Sex difference in long-term clinical outcomes after percutaneous coronary intervention

- A propensity-matched analysis of National Health Insurance data in Republic of Korea

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Disclosures

- No conflicts of interest or financial disclosures to report

Sex-disparities, True or False ?

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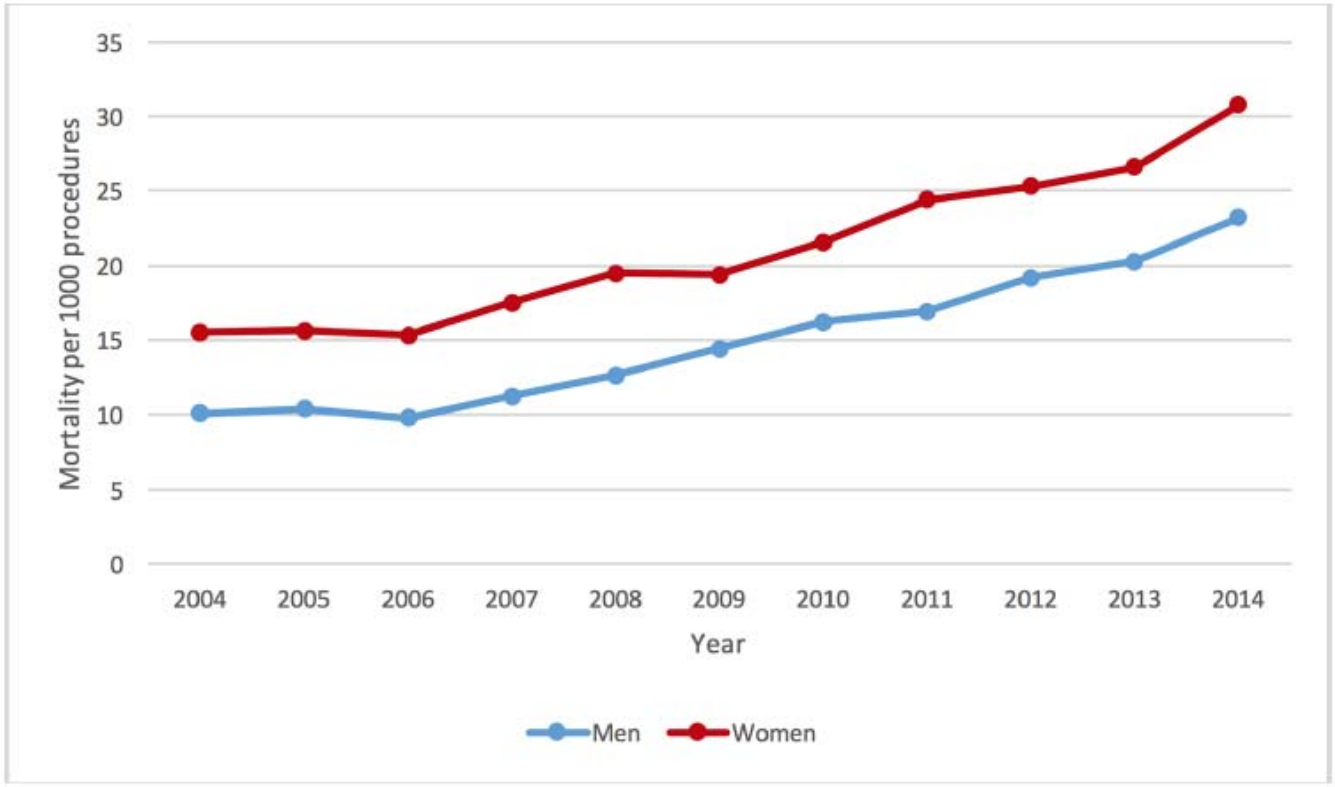
Female patients in randomized trials

- Under-represented, accounting for ~25% of patients
  - Comorbidities
  - Child-bearing potential
  - Older age

Chieffo A, EuroIntervention 2018

Annual rates of mortality for men and women per 1000 records.

Source, National Inpatient Sample Data, 2004 – 2014
N = 6,601,526



Potts J, *PLoS One* 2018

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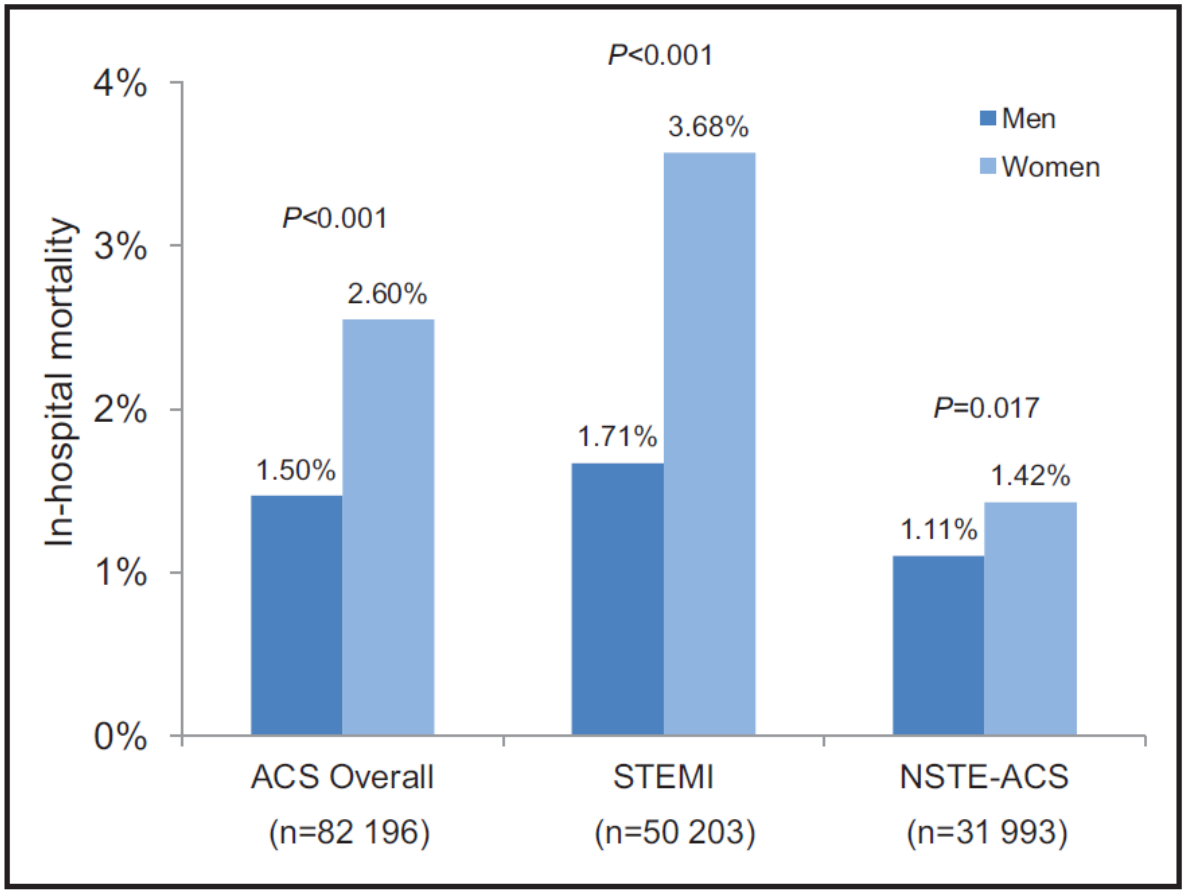
In-hospital mortality

Source, CCC-ACS project, 2014 – 2018
N = 82,196



Hao Y, *Circulation* 2019

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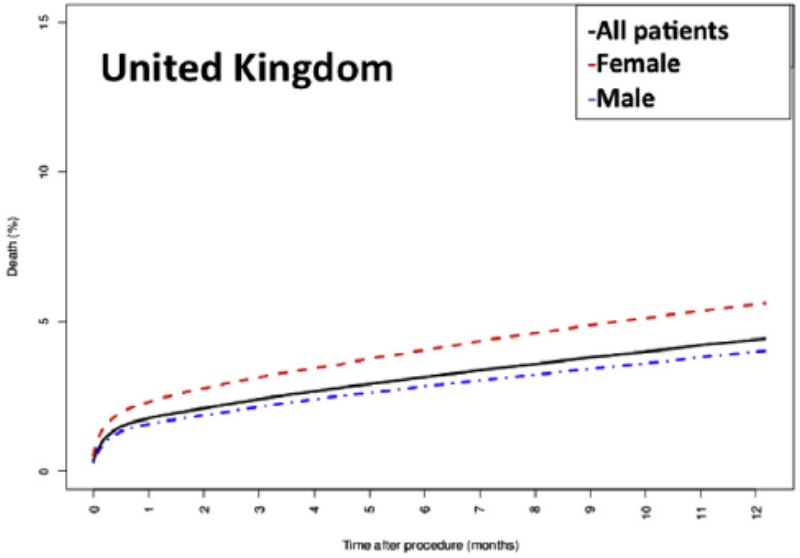
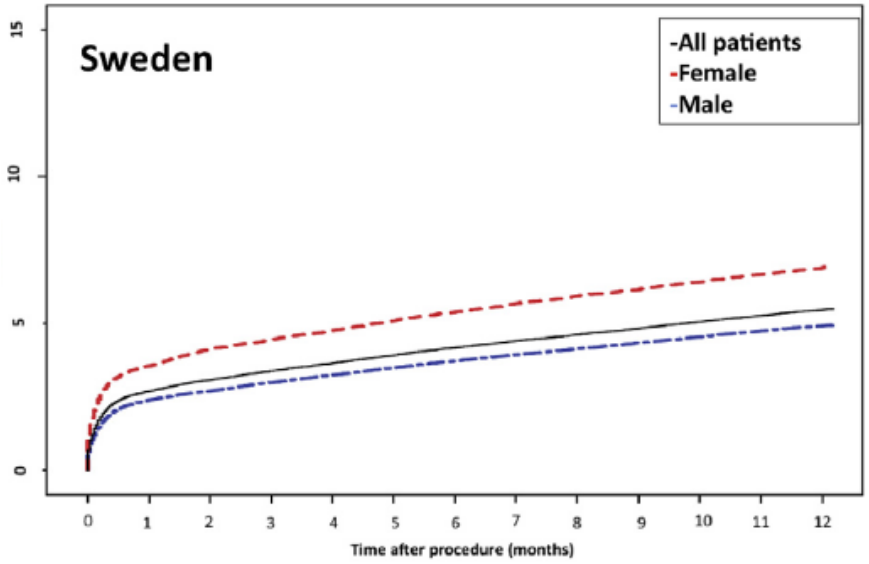
1 year all-cause mortality

Source, BCIS and the SCAAR registry, 2007 – 2011
N = 368,492/89,769



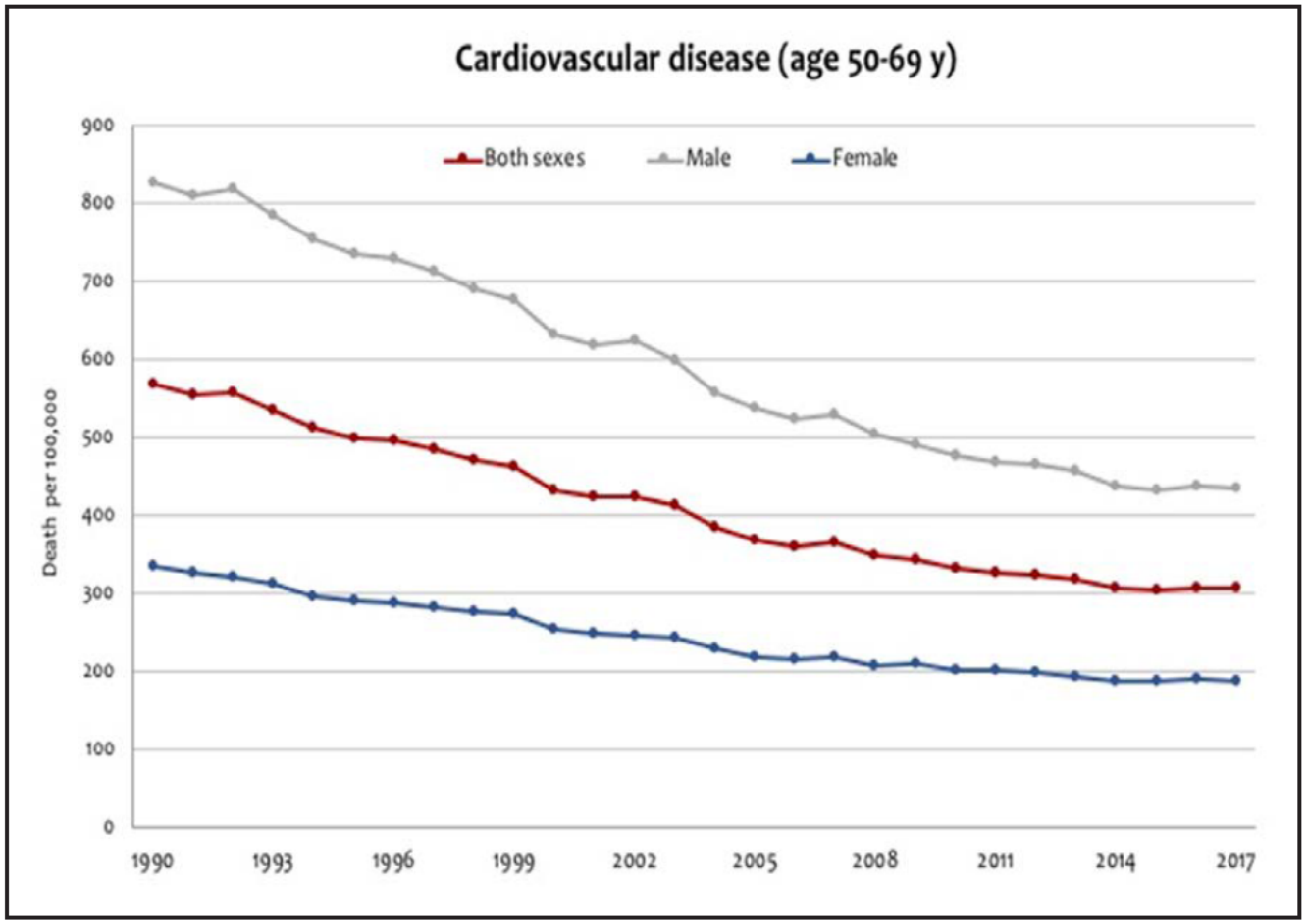
No. at risk	0 months	1 month	6 months	12 months
Female	85546	83586	82095	80744
Male	245913	242070	238954	236035



No. at risk	0 months	1 month	6 months	12 months
Female	24412	24189	22915	22533
Male	65357	62996	61331	61336

Kunadian V, *Am J Cardiol* 2017

Cardiovascular mortality during 3 decades



Evolution of cardiovascular mortality between 1990 and 2017.

