

## Appendix 1. SEARCH STRATEGY

### Search terms

In the first stage, broad search terms were used and in the second stage, more focused terms were used:

1. “prevention”, “policy”, “health systems”, “cardiovascular”, “drugs”
2. “barriers”, “facilitators”

### Databases

Stage 1 search: Pubmed

Stage 2 search: Global Health, Cochrane, Latin American and Caribbean Health Sciences Literature (LILACS), Africa-Wide Information, Index Medicus for the South-East Asian Region (IMSEAR), Index Medicus for the Eastern Mediterranean Region (IMEMR) Western Pacific Rim Region Index Medicus (WPRIM), (Sociofile, PsychLit, PAIS, IBSS, IPSA and HealthStar), Health System Evidence ([www.healthsystemsevidence.org](http://www.healthsystemsevidence.org)) and EVIPnet.

HMIC (Health Management)

EMBase (pharma-OVID)

Psychinfo(Ovid)

Stage 3 search: Review of relevant articles, conference proceedings, expert opinion

### Stage 1 search

#### Search terms

("humans"[All Fields]) AND ((((\*prevention/) AND ((((((  
((( (\*policy) OR \*health systems) OR  
\*delivery of healthcare/) OR \*primary healthcare/) OR \*h  
ealth services accessibility/) OR  
\*health services research/) OR \*financing, government/))  
AND (((((((((cardiovascular disease/  
OR \*myocardial infarction/) OR \*acute coronary syndromes)  
OR (\* AND ((ischaemic OR  
coronary) AND heart disease))) OR (\*peripheral AND (vascu  
lar OR arterial) AND disease))  
OR \*cerebrovascular disease/) OR (\*stroke OR transient isc  
haemic attacks)))))) AND (drugs  
OR medicines OR medications))

#### Search Strategy used for Pubmed

("humans"[All Fields]) AND ((((\*prevention/) AND (((((((((( (\*policy) OR \*health systems)  
OR \*delivery of healthcare/) OR \*primary healthcare/) OR \*health services  
accessibility/) OR \*health services research/) OR \*financing, government/)) AND  
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syndromes) OR (\* AND ((ischaemic OR coronary) AND heart disease))) OR  
(\*peripheral AND (vascular OR arterial) AND disease)) OR \*cerebrovascular  
disease/) OR (\*stroke OR transient ischaemic attacks)))))) AND (drugs OR medicines  
OR medications))

### Search Strategy used for Pubmed

1. \*cardiovascular disease/ (1925838)
2. \*myocardial infarction/ (196118)
3. \*acute coronary syndromes/ (23620)
4. \*((ischaemic OR coronary) AND heart disease) (829052)
5. \*peripheral AND (vascular OR arterial) AND disease (32365)
6. \*cerebrovascular disease/ (288502)
7. \*stroke OR transient ischaemic attacks (223015)
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 (2074187)
9. \*policy/ (249454)
10. \*health systems/ (152720)
11. \*delivery of healthcare/ (807321)
12. \*primary healthcare/ (171255)
13. \*health services accessibility/ (84317)
14. \*health services research/ (262948)
15. \*financing, government/ (82785)
16. 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 (1280713)
17. 16 AND 8 (74709)
18. \*prevention/ (1252177)
19. 17 AND 18 (20526)
20. drugs OR medicines OR medications (1169931)
21. 19 AND 20 (2367)
22. "humans"[species] (13303958)
23. 21 AND 22 (2252)
24. barriers OR facilitators (73319)
25. 23 AND 24 (2442)

### **Stage 2 search**

Search of additional databases (131 additional references). Total 2573 references from Stage 1&2 searches. Eliminating duplicates led to 2188 references.

### **Stage 3 search**

Searching reference lists (18) and forward citation searching (40)

Supplementary Table 1a. Summary of findings of studies examining the associations of barriers/facilitators and adherence.

