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Sex differences in the prescription of anti-hypertensive medications

Perspective from the clinic

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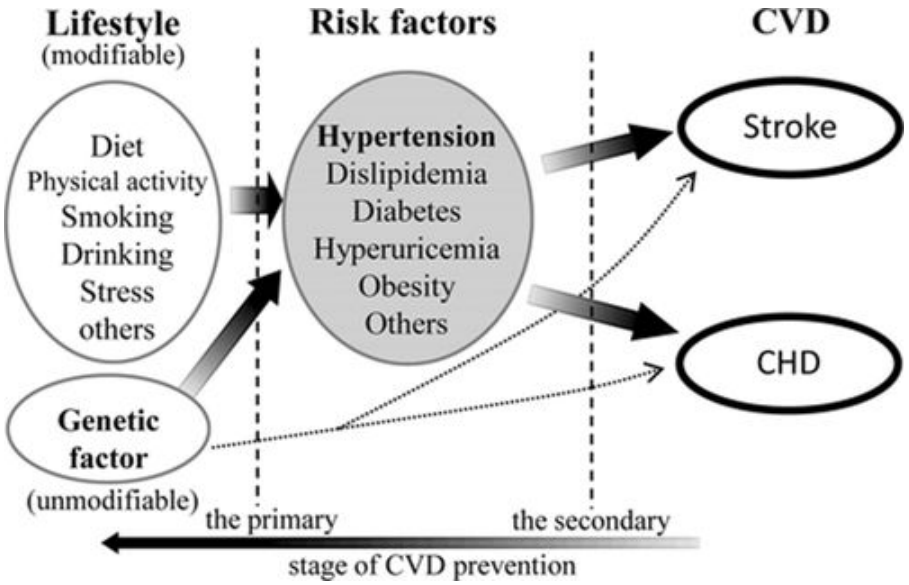
Hypertension and cardiovascular disease

10.4 million deaths worldwide[1]



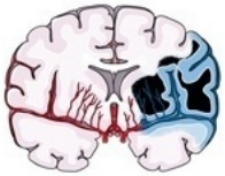
Often unrecognised or undertreated[2]

[1] GBD 2017 Risk Factor Collaborators, The Lancet, 2018
[2] Beaney et al., Lancet Glob Health, 2018
Kokubo, Hypertension, 2014

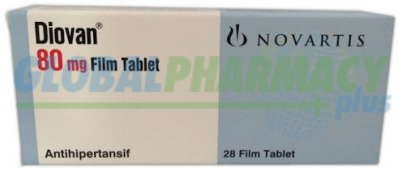
Anti-hypertensive medication

PHARMACOLOGICAL CLASSES

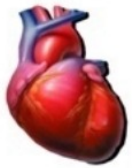
Centrally acting agents
Betablockers



1 Pill



Betablockers
CCBs (Verapamil, dilatiazem)

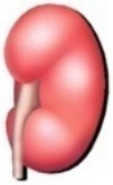


1 Pill

CCBs (Dihydropyridines)
ACE Inhibitors
ARBs
Renin inhibitors
Alpha-1 adrenergic R. antagonists
Direct vasodilators

2 Pills

Diuretics
ACE Inhibitors
ARBs
Renin inhibitors
Betablockers



Laurent, Pharmacological Research, 2017

Sex differences in hypertension treatment?

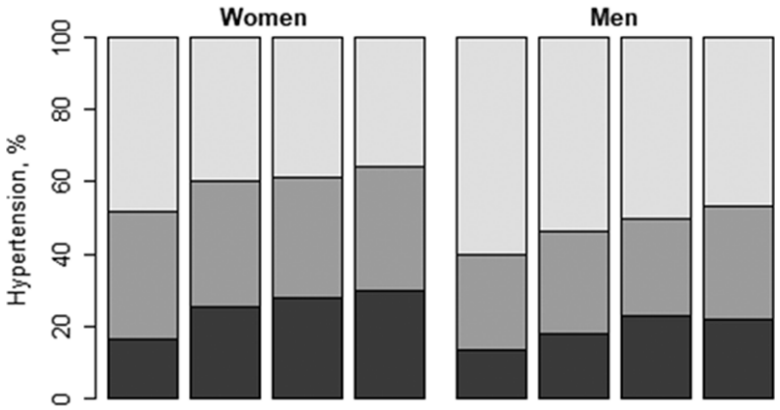
Blood pressure-lowering regimens are equally effective in men and women[1]

Sex differences in medication prescription preferences[2,3]

Diuretics, beta-blockers, ARBs (?)