Diaz R. *Circulation* 2019

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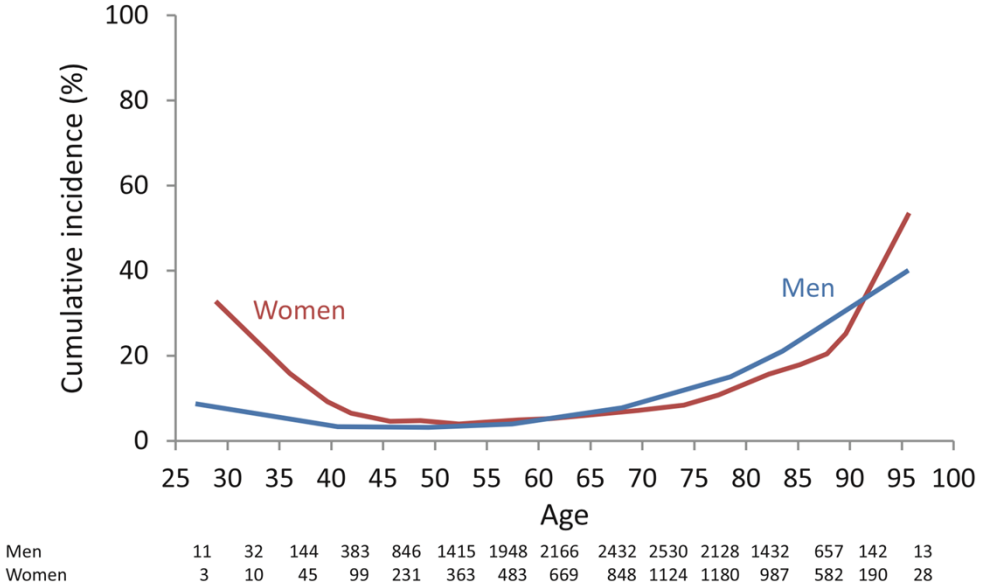
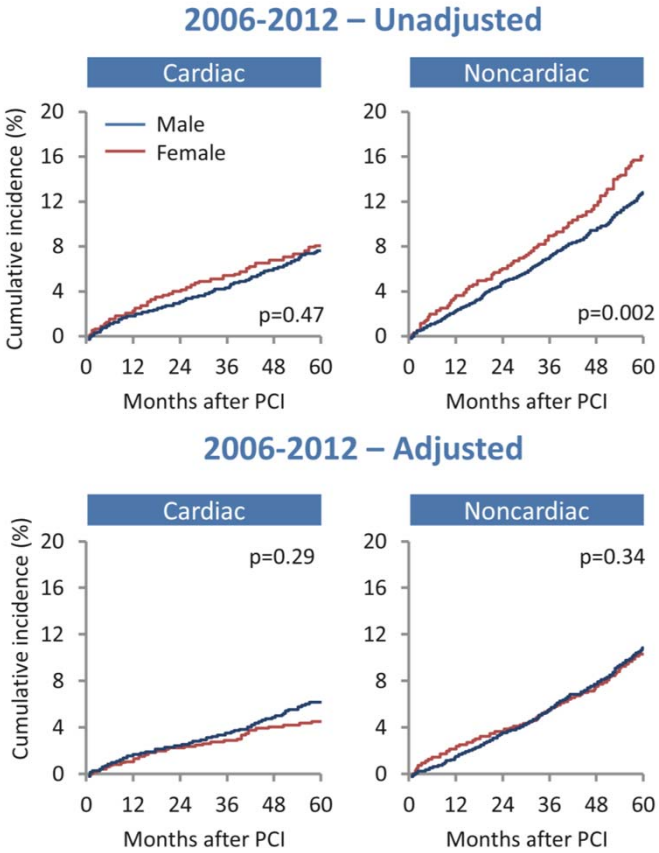
5-year cardiac death stratified by sex: no difference after adjustment

Source, Mayo PCI registry, 1991 – 2012
N = 23,127





Raphael, Circ Int 2018

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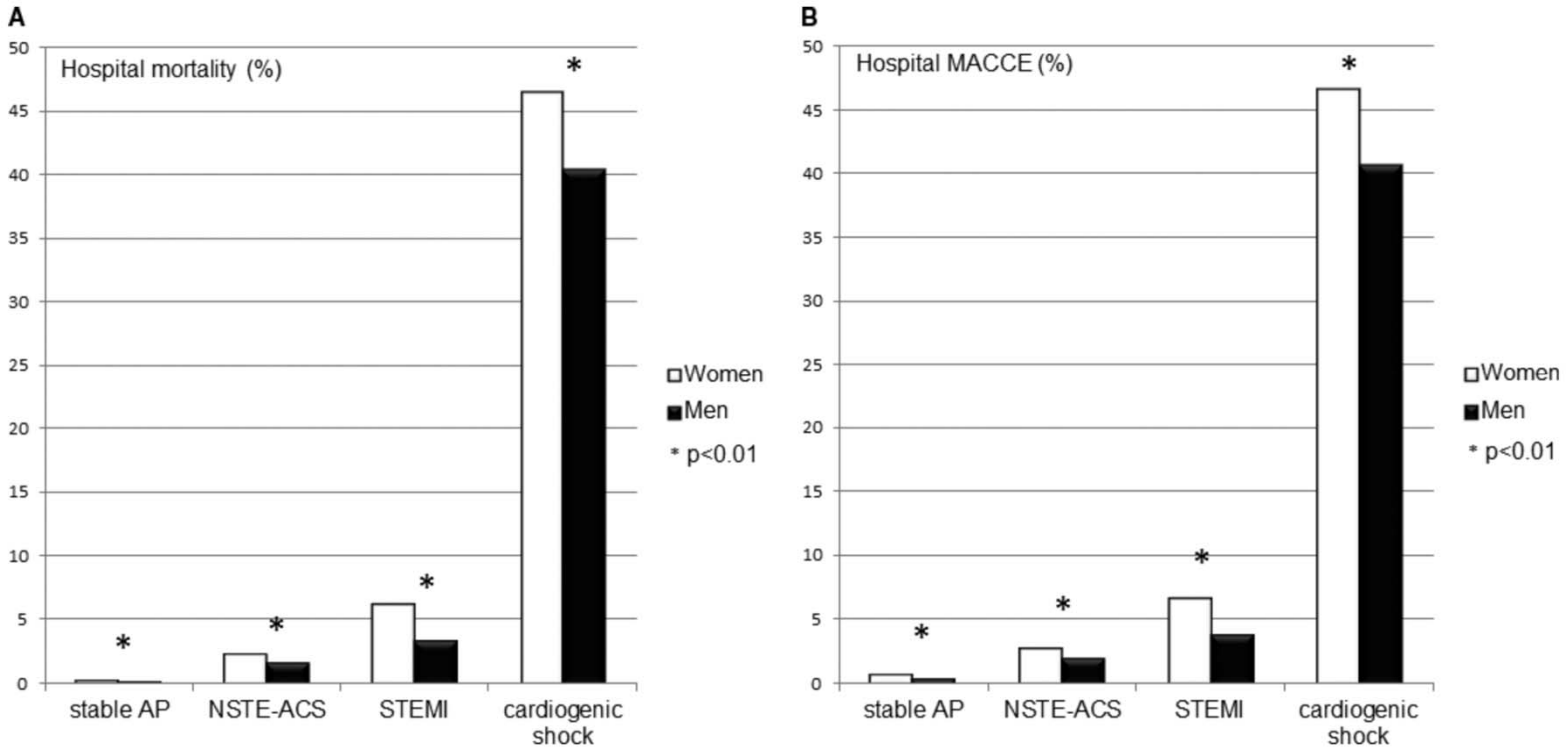
German data

Source, German PCI registry, 2007 – 2009

N = 185,312

Further analysis: sex difference (+) only in STEMI



Heer, JAHA 2017

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Aim of study

- To investigate the sex difference in the 5-year outcome after percutaneous coronary intervention using real-world data.

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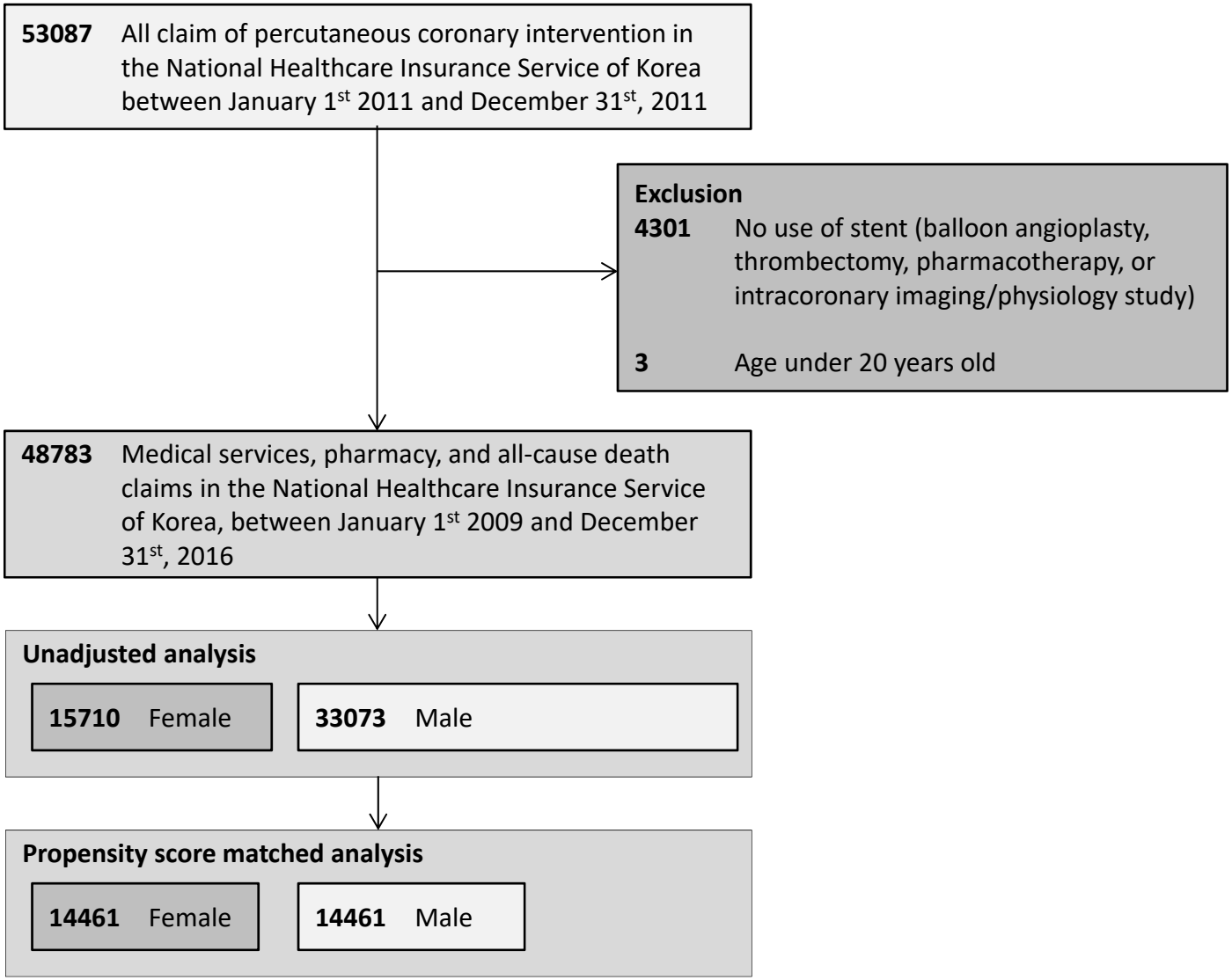
Study flow chart



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Clinical outcomes

- Primary endpoint
  - Death during 5 year follow-up

- Secondary end point
  - Major adverse clinical event (MACE) defined as composite of death, repeat revascularization, critic ally ill cardiovascular status, or stroke, and each of MACE
    - Critically ill cardiovascular status defined by any claims that
      - Cardiogenic shock, which included resuscitation, endotracheal intubation and mechanical ventilation
      - Use of hemodynamic support device including IABP or ECMO

