

SUPPLEMENT 1: METHOD

For this narrative review, the following search was performed in PubMed, Embase, and Web of Science with an update on April 20, 2021 (table). Duplicates and articles not written in English were excluded (Figure 1). The remaining articles were screened based on title and abstract and the full text of relevant articles was screened by one author (MYK) and were deemed relevant for this review if 1) the study population consisted of only stable chest pain patients, AND 2) the CCS was determined on cardiac CT without intravenous contrast, AND EITHER 3) diagnostic evaluation of coronary artery disease as the primary endpoint was performed, described per CCS category, OR 4) prognostic evaluation of major adverse cardiovascular events (MACE) as outcome was performed, described per CCS category. The references of the articles that fulfilled the previous criteria were also screened and relevant articles were included. Articles were excluded if: no full text could be found, the article did not meet the primary endpoints, the article determined CCS through contrast-enhanced CT scans, the article described guidelines, study protocols, editorials, or validation tools or primarily focused on specific patient populations (e.g., asymptomatic patients, patients with diabetes, rheumatoid arthritis), cost-effectiveness, biomarkers, or risk factors. In addition, reviews were excluded, for example, those that primarily focused on asymptomatic and symptomatic chest pain patients together, acute chest pain patients, or different (CT) technical applications.

This search included 2398 articles (Figure 1). Duplicate articles and articles not written in English were excluded leaving 1627 articles to be screened based on title and abstract. The full text of the remaining 223 articles was screened, resulting in the exclusion of 190 articles. The references of the remaining 33 articles were then screened resulting in a 9 additional articles. The flowchart (Figure 1) shows the result of the search and the inclusion and exclusion criteria. Eventually, a total of 42 articles were included in this review. Of these, 19 focused on the diagnostic value of CCS and 13 on the prognostic value of CCS. 10 articles described both the diagnostic and prognostic value of CCS.

Table: Searches performed in PubMed, Embase, and Web of Science	
PubMed	("Tomography"[Mesh] OR "Tomography, X-Ray Computed"[Mesh] OR computed tomograph*[tiab] OR computerized tomography[tiab] OR CT [tiab] OR CT scan*[tiab] OR imaging test*[tiab] OR cardiac CT[tiab]) AND ("Chest Pain"[Mesh] OR chest pain*[tiab] OR angina pectoris[tiab] OR angina[tiab] OR typical chest pain*[tiab] OR atypical chest pain*[tiab] OR non-specific chest pain*[tiab]) AND ("Vascular Calcification"[Mesh] AND "Coronary Vessels"[Mesh] OR Coronary artery calcium score*[tiab] OR coronary calcium score*[tiab] OR CAC[tiab]OR CCS[tiab] OR 'coronary artery calcification'[tiab] OR coronary calcification* [tiab] OR coronary artery calcium[tiab] OR calcium score*[tiab] OR calcification*[tiab] OR calcium[tiab] OR calcified[tiab] OR Agatston score[tiab]).
Embase	'computer assisted tomography'/exp OR 'x-ray computed tomography'/exp OR 'computed tomograph*':ti,ab,kw OR 'computerized tomography':ti,ab,kw OR 'CT':ti,ab,kw OR 'CT scan*':ti,ab,kw OR 'imaging test*':ti,ab,kw OR 'cardiac CT':ti,ab,kw AND 'thorax pain'/exp OR 'angina pectoris'/exp OR 'typical chest pain*':ti,ab,kw OR 'atypical chest pain*':ti,ab,kw OR 'non-specific chest pain*':ti,ab,kw AND 'coronary artery calcium score'/exp OR 'CAC':ti,ab,kw OR 'CCS':ti,ab,kw OR 'calcification*':ti,ab,kw OR 'Agatston score':ti,ab,kw
Web of Science	TS= 'computed tomography OR 'CT scan' OR 'Cardiac CT' AND TS= 'Chest Pain*' OR 'angina pectoris' OR 'typical chest pain*' OR 'atypical chest pain*' OR 'non-specific chest pain*' AND TS= 'coronary calcium score*' OR 'Coronary artery calcium score*' OR 'CAC' OR 'CCS' OR coronary artery calcification* OR 'coronary calcification*' OR 'calcium score*' OR 'calcification*' OR 'calcified' OR 'Agatston score'
Mesh=Medical Subject Headings. tiab= title and abstract. exp= exact Emtree term, exploded. ti.ab.kw= title, abstract and keywords. TS= topic.	

