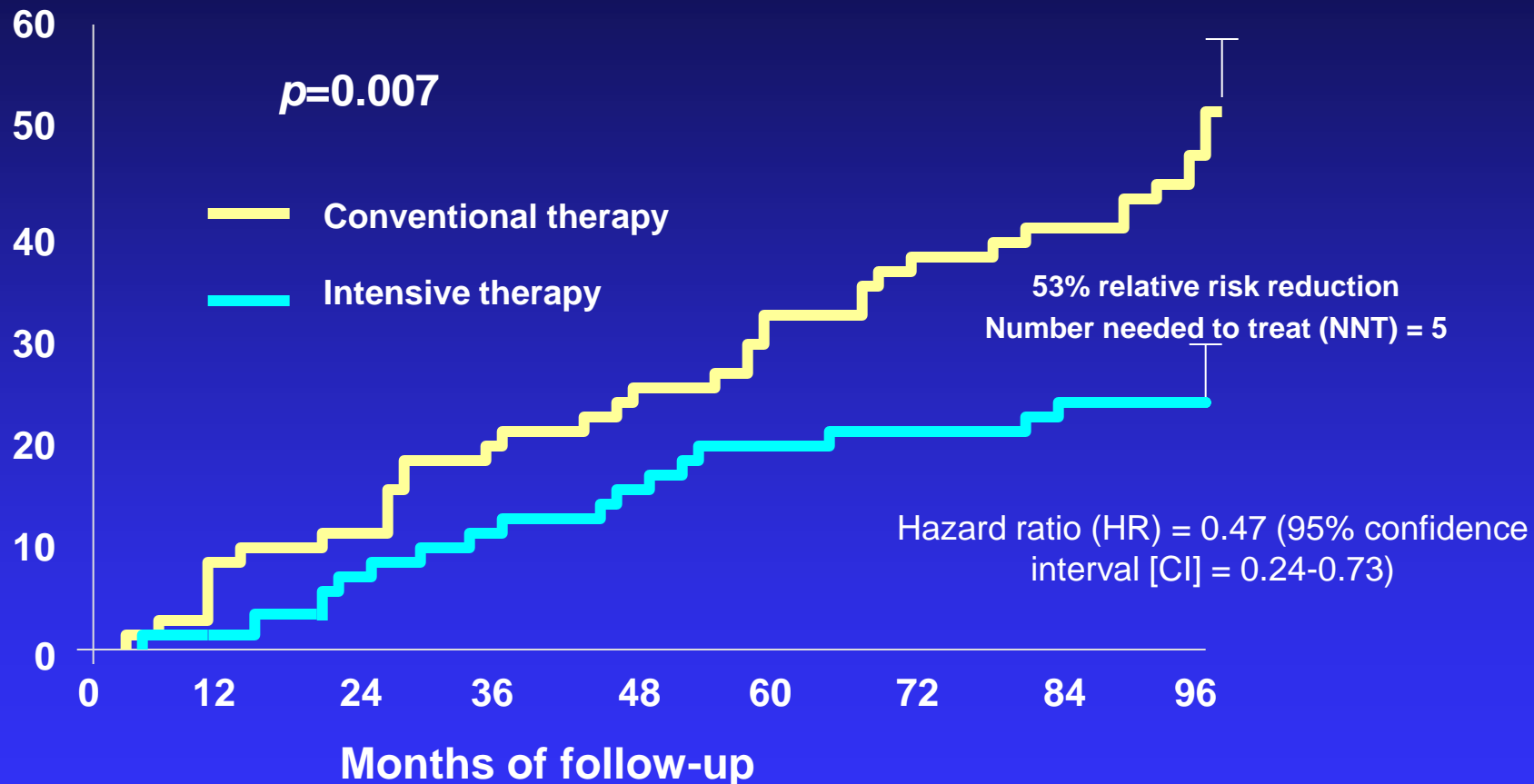


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**What is the early evidence showing the effectiveness of global risk management strategies?**