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Baseline characteristics

	Unadjusted				PSM strarified by age			
	Women	Men	p-value	SMD	Women	Men	p-value	SMD
N	15710	33073			14461	14461		
Demographics								
Age	69.71 (9.70)	61.97 (11.14)	<0.001	0.741	68.84 (9.49)	68.79 (9.45)	0.698	0.005
Clinical risk factors and prior medical history								
Hypertension	13314 (84.7)	23260 (70.3)	<0.001	0.351	12110 (83.7)	12213 (84.5)	0.101	0.019
Diabetes	4473 (28.5)	7609 (23.0)	<0.001	0.125	4085 (28.2)	4185 (28.9)	0.198	0.015
Hyperlipidemia	11434 (72.8)	21174 (64.0)	<0.001	0.189	10548 (72.9)	10584 (73.2)	0.643	0.006
Dialysis	390 (2.5)	734 (2.2)	0.075	0.017	385 (2.7)	414 (2.9)	0.315	0.012
Malignancy	614 (3.9)	1686 (5.1)	<0.001	0.057	611 (4.2)	590 (4.1)	0.556	0.007
Stroke	885 (5.6)	1465 (4.4)	<0.001	0.055	811 (5.6)	867 (6.0)	0.167	0.017
Resuscitation	28 (0.2)	78 (0.2)	0.241	0.013	23 (0.2)	27 (0.2)	0.671	0.007
Angina	2798 (17.8)	5277 (16.0)	<0.001	0.05	2662 (18.4)	2663 (18.4)	1	<0.001
AMI	1389 (8.8)	3187 (9.6)	0.005	0.027	1294 (8.9)	1375 (9.5)	0.104	0.019
Revascularization	940 (6.0)	2323 (7.0)	<0.001	0.042	910 (6.3)	949 (6.6)	0.362	0.011
PCI	919 (5.8)	2257 (6.8)	<0.001	0.04	889 (6.1)	917 (6.3)	0.512	0.008
CABG	25 (0.2)	84 (0.3)	0.049	0.021	25 (0.2)	42 (0.3)	0.05	0.024
Clinical presentation at index PCI								
Diagnosis			<0.001	0.15			0.529	0.013
Angina	10542 (67.1)	19831 (60.0)			9881 (68.3)	9838 (68.0)		
NSTEMI	1912 (12.2)	5103 (15.4)			1698 (11.7)	1668 (11.5)		
STEMI	3256 (20.7)	8139 (24.6)			2882 (19.9)	2955 (20.4)		
Critically ill cardiovascular status	1064 (6.8)	1911 (5.8)	<0.001	0.041	899 (6.2)	891 (6.2)	0.864	0.002
Resusication	435 (2.8)	908 (2.7)	0.906	0.001	368 (2.5)	378 (2.6)	0.738	0.004
Mechanical ventilation	897 (5.7)	1610 (4.9)	<0.001	0.038	759 (5.2)	767 (5.3)	0.854	0.002
IABP	319 (2.0)	647 (2.0)	0.606	0.005	264 (1.8)	277 (1.9)	0.602	0.007
ECMO	61 (0.4)	194 (0.6)	0.006	0.028	56 (0.4)	78 (0.5)	0.069	0.022
Procedural characteristics at index PCI							0.821	0.007
Stent used			0.073	0.022	680 (4.7)	698 (4.8)		
BMS	733 (4.7)	1697 (5.1)			1114 (7.7)	1130 (7.8)		
DES 1st generation	1184 (7.5)	2431 (7.4)			12667 (87.6)	12633 (87.4)		
DES 2nd generation	13793 (87.8)	28945 (87.5)			1.09 (0.39)	1.09 (0.39)	0.833	0.002
Stent number used	1.09 (0.39)	1.09 (0.39)	0.112	0.015	1.09 (0.39)	1.09 (0.39)	0.695	0.005

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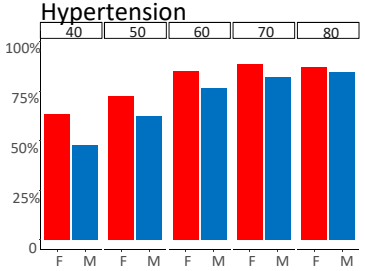
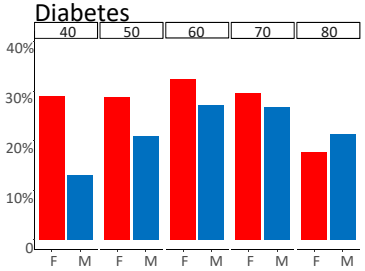
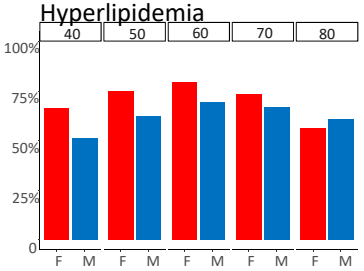
Hypertension



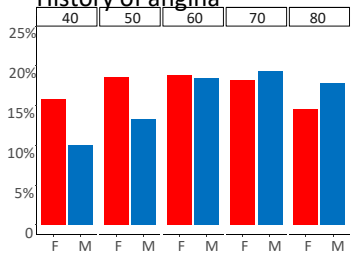
Diabetes



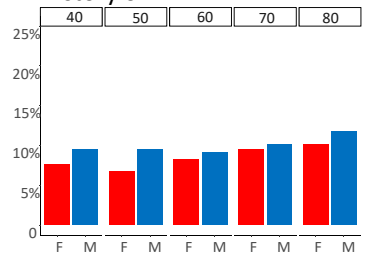
Hyperlipidemia



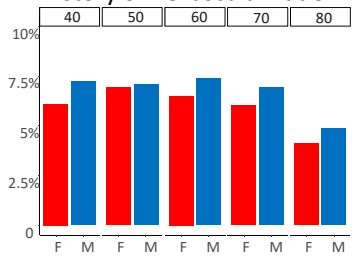
History of angina



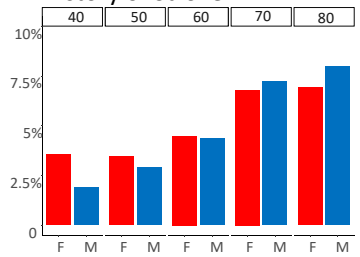
History of AMI



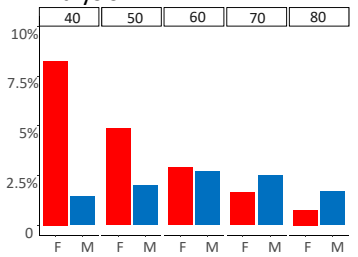
History of Revascularization



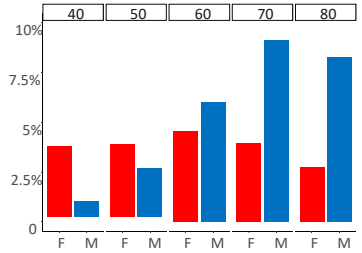
History of Stroke



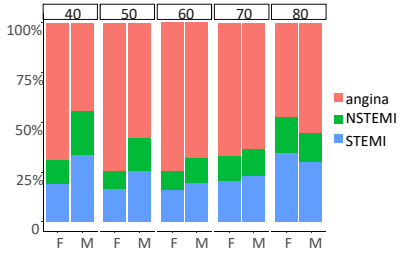
Dialysis



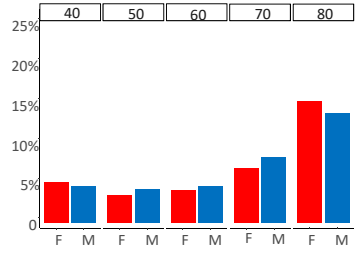
Malignancy



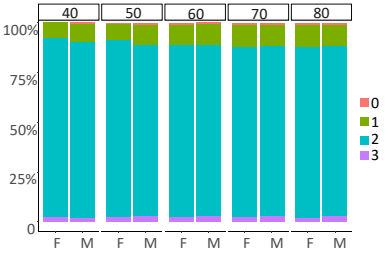
Diagnosis at index PCI



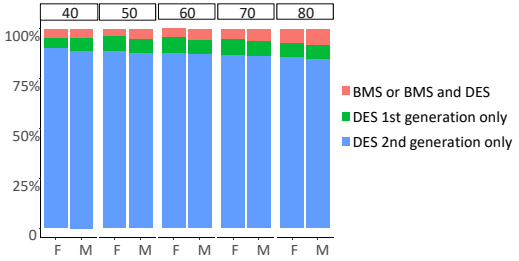
Shock



Stent number used in PCI



Stent material



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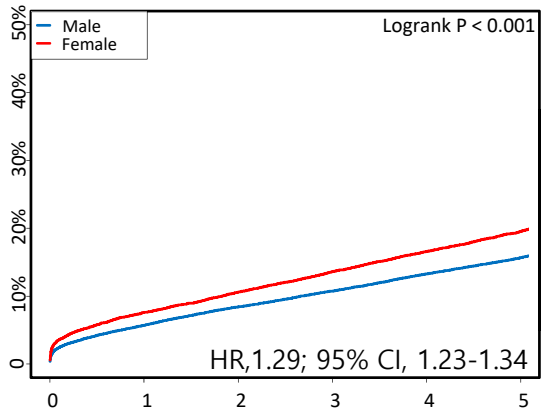
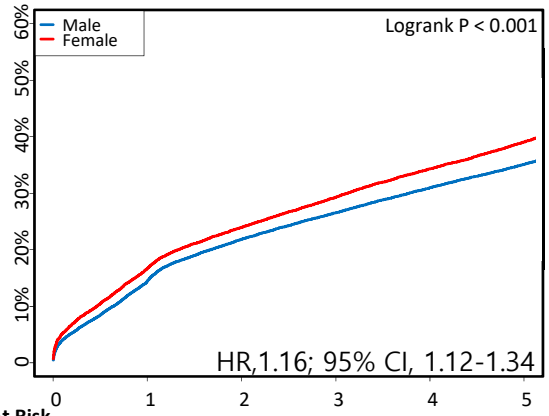
Clinical outcomes of crude group

Death



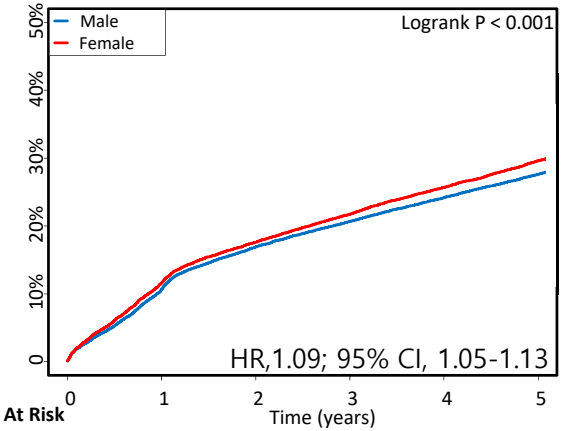
No. At Risk						
Male	33073	31106	30153	29322	28409	25999
Female	15710	14489	13999	13506	13017	12041

MACE



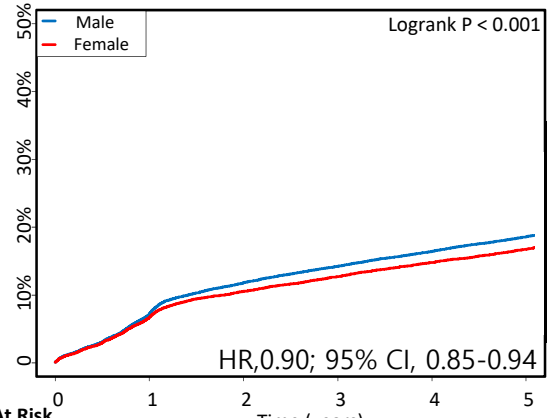
No. At Risk						
Male	33073	28212	25726	24138	22625	19957
Female	15710	13061	11910	11056	10258	9104

Non-fatal MACE



No. At Risk						
Male	33073	28212	25726	24138	22625	19957
Female	15710	13061	11910	11056	10258	9104

Revascularization



No. At Risk						
Male	33073	28923	26709	25301	23929	21358
Female	15710	13546	12572	11856	11165	10101

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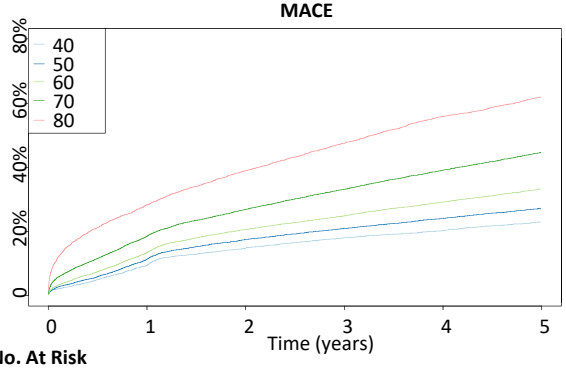
Clinical outcomes stratified according to ages

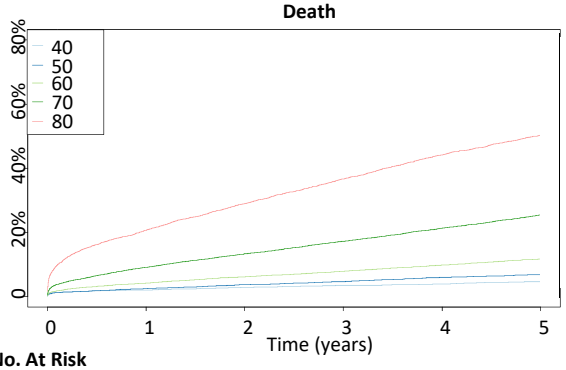
MACE



No. At Risk

40	5027	4533	4258	4083	3953	3477
50	11237	9930	9228	8828	8456	7536
60	14844	12820	11727	11073	10422	9381
70	13718	11160	10015	9144	8320	7248
80	3957	2830	2408	2066	1732	1419

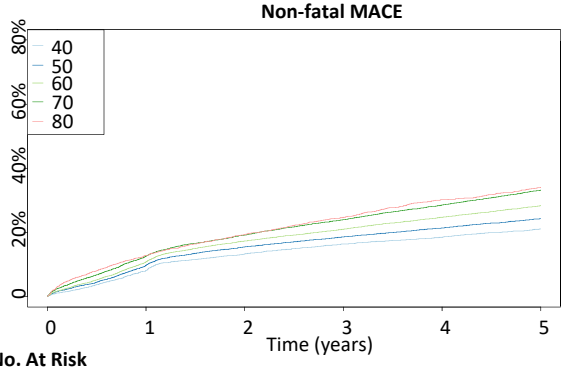
Death



No. At Risk

40	5027	4903	4856	4810	4762	4303
50	11237	10929	10769	10639	10468	9667
60	14844	14185	13860	13570	13264	12438
70	13718	12445	11868	11317	10745	9779
80	3957	3133	2799	2492	2187	1853

