The Malmö Diet and Cancer Study Department of Clinical Sciences Skåne University Hospital, Malmö Lund University

# Malmö Diet and Cancer Study incl. CV-cohort

# Cardiovascular Endpoints

End of follow-up: 31 December 2016 Report: 4 April 2018

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#### **General information**

All cardiovascular disease groups, except *atrial fibrillation* and *flutter* events, can have both prevalent and incident outcomes at the individual level.

Prevalent: date of diagnosis ≤ date of entry Incident: date of diagnosis > date of entry

Abbreviations:

CABG = Coronary Artery Bypass Graft surgery

MACE = Major Adverse Coronary Events

PCI = Percutaneous Coronary artery Intervention

# Amendments and implementation of new procedures

#### Year\* Description

2017 - Added the variables cgdat\_ep, fucg, pcdat\_ep, fupc

- Included all secondary diagnoses (currently max 31) in the Patient Register and added two more groups of the source-variables for the disease groups CABG, atrial fibrillation/flutter, aortic stenosis (both "as" and "ay")
- Removed events which have occurred after the date of emigration (if available)
- 2015 Validation of stroke events by means of the Stroma register started in 1989 and ceased in year 2013, the latest year with complete validated data was 2010. New non-validated stroke events from hospitals in Malmö were included as endpoints, but only events after 2010.
  - Atrial fibrillation and flutter events from the Hospital-based outpatient care (Öppenvårdsregistret) were included as endpoints. Previously only data from the Hospital Discharge Register (Slutenvårdsregistret) and the Cause-of-Death Register were included.
  - As a consequence of the amendments above the coding of the source variables pr\_stso, stso and afso was changed. The coding of the variable pr\_st was also modified.
- 2014 Introduced a separate last follow-up date for stroke.
- 2012 The original value for the recidive date in the Recidive Registry (part of the Stroma Registry) is composed of year and month (i.e. YYYYMM; day is missing). By default the day has been set to 15 in previous endpoint updates. Nevertheless, a few individuals have died a few days before day 15, which was not taken into account previously. However, in the new update the recidive date has been changed for such cases to date of death.
- 2011 Five new endpoints were added to the cardiovascular endpoint update: CABG surgery event, PCI event, MACE event (coronary event, CABG or PCI), Aortic stenosis event (based on ICD code), and Aortic stenosis event (based on surgery code).
  - In order to relate the cardiovascular events to the date at rescreening (2007-2012), a new file was created, parallell to the ordinary file with baseline screening date (1991-1996).
  - Information of reused (återanvända) Personal Identity Numbers (PIN) was taken into account, diagnoses appearing after the date of death of an MDC participating individual were removed.
  - For individuals with changed PINs, data with the new PIN (death, emigration) were included in the endpoint update.
  - Date of death as given by SCB has been used (previously dates from SoS were used)
  - One individual in the MDC cohort (not in CV cohort) was identified with two different PINs, the latest PIN was removed. The new MDC cohort number is 30 446.

<sup>\*</sup> The year when the endpoint update was made, usually the year after last follow-up year.

#### 1. Cohorts

#### Baseline 1991-1996

Background population: 74 137

Men: 31 513 Women: 42 624

#### Malmö Diet and Cancer Study (MDC) cohort

Individuals qualify to the MDC cohort if they participated in at least one part of the Malmö Diet and Cancer Study.

Total: 30 446

Men: 12 120 Women: 18 326

#### Cardiovascular (CV) cohort

Every other individual in the MDC cohort screened between 1991 to 1994 was invited to a CV project which included a B-mode carotid ultrasound examination for determination of carotid intima-media thickness and plaques. Out of 6 103 individuals which accepted the invitation about 5 500 further participated in an extended examination, including laboratory analyses.

Total: 6 103

Men: 2 572 Women: 3 531

# CV-rescreening 2007-2012 (CV-AUS)

All individuals in the CV-cohort, alive, not emigrated, and living in southern Sweden, were invited to rescreening during 2007-2012. In total 3 734 individuals participated in the study out of the original number 6 103.