Barriers/ Facilitators	Study (Author, Year, Setting)	Context	Study Design	Sample Size	Study details	Outcome	Relevant findings (95% confidence intervals given where available)
Patient counselling	O'Carroll R, 2013 (UK) (21)	First stroke/TIA	RCT	62	Intervention= two-physician-led counselling sessions aimed at increasing adherence	Adherence to antihypertensive medication at 3 months Electronic pill bottle & self-report	<b>Intervention vs control: by electronic pill count, percentage of doses taken on schedule-96.8% vs 87.4%, mean difference 9.8 %, 95 % CI 0.2-16.2; p=0.048</b>
	Hornnes N, 2011 (Denmark) (22)	Acute stroke/TIA	RCT	349	Intervention= 4 home visits by a nurse with individually tailored counselling on a healthy lifestyle.	Adherence to antihypertensive therapy at 1 year Self-report	Intervention vs control: 98% vs 99%, OR 0.88, 95% CI 0.54-1.44 ; p=0.50
	Maron DJ, 2010 (USA and Canada) (39)	Stable CHD	Prospective cohort	2287	Nurse-led case management nested in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial. CVD drugs provided at no cost.	Adherence and persistence to 4D at 5 years Self-report	<b>Persistence increased from baseline to 5 years as follows: antiplatelets 87% to 96%, (OR 3.58, 95% CI 2.48-5.18); beta-blockers 69% to 85% (OR 2.54, 2.06-3.15); ARBs 46% to 72%(OR 3.02, 2.53-3.60), statins 64% to 93%(OR 7.51, 5.67-9.94), 4D 28% to 53% (OR 2.90, 95% CI 2.44-3.43) (all p&lt;0.001).</b> Adherence was 97% at 6 months and 95% at 5 years.
	McManus JA, 2009 (UK) (23)	Stroke in hospital	RCT	102	Intervention = 3-month,nurse-led health counselling with written and verbal information on lifestyle.	Adherence and persistence to 4D at 3 years Self-report	Persistence: 95% vs 89%, OR 3.00, 0.57-15.7 (p=0.19) for antiplatelets 97% vs 95%, OR 1.02, 0.55-1.91 (p=0.95) for antihypertensives 88% vs 89%, OR 1.03, 0.25- 4.14 (p=0.97) for statins Adherence to 4D: 78% vs 92%, OR 0.30, 0.07-1.24 (p=0.10)
	Faulkner MA, 2000 (USA) (17)	CABG	RCT	30	Intervention=weekly pharmacy-led telephone contact for 12 weeks	Adherence to lovastatin at 1 year and 2 years Prescription fill rate	<b>Intervention vs control: 67% vs 33%; p&lt;0.05 at 1 year and 60% vs 27%; p&lt;0.05 at 2 years (chi-squared test reported)</b> At 1 yr, OR 4.00, 0.88-18.26; p=0.07, and at 2 yrs, OR 4.13, 0.88-19.27; p=0.07
Hospital quality improvement programmes	Bushnell C, 2011 (USA)(30)	Ischemic stroke/TIA in hospital	Retrospective cohort	2457	Guideline implementation in the Adherence eValuation After Ischemic stroke-Longitudinal (AVAIL) Registry in a sample of hospitals participating in the Get With The Guidelines-Stroke program	Persistence and adherence to 4D at 1 year Self report	<b>Persistence and adherence associated with: number of medications prescribed at discharge (OR=1.08, 1.04-1.11; p&lt;0.001 per 1 decrease); and follow-up appointment with primary care physician (OR=1.72, 1.12-2.52; p= 0.006).</b>
	Johnston C, 2010 (USA) (19)	Ischaemic stroke in hospital	RCT	3361	Intervention: assistance in the development and implementation of standardized stroke discharge orders.	Adherence to statin at 6 months Prescription fill rate	Intervention vs non-intervention hospitals, At hospital level: OR, 1.26; 0.70 -2.30; p=0.36. <b>At individual level: OR, 1.29, 1.04-1.60; p=0.02.</b>
	Jackevicius CA, 2008 (Canada) (31)	AMI in hospital	Retrospective cohort	4591	Quality improvement of care in the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) study registry in Ontario	Adherence to 4D at 120 days Prescription fill rate	<b>PredischARGE medication counselling: OR 1.61, 1.26-2.04; p=0.0001</b> <b>Cardiologist (vs GP) as doctor responsible for patient's care: OR 1.80, 1.34-2.43; p=0.0001.</b> Teaching vs other hospital: OR 1.35,0.93-1.97;p=0.11
Generic versus branded drugs	O'Brien EC, 2015 (USA) (37)	NSTEMI in hospital	Retrospective cohort	1421	NSTEMI patients: 65 years old discharged on a statin in 2006 from USA hospitals.	Adherence to statins at 1 year Prescription refill rate	Generic vs brand users: 86.0% [IQR = 42.6%-97.2%] vs 84.1% [IQR = 53.4%-97.0%]), (p= 0.97)
Complexity of treatment regimen	Castellano JM, 2014 (Argentina, Brazil, Italy, Paraguay &Spain)(25)	Aged >40 years with acute MI in last 2 years	Cross-sectional study	2118	In a single visit, data was gathered to estimate prescription, adherence and barriers to adherence for aspirin, ACEIs, beta-blockers, and statins	Adherence to 4D Self report	<b>Nonadherence was associated with age&lt;50years (OR 1.50, 95% CI 1.08-2.09; p=0.015), depression (OR 1.07, 95% CI 1.04-1.09; p&lt;0.001), being on a complex medication regimen (OR 1.42, 95% CI 1.00-2.02: p=0.047) and lower level of social support (OR 0.94 0.92-0.96; p&lt;0.001)</b>
Fixed dose combination therapy	Thom S, 2013 (India, Europe) (20)	High CV risk	RCT	1698	Intervention=FDC (containing either: 75 mg aspirin, 40 mg simvastatin, 10 mg lisinopril, and 50 mg atenolol or 75 mg aspirin, 40 mg simvastatin, 10 mg lisinopril and 12.5 mg hydrochlorothiazide)	Adherence to 4D at 15 months Self report	<b>FDC vs separate medications: RR 1.29, 95% CI 1.22-1.36; p&lt;0.0001</b>
	Castellano JM, 2014 (Argentina, Brazil, Italy, Paraguay and Spain) (25)	Aged >40 years with MI within last 2 years.	RCT	695	Intervention=FDC (containing aspirin 100 mg, simvastatin 40 mg, and ramipril 2.5, 5, or 10 mg)	Adherence at 9 months Self report and pill count	<b>FDC vs separate medications: RR 1.24, 95% CI 1.06 to 1.47; p= 0.009</b>
	Selak V, 2014 (New Zealand)(28)	High CV risk	RCT	233	Intervention=FDC (with two versions available: aspirin 75 mg, simvastatin 40 mg, and lisinopril 10 mg with either atenolol 50 mg or hydrochlorothiazide 12.5 mg).	Adherence to 4D at 12 months Self report	<b>FDC vs separate medications: RR 1.50, 95% CI 1.25-1.82; p&lt;0001</b>
	Patel A, 2015 (Australia, New Zealand)(26)	High CV risk	RCT	381	Intervention=FDC (containing aspirin 75 mg, simvastatin 40 mg, lisinopril 10 mg and either atenolol 50 mg or hydrochlorothiazide 12.5 mg)	Adherence to 4D at 18 months (median follow-up) Self report	<b>FDC vs separate medications: RR 1.26, 95% CI 1.08-1.48; p&lt;0001</b>