Non-fatal MACE



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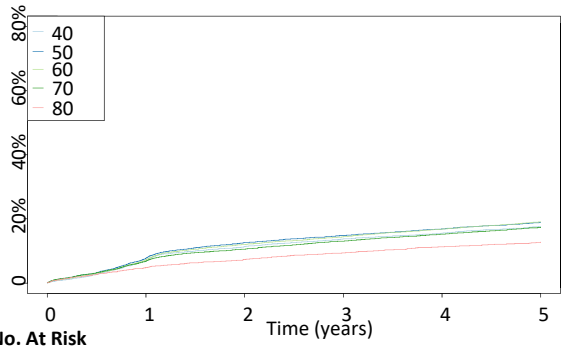
60	14844	12820	11727	11073	10422	9381
70	13718	11160	10015	9144	8320	7248
80	3957	2830	2408	2066	1732	1419

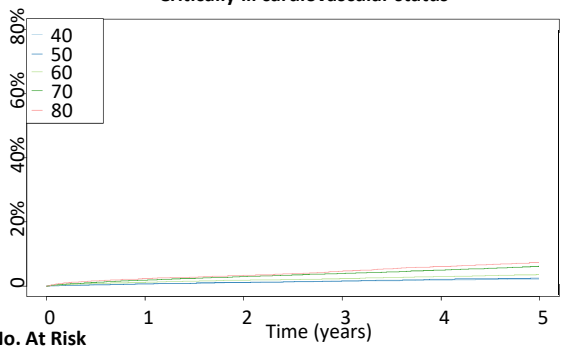
Revascularization



No. At Risk

40	5027	4571	4316	4164	4042	3570
50	11237	10093	9444	9103	8764	7893
60	14844	13178	12232	11681	11121	10151
70	13718	11632	10676	9928	9208	8208
80	3957	2995	2613	2281	1959	1637

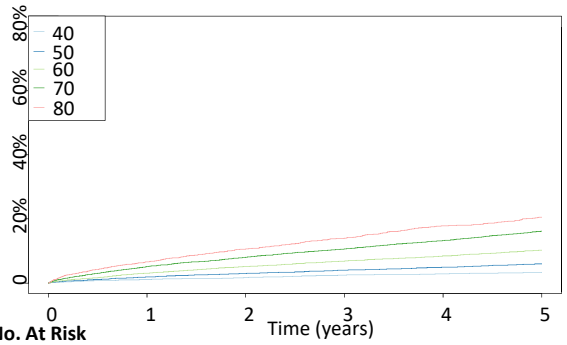
Critically ill cardiovascular status



No. At Risk

40	5027	4899	4847	4798	4744	4285
50	11237	10912	10751	10615	10445	9645
60	14844	14166	13835	13544	13236	12409
70	13718	12419	11837	11284	10709	9737
80	3957	3128	2794	2486	2180	1848

Stroke



No. At Risk

40	5027	4853	4783	4703	4640	4175
50	11237	10741	10495	10280	10053	9184
60	14844	13800	13254	12793	12352	11398
70	13718	11934	11125	10403	9685	8615
80	3957	2962	2580	2254	1920	1592

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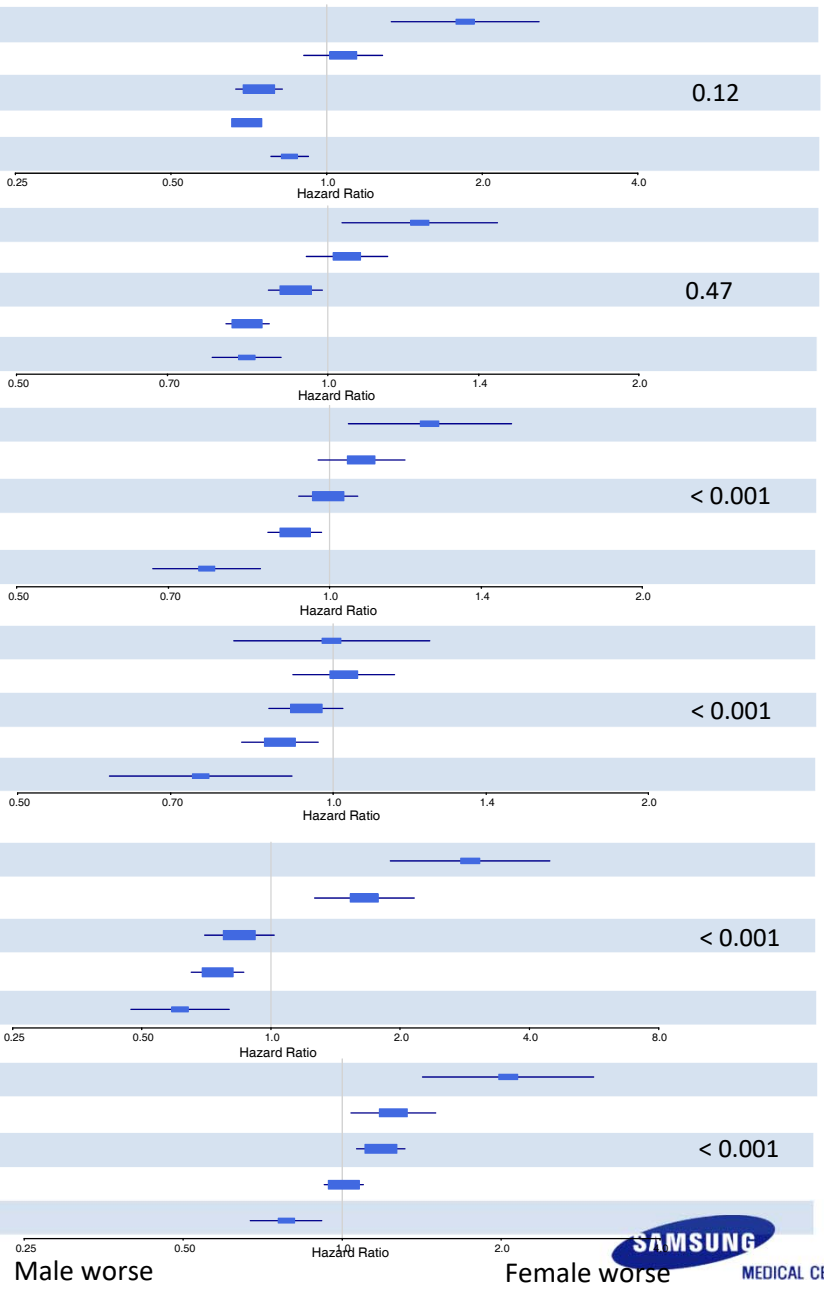
HR of female compared to male stratified by age group

		Total	Event	HR (95% CI)	P-value	P for interaction
Death	Age ≤ 40	5027	249	1.85 (1.34 - 2.58)	< 0.001	
	Age < 50	11237	851	1.08 (0.90 - 1.28)	0.407	
	Age < 60	14844	1937	0.74 (0.67 - 0.82)	< 0.001	0.12
	Age < 70	13718	3935	0.70 (0.66 - 0.75)	< 0.001	
	Age ≥ 80	3957	2182	0.85 (0.78 - 0.92)	< 0.001	
MACCE	Age ≤ 40	5027	1224	1.23 (1.03 - 1.46)	0.02	
	Age < 50	11237	3236	1.04 (0.95 - 1.14)	0.35	
	Age < 60	14844	5217	0.93 (0.88 - 0.99)	0.019	0.47
	Age < 70	13718	6582	0.84 (0.80 - 0.88)	< 0.001	
	Age ≥ 80	3957	2620	0.84 (0.77 - 0.90)	< 0.001	
Non-fatal MACCE	Age ≤ 40	5027	1108	1.25 (1.04 - 1.50)	0.016	
	Age < 50	11237	2814	1.07 (0.98 - 1.18)	0.15	
	Age < 60	14844	4255	1.00 (0.93 - 1.06)	0.919	< 0.001
	Age < 70	13718	4387	0.93 (0.87 - 0.98)	0.012	
	Age ≥ 80	3957	1088	0.76 (0.68 - 0.86)	< 0.001	
Revascularization	Age ≤ 40	5027	917	1.00 (0.80 - 1.24)	0.981	
	Age < 50	11237	2169	1.02 (0.92 - 1.15)	0.676	
	Age < 60	14844	2792	0.94 (0.87 - 1.02)	0.152	< 0.001
	Age < 70	13718	2208	0.89 (0.82 - 0.97)	0.006	
	Age ≥ 80	3957	382	0.75 (0.61 - 0.91)	0.005	
Cardiogenic shock	Age ≤ 40	5027	114	2.91 (1.9 - 4.46)	< 0.001	
	Age < 50	11237	286	1.65 (1.26 - 2.16)	< 0.001	
	Age < 60	14844	558	0.84 (0.70 - 1.02)	0.073	< 0.001
	Age < 70	13718	807	0.75 (0.65 - 0.86)	< 0.001	
	Age ≥ 80	3957	224	0.61 (0.47 - 0.80)	< 0.001	
Stroke	Age ≤ 40	5027	183	2.06 (1.42 – 3.00)	< 0.001	
	Age < 50	11237	696	1.25 (1.04 - 1.50)	0.018	
	Age < 60	14844	1552	1.18 (1.07 - 1.31)	0.002	< 0.001
	Age < 70	13718	2117	1.01 (0.93 - 1.10)	0.868	
	Age ≥ 80	3957	638	0.78 (0.67 - 0.92)	0.002	



Male worse

Female worse

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Baseline characteristics

	Unadjusted				PSM strarified by age			
	Women	Men	p-value	SMD	Women	Men	p-value	SMD
N	15710	33073			14461	14461		
Demographics								
Age	69.71 (9.70)	61.97 (11.14)	<0.001	0.741	68.84 (9.49)	68.79 (9.45)	0.698	0.005
Clinical risk factors and prior medical history								
Hypertension	13314 (84.7)	23260 (70.3)	<0.001	0.351	12110 (83.7)	12213 (84.5)	0.101	0.019
Diabetes	4473 (28.5)	7609 (23.0)	<0.001	0.125	4085 (28.2)	4185 (28.9)	0.198	0.015
Hyperlipidemia	11434 (72.8)	21174 (64.0)	<0.001	0.189	10548 (72.9)	10584 (73.2)	0.643	0.006
Dialysis	390 (2.5)	734 (2.2)	0.075	0.017	385 (2.7)	414 (2.9)	0.315	0.012
Malignancy	614 (3.9)	1686 (5.1)	<0.001	0.057	611 (4.2)	590 (4.1)	0.556	0.007
Stroke	885 (5.6)	1465 (4.4)	<0.001	0.055	811 (5.6)	867 (6.0)	0.167	0.017
Resuscitation	28 (0.2)	78 (0.2)	0.241	0.013	23 (0.2)	27 (0.2)	0.671	0.007
Angina	2798 (17.8)	5277 (16.0)	<0.001	0.05	2662 (18.4)	2663 (18.4)	1	<0.001
AMI	1389 (8.8)	3187 (9.6)	0.005	0.027	1294 (8.9)	1375 (9.5)	0.104	0.019
Revascularization	940 (6.0)	2323 (7.0)	<0.001	0.042	910 (6.3)	949 (6.6)	0.362	0.011
PCI	919 (5.8)	2257 (6.8)	<0.001	0.04	889 (6.1)	917 (6.3)	0.512	0.008
CABG	25 (0.2)	84 (0.3)	0.049	0.021	25 (0.2)	42 (0.3)	0.05	0.024
Clinical presentation at index PCI								
Diagnosis			<0.001	0.15			0.529	0.013
Angina	10542 (67.1)	19831 (60.0)			9881 (68.3)	9838 (68.0)		
NSTEMI	1912 (12.2)	5103 (15.4)			1698 (11.7)	1668 (11.5)		
STEMI	3256 (20.7)	8139 (24.6)			2882 (19.9)	2955 (20.4)		
Critically ill cardiovascular status	1064 (6.8)	1911 (5.8)	<0.001	0.041	899 (6.2)	891 (6.2)	0.864	0.002
Resusication	435 (2.8)	908 (2.7)	0.906	0.001	368 (2.5)	378 (2.6)	0.738	0.004
Mechanical ventilation	897 (5.7)	1610 (4.9)	<0.001	0.038	759 (5.2)	767 (5.3)	0.854	0.002
IABP	319 (2.0)	647 (2.0)	0.606	0.005	264 (1.8)	277 (1.9)	0.602	0.007
ECMO	61 (0.4)	194 (0.6)	0.006	0.028	56 (0.4)	78 (0.5)	0.069	0.022
Procedural characteristics at index PCI							0.821	0.007
Stent used			0.073	0.022	680 (4.7)	698 (4.8)		
BMS	733 (4.7)	1697 (5.1)			1114 (7.7)	1130 (7.8)		
DES 1st generation	1184 (7.5)	2431 (7.4)			12667 (87.6)	12633 (87.4)		
DES 2nd generation	13793 (87.8)	28945 (87.5)			1.09 (0.39)	1.09 (0.39)	0.833	0.002
Stent number used	1.09 (0.39)	1.09 (0.39)	0.112	0.015	1.09 (0.39)	1.09 (0.39)	0.695	0.005

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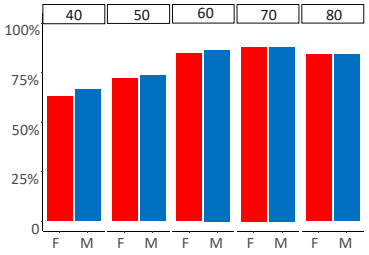
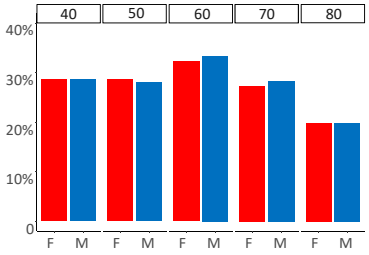
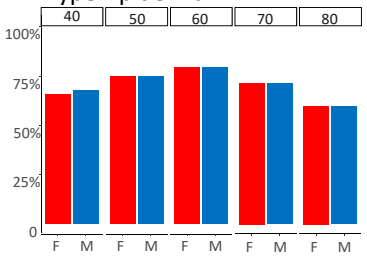
Hypertension