Total: 3 734

Men: 1 522 Women: 2 212

#### 2. Time of follow-up

Number of person-years from date of entry to death, lost to follow-up or to 31 December 2016.

	Baseline MDC (n=30 446)*	CV (n=6103)**	Rescreening CV-AUS (n=3 734)
Total	599 738	127 609	25 618
Men	227 833	51 693	10 303
Women	371 905	75 916	15 316

<sup>\*</sup> Six individuals (3 males, 3 females) out of 30 446 lack follow-up time due to missing screening date.

<sup>\*\*</sup> One individual (male) out of 6 103 lack follow-up time due to missing screening date

# 3. Summary of prevalent and incident events by disease group

Number of individuals with first prevalent and/or first incident cardiovascular disease until 31 December 2016 by cohort and disease group.

	Baselin	e					Rescreening			
	MDC (	MDC (n=30 446)			CV (n=6 103)			CV-AUS (n=3 734)		
Disease group	Prev	Inc	Inc 2016	Prev	Inc	Inc 2016	Prev	Inc	Inc 2016	
Coronary events	600	3 864	157	102	768	34	219	215	31	
Stroke	344	3 353	144	48	677	37	142	217	30	
Heart failure	87	2 070	142	13	415	34	47	156	29	
Atrial fibrillation or flutter	312	5 078	345	58	1 079	83	253	418	68	
CABG surgery	335	2 624	100	49	535	24	229	159	27	
PCI	41	1 621	76	4	326	20	106	123	23	
MACE (coronary events, CABG or PCI)	774	4 772	190	131	939	39	308	277	40	
Aortic stenosis (based on ICD code)	64	867	65	11	175	12	35	86	9	
Aortic stenosis (based on surgery code)	30	300	26	3	71	4	24	23	4	

# **REFERENCE TIME POINT AT BASELINE (tables 4-13)**

# 4. Incident cardiovascular events by year of diagnosis – Part 1

Number of individuals with first incident coronary, stroke, heart failure and/or atrial fibrillation/flutter events until 31 December 2016 in the MDC and CV cohorts by year of diagnosis.

	Corona	ry events	Stroke		Heart failure <sup>*</sup>				Atrial fibrillation/ flutter**		
Year	MDC	CV	MDC	CV	MDC	MDC CV			MDC	CV	
					Pre MI	Post MI	Pre MI	Post MI			
1991	3		2						1		
1992	9	6	12	4	2	2	1	2	5		
1993	29	10	21	8	5	2	2	1	16	6	
1994	50	17	47	17	9	1	7	1	31	17	
1995	97	19	74	20	25	6	7	2	42	15	
1996	128	24	94	14	26	13	7	2	68	14	
1997	128	24	103	20	25	11	6	1	85	20	
1998	146	25	117	17	29	14	6		92	16	
1999	154	27	120	25	38	14	8	4	95	18	
2000	149	28	144	37	49	17	8	1	109	18	
2001	152	24	146	27	41	8	8		174	28	
2002	165	33	151	29	49	11	6	4	198	48	
2003	200	44	151	30	41	27	6	4	206	49	
2004	194	26	139	23	64	31	14	5	217	40	
2005	195	46	162	30	59	32	11	6	233	49	
2006	200	32	200	30	71	32	16	3	275	45	
2007	217	39	160	25	70	26	6	6	241	32	
2008	209	47	179	21	89	42	18	6	304	65	
2009	200	41	178	51	78	32	15	7	351	75	
2010	206	38	125	27	86	27	26	5	309	71	
2011	192	48	186	41	106	31	19	11	357	65	
2012	167	29	177	38	96	45	19	9	346	79	
2013	176	43	189	35	92	31	25	3	329	75	
2014	186	32	173	38	127	41	18	8	320	68	
2015	155	32	159	33	122	33	23	8	329	83	
2016	157	34	144	37	95	47	28	6	345	83	
Total	3 864	768	3 353	677	1 494	576	310	105	5 078	1 079	

<sup>\*</sup> Incident heart failure events were splitted into following groups:

Pre MI = heart failure at least one day before a possible acute myocardial infarction

Post MI = heart failure on the same day or after a non-fatal acute myocardial infarction (incl. possible prevalent MI)

Acute myocardial infarction were identified through ICD8/9=410 and ICD10=I21 in the Hospital Discharge Register

<sup>\*\*</sup> No incident atrial fibrillation/flutter event is recorded if the individual has a prevalent event

# 5. Incident cardiovascular events by year of diagnosis – Part 2

Number of individuals with first incident CABG, PCI, MACE, aortic stenosis (ICD and surgery) events until 31 December 2016 in the MDC and CV cohorts by year of diagnosis.

	CABG	surgery	PCI		MACE	MACE		tenosis	Aortic stenosis (surgery)	
Year	MDC	CV	MDC	CV	MDC	CV	MDC	CV	MDC	CV
1991	1				4					
1992	8	1	3	1	18	7	1			
1993	16	6	6	2	41	14	5	1	2	
1994	42	16	10	4	76	26	7	4	3	2
1995	53	9	4	1	133	25	8	2	3	2
1996	79	15	13	2	178	34	22	8	7	4
1997	85	15	14	3	178	32	19	5	13	5
1998	89	17	48	10	186	33	12	2	10	2
1999	106	13	59	7	217	32	12	1	8	1
2000	103	22	53	13	198	39	12	3	6	2
2001	123	15	85	11	218	31	22	8	4	
2002	142	25	7	1	209	39	22	4	8	1
2003	152	31	108	26	244	48	29	1	13	2
2004	153	30	105	12	250	35	30	7	11	3
2005	143	35	93	21	231	56	40	8	11	6
2006	158	27	120	15	248	44	54	9	23	4
2007	145	27	102	17	248	46	48	6	16	7
2008	144	34	110	21	248	55	38	6	10	2
2009	135	32	102	26	238	53	54	11	20	4
2010	137	34	102	27	241	53	50	8	27	7
2011	113	26	96	22	209	53	73	13	12	2
2012	94	19	70	12	193	33	71	15	15	1
2013	92	20	76	20	192	41	60	13	18	2
2014	119	19	86	13	205	32	58	11	16	3
2015	92	23	73	19	179	39	55	17	18	5
2016	100	24	76	20	190	39	65	12	26	4
Total	2 624	535	1 621	326	4 772	939	867	175	300	71

# 6. Coronary events by diagnosis

Number of individuals with first prevalent and/or first incident coronary events until 31 December 2016 in the MDC and CV cohorts by diagnosis group.

		MDC cohe	ort (n=30 4	146)	CV cohort (n=6 103)		
Diagnosis	ICD-9	Prevalent	Incident	Incident 2016	Prevalent	Incident	Incident 2016
Acute myocardial infarction	410	600	3 355	124	102	679	26
Other acute and subacute forms of ischemic heart disease	411		4				
Old myocardial infarction	412		10				
Angina pectoris	413		2				
Other forms of chronic ischemic heart disease	414		493	33		89	8
Total		600	3 864	157	102	768	34

# 7. Incident coronary events by diagnosis and source

Number of individuals with first incident coronary event until 31 December 2016 in the MDC cohort by diagnosis group and source of information.

Diagnosis	ICD-9	Hospital Discharge Register	Cause-of- death Register	Total
Acute myocardial infarction	410	2 830	525	3 355
Other acute and subacute forms of ischemic heart disease	411		4	4
Old myocardial infarction	412		10	10
Angina pectoris	413		2	2
Other forms of chronic ischemic heart disease	414		493	493
Total		2 830	1 034	3 864

# 8. Stroke events by diagnosis

Number of individuals with first prevalent and/or first incident stroke events until 31 December 2016 in the MDC and CV cohorts by diagnosis group.