# Steno-2: Effects on Combined CV Outcomes



# Effect of long-term modest reductions in CV risk factors



# “Combination Pill” / “Polypill”

- Yusuf /Peto: Propose combination pill of ACEI, BB, ASA and statin in secondary prevention to reduce risk by 75%.
- Wald /Law: 3 BP lowering drugs at half doses + statin + ASA+ folate: Could reduce CVD by 80 to 90%!
- Give it to all over 55 yrs without measuring anything else!  
Excellent tolerability

# TIPS: Components of each Groups vs Low dose Polycap

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Antiplatelet	ASA	100 mg/d
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Statin	Simvastatin	20 mg/d
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ACE-Inhibitors	Ramipril	5 mg/d
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Beta-blocker	Atenolol	50 mg/d
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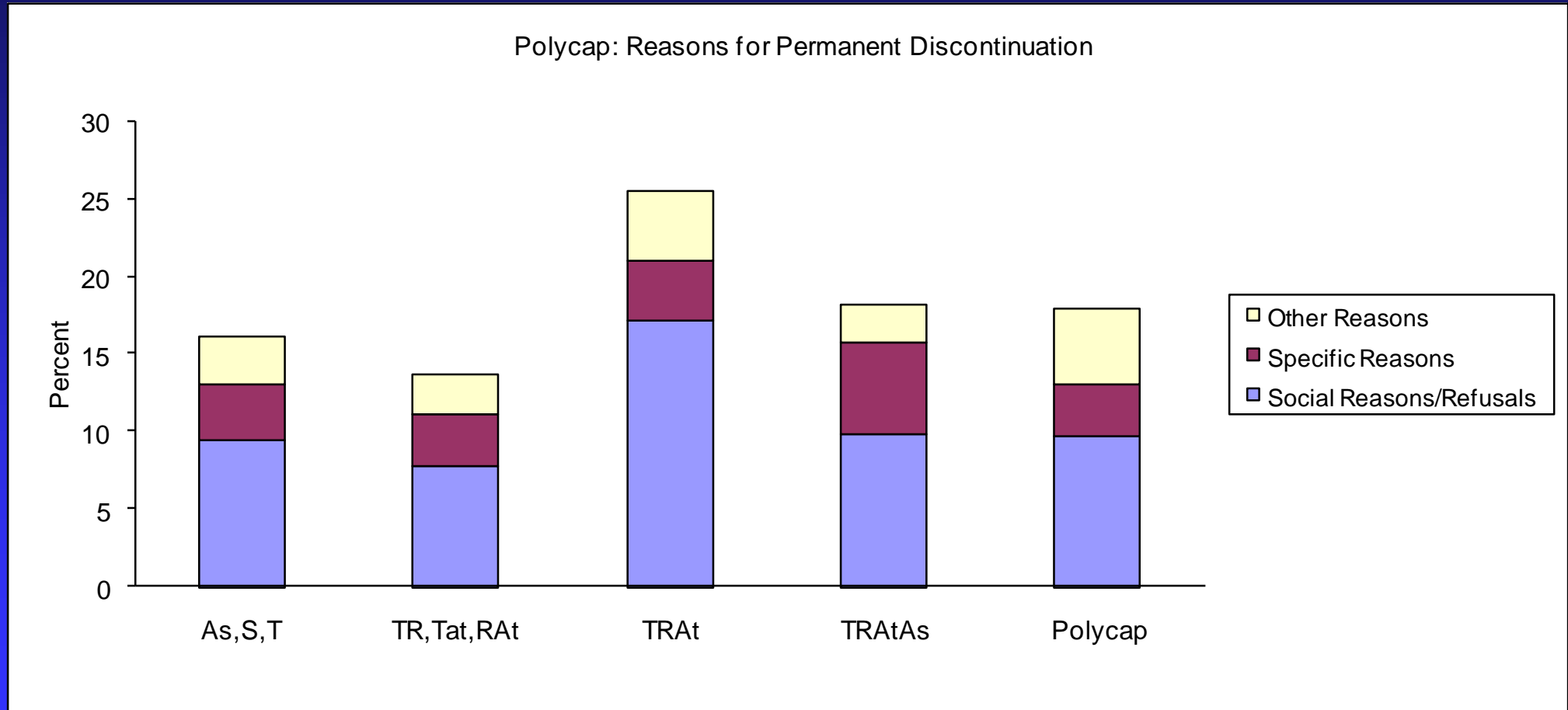
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Diuretic	Hydrochlorothiazide	12.5 mg/d
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Polycap	All of the above	
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# TIPS: Reasons for Permanent Discontinuation of Study Drug