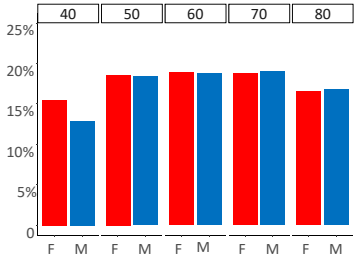
Diabetes



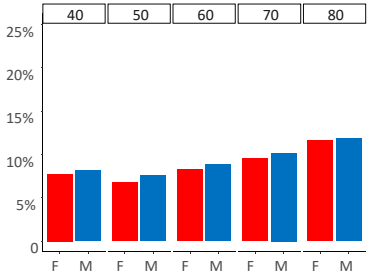
Hyperlipidemia



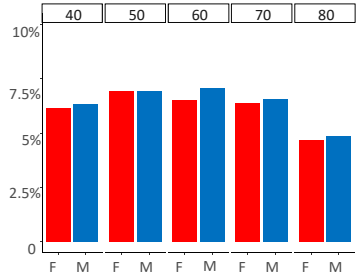
History of angina



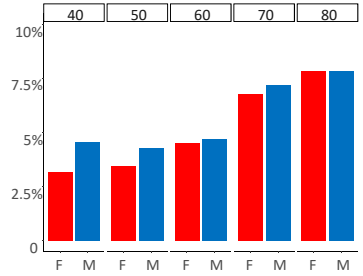
History of AMI



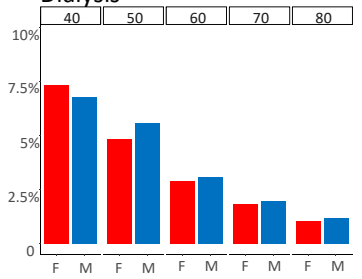
History of Revascularization



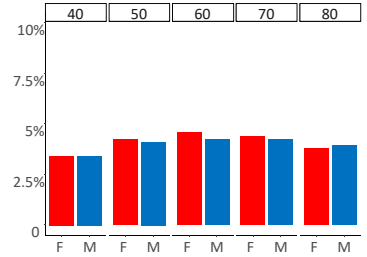
History of Stroke



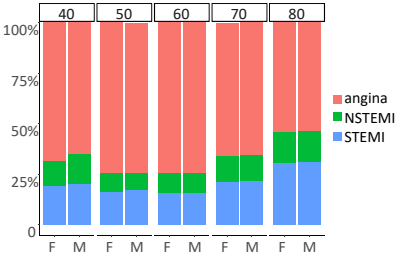
Dialysis



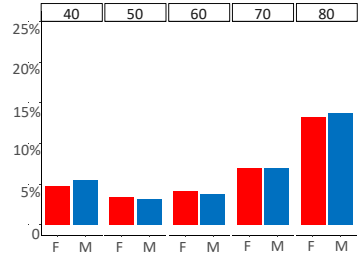
Malignancy



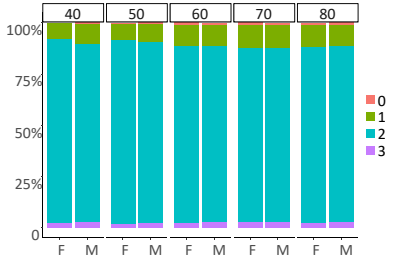
Diagnosis at index PCI



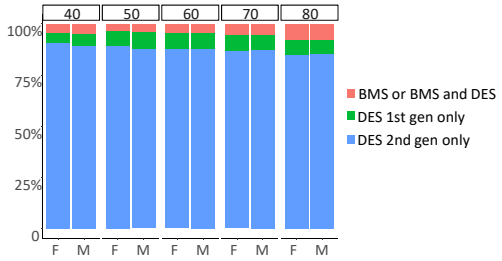
Shock



Stent number used in PCI



Stent material



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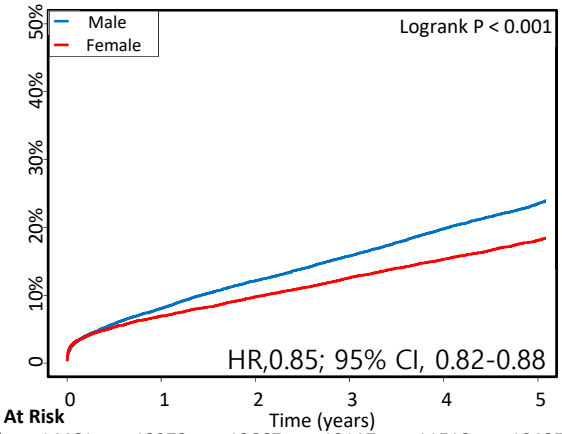
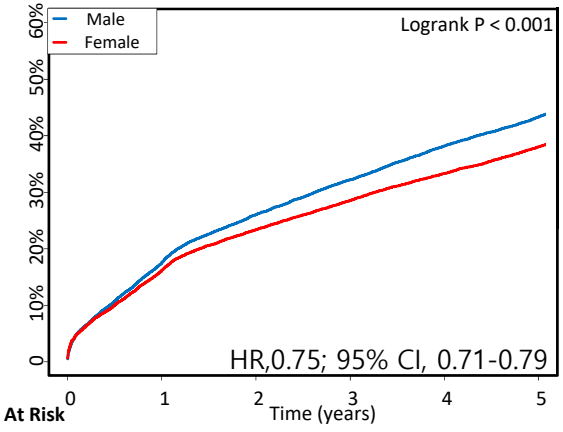
Clinical outcomes of propensity-score matched group

Death



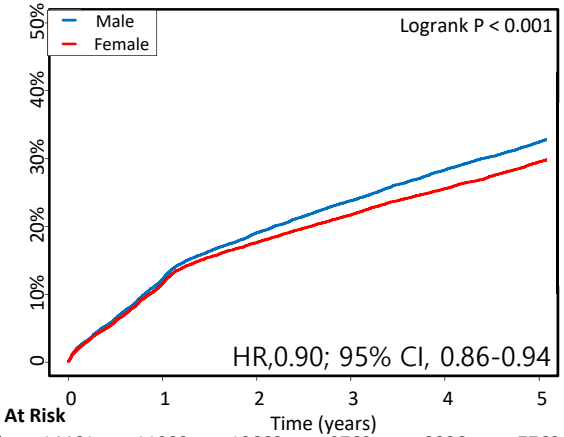
No. At Risk						
Male	14461	13273	12667	12117	11518	10485
Female	14461	13431	13006	12581	12169	11282

MACE



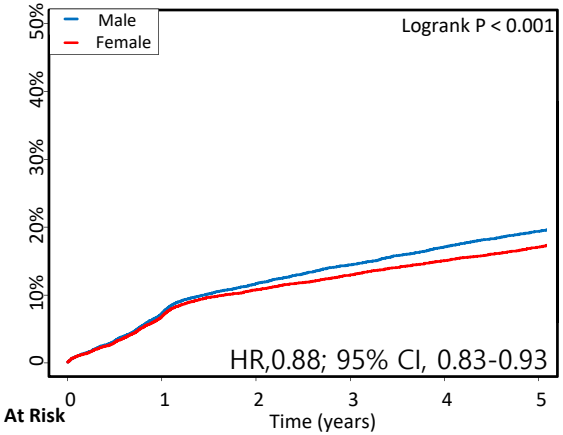
No. At Risk						
Male	14461	11902	10663	9763	8886	7762
Female	14461	12103	11051	10289	9587	8518

Non-fatal MACE



No. At Risk						
Male	14461	11902	10663	9763	8886	7762
Female	14461	12103	11051	10289	9587	8518

Revascularization



No. At Risk						
Male	14461	12346	11260	10464	9650	8549
Female	14461	12544	11651	11019	10413	9434

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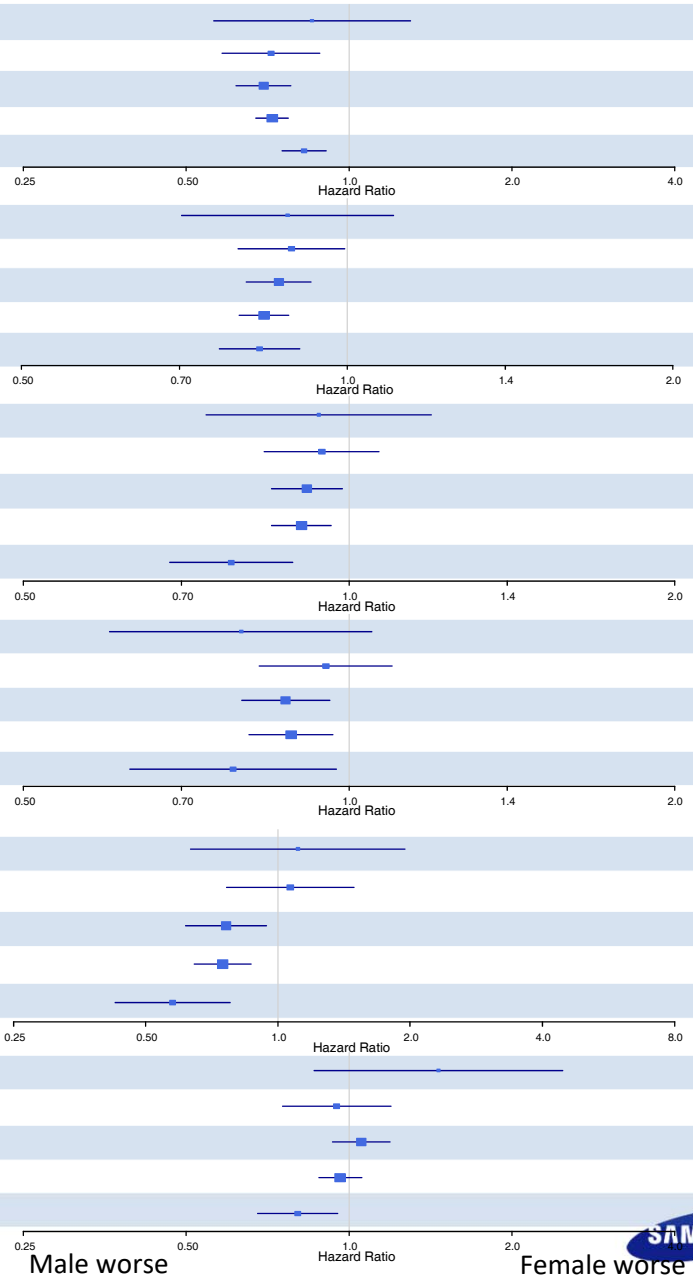
HR of female compared to male stratified by age group in PSM population

		Total	Event	HR (95% CI)	P-value	P for interaction
Death						
	Age ≤ 40	1008	88	0.85 (0.56 - 1.30)	0.46	
	Age < 50	3810	366	0.72 (0.58 - 0.88)	0.002	
	Age < 60	9092	1165	0.70 (0.62 - 0.78)	< 0.001	0.044
	Age < 70	11810	3323	0.72 (0.67 - 0.77)	< 0.001	
	Age ≥ 80	3202	1763	0.83 (0.75 - 0.91)	< 0.001	
MACCE						
	Age ≤ 40	1008	302	0.88 (0.70 - 1.10)	0.272	
	Age < 50	3810	1200	0.89 (0.79 - 0.99)	0.04	
	Age < 60	9092	3266	0.87 (0.81 - 0.93)	< 0.001	0.286
	Age < 70	11810	5643	0.84 (0.80 - 0.88)	< 0.001	
	Age ≥ 80	3202	2126	0.83 (0.76 - 0.90)	< 0.001	
Non-fatal MACCE						
	Age ≤ 40	1008	268	0.94 (0.74 - 1.19)	0.598	
	Age < 50	3810	1034	0.94 (0.84 - 1.07)	0.351	
	Age < 60	9092	2712	0.91 (0.85 - 0.99)	0.02	0.08
	Age < 70	11810	3830	0.90 (0.85 - 0.96)	0.002	
	Age ≥ 80	3202	907	0.78 (0.68 - 0.89)	< 0.001	
Revascularization						
	Age ≤ 40	1008	200	0.80 (0.60 - 1.05)	0.106	
	Age < 50	3810	767	0.95 (0.83 - 1.10)	0.492	
	Age < 60	9092	1760	0.87 (0.80 - 0.96)	0.005	0.51
	Age < 70	11810	1927	0.88 (0.81 - 0.97)	0.007	
	Age ≥ 80	3202	321	0.78 (0.63 - 0.97)	0.028	
Cardiogenic shock						
	Age ≤ 40	1008	49	1.11 (0.63 - 1.95)	0.716	
	Age < 50	3810	139	1.07 (0.77 - 1.49)	0.704	
	Age < 60	9092	349	0.76 (0.62 - 0.94)	0.012	0.004
	Age < 70	11810	703	0.75 (0.65 - 0.87)	< 0.001	
	Age ≥ 80	3202	180	0.58 (0.43 - 0.78)	< 0.001	
Stroke						
	Age ≤ 40	1008	57	1.46 (0.86 - 2.48)	0.159	
	Age < 50	3810	288	0.95 (0.75 - 1.20)	0.653	
	Age < 60	9092	1037	1.05 (0.93 - 1.19)	0.401	0.023
	Age < 70	11810	1856	0.96 (0.88 - 1.06)	0.422	
	Age ≥ 80	3202	535	0.80 (0.68 - 0.95)	0.012	



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Why sex-disparities?

- Adjust with risk factors
- Worse presentation and Inadequate pharmacotherapy

Why sex-disparities?

