

CVD Update 2018

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WHI CVD Outcomes

MRC (N=44,174)

- CVD death=4203
- CHD death=1917
- Incident CHD=3185
- MI=2254
- CABG/PTCA=2899
- HF=2583
- A Fib=1233
- Valvular=342

SRC (N=117,634)

- CVD death=9714
- CHD death=4060
- Stopped adjudicating after 2005

HF Paper Proposals and Abstracts

- 12 Paper Proposals
- 2 Consortium papers published
- 1 Paper in resubmission
- 5 Abstracts presented at Scientific sessions: AHA Epi, ACC,

Walking and HFpEF and HFrEF

Xiaochen Lin

Table 7. Association between tertiles of energy expenditure from walking (MET-hr/wk) and HFpEF and HFrEF in UNC Subcohort (N=37,780).¹

Energy Expenditure from Walking (MET-hr/wk)	No. of HF Cases	No. of Person-years	Model 1 ²			Model 2 ³			Model 3 ⁴		
			Multivariate-adjusted			Multivariate+vigorous PA adjusted			Multivariate+vigorous PA+potential mediators adjusted		
			HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
HFpEF											
Below median: [0.00, 2.00]	1010	244007	1.00			1.00			1.00		
Above median: (2.00, 40.8]	754	244940	0.82 [0.74, 0.90]		<0.001	0.82 [0.74, 0.91]		<0.001	0.83 [0.74, 0.92]		<0.001
HFrEF											
Below median: [0.00, 2.00]	549	244007	1.00			1.00			1.00		
Above median: (2.00, 40.8]	472	244940	0.84 [0.74, 0.96]		0.01	0.84 [0.74, 0.96]		0.01	0.85 [0.74, 0.97]		0.02

1. All HR and 95% CI are estimated from multivariate Cox proportional hazard models.

2. Model 1 is adjusted for age, OS/CT indicator, ethnicity, region, education, income, smoking status, alcohol consumption, BMI, hormone therapy (HT) usage status, alternative health eating index (AHEI), family history of MI, and history of hysterectomy.

3. Model 2 is adjusted for covariates adjusted in Model 1, as well as MET-hr/wk from vigorous PA.

4. Model 3 is adjusted for covariates in Model 2, as well as potential causal mediators, including diabetes, hypertension and hypercholesterolemia.

Walking Duration, Frequency or Speed ?

Table 8. Association of walking frequencies, duration and speed with HFpEF in UNC Subcohort (N=37,780).¹

	No. of HF Cases	No. of Person-years	Model 1 ²			Model 2 ³			Model 3 ⁴		
			HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
HFpEF											
Walking Frequencies											
Rarely or never	383	95547	1.00			1.00			1.00		
1-3 times/month	321	84820	1.00[0.85, 1.19]		0.96	1.00[0.85, 1.19]		0.96	0.99[0.83, 1.16]		0.86
1 time/wk	278	56101	1.13[0.95, 1.36]		0.18	1.13[0.95, 1.36]		0.18	1.12[0.93, 1.34]		0.24
2-3 times/wk	475	142289	0.99[0.84, 1.17]		0.92	0.99[0.84, 1.17]		0.92	0.99[0.84, 1.17]		0.92
4-6 times/wk	363	109021	1.09[0.87, 1.36]		0.48	1.09[0.87, 1.36]		0.48	1.06[0.85, 1.34]		0.60
7 or more times/wk	107	40220	0.91[0.65, 1.26]		0.56	0.91[0.65, 1.26]		0.56	0.92[0.66, 1.28]		0.62

2. Model 1 is adjusted for age, OS/CT indicator, ethnicity, region, education, income, smoking status, alcohol consumption, BMI, hormone therapy (HT) usage status, alternative health eating index (AHEI), family history of MI, history of hysterectomy and MET-hr/wk from walking.

3. Model 2 is adjusted for covariates adjusted in Model 1, as well as MET-hr/wk from vigorous PA.

4. Model 3 is adjusted for covariates in Model 2, as well as potential causal mediators, including diabetes, hypertension and hypercholesterolemia.

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	No. of HF Cases	No. of Person-years	Model 1 ²			Model 2 ³			Model 3 ⁴		
			Multivariate+MET-hr/wk from walking adjusted			Multivariate+MET-hr/wk from walking+MET-hr/wk from vigorous PA adjusted			Multivariate+MET-hr/wk from walking+MET-hr/wk from vigorous PA+potential mediators adjusted		
			HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
HFpEF											
Walking Duration											
Less than 20 min	512	114428	1.00			1.00			1.00		
20-39 min	631	180217	0.88[0.77, 1.00]		0.05	0.88[0.77, 1.00]		0.05	0.87[0.76, 1.00]		0.04
40-59 min	147	63198	0.69[0.54, 0.87]		0.002	0.69[0.54, 0.87]		0.002	0.70[0.55, 0.89]		0.004
1 hr or more	101	37724	0.95[0.71, 1.28]		0.74	0.95[0.71, 1.27]		0.73	0.97[0.72, 1.31]		0.83

2. Model 1 is adjusted for age, OS/CT indicator, ethnicity, region, education, income, smoking status, alcohol consumption, BMI, hormone therapy (HT) usage status, alternative health eating index (AHEI), family history of MI, history of hysterectomy and MET-hr/wk from walking.