Barriers/ Facilitators	Study (Author, Year, Setting)	Context	Study Design	Sample Size	Study details	Outcome	Relevant findings (95% confidence intervals given where available)
Co-payments for medical care	Winkelmayr WC, 2007 (Austria) (34)	AMI in hospital	Retrospective cohort	4105	The association between copayments and outpatient use of beta-blockers, statins, and ACEI/ARB in Austrian MI patients	Adherence at 120 days Prescription refill rate	<b>Adherence (waived co-payments vs co-payment): OR 1.35; 95% CI 1.10–1.67 for ACEI/ARB, OR 1.09; 0.89–1.35 for <math>\beta</math>-blocker and OR 1.09;0.89–1.34 for statin</b>
	Ye X, 2007 (USA) (35)	CHD and hospital-initiated statin	Retrospective cohort	5548	Databases containing inpatient admission, outpatient, enrollment, and pharmacy claims from 1999 to 2003 to study associations with copayments.	Adherence to statins at 1 year Prescription refill rate	<b>Non-adherence (co- payment <math>\geq</math>\$20 vs co-payment <math>&lt;</math>\$10): OR 0.42; 95% CI, 0.36–0.49.</b>
Insurance and prescription cost assistance	Choudhry NK, 2011 (USA) (27)	AMI in hospital	RCT	5855	intervention= full prescription coverage by insurance-plan sponsor	Adherence to 4D at 394 days (median follow-up) Prescription refill rate	<b>Full-coverage vs usual coverage: OR 1.41, 95% CI 1.18-1.56; p&lt;0.001 for 4D and p&lt;0.001 for all individual drug classes.</b>

Supplementary Table 1b. Summary of findings of studies examining the associations of barriers/facilitators and persistence.