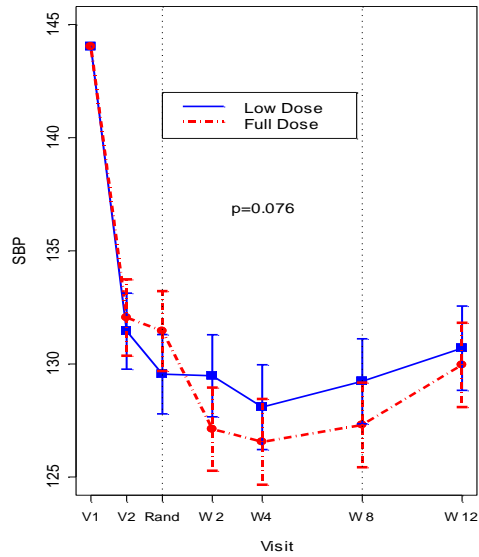
# Estimated reductions in CHD/Stroke of a low dose Polycap in Those With Average Risk Factor Levels

		% Relative Reduction		
		Reduction in Risk Factors	CHD	Stroke
LDL-C (mmol/L)	Est (Simv 20)	0.80	27%	8%
DBP (mmHg)	Est (3, ½ dose)	5.7	24%	33%
Platelet function	Est (ASA 100 mg)	Similar	32%*	16%
Combined	Est	-	<b>62%</b>	<b>48%</b>