ACE-inhibitors, CCBs

Poor blood pressure control overall, but better in women[4,5]



[1] Turnbull et al., Eur Heart J, 2008
[2] Wallentin et al., J Clin Hypertens, 2018
[3] Deborde et al., J Hypertens., 2018
[4] Peters et al., Circulation, 2019
[5] Redfern et al., Hypertension Research, 2019

Dutch cardiovascular risk management

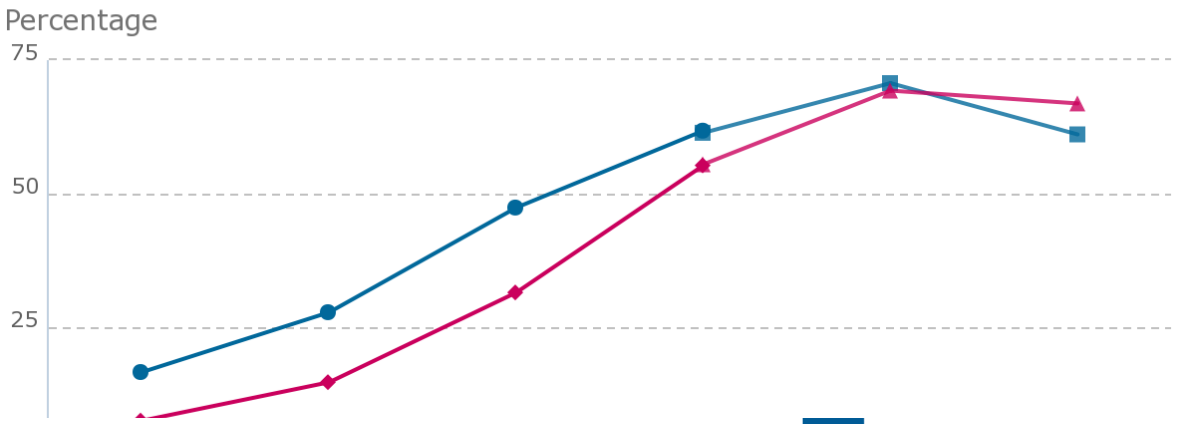
High risk Tienjaarsrisico op sterfte aan HVZ met **SCORE ≥ 10%**	Lifestyle + medication	Stepwise increase starting with **monotherapy**
Intermediate risk Ernstig verhoogde enkele risicofactor (TC > 8 mmol/l of bloeddruk ≥ 180 mmHg) Tienjaarsrisico op sterfte aan HVZ met **SCORE ≥ 5% en < 10%**	Lifestyle + consider medication	
Low risk Tienjaarsrisico op sterfte aan HVZ met **SCORE < 5%**. Veel personen van middelbare leeftijd vallen in deze categorie.	Lifestyle only	

Praktische handleiding bij de NHG-standaard CVRM 2019

How about hypertension in the Netherlands?

Prevalentie verhoogde bloeddruk

Nederland de Maat Genomen (30 tot 70-jarigen), LASA (60 tot 100-jarigen)



26.2%

37.4%

Volksgezondheidenzorg.info

https://www.volksgezondheidenzorg.info/onderwerp/bloeddruk/cijfers-context/huidige-situatie

Research question

Are current cardiovascular primary prevention practices focussed on high blood pressure in line with the Dutch cardiovascular risk management guidelines?

Are there sex differences?

- Guideline adherence
- Medication choice
- Medication dose

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Study population

All patients prescribed anti-hypertensive medications before first visit (n = 4,409)

Regular care database

Cardiology Centers of the Netherlands

Seen between 2007-2018

Standardised cardiac work-up

Selection of anti-hypertensive medications

Based on the Dutch general practitioner guidelines (2019)

ACEIs

ARBs

CCBs

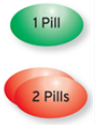
Thiazide diuretics

Beta-blockers

Calculate dose as percentage of recommended start dose

Baseline table

	Men (n = 1792)	Women (n = 2617)
Age (years)	63 (± 10)	64 (± 10)
Body mass index (kg/m^2)	28.1 (± 4.2)	28.1 (± 5.3)
Systolic blood pressure (mmHg)	151 (21)	149 (22)
10-year cardiovascular mortality risk (SCORE)	**5.3 [2.7-10.2]**	**2.9 [1.0-6.8]**
Diabetes mellitus (n,%)	310 (17.3)	326 (12.5)
Dyslipidaemia (n,%)	387 (21.6)	582 (22.2)
Current smoker (n,%)	510 (28.5)	716 (27.4)
Total number of anti-hypertensive pills (n,%) 1 2 3 4	 1679 (93.7) 105 (5.9) 8 (0.4) 0 (0.0)	 2417 (92.4) 183 (7.0) 15 (0.6) 2 (0.1)
Cardiovascular management risk group (n, %) Low risk Intermediate risk High risk **Unknown**	 502 (28.0) 297 (16.6) 276 (15.4) **717 (40.0)**	 939 (35.9) 288 (11.0) 245 (9.4) **1145 (43.8)**