- **Adjust with risk factors**

- Worse presentation and Inadequate pharmacotherapy

Higher prevalence of hyperlipidemia in older female

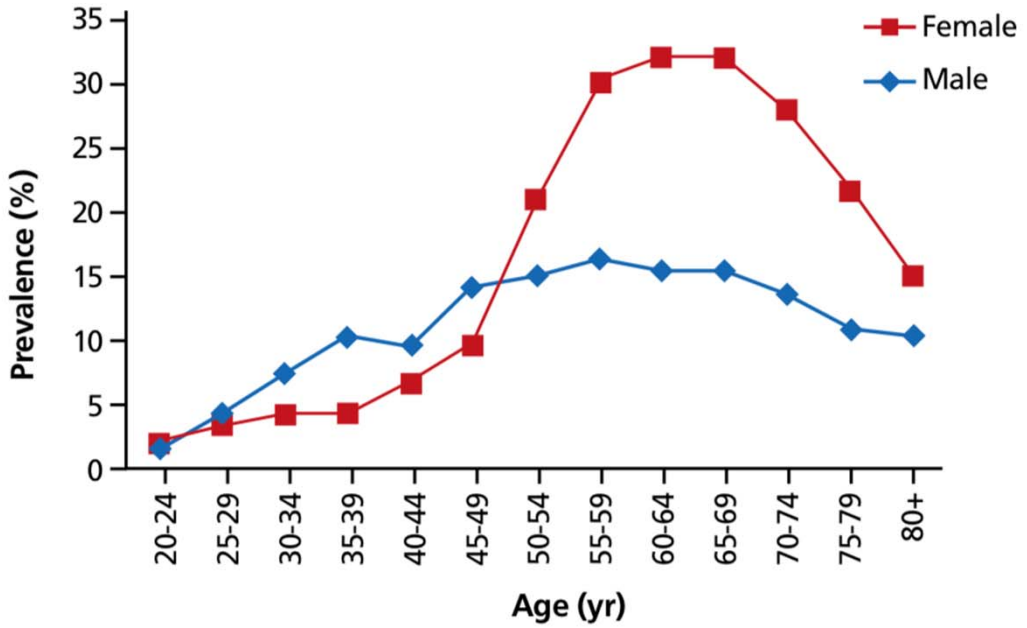

Figure 1. Sex and age-specific prevalence of hypercholesterolemia among Korean adults. Definition of total cholesterol: ≥240 mg/dL or use of lipid-lowering drugs (Data from Ministry of Health and Welfare; Korea Centers for Disease Control and Prevention. Korea health statistics 2012: Korea National Health and Nutrition Examination Survey (KNHANES V-3). Seoul: Ministry of Health and Welfare; 2013) [6].

Kim HC, JKMA 2016

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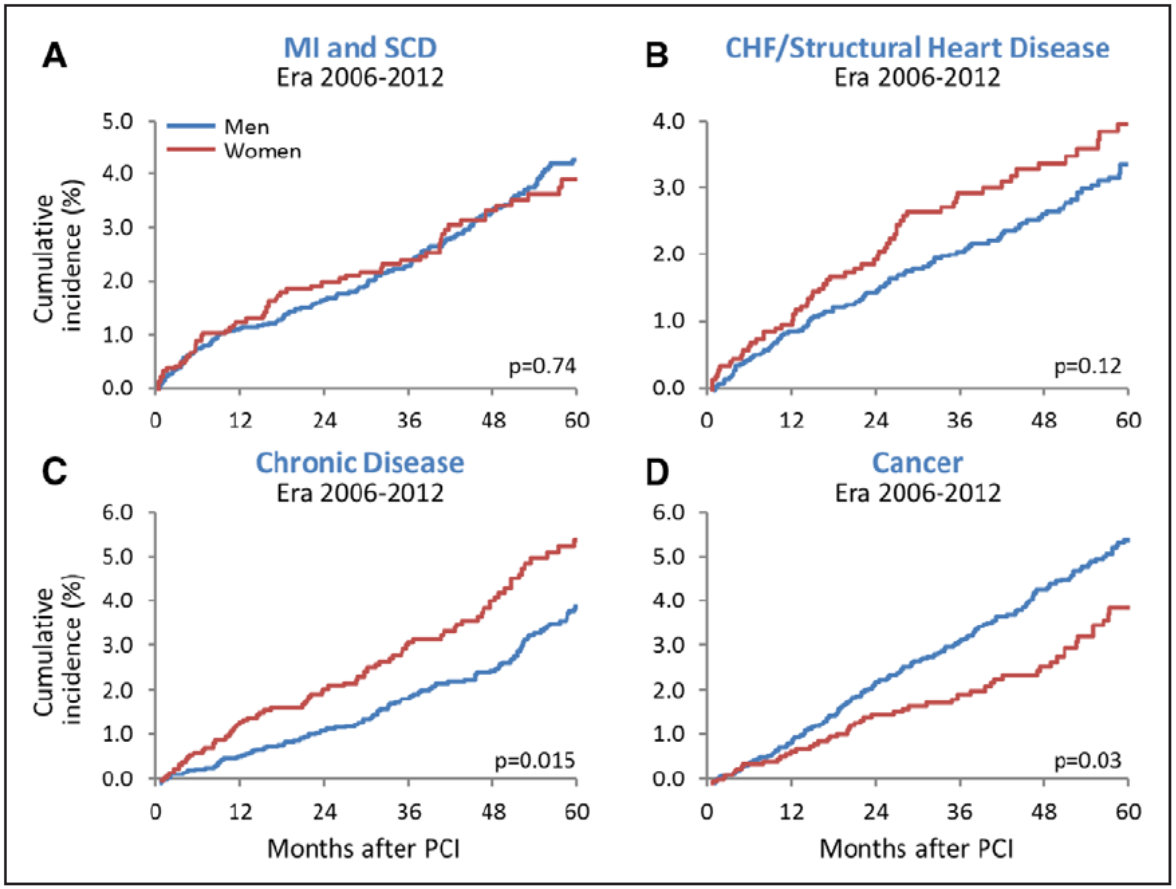
Higher prevalence of chronic disease in female

Source, Mayo PCI registry, 1991 – 2012
N = 23,127



Raphael CE,. *Circ Cardiovasc Interv* 2018

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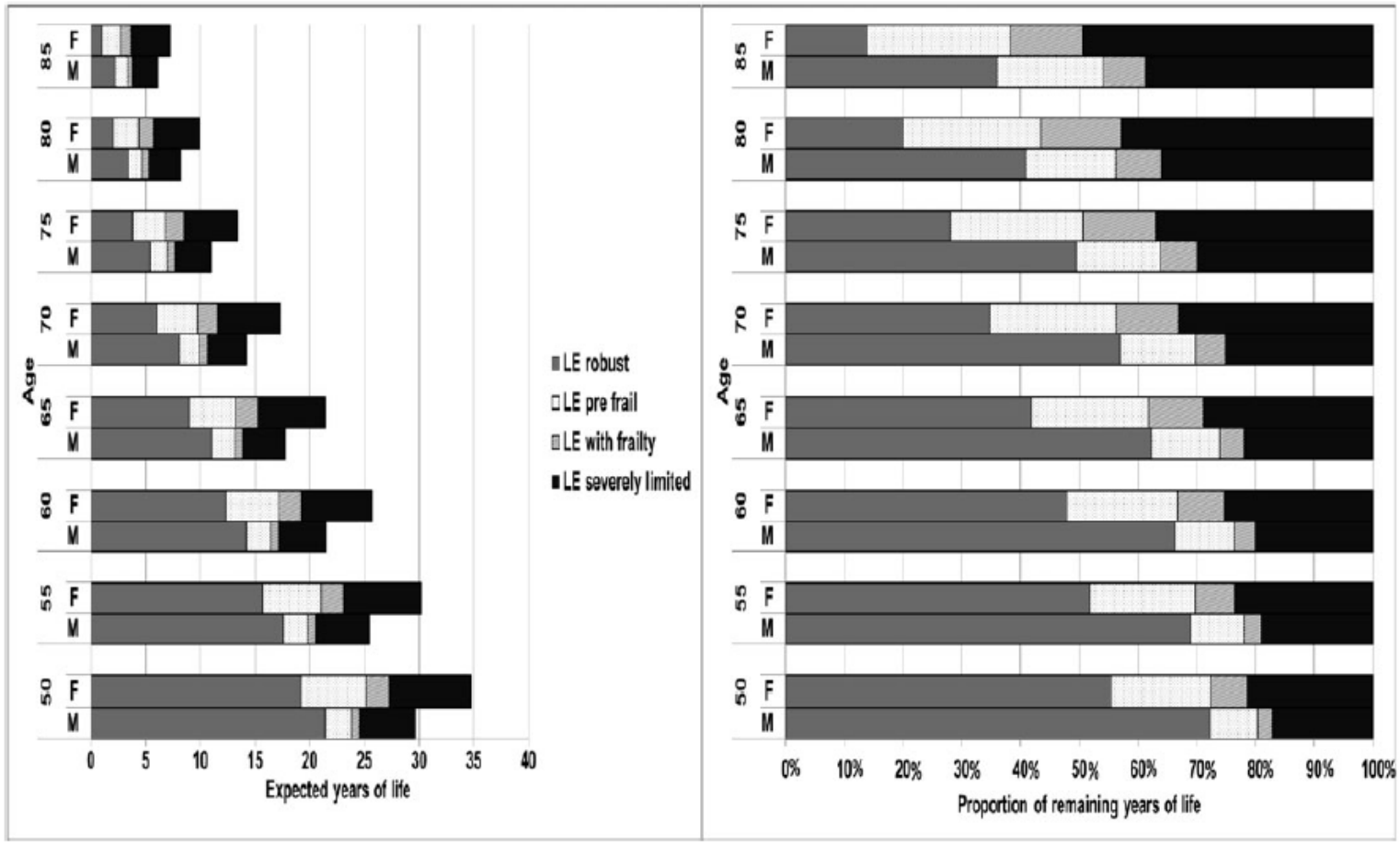
Longer life expectancy in eldery female with frailty

Source, Survey of Health, Ageing and Retirement in Europe, 2011 – 2012
N = 50,351



Romero-Ortuno R, *Age Ageing* 2014

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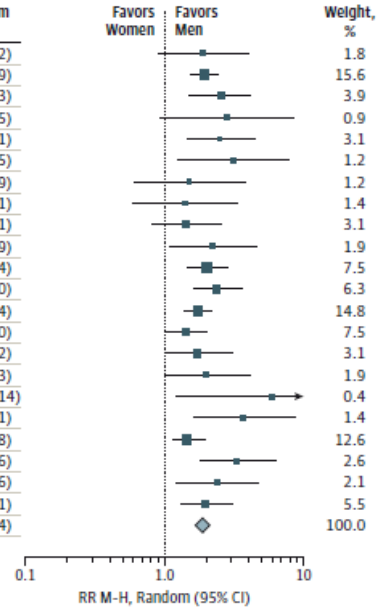
Meta-analysis of inhospital mortality according to sex

A

Source	Women No. of Events	Women Total, No.	Men No. of Events	Men Total, No.	RR M-H, Random (95% CI)	Weight, %
Anupkumar et al,[5] 2013	9	92	25	484	1.89 (0.91-3.92)	1.8
Berger and Brown,[6] 2006	175	2619	217	6396	1.97 (1.62-2.39)	15.6
Birkemeyer et al,[7] 2013	28	276	33	828	2.55 (1.57-4.13)	3.9
Da Silva et al,[8] 2011	7	125	6	303	2.83 (0.97-8.25)	0.9
De Luca et al,[9] 2004	21	353	28	1195	2.54 (1.46-4.41)	3.1
Eitel et al,[10] 2012	10	96	8	239	3.11 (1.27-7.65)	1.2
Feliciano et al,[11] 2005	7	72	11	173	1.53 (0.62-3.79)	1.2
Ferrante et al,[12] 2011	8	138	14	343	1.42 (0.61-3.31)	1.4
Ferrante et al,[13] 2012	17	179	37	565	1.45 (0.84-2.51)	3.1
Ge et al,[14] 2009	70	550	8	142	2.26 (1.11-4.59)	1.9
Hannan et al,[15] 2000	62	686	71	1605	2.04 (1.47-2.84)	7.5
Hurtado-Martinez et al,[16] 2006	40	183	59	655	2.43 (1.68-3.50)	6.3
Jackson et al,[17] 2011	153	2544	212	6167	1.75 (1.43-2.14)	14.8
Kosuge et al,[18] 2006	51	790	98	2191	1.44 (1.04-2.00)	7.5
Kunadian et al,[19] 2013	21	844	29	2020	1.73 (0.99-3.02)	3.1
Liu and Weimin,[20] 2013	11	123	20	455	2.03 (1.00-4.13)	1.9
Peixoto et al,[21] 2006	6	66	2	133	6.05 (1.25-29.14)	0.4
Srimahachota et al,[22] 2004	12	52	8	131	3.78 (1.64-8.71)	1.4
Toyota et al,[23] 2013	104	1197	185	3182	1.49 (1.19-1.88)	12.6
Vakili et al,[24] 2001	25	317	17	727	3.37 (1.85-6.16)	2.6
Zanchi et al,[25] 2009	14	124	17	364	2.42 (1.23-4.76)	2.1
Zhang et al,[26] 2010	36	468	60	1574	2.02 (1.35-3.01)	5.5
Total	887	11894	1165	29872	1.93 (1.75-2.14)	100.0

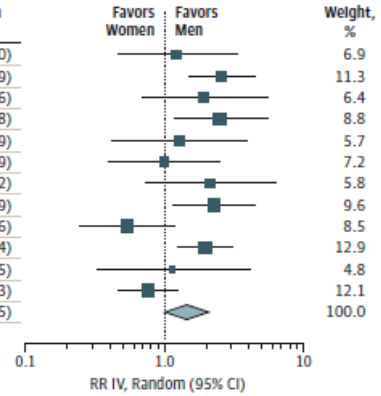
Heterogeneity: $\tau^2 = 0.01$; $\chi^2_{21} = 24.38$, ($P = .27$); $I^2 = 14\%$
Test for overall effect: $Z = 12.74$ ($P < .001$)



B

Source	log (RR)	SE	RR IV, Random (95% CI)	Weight, %
Berger and Brown,[6] 2006	0.223	0.48	1.25 (0.49-3.20)	6.9
De Luca et al,[9] 2004	0.95	0.27	2.59 (1.52-4.39)	11.3
Eitel et al,[10] 2012	0.66	0.51	1.93 (0.71-5.26)	6.4
Hurtado-Martinez et al,[16] 2006	0.92	0.38	2.51 (1.19-5.28)	8.8
Jackson et al,[17] 2011	0.26	0.56	1.30 (0.43-3.89)	5.7
Kosuge et al,[18] 2006	0.0099	0.46	1.01 (0.41-2.49)	7.2
Srimahachota et al,[22] 2004	0.765	0.55	2.15 (0.73-6.32)	5.8
Vakili et al,[24] 2001	0.83	0.343	2.29 (1.17-4.49)	9.6
Valente et al,[27] 2012	-0.612	0.39	0.54 (0.25-1.16)	8.5
Yamane et al,[28] 2011	0.667	0.21	1.95 (1.29-2.94)	12.9
Zanchi et al,[25] 2009	0.14	0.63	1.15 (0.33-3.95)	4.8
Zhang et al,[26] 2010	-0.26	0.24	0.77 (0.48-1.23)	12.1
Total			1.48 (1.07-2.05)	100.0

Heterogeneity: $\tau^2 = 0.17$; $\chi^2_{11} = 25.28$, ($P = .008$); $I^2 = 56\%$
Test for overall effect: $Z = 2.38$ ($P = .02$)



Pancholy SB, *JAMA Intern Med* 2014

SAMSUNG MEDICAL CENTER

Why sex-disparities?