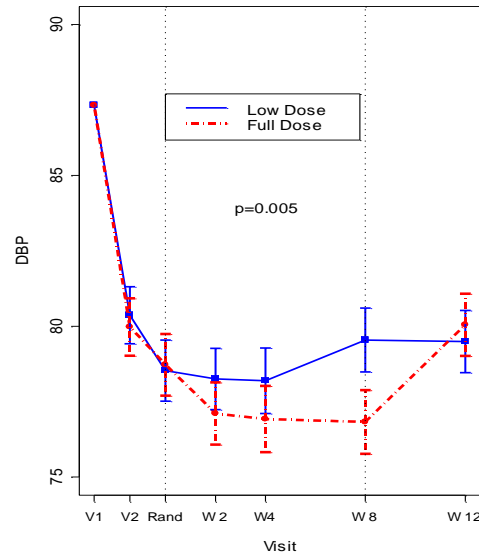
\*RCTs suggest a smaller benefit

# Changes in BP with Full dose vs low dose Polycap: TIPS-2

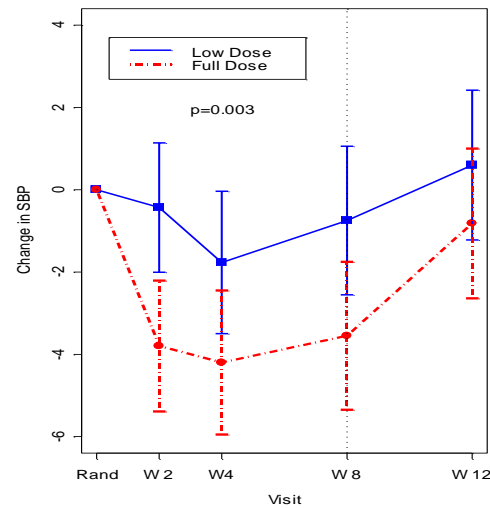
Systolic BP



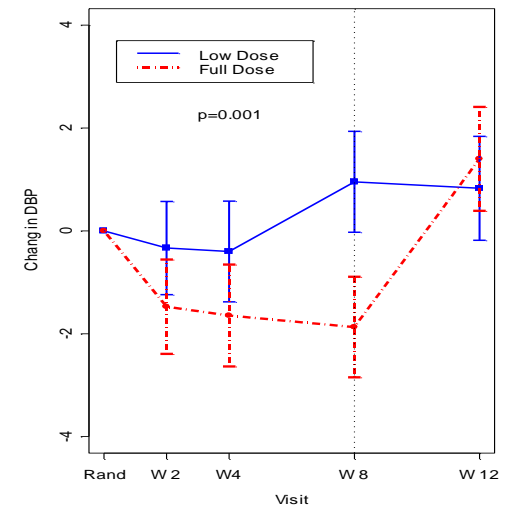
Diastolic BP



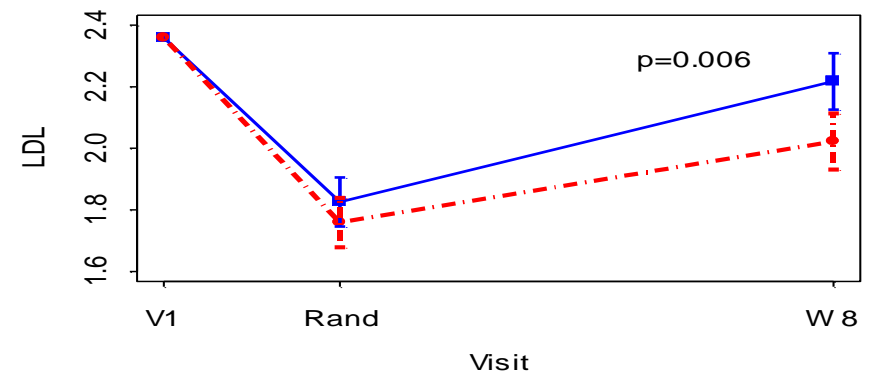
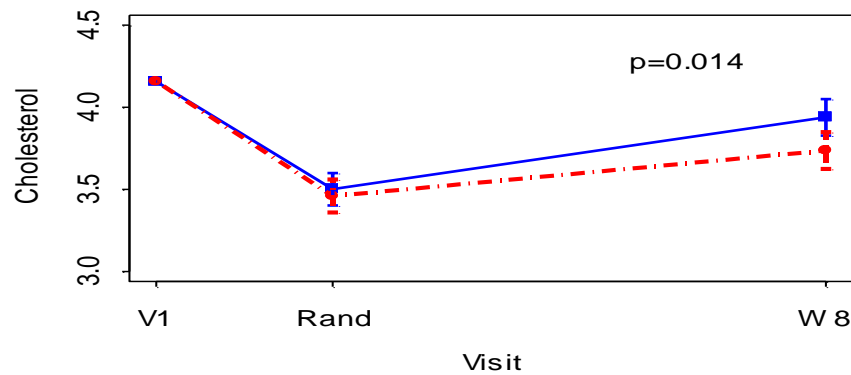
Systolic BP