Adherence to guidelines in men

Patients	Low risk (n =502)	Intermediate risk (n = 297)	High risk (n = 276)
Total number of anti-hypertensive pills (n,%)			
1	**468 (93.2)**	**281 (94.6)**	**253 (91.7)**
2	31 (6.2)	15 (5.1)	19 (6.9)
3	3 (0.6)	1 (0.3)	4 (1.4)

Prescriptions	Low risk (n =695)	Intermediate risk (n = 429)	High risk (n =400)
Compounds per pill (n,%)			
1	620 (89.2)	371 (86.5)	337 (84.2)
2	**73 (10.5)**	**57 (13.3)**	**62 (15.5)**
3	2 (0.3)	1 (0.2)	1 (0.2)
Percentage of recommended start dose (n, %)			
< 50	10 (1.4)	4 (0.9)	6 (1.5)
50-100	46 (6.6)	23 (5.4)	18 (4.5)
100	333 (47.9)	194 (45.2)	189 (47.2)
> 100	**306 (44.0)**	**208 (48.5)**	**187 (46.8)**

Adherence to guidelines in women

Patients	Low risk (n = 939)	Intermediate risk (n = 288)	High risk (n = 245)
Total number of anti-hypertensive pills (n,%)			
1	**873 (93.0)**	**269 (93.4)**	**218 (89.0)**
2	63 (6.7)	19 (6.6)	26 (10.6)
3	3 (0.3)	0 (0.0)	1 (0.4)

Prescriptions	Low risk (n = 1318)	Intermediate risk (n = 416)	High risk (n = 365)
Compounds per pill (n,%)			
1	1179 (89.5)	364 (87.5)	320 (87.7)
2	**138 (10.5)**	**51 (12.3)**	**43 (11.8)**
3	1 (0.1)	1 (0.2)	2 (0.5)
Percentage of recommended start dose (n, %)			
< 50	25 (1.9)	5 (1.2)	3 (0.8)
50-100	128 (9.7)	26 (6.2)	21 (5.8)
100	684 (51.9)	204 (49.0)	197 (54.0)
> 100	**481 (36.5)**	**181 (43.5)**	**144 (39.5)**

High risk men and high risk women

Patients	High risk men (n = 276)	High risk women (n = 245)
Systolic blood pressure (mmHg)	165 (18)	169 (21)
10-year cardiovascular mortality risk (SCORE)	15.1 [11.9-22.1]	16.6 [12.5-25.6]
Total number of anti-hypertensive pills (n,%)		
1	253 (91.7)	218 (89.0)
2	**19 (6.9)**	**26 (10.6)**
3	4 (1.4)	1 (0.4)

Prescriptions	High risk men (n =400)	High risk women (n = 365)
Compounds per pill (n,%)		
1	337 (84.2)	320 (87.7)
2	**62 (15.5)**	**43 (11.8)**
3	1 (0.2)	2 (0.5)
Percentage of recommended start dose (n, %)		
< 50	6 (1.5)	3 (0.8)
50-100	18 (4.5)	21 (5.8)
100	189 (47.2)	197 (54.0)
> 100	**187 (46.8)**	**144 (39.5)**

Antihypertensive medication by sex

	Prescriptions for men (n = 2639)	Prescriptions for women (n = 3790)
ACE-inhibitors (n,%)	**601 (22.8)**	**640 (16.9)**
ARBs (n,%)	539 (20.4)	789 (20.8)
Beta-blockers (n,%)	**691 (26.2)**	**1215 (32.1)**
Thiazide diuretics (n,%)	634 (24.0)	933 (24.6)
CCBs (n,%)	488 (18.5)	645 (17.0)
Compounds per pill (n,%)		
1	2334 (88.4)	3368 (88.9)
2	296 (11.2)	412 (10.9)
3	9 (0.3)	10 (0.3)
Percentage of recommended start dose (n, %)		
< 50	29 (1.1)	68 (1.8)
50-100	153 (5.8)	319 (8.4)
100	1215 (46.0)	1915 (50.5)
> 100	**1242 (47.1)**	**1488 (39.3)**

Summary

Majority of intermediate and high risk patients still receive monotherapy

- Men more often dual combination pills
- Women more often multiple separate pills

Women more often prescribed beta-blockers

Men more often prescribed ACEIs

Women overall lower doses than men, even in high risk group

Acknowledgements

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