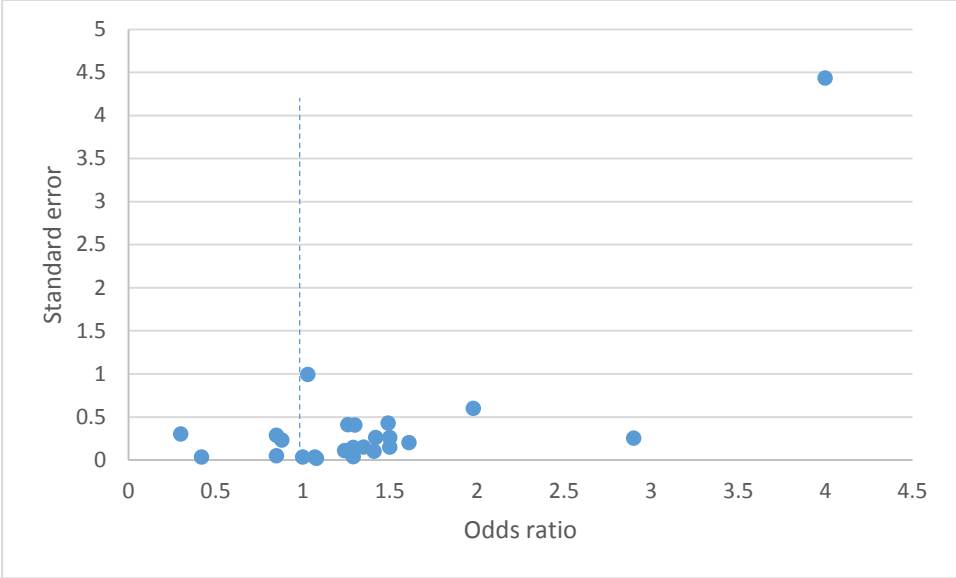
Barriers/ Facilitators	Study (Author, Year, Setting)	Context	Study Design	Sample Size	Study details	Outcome	Relevant findings (95% confidence intervals given where available)
Patient counselling	Maron DJ, 2010 (USA and Canada) (39)	Stable CHD	Prospective cohort	2287	Nurse-led case management nested in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial. CVD drugs provided at no cost.	Adherence and persistence to 4D at 5 years Self-report	<b>Persistence increased from baseline to 5 years as follows: antiplatelets 87% to 96%, (OR 3.58, 95% CI 2.48-5.18); beta-blockers 69% to 85% (OR 2.54, 2.06-3.15); ARBs 46% to 72%(OR 3.02, 2.53-3.60), statins 64% to 93%(OR 7.51, 5.67-9.94), 4D 28% to 53% (OR 2.90, 95% CI 2.44-3.43) (all p&lt;0.001).</b> Adherence was 97% at 6 months and 95% at 5 years (OR 0.60, 0.40-0.90, p=0.013).
	McManus JA, 2009 (UK) (23)	Stroke in hospital	RCT	102	Intervention = 3-month,nurse-led health counselling with written and verbal information on lifestyle.	Adherence and persistence to 4D at 3 years Self-report	Persistence: 95% vs 89%, OR 3.00, 0.57-15.7 (p=0.19) for antiplatelets 97% vs 95%, OR 1.02, 0.55-1.91 (p=0.95) for antihypertensives 88% vs 89%, OR 1.03, 0.25- 4.14 (p=0.97) for statins Adherence to 4D: 78% vs 92%, OR 0.30, 0.07-1.24 (p=0.10)
	Hohmann C, 2009 (Germany) (29)	Ischemic stroke/TIA in hospital	Non-randomized, controlled intervention trial	255	Intervention=hospital pharmacist counselling before discharge and plan for out-patient care plus counselling by community pharmacists	Persistence to aspirin and clopidogrel at 1 year Self-reported and GP-reported	Intervention: 38.7% vs 32.7%, OR 1.30, 0.73-2.31; p=0.37 for aspirin and 26.7% and 30.1%, OR 0.85, 0.46-1.57; p=0.60 for clopidogrel
	Lafitte M, 2009 (France) (36)	ACS in hospital	Prospective cohort	660	3 months after discharge for ACS, consecutive patients were invited to join a comprehensive risk factor management programme	Persistence to 4D at 20 months (mean follow-up) Self-report	At follow-up and baseline respectively but no control group reported: 86% vs 98% for beta blocker or a calcium antagonist, 88% vs 94% for statin, 96% vs 100% for antiplatelet, 62% vs 82% for ACEI/ARB, 76% vs 92% for 4D
	Yilmaz MB, 2005 (Turkey) (24)	On statin for secondary prevention in hospital	RCT	202	Intervention=counselling regarding efficacy, pharmacokinetic profile, and side effects of their statins.	Persistence to statin therapy at 15 months (median follow-up) Self-report	<b>62.7% versus 46%; OR=1.98, 1.13-3.47; p=0.017</b>