- Adjust with risk factors
- Worse presentation and Inadequate pharmacotherapy

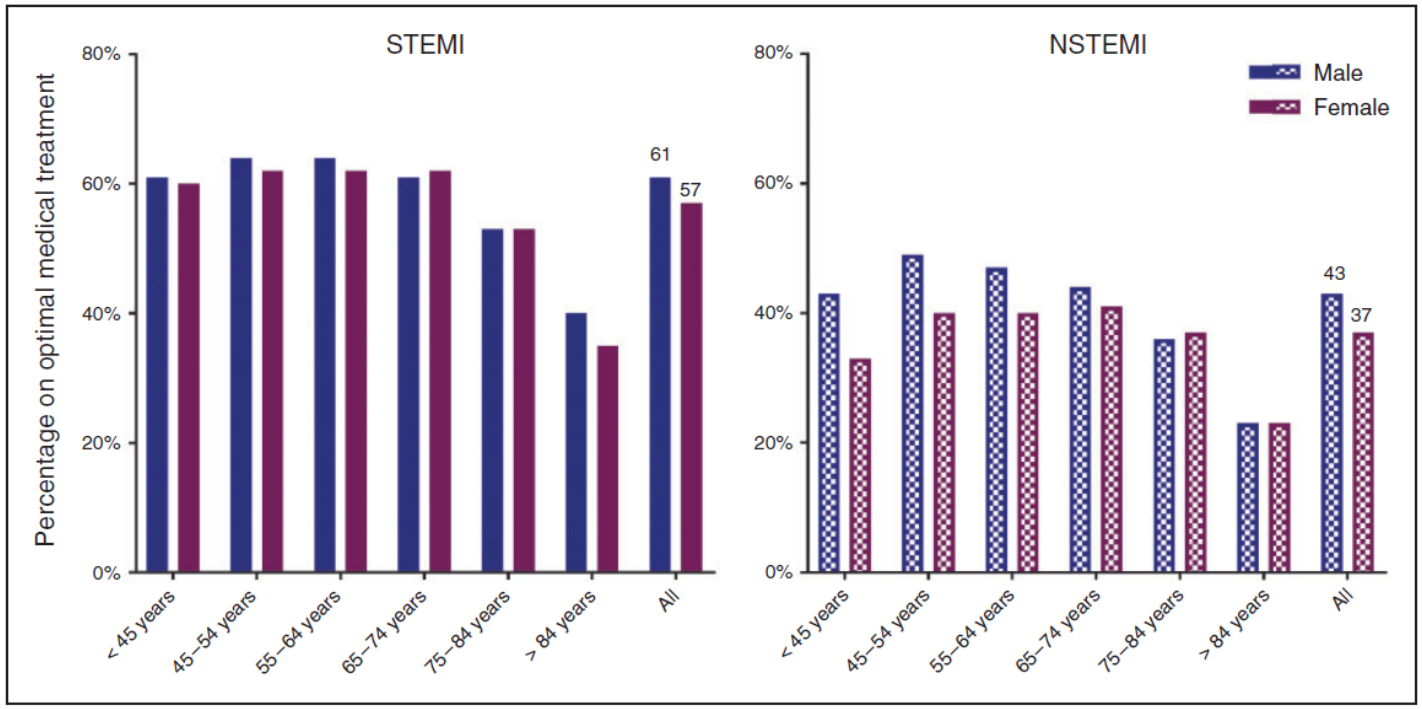
Chest pain in ACS

Source	Study Characteristic							Proportion Without Chest Pain, %		
	Study Description	Patient Population	Study Years	Sample Size	Mean Age, y	Age Adjusted	Race Adjusted	Men	Women	All
Brieger et al,[37] 2004	GRACE Registry	ACS	1999-2002	20 881	65.8	Yes	No	7.3	10.6	8.4
Canto et al,[8] 2000	National MI Registry	MI	1994-1998	434 877	69.3	Yes	Yes	28.6	38.6	32.7
Canto et al,[38] 2002	Alabama UA Registry	UA	1993-1999	4167	72.3	Yes	Yes	50.2	53.0	51.7
Culić et al,[39] 2002	CCUs Croatia	MI	1990-1995	1996	58.8	Yes	No	12.4	20.3	14.8
Dorsch et al,[7] 2001	United Kingdom	MI	1995	2096	70.6	Yes	No	17.6	24.6	20.1
Goldberg et al,[40] 1998	Worcester MI Study	MI	1986-1988	1360	67.7	Yes	No	18.0	23.0	20.0
Milner et al,[41] 2004	Worcester MI Study	MI	1997-1999	2073	70.2	Yes	No	30.9	45.8	37.3
Roger et al,[42] 2000	Olmsted County, Minnesota	UA	1985-1992	2271	63.0	Yes	No	25.0	19.0	22.0
Stern et al,[43] 2004	26 Hospitals, CCU, Israel	ACS	2000	2113	64.9	Yes	No	18.7	29.7	21.7
Cumulative	. . .	. . .	. . .	. . .	. . .	. . .	. . .	27.4 (76 036 of 276 933)	37.5 (73 003 of 194 797)	31.6 (149 039 of 471 730)

Canto JG, Arch Intern Med 2007

Medical adherence between male and female.

Source, Dutch Hospital Care Information System, 2012 – 2013
N = 59,534



- Optimal medical adherence (aspirin , p2y12-inhibitor, statin, beta-blocker and ACEi/ARB

Eindhoven DC, *Eur J Prev Cardiol* 2017

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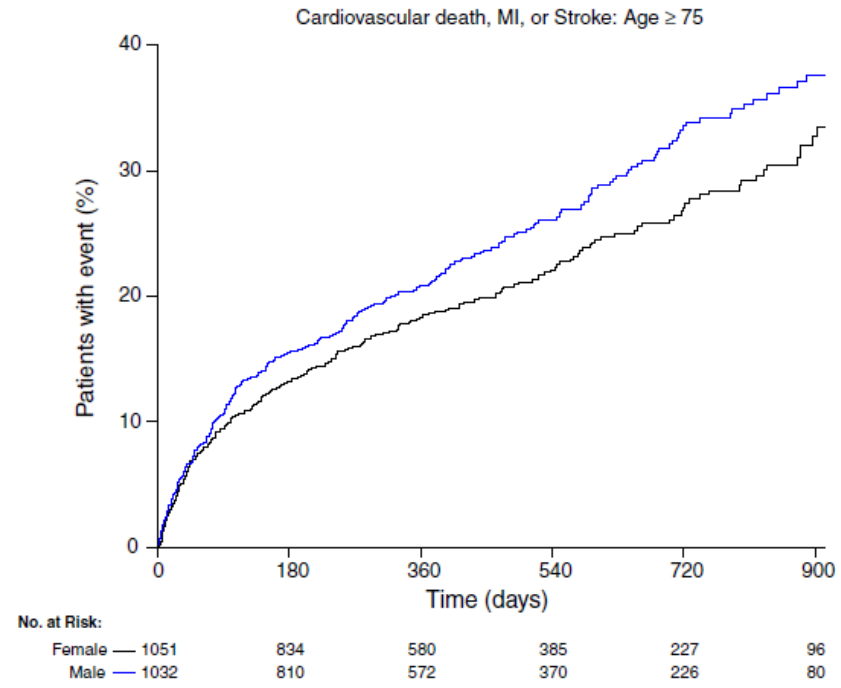
Outcome in the condition of controlled medical adherence

- TRILOGY ACS substudy



Clemmensen P, *Am Heart J* 2015

Outcome in the condition of controlled medical adherence

- DAPT substudy

Outcome	Women (N=2925)	Men (N=8723)	Log-Rank *P* Value	Two-Sided *P* Value for Difference	Adjusted *P* Value*
Stent thrombosis or MI	3.3%	3.0%	0.47		0.17
Stent thrombosis	0.71%	0.91%	0.23		0.87
ARC definite	0.67%	0.80%	0.39		0.99
ARC probable	0.04%	0.13%	0.20		0.86
MI	3.2%	3.0%	0.47		0.17
Stent thrombosis-related	0.67%	0.88%	0.23		0.85
MACCE (death, MI, stroke)	4.9%	5.1%	0.93		0.12
Death	1.1%	1.9%	0.01		0.06
Cardiac	0.50%	1.0%	0.004		0.13
Vascular	0.11%	0.08%	0.75		0.34
Noncardiovascular	0.54%	0.76%	0.46		0.11
All stroke	1.0%	0.75%	0.13		0.30
Ischemic stroke	0.71%	0.56%	0.28		0.46
Hemorrhagic stroke	0.29%	0.18%	0.19		0.12
Type uncertain	0.04%	0.01%	0.43		1.0

Berry NC, *Circ Cardiovasc Interv* 2018

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Limitations

- The source data was administrative claims which lack of specific codes for specific conditions and may not capture patient reported outcome.

- The detailed clinical data including severity of disease, laboratory tests, or life styles such as smoking were not available.

- The results of cardiac biomarkers, electrocardiography, or coronary angiography were not available in administrative database, hence the exact clinical presentation could not be explained.

Conclusions

- Female generally showed worse outcome after PCI.
- After adjustment of baseline conditions, female showed better outcome than male.
- The apparent higher risk of female was affected by older age and accompanying higher comorbidities than male.

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THANK YOU!

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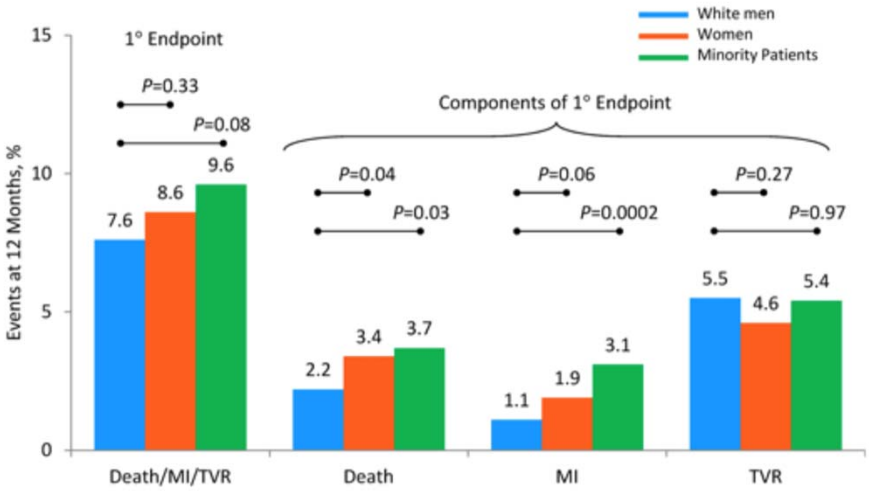
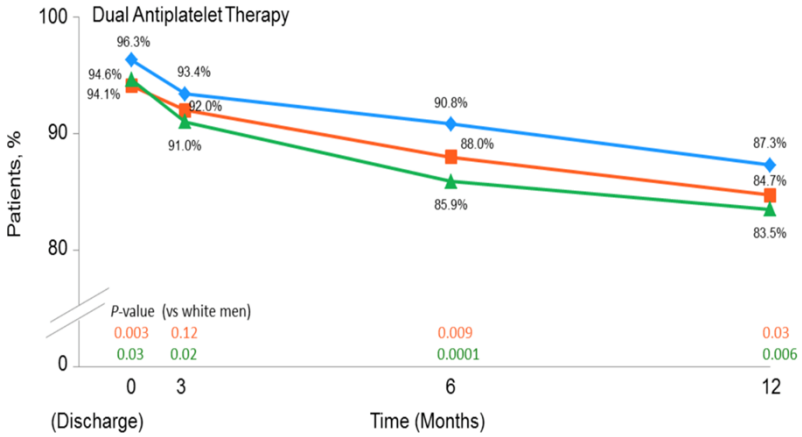
Similar primary endpoint but higher non-stent related MI

Source: PLATINUM Diversity and PROMUS Element Plus Post-Approval Study Pooled Analysis