► **Supplementary Table 1** Diagnostic value of CCS 0 in stable chest pain patients.

First author (year)	Population (N, % men, mean age ± SD)	CT system	cCTA ≥ 50 % luminal stenosis N (%)	Total number of patients with a CCS 0 N (%*)	Total number of CCS 0 patients with OCAD N (%)	Total number of CCS 0 patients with non-OCAD N (%)
Low pre-test probability						
Kwon (2011)	N = 3979, 44 % men Age: 60 ± 10	64-slice MDCT	622 (16)	2406 (61)	90 (3.7)	n.r.
Nicoll (2016)	N = 5515, 61 % men Age: 60 ± 12	64-slice MDCT	1538 (28)	1897 (34)	109 (5.7)	n.r.
Yerramasu (2014)	N = 300, 48 % men Age: 60.6 ± 9.6	First-generation DSCCT	90 (30)	131 (44)	2 (1.5) [§]	n.r.
Wang (2019)	N = 1753, 46 % men Age: 57 ± 12	Second-generation DSCCT	222 (15)	915 (52)	14 (1.9)	63 (7)
Low and intermediate pre-test probability						
van Werkhoven (2009)	N = 432, 59 % men Age: 58 ± 11	64-slice MDCT	109 (25)	70 (34)	9 (7.2)	9 (18)
van Werkhoven (2010)	N = 576, 47 % men Age: 56 ± 12 Typical: 21 %, atypical: 43 %, non-anginal: 36 %	64-slice MDCT	168 (29)	242 (42)	14 (5.8)	n.r.
Villines (2011)	N = 10 037, 56 % men Age: 57 ± 11 Typical: 13 %	64-slice MDCT	2069 (21)	5128 (51)	244 (5.1)	667 (13)
Kim (2012)	N = 2088, 49 % men Age: 59 ± 10 Typical: 16 %, atypical: 44 %, non-anginal: 40 %	64-slice MDCT	444 (21)	1114 (53)	48 (2.2)	n.r.
Born (2016)	N = 1551, 38 % men Age: 58 ± 10	64-slice MDCT	214 (14)	739 (48)	23 (3.1)	62 (8.4)
Van der Zant (2015)	N = 1014, 0 % men Age: 59 ± 10 Atypical: 100 %	Second-generation DSCCT	494 (49)	557 (55)	8 (1.5)**	37 (7)**
Senoner (2020)	N = 1451, 49 % men Age: 53 ± 11 Symptomatic: 66 %, asymptomatic: 34 %	Second-generation DSCCT	93 (6)	1289 (89)	66 (5.1)	268 (21)

► Supplementary Table 1 (Continuation)