Hospital quality improvement programmes	Bushnell C, 2011 (USA)(30)	Ischemic stroke/TIA in hospital	Retrospective cohort	2457	Guideline implementation in the Adherence eValuation After Ischemic stroke–Longitudinal (AVAIL) Registry in a sample of hospitals participating in the Get With The Guidelines–Stroke program	Persistence and adherence to 4D at 1 year Self report	<b>Persistence and adherence associated with: number of medications prescribed at discharge (OR=1.08, 1.04-1.11; p&lt;0.001 per 1 decrease); and follow-up appointment with primary care physician (OR=1.72, 1.12-2.52; p=0.006).</b>
	Khanderia U, 2005 (USA) (40)	CABG in hospital	Retrospective case-control	403	A Physician education protocol to implement statin in all patients admitted for CABG.	Persistence to statins at 6 months Self-report	Intervention vs control: 67% vs 58%, OR 1.49, 0.88-2.55; p=0.14
Site of care and home circumstances of patients	Glader E-L, 2010 (Sweden) (32)	Acute stroke in hospital	Prospective cohort	21077	A 1-year cohort (September 2005–August 2006) from the Swedish Stroke Register.	Persistence with 4D at 1 year Prescription fill rate	<b>Institutional living correlated with persistence for all drug classes (p=0.001). Stroke unit care was associated with persistence for statins (p=0.007). Support by next-of-kin associated with persistence for antihypertensives (p=0.001).</b>
Physician education/training	Ko DT, 2005 (Canada) (18)	AMI aged≥65 years in hospital	Retrospective cohort	63301	Evaluation on whether care by International medical graduates(IMGs) is a determinant of poor persistence and worse outcomes after AMI versus care by Canadian medical graduates (CMGs)	Persistence to 4D at 90 days Prescription refill	Adjusted OR(IMG/Canadian): aspirin 1.00 95% CI (0.94 - 1.06); BB 1.01 (0.94 - 1.08); ACEI <b>1.07 (1.01 - 1.14); statins 1.10 (1.01-1.20)</b>
	Harats D, 2005 (Israel) (33)	CHD in hospital	Cross-sectional then prospective Cohort	2994	Brief educational sessions with physicians to review National guidelines to ascertain physician's awareness	Persistence to statins at 8 weeks Self-report	Intervention vs control: <b>57% vs 45%. (p&lt;0001)</b>
Insurance and prescription cost assistance	Mathews R, 2015 (USA) (38)	ACS in hospital	Prospective cohort	7955	Within the Treatment with Adenosine Diphosphate Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome (TRANSLATE-ACS) study.	Persistence to 4D at 6 months Self-report	<b>Non-persistence less likely with private insurance (OR 0.85, 95% CI 0.76-0.95),prescription cost assistance (OR 0.63, 0.54-0.75),and clinic follow-up arranged pre-discharge (OR 0.89, 0.80-0.99)</b>