		MDC cohe	ort (n=30 4	146)	CV cohort (n=6 103)		
Diagnosis	ICD-9	Prevalent	Incident	Incident 2016	Prevalent	Incident	Incident 2016
Unknown	-	14	31		3	6	
Subarachnoid hemorrhage	430	49	108	3	7	20	
Intracerebral hemorrhage	431	35	415	17	3	89	4
Occlusion of cerebral arteries	434	206	2 738	120	30	550	31
Acute, but ill-defined, cerebrovascular disease	436	40	61	4	5	12	2
Total		344	3 353	144	48	677	37

# 9. Incident stroke events by diagnosis and source

Number of individuals with first incident stroke event until 31 December 2016 in the MDC cohort by diagnosis group and source of information.

Diagnosis	ICD-9	•	Stroma register (also in HDR)*	HDR*, outside Malmö	HDR*, Malmö after 2010	Recidiv register	Total
Unknown	-					31	31
Subarachnoid hemorrhage	430	3	54	28	23		108
Intracerebral hemorrhage	431	17	241	48	109		415
Occlusion of cerebral arteries	434	209	1 572	270	687		2 738
Acute, but ill-defined, cerebrovascular disease	436	10	7	14	30		61
Total		239	1 874	360	849	31	3 353

<sup>\*</sup> HDR = Hospital Discharge Register

#### 10. Heart failure events by diagnosis

Number of individuals with first prevalent and/or first incident heart failure events until 31 December 2016 in the MDC and CV cohorts by diagnosis group.

		MDC	MDC cohort (n=30 446)					CV cohort (n=6 103)			
Diagnosis ICD		Prevalent*		Incident*		Incident	Prevalent*		Incident*		Incident
	ICD-10	pre MI	post MI	pre MI	post MI	2016	pre MI	post MI	pre MI	post MI	2016
Heart failure	428	57	30	1 479	572	142	8	5	309	103	34
Hypertensive heart disease with (congestive) heart failure	I11.0			15	4				1	2	
Total		57	30	1 494	576	142	8	5	310	105	34

<sup>\*</sup> Prevalent and incident heart failure events were splitted into following groups:

Pre MI = heart failure at least one day before a possible acute myocardial infarction

Post MI = heart failure on the same day or after a non-fatal acute myocardial infarction (incl. possible prevalent MI)

Acute myocardial infarction were identified through ICD8/9=410 and ICD10=I21 in the Hospital Discharge Register

# 11. Incident heart failure events by diagnosis and source

Number of individuals with first incident heart failure event until 31 December 2016 in the MDC cohort by diagnosis group and source of information.

Diagnosis	ICD-9/	Hospital Dis	Hospital Discharge Register*			
	ICD-10	Pre MI	Post MI			
Heart failure	428	1 479	572	2 051		
Hypertensive heart disease with (congestive) heart failure	I11.0	15	4	19		
Total		1 494	576	2 070		

<sup>\*</sup> Incident heart failure events were splitted into following groups:

Pre MI = heart failure at least one day before a possible acute myocardial infarction

Post MI = heart failure on the same day or after a non-fatal acute myocardial infarction (incl. possible prevalent MI)

Acute myocardial infarction were identified through ICD8/9=410 and ICD10=I21 in the Hospital Discharge Register

# 12. Atrial fibrillation and flutter events by diagnosis

Number of individuals with first prevalent or first incident atrial fibrillation and flutter events until 31 December 2016 in the MDC and CV cohorts. Only the first event of an individual is recorded, thus no incident event is recorded if the individual has a prevalent event.

		MDC cohort (n=30 446)			CV cohort (n=6 103)		
Diagnosis	ICD-9	Prevalent	Incident	Incident 2016	Prevalent		Incident 2016
Atrial fibrillation and flutter	427D	312	5 078	345	58	1 079	83

# 13. Incident atrial fibrillation and flutter events by diagnosis and source

Number of individuals with first incident atrial fibrillation and flutter event until 31 December 2016 in the MDC cohort by diagnosis group and source of information. Only the first event of an individual is recorded, thus no incident event is recorded if the individual has a prevalent event.

Diagnosis		Discharge	based out-	Cause-of- death Register	Total
Atrial fibrillation and flutter	427D*	3 745	1 296	37	5 078

<sup>\*</sup> Corresponding code in the Cause-of-death Register is 4273