First author (year)	Population (N, % men, mean age ± SD)	CT system	cCTA ≥ 50 % luminal stenosis N (%)	Total number of patients with a CCS 0 N (%)	Total number of CCS 0 patients with OCAD N (%)	Total number of CCS 0 patients with non-OCAD N (%)
Intermediate pre-test probability						
Hulten (2014)	N = 1145, 63 % men Age: 55 ± 12	64-slice MDCT	285 (42)	83 (7.3)	9 (1.9)	81 (17)
Nieman (2009)	N = 471, 57 % men Age: 56 ± 10 Typical: 31 %, atypical: 53 %, non-anginal: 16 %	First-generation DSCT	140 (31) ^y	175 (37)	3 (2)	n.r.
Meyer (2012)	N = 383, 62 % men Age: 58 ± 13 Typical: 81 %, atypical: 19 %	First-generation DSCT	114 (30)	121 (32)	0 (0)	n.r.
Kaczmarek (2013)	N = 1132, 47 % men Age: 58.7 ± 10.9	First-generation DSCT	272 (24)	668 (59) ^{***}	56 (8.4) ^{***}	n.r.
Intermediate and high pre-test probability						
Gottlieb (2010)	N = 291, 73 % men Age: 59 ± 10	64-slice MDCT	163 (56)	72 (25)	14 (19)	n.r.
Dedic (2013)	N = 756, 51 % men Age: 56 ± 10	First-generation DSCT	10 (1)	281 (37)	10 (3.6)	n.r.
High pre-test probability						
LaMont (2002)	N = 153, 76 % men Age: 58 ± 9 Typical: 37 %, atypical: 39 %, non-anginal: 24 %	Electron beam CT	112 (73)	29 (19)	2 (7)	n.r.
Drosch (2010)	N = 500, 75 % men Age: 63 ± 10	16 or 64-slice MDCT	16 (3) ^y	61 (12)	16 (26)	45 (74)
Type of symptoms						
Ho (2008)	N = 664, 84 % men Age: 62 ± 9 Atypical: 10 %	64-slice MDCT	86 (13)	92 (14)	0 (0)	n.r.
Akram (2009)	N = 210, 47 % men Age: 57 ± 11.8 Typical/atypical: 64 %, non-anginal: 36 %	64-slice MDCT	28 (21)	70 (34)	4 (5.7)	n.r.
Knez (2004)	N = 2115, 66 % men Age: 62 Typical/atypical: 80 %, non-anginal: 20 %	Electron beam CT	1255 (59)	334 (16)	8 (2.4)	n.r.

▶ Supplementary Table 1 (Continuation)

First author (year)	Population (N, % men, mean age ± SD)	CT system	cCTA ≥ 50 % luminal stenosis N (%)	Total number of patients with a CCS 0 N (%) [*]	Total number of CCS 0 patients with OCAD N (%)	Total number of CCS 0 patients with non-OCAD N (%)
Geluk (2008)	N = 304, 56 % men Age: 55 Typical: 19 %, atypical: 74 %, other [‡] : 7 %	Electron beam CT	38 (13)	159 (52) ^{***}	0 (0)	2 (15)
Ueda (2012)	N = 753, 70 % men Age: 64.7 ± 10.7 Typical: 29 %, atypical: 20 %, asymptomatic [‡] : 51 %	First generation DSCT	189 (25)	260 (35)	8 (3.1)	n.r.
Pre-test probability or type of symptoms not reported						
Schmermund (2000)	N = 323, 77 % men Age: 55 ± 11	Electron beam CT	179 (55)	117 ^{***}	17 (15)	n.r.
Feldman (2000)	N = 22, 82 % men Age: 59.6 ± 9	Helical CT: double layers of detectors	16 (89)	8 (37)	2 (25)	2 (25)
Kiani (2020)	N = 219, 55 % men Age: 63 ± 12.39	192-slice MDCT	97 (44)	128 ^{***}	36 (28)	n.r.

Note: SD = standard deviation. CT = computed tomography. CCS = coronary calcium score. cCTA = coronary computed tomography angiography.

CAD = coronary artery disease. MDCT = multi-detector CT. DSCT = dual-source CT. Non-OCAD = non-obstructive coronary artery disease, luminal stenosis < 50 %. n.r. = not reported in the article.

^{*} percentage of patients with a CCS 0 in relation to the total population of the study.

^{**} due to non-calcified plaques.

^{***} CCS ≤ 10 or ≤ 15 or ≤ 100.

^a clinical suspicion of CAD based on prior testing (e. g., resting ECG, exercise ECG test).

[‡] Based on invasive coronary angiography.

[§] based on ≥ 70 % stenosis.

[‡] arrhythmia, collapse, screening.