Supplementary Table 1c. Summary of findings of studies examining the associations of barriers/facilitators and adherence/persistence by drug class.

Study (Author, Year, Setting)	Context	Study Design	Sample Size	Study details	Outcome	Relevant findings (95% confidence intervals given where available)
<b>4D</b>						
Maron DJ, 2010 (USA and Canada) (39)	Stable CHD	Prospective cohort	2287	Nurse-led case management nested in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial. CVD drugs provided at no cost.	Adherence and persistence to 4D at 5 years Self-report	<b>Persistence increased from baseline to 5 years as follows: antiplatelets 87% to 96%, (OR 3.58, 95% CI 2.48-5.18); beta-blockers 69% to 85% (OR 2.54, 2.06-3.15); ARBs 46% to 72%(OR 3.02, 2.53-3.60), statins 64% to 93%(OR 7.51, 5.67-9.94), 4D 28% to 53% (OR 2.90, 95% CI 2.44-3.43) (all p&lt;0.001).</b> Adherence was 97% at 6 months and 95% at 5 years.
McManus JA, 2009 (UK) (23)	Stroke in hospital	RCT	102	Intervention = 3-month,nurse-led health counselling with written and verbal information on lifestyle.	Adherence and persistence to 4D at 3 years Self-report	Persistence: 95% vs 89%, OR 3.00, 0.57-15.7 (p=0.19) for antiplatelets 97% vs 95%, OR 1.02, 0.55-1.91 (p=0.95) for antihypertensives 88% vs 89%, OR 1.03, 0.25- 4.14 (p=0.97) for statins Adherence to 4D: 78% vs 92%, OR 0.30, 0.07-1.24 (p=0.10)
Lafitte M, 2009 (France) (36)	ACS in hospital	Prospective cohort	660	3 months after discharge for ACS, consecutive patients were invited to join a comprehensive risk factor management programme	Persistence to 4D at 20 months (mean follow-up) Self-report	At follow-up and baseline respectively but no control group reported: 86% vs 98% for beta blocker or a calcium antagonist, 88% vs 94% for statin, 96% vs 100% for antiplatelet, 62% vs 82% for ACEI/ARB, 76% vs 92% for 4D
Bushnell C, 2011 (USA)(30)	Ischemic stroke/TIA in hospital	Retrospective cohort	2457	Guideline implementation in the Adherence eValuation After Ischemic stroke-Longitudinal (AVAIL) Registry in a sample of hospitals participating in the Get With The Guidelines-Stroke program	Persistence and adherence to 4D at 1 year Self report	<b>Persistence and adherence associated with: number of medications prescribed at discharge (OR=1.08, 1.04-1.11; p&lt;0.001 per 1 decrease); and follow-up appointment with primary care physician (OR=1.72, 1.12-2.52; p=0.006).</b>
Jackevicius CA, 2008 (Canada) (31)	AMI in hospital	Retrospective cohort	4591	Quality improvement of care in the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) study registry in Ontario	Adherence to 4D at 120 days Prescription fill rate	<b>Predischarge medication counselling: OR 1.61, 1.26-2.04; p=0.0001</b> <b>Cardiologist (vs GP) as doctor responsible for patient's care: OR 1.80, 1.34-2.43; p=0.0001.</b> Teaching vs other hospital: OR 1.35,0.93-1.97;p=0.11
Glader E-L, 2010 (Sweden) (32)	Acute stroke in hospital	Prospective cohort	21077	A 1-year cohort (September 2005-August 2006) from the Swedish Stroke Register.	Persistence with 4D at 1 year Prescription fill rate	<b>Institutional living correlated with persistence for all drug classes (p=0.001). Stroke unit care was associated with persistence for statins (p=0.007).</b> <b>Support by next-of-kin associated with persistence for antihypertensives (p=0.001).</b>
Castellano JM, 2014 (Argentina, Brazil, Italy, Paraguay &Spain)(25)	Aged >40 years with acute MI in last 2 years	Cross-sectional study	2118	In a single visit, data was gathered to estimate prescription, adherence and barriers to adherence for aspirin, ACEIs, beta-blockers, and statins	Adherence to 4D Self report	<b>Nonadherence was associated with age&lt;50years (OR 1.50, 95% CI 1.08-2.09; p=0.015), depression (OR 1.07, 95% CI 1.04-1.09; p&lt;0.001), being on a complex medication regimen (OR 1.42, 95% CI 1.00-2.02: p=0.047) and lower level of social support (OR 0.94 0.92-0.96; p&lt;0.001)</b>
Thom S, 2013 (India, Europe) (20)	High CV risk	RCT	1698	Intervention=FDC (containing either: 75 mg aspirin, 40 mg simvastatin, 10 mg lisinopril, and 50 mg atenolol or 75 mg aspirin, 40 mg simvastatin, 10 mg lisinopril and 12.5 mg hydrochlorothiazide)	Adherence to 4D at 15 months Self report	<b>FDC vs separate medications: RR 1.29, 95% CI 1.22-1.36; p&lt;0.0001</b>
Selak V, 2014 (New Zealand)(28)	High CV risk	RCT	233	Intervention=FDC (with two versions available: aspirin 75 mg, simvastatin 40 mg, and lisinopril 10 mg with either atenolol 50 mg or hydrochlorothiazide 12.5 mg).	Adherence to 4D at 12 months Self report	<b>FDC vs separate medications: RR 1.50, 95% CI 1.25-1.82; p&lt;0001</b>
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Ko DT, 2005 (Canada) (18)	AMI aged≥65 years in hospital	Retrospective cohort	63301	Evaluation on whether care by International medical graduates (IMGs) is a determinant of poor persistence and worse outcomes after AMI versus care by Canadian medical graduates (CMGs)	Persistence to 4D at 90 days Prescription refill	Adjusted OR(IMG/Canadian): aspirin 1.00 95% CI (0.94 - 1.06); BB 1.01 (0.94 - 1.08); ACEI 1.07 (1.01 - 1.14); statins 1.10 (1.01-1.20)
Choudhry NK, 2011 (USA) (27)	AMI in hospital	RCT	5855	Intervention= full prescription coverage by insurance-plan sponsor	Adherence to 4D at 394 days (median follow-up) Prescription refill rate	<b>Full-coverage vs usual coverage: OR 1.41, 95% CI 1.18-1.56; p&lt;0.001 for 4D and p&lt;001 for all individual drug classes.</b>
Mathews R, 2015 (USA) (38)	ACS in hospital	Prospective cohort	7955	Within the Treatment with Adenosine Diphosphate Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome (TRANSLATE-ACS) study.	Persistence to 4D Self-report	<b>Non-persistence less likely with private insurance (OR 0.85, 95% CI 0.76-0.95),prescription cost assistance (OR 0.63, 0.54-0.75),and clinic follow-up arranged pre-discharge (OR 0.89, 0.80-0.99)</b>