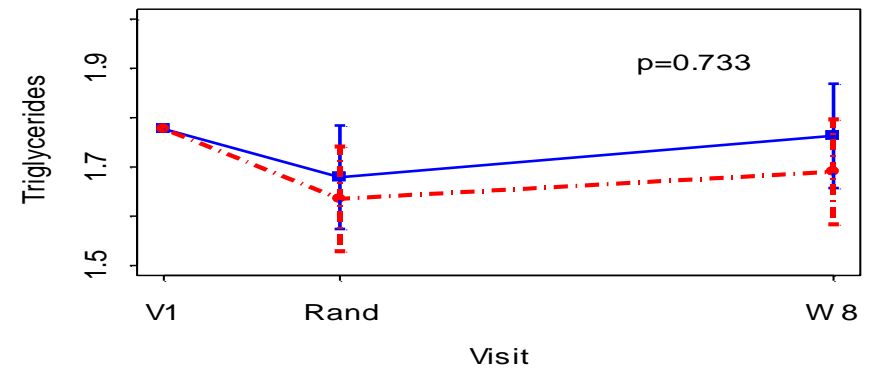
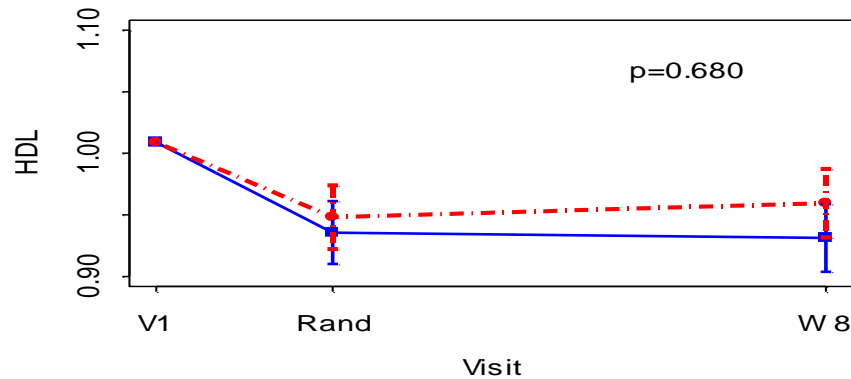
Diastolic BP



# Changes in lipids with full dose vs low dose Polycap: TIPS-2



— Low Dose  
- - Full Dose





# Estimated reductions in CHD/Stroke of a Full dose Polycap in Those With Average Risk Factor Levels

		% Relative Reduction		
		Reduction in Risk Factors	CHD	Stroke
LDL-C (mmol/L)	Est (Simv 40)	1.1	35%	15%
DBP (mmHg)	Est (3, full dose)	10.0	40%	50%
Platelet function	Est (ASA 100 mg)	Similar	32%*	16%
Combined	Est	-	<b>70 to 80%</b>	<b>65 to 75%</b>

\* RCTs suggest a smaller benefit

# Trials with the Polypill

Authors	Components (dose in mg)	No	$\Delta$ BP (mmHg)	$\Delta$ LDL (mmol/L)	Proj RRR in CVD
1. TIPS-1 (Lancet 2009)	ASA (100), Ram (5), HTZ (12.5), AT (50), Simv (20)	2053	-7.4/-5.6	0.80	~55%
2. TIPS-2 (unpublished)	Double of above	510 (?)	-12/-7.5*	1.0*	~65%*
3. PILL Collab (PLOS One 2011)	ASA (75), Lis (10, HCTZ (12.5), Simv (20)	378	-9.9/5.3	0.8	~50%
4. Malekzadeh (Int J Clin Pract 2010)	ASA (81), Enal (2.5), HCTZ (12.5), Atorv (20)	475 (348 completed)	-4.5/-1.6	0.46	~25%

# Who should get the polypill ?

- *ON CURRENT EVIDENCE:*

Those with established vascular disease (v high risk).

Those without vascular disease, but at hi risk( >2% /yr) eg. hi risk hypertension, diabetes or multiple RF.

- *POTENTIAL:*

Moderate risk individuals eg >55 yrs + additional RF (trials underway: HOPE-3 and TIPS- 3).

- *FUTURE:*

All >55 yrs(????!!!!)

# The Polycap to revolutionize prevention

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- Low cost(<\$ 5 to 10/mo), simple (little dose titration), safe, well tolerated (so no monitoring).
- Can the polycap be used by NPHW (using algorithms and phys mentorship) for secondary and hi risk prim prev (diabetes, hypertension)?
- Physician involved only with complex patients, “resistant” risk factors or side-effects?