1-year FU
N= 1,501





Batchelor, JAMA Cardiol 2017

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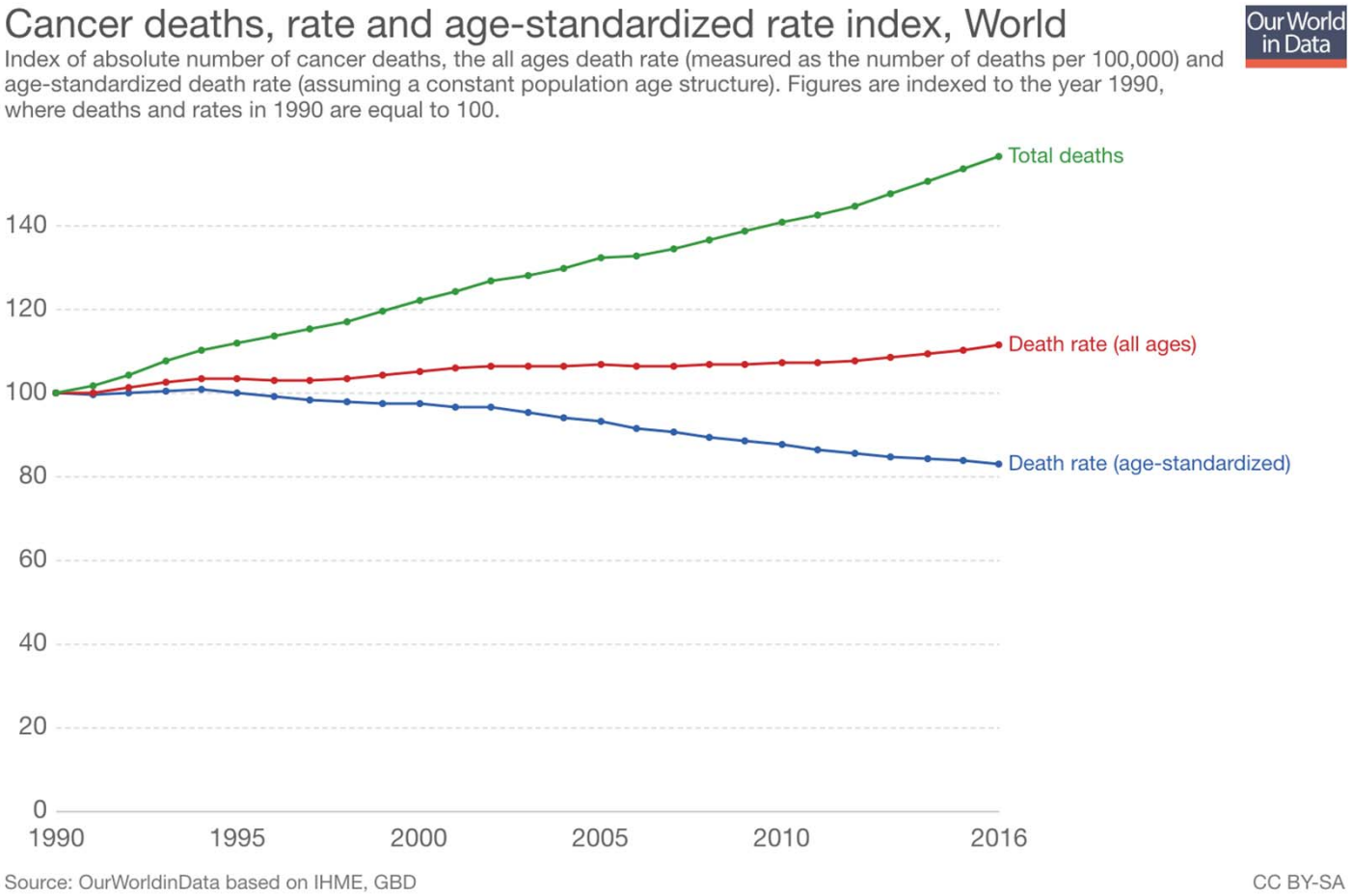
Increased total death but decreased age-standardized death rate



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Clinical outcomes

	Crude population				Propensity-score matched population			
	Female (N = 15710)	Male (N = 33073)	Unadjusted HR (95% CI)	P-value	Female (N = 14461)	Male (N = 14461)	Propensity-score adjusted HR (95% CI)	P-value
Death	3430 (21.8)	5724 (17.3)	1.29 (1.23-1.34)	<0.001	2930 (20.3)	3775 (26.1)	0.85 (0.82 - 0.88)	<0.001
MACE	6579 (41.9)	12300 (37.2)	1.16 (1.12-1.19)	<0.001	5889 (40.7)	6648 (46.0)	0.75 (0.71 - 0.79)	<0.001
Non-fatal MACE	4570 (29.1)	9082 (27.5)	1.09 (1.05-1.13)	<0.001	4227 (29.2)	4524 (31.3)	0.90 (0.86 - 0.94)	<0.001
Revascularization	2507 (16.0)	5961 (18.0)	0.90 (0.85-0.94)	<0.001	2370 (16.4)	2605 (18.0)	0.88 (0.83 - 0.93)	<0.001

Higher prevalence of several comorbidities in female

Table 2. Prevalence of Chronic Medical Conditions in Men and Women; Change in Log Odds of Medical Condition with a 1-Year Increase in Age (Slope) Across the Age Span 65 to 100 for Each Sex; Age and Sex Interaction

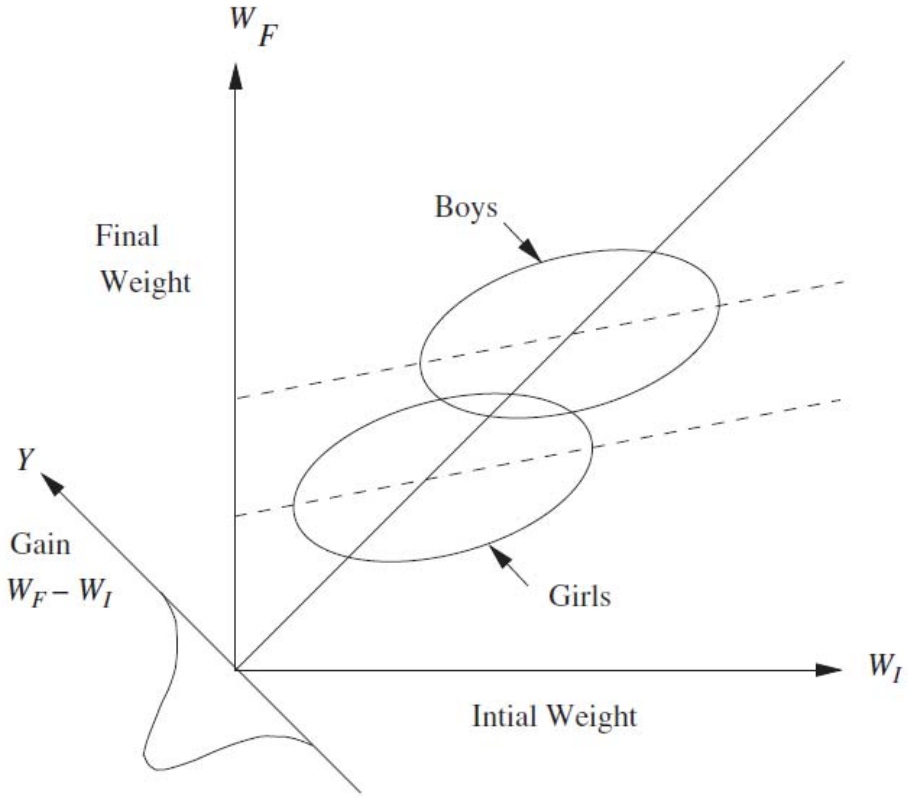
Medical Condition	Women,%	Men,%	*P*-Value[a]	Women, Slope Age[b]	Women, *P*-Value[c]	Men, Slope Age	Men, *P*-Value[c]	Age by Sex, *P*-Value[d]
Atrial fibrillation	11	14	.01	0.029	<.001	0.034	<.001	.91
Anemia	20	17	.005	0.013	.004	0.019	.02	.91
Arthritis	35	26	<.001	0.026	<.001	0.036	<.001	.58
Atherosclerosis	20	24	<.001	0.014	.002	0.012	.08	.91
Benign prostatic hyperplasia	NA	13	NA	NA	NA	0.027	.003	NA
Congestive heart failure	21	18	.003	0.020	<.001	0.024	.002	.91
Constipation	10	10	.75	0.007	.28	0.007	.53	.96
Chronic obstructive pulmonary disease	14	20	<.001	−0.029	<.001	−0.015	.06	.45
Cerebrovascular disease	19	24	<.001	−0.017	<.001	−0.020	.006	.91
Dementia	52	45	<.001	0.035	<.001	0.034	<.001	.95
Depression	37	31	<.001	−0.005	.13	−0.008	.21	.91
Diabetes mellitus	23	26	.002	−0.056	<.001	−0.033	<.001	.01
Gastroesophageal reflux disease	23	23	.66	3×10^{-4}	.98	−0.007	.38	.82
Hypertension	56	53	.08	0.005	.22	−0.018	.003	.006
Lipid disorder	9	11	.03	−0.045	<.001	−0.046	<.001	.95
Osteoporosis	21	5	.001	0.028	<.001	0.022	.17	.91
Parkinson's disease	6	10	<.001	−0.045	<.001	0.007	.52	<.001
Peripheral vascular disease	11	14	<.001	0.001	.96	−0.005	.62	.91
Renal failure	3	5	<.001	−0.027	.006	−0.010	.52	.81
Thyroid disorders	20	9	<.001	0.011	.008	0.037	.002	.11
All vascular disease	41	49	<.001	-7×10^{-5}	.98	−0.002	.67	.91

Moore KL, *J Am Geriatr Soc* 2012

Why sex-disparities?

- Adjust with risk factors, stent number, ACS/non-ACS
- Worse clinical presentation and inadequate pharmacotherapy?
- Lord's paradox

Lord's paradox



ow how the
d if there had
olled differences."

Statistician 1 :
Weight gain between boys and girls shows no differences (Solid line)

Statistician 2 :
Weight gain between boys and girls shows differences (Dotted line) after initial weight adjustment.

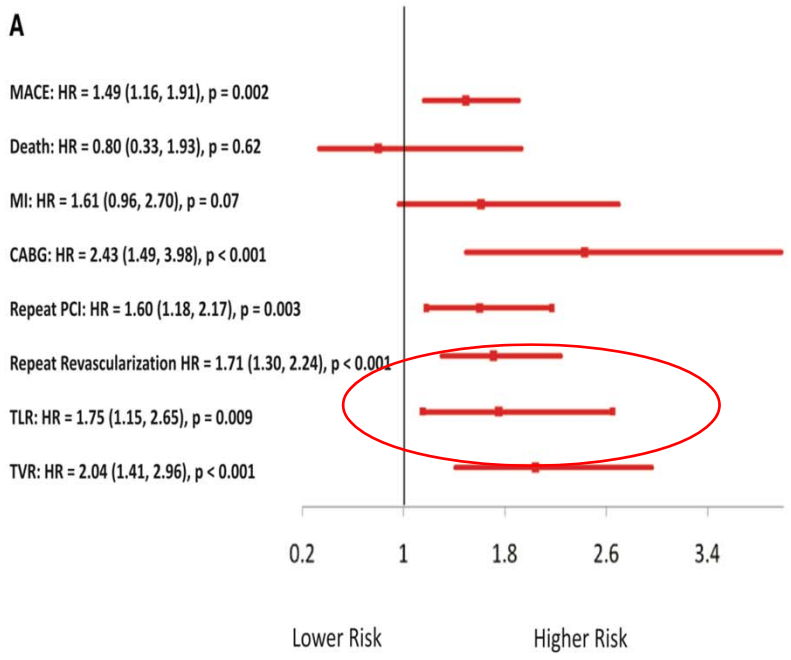
Pearl J. Lord's Paradox Revisited – (Oh Lord! Kumbaya!). *J Causal Inference* 2016

Young women have less severe CAD but increased risk of TLF/TVF

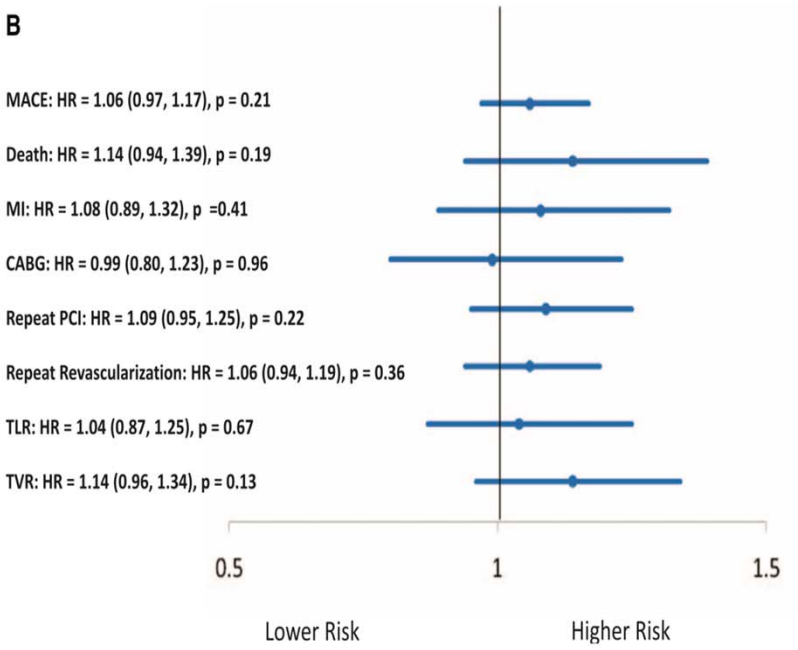
Source, NHLBI dynamic PCI registry, 1997 – 2006

N = 10963

Women age < 50 vs men age < 50



Women age >= 50 vs men age >= 50



Epps, Circ Qual Outcomes 2016

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