Study (Author, Year, Setting)	Context	Study Design	Sample Size	Study details	Outcome	Relevant findings (95% confidence intervals given where available)
<b>Antihypertensive</b>						
O'Carroll R, 2013 (UK) (21)	First stroke/TIA	RCT	62	Intervention= two-physician-led counselling sessions aimed at increasing adherence	Adherence to antihypertensive medication at 3 months Electronic pill bottle & self-report	<b>Intervention vs control: by electronic pill count, percentage of doses taken on schedule-96.8% vs 87.4%, mean difference 9.8 %, 95 % CI 0.2-16.2; p=0.048</b>
Hornnes N, 2011 (Denmark) (22)	Acute stroke/TIA	RCT	349	Intervention= 4 home visits by a nurse with individually tailored counselling on a healthy lifestyle.	Adherence to antihypertensive therapy at 1 year Self-report	Intervention vs control: 98% vs 99%, OR 0.88, 95% CI 0.54-1.44 ; p=0.50
<b>Antiplatelet</b>						
Hohmann C, 2009 (Germany) (29)	Ischemic stroke/TIA in hospital	Non-randomized, controlled intervention trial	255	Intervention=hospital pharmacist counselling before discharge and plan for out-patient care plus counselling by community pharmacists	Persistence to aspirin and clopidogrel at 1 year Self-reported and GP-reported	Intervention: 38.7% vs 32.7%, OR 1.30, 0.73-2.31; p=0.37 for aspirin and 26.7% and 30.1%, OR 0.85, 0.46-1.57; p=0.60 for clopidogrel
<b>Statin</b>						
Faulkner MA, 2000 (USA) (17)	CABG	RCT	30	Intervention=weekly pharmacist-led telephone contact for 12 weeks	Adherence to lovastatin at 1 year and 2 years Prescription fill rate	<b>Intervention vs control: 67% vs 33%; p&lt;0.05 at 1 year and 60% vs 27%; p&lt;0.05 at 2 years (chi-squared test reported)</b> At 1 yr, OR 4.00, 0.88-18.26; p=0.07, and at 2 yrs, OR 4.13, 0.88-19.27; p=0.07
Yilmaz MB, 2005 (Turkey) (24)	On statin for secondary prevention in hospital	RCT	202	Intervention=counselling regarding efficacy, pharmacokinetic profile, and side effects of their statins.	Persistence to statin therapy at 15 months (median follow-up) Self-report	<b>62.7% versus 46%; OR=1.98, 1.13-3.47; p=0.017</b>
Johnston C, 2010 (USA) (19)	Ischaemic stroke in hospital	RCT	3361	Intervention: assistance in the development and implementation of standardized stroke discharge orders.	Adherence to statin at 6 months Prescription fill rate	Intervention vs non-intervention hospitals. At hospital level: OR, 1.26; 0.70 –2.30; p=0.36. <b>At individual level: OR, 1.29, 1.04-1.60; p=0.02.</b>
Khanderia U, 2005 (USA) (40)	CABG in hospital	Retrospective case-control	403	A Physician education protocol to implement statin in all patients admitted for CABG.	Persistence to statins at 6 months Self-report	Intervention vs control: 67% vs 58%, OR 1.49, 0.88-2.55; p=0.14
O'Brien EC, 2015 (USA) (37)	NSTEMI in hospital	Retrospective cohort	1421	NSTEMI patients ≥ 65 years old discharged on a statin in 2006 from USA hospitals.	Adherence to statins at 1 year Prescription refill rate	Generic vs brand users: 86.0% [IQR = 42.6%-97.2%] vs 84.1% [IQR = 53.4%-97.0%], (p= 0.97)
Harats D, 2005 (Israel) (33)	CHD in hospital	Cross-sectional then prospective Cohort	2994	Brief educational sessions with physicians to review National guidelines to ascertain physician's awareness	Persistence to statins at 8 weeks Self-report	Intervention vs control: <b>57% vs 45%. (p&lt;0001)</b>
Ye X, 2007 (USA) (35)	CHD and hospital-initiated statin	Retrospective cohort	5548	Databases containing inpatient admission, outpatient, enrollment, and pharmacy claims from 1999 to 2003 to study associations with copayments.	Adherence to statins at 1 year Prescription refill rate	<b>Non-adherence (co- payment ≥\$20 vs co-payment &lt;\$10): OR 0.42; 95% CI, 0.36–0.49.</b>
<b>Beta-blockers, statins and ACEI/ARB</b>						
Winkelmayer WC, 2007 (Austria) (34)	AMI in hospital	Retrospective cohort	4105	The association between copayments and outpatient use of beta-blockers, statins, and ACEI/ARB in Austrian MI patients	Adherence at 120 days Prescription refill rate	<b>Adherence (waived co-payments vs co-payment): OR 1.35; 95% CI 1.10–1.67 for ACEI/ARB, OR 1.09; 0.89–1.35 for β-blocker and OR 1.09;0.89–1.34 for statin</b>
<b>Beta-blockers, statins and ACEI/ARB</b>						
Castellano JM, 2014 (Argentina, Brazil, Italy, Paraguay and Spain) (25)	Aged >40 years with MI within last 2 years.	RCT	695	Intervention=FDC (containing aspirin 100 mg, simvastatin 40 mg, and ramipril 2.5, 5, or 10 mg)	Adherence to 4D at 9 months Self report and pill count	<b>FDC vs separate medications: RR 1.24, 95% CI 1.06 to 1.47; p= 0.009</b>