3. Model 2 is adjusted for covariates adjusted in Model 1, as well as MET-hr/wk from vigorous PA.

4. Model 3 is adjusted for covariates in Model 2, as well as potential causal mediators, including diabetes, hypertension and hypercholesterolemia.

Walking Duration, Frequency or Speed ?

Table 8. Association of walking frequencies, duration and speed with HFpEF in UNC Subcohort (N=37,780).¹

	No. of HF Cases	No. of Person-years	Model 1 ²			Model 2 ³			Model 3 ⁴		
			Multivariate+MET-hr/wk from walking adjusted			Multivariate+MET-hr/wk from walking+MET-hr/wk from vigorous PA adjusted			Multivariate+MET-hr/wk from walking+MET-hr/wk from vigorous PA+potential mediators adjusted		
			HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
HFpEF											
Walking Speed											
Casual	444	87925	1.00			1.00			1.00		
Average	652	189505	0.72[0.63, 0.83]	<0.001		0.72[0.63, 0.83]	<0.001		0.76[0.66, 0.88]	<0.001	
Fast	189	95337	0.57[0.46, 0.70]	<0.001		0.57[0.46, 0.70]	<0.001		0.61[0.49, 0.76]	<0.001	

2. Model 1 is adjusted for age, OS/CT indicator, ethnicity, region, education, income, smoking status, alcohol consumption, BMI, hormone therapy (HT) usage status, alternative health eating index (AHEI), family history of MI, history of hysterectomy and MET-hr/wk from walking.

3. Model 2 is adjusted for covariates adjusted in Model 1, as well as MET-hr/wk from vigorous PA.

4. Model 3 is adjusted for covariates in Model 2, as well as potential causal mediators, including diabetes, hypertension and hypercholesterolemia.

Walking Speed is strongly associated with HF, HFpEF but not HFrEF

Table 1. Association of walking speed with heart failure, additionally adjusting for the status of meeting the AHA recommendation (7.5 MET-hr/wk).

	Walking Speed	No. of HF Cases	No. of Person-years	HR	95% CI	<i>P</i>
Total HF	Casual	791	87925	1.00		
	Average	1190	189505	0.72 [0.67, 0.86]		<0.001
	Fast	374	95337	0.59 [0.50, 0.72]		<0.001
HFpEF	Casual	444	87925	1.00		
	Average	652	189505	0.72 [0.63, 0.83]		<0.001
	Fast	189	95337	0.57 [0.46, 0.70]		<0.001
HFrEF	Casual	247	87925	1.00		
	Average	369	189505	0.84 [0.70, 1.01]		0.07
	Fast	142	95337	0.89 [0.69, 1.15]		0.36

1. All HR and 95% CI are estimated from multivariable Cox proportional hazard model, adjusting for the indicator of meeting the AHA recommendation (\geq vs. $<$ 7.5 MET-hr/wk), along with age, OS/CT indicator, ethnicity, region, education, income, smoking status, alcohol consumption, BMI, hormone therapy (HT) usage status, alternative health eating index (AHEI), family history of MI, history of hysterectomy and MET-hr/wk from walking.

CKD strongly associated with HFpEF less so with HFrEF

	Kidney Function Using e-GFR ^{&}			
	Level 1 (e-GFR<45)	Level 2 (45 ≤ e-GFR <60)	Level 3 (60 ≤ e-GFR <90)	Level 4 (e-GFR ≥90)
<i>n</i>	217	1,039	10,924	10,948
Total # Person-years	1,881	11,212	127,516	131,714
Any HF				
# Cases	48	121	779	538
Age-adjusted HF Rate*	25.78 (23.97, 27.74)	10.91 (10.61, 11.23)	6.25 (6.19, 6.31)	4.17 (4.13, 4.21)
<i>Hazards Ratios with 95% Confidence Intervals</i>				
Age-adjusted	4.66 (4.19, 5.18)	1.64 (1.52, 1.77)	0.87 (0.83, 0.90)	(ref)
Multiple Variable Adjusted Model ^a	3.23 (2.90, 3.60)	1.40 (1.30, 1.51)	0.91 (0.87, 0.95)	(ref)
HF-PEF				
# Cases	25	61	389	248
Age-adjusted HF-PEF Rate*	13.35 (12.37, 14.40)	5.49 (5.34, 5.65)	3.12 (3.09, 3.15)	1.92 (1.90, 1.94)
<i>Hazards Ratios with 95% Confidence Intervals</i>				
Age-adjusted	6.63 (5.70, 7.71)	2.30 (2.07, 2.56)	1.04 (0.98, 1.11)	(ref)
Multiple Variable Adjusted Model ^a	4.77 (4.09, 5.57)	2.02 (1.81, 2.24)	1.11 (1.04, 1.18)	(ref)
HF-REF				
# Cases	11	40	275	209
Age-adjusted HF-REF Rate*	5.96 (5.54, 6.40)	3.60 (3.50, 3.70)	2.21 (2.19, 2.23)	1.62 (1.60, 1.64)
<i>Hazards Ratios with 95% Confidence Intervals</i>				
Age-adjusted	2.21 (1.78, 2.74)	1.20 (1.06, 1.37)	0.73 (0.68, 0.78)	(ref)
Multiple Variable Adjusted Model ^a	1.46 (1.18, 1.82)	0.99 (0.87, 1.12)	0.77 (0.72, 0.83)	(ref)