Supplementary Figure 1. Funnel plot for publication bias





## Appendix 2. Cochrane tool for assessment of risk of bias

Bias domain	Source of bias	Support for judgment	Review authors' judgment (assess as low, unclear or high risk of bias)
Selection bias	Random sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence
	Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen before or during enrolment	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment
Performance bias	Blinding of participants and personnel*	Describe all measures used, if any, to blind trial participants and researchers from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Detection bias	Blinding of outcome assessment*	Describe all measures used, if any, to blind outcome assessment from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Detection bias due to knowledge of the allocated interventions by outcome assessment
Attrition bias	Incomplete outcome data*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomised participants), reasons for attrition or exclusions where reported, and any reinclusions in analyses for the review	Attrition bias due to amount, nature, or handling of incomplete outcome data
Reporting bias	Selective reporting	State how selective outcome reporting was examined and what was found	Reporting bias due to selective outcome reporting
Other bias	Anything else, ideally prespecified	State any important concerns about bias not covered in the other domains in the tool	Bias due to problems not covered elsewhere

### Appendix 3. Tool for assessing risk of bias for observational studies

Type of bias	Study design			
	Cross sectional	Case control	Cohort	Ecological
Selection bias	Was the study population selected appropriate?			
	Was the sample representative of its target population?	Were the controls randomly selected from the same population as the cases?	Was an appropriate control group used?  Was follow up sufficiently complete? (>80%)	Were the subjects representative of the group, place, or population of interest?
Differential misclassification	Did the assessment of the exposure or outcome differ according to the patient status?	Did the exposure assessment differ for cases and controls?	Did the outcome assessment differ for exposed and non exposed?	Were the exposure and outcome variables measured and defined in the same or a similar way across the different groups studied?
Non-differential misclassification	Were valid methods used for measuring medication adherence and persistence?			
Confounding	Was any strategy undertaken to control for potential confounders?			
	<ol style="list-style-type: none"> <li>1. At the design stage (restriction, matching)</li> <li>2. At the analysis stage (stratification, multivariable analysis)</li> </ol>			

**Define each domain as low risk of bias, unclear risk of bias or high risk of bias**