HF = Heart Failure; HF-PEF = Preserved Ejection Fraction Heart Failure; HF-REF = Reduced Ejection Fraction Heart Failure

* - # Cases/1,000 person-years follow up (adjusted for age within sample)

a - Adjusted for age, body mass index, race, education, income, systolic blood pressure, current smoking, baseline history of medical conditions (diabetes, hypertension, coronary heart disease, atrial fibrillation)

& - ml/min/1.73m²

Note: Kidney function trend *p*-value<0.001 for all HF and HF-PEF models.

Calibrated Dietary Sodium associated with HFpEF and HFrEF

	Quintile of Calibrated Intake					P for trend	HR per sd (95% CI)
	Q1	Q2	Q3	Q4	Q5		
HFpEF							
Dietary sodium							
Cases/Person-years	192/74151	153/79329	126/81469	113/80358	154/79352		
Model 1	1.00	0.91 (0.73, 1.13)	0.94 (0.74, 1.18)	0.99 (0.78, 1.26)	1.81 (1.44, 2.29)	<0.001	1.21 (1.12, 1.31)
Model 2	1.00	1.11 (0.88, 1.40)	1.21 (0.94, 1.57)	1.39 (1.05, 1.84)	2.72 (2.01, 3.68)	<0.001	1.40 (1.26, 1.55)
Dietary potassium							
Cases/Person-years	127/71016	175/76447	163/79716	155/82066	118/85413		
Model 1	1.00	1.10 (0.87, 1.39)	0.96 (0.75, 1.23)	0.96 (0.75, 1.22)	0.85 (0.65, 1.11)	0.14	0.94 (0.86, 1.02)
Model 2	1.00	1.15 (0.87, 1.53)	1.05 (0.77, 1.44)	1.06 (0.76, 1.49)	1.01 (0.69, 1.48)	0.76	0.98 (0.87, 1.11)
Sodium:potassium ratio							
Cases/Person-years	164/80329	153/81591	145/80387	131/78073	145/74277		
Model 1	1.00	1.05 (0.84, 1.31)	1.09 (0.87, 1.36)	1.15 (0.91, 1.45)	1.66 (1.31, 2.10)	<0.001	1.19 (1.10, 1.28)
Model 2	1.00	1.12 (0.89, 1.41)	1.23 (0.97, 1.57)	1.40 (1.06, 1.83)	2.20 (1.60, 3.04)	<0.001	1.32 (1.18, 1.47)
HFrEF							
Dietary sodium							
Cases/Person-years	106/73533	86/78636	84/80488	75/79437	81/78771		
Model 1	1.00	0.91 (0.68, 1.21)	1.05 (0.78, 1.42)	1.07 (0.78, 1.46)	1.40 (1.02, 1.93)	0.03	1.13 (1.01, 1.25)
Model 2	1.00	1.10 (0.81, 1.50)	1.27 (0.91, 1.78)	1.32 (0.91, 1.90)	1.78 (1.19, 2.69)	0.005	1.22 (1.06, 1.39)
Dietary potassium							
Cases/Person-years	102/70234	94/75716	91/78865	86/81327	59/84725		
Model 1	1.00	0.76 (0.57, 1.02)	0.72 (0.53, 0.97)	0.71 (0.52, 0.95)	0.55 (0.39, 0.77)	<0.001	0.83 (0.75, 0.92)
Model 2	1.00	0.81 (0.57, 1.16)	0.82 (0.55, 1.20)	0.89 (0.59, 1.35)	0.71 (0.44, 1.14)	0.13	0.90 (0.77, 1.05)
Sodium:potassium ratio							
Cases/Person-times	88/79741	87/80691	88/79625	76/77266	93/73543		
Model 1	1.00	1.09 (0.81, 1.46)	1.18 (0.88, 1.59)	1.15 (0.84, 1.57)	1.69 (1.24, 2.31)	0.001	1.18 (1.07, 1.31)
Model 2	1.00	1.12 (0.82, 1.52)	1.20 (0.87, 1.65)	1.11 (0.78, 1.60)	1.57 (1.03, 2.40)	0.06	1.15 (1.00, 1.32)