► **Supplementary Table 2** Diagnostic value of CCS > 0 in stable chest pain patients.

First author (year)	Population (N, % men, mean age, SD)	CT system	Total number of patients with CCS > 0 N (%)	Total number of CCS > 0 patients with OCAD N (%)	Total number of patients per CCS > 0 category (N)	Total number of OCAD per CCS > 0 category N (%)
Low pre-test probability						
Kwon (2011)	N = 3979, 44 % men Age: 60 ± 10	64-slice MDCT	1573 (40)	532 (34)	1–10 (287) 11–100 (708) 101–400 (369) >400 (209)	34 (12) 162 (23) 180 (49) 156 (75)
Nicoll (2016)	N = 5515, 61 % men Age: 60 ± 12	64-slice MDCT	3528 (64)	1429 (41)		
Yerramasu (2014)	N = 300, 48 % men Age: 60.6 ± 9.6	First-generation DSCT	169 (56)	54 (32)	1–400 (136) >400 (33)	27 (20)§ 27 (82)§
Wang (2019)	N = 1753, 46 % men Age: 57 ± 12	Second-generation DSCT	838 (48)	208 (30)	> 0 (838) > 100 (91)	208 (30) 61 (67)
Low and intermediate pre-test probability						
van Werkhoven (2009)	N = 432, 59 % male Age: 58 ± 11	64-slice MDCT	285 (66)	103 (36)	1–99 (122) 100–399 (75) 400–999 (56) > 1000 (32)	20 (16) 32 (44) 29 (52) 22 (69)
van Werkhoven (2010)	N = 576, 47 % men Age: 56 ± 12 Typical: 21 %, atypical: 43 %, non-anginal: 36 %	64-slice MDCT	334 (58)	154 (46)	1–400 (260) >400 (74)	94 (36) 60 (81)
Villines (2011)	N = 10037, 56 % men Age: 57 ± 11 Typical: 13 %	64-slice MDCT	4909 (49)	1825 (44)		
Kim (2012)	N = 2088, 49 % men Age: 59 ± 10 Typical: 16 %, atypical: 44 %, non-anginal: 40 %	64-slice MDCT	974 (47)	396 (41)		
Bom (2016)	N = 1551, 38 % men Age: 58 ± 10	64-slice MDCT	812 (52)	n.r.	0.1–100 (498) 100–400 (215) >400 (99)	n.r. n.r. n.r.
Van der Zant (2015)	N = 1014, 0 % men Age: 59 ± 10 Atypical: 100 %	Second-generation DSCT	457 (45)	49 (11)		

▶ Supplementary Table 2 (Continuation)							
First author (year)	Population (N, % men, mean age, SD)	CT system	Total number of patients with CCS > 0 N (%)	Total number of patients with CCS > 0 N (%)	Total number of patients per CCS > 0 category (N)	Total number of patients per CCS > 0 category N (%)	Total number of OCAD per CCS > 0 category N (%)
Senoner (2020)	N = 1451, 49 % men Age: 53 ± 11 Symptomatic: 66 %, asymptomatic*: 34 %	Second-generation DSCT	162 (11)**	27 (17)			
Intermediate pre-test probability							
Hulten (2014)	N = 1145, 63 % men Age: 55 ± 12	64-slice MDCT	662 (58)	278 (42)			
Nieman (2009)	N = 471, 57 % men Age: 56 ± 10 Typical: 31 %, atypical: 53 %, non-anginal: 16 %	First-generation DSCT	288 (61)	137 (48)	0.1–10 (48)	5 (10)	
					11–100 (101)	37 (37)	
					101–400 (74)	37 (51)	
					>400 (65)	58 (94)	
Meyer (2012)	N = 383, 62 % men Age: 58 ± 13 Typical: 81 %, atypical: 19 %	First-generation DSCT	262 (68)	104 (40)	0.1–10 (63)	6 (3.8)	
					10.1–100 (66)	15 (23)	
					100.1–400 (63)	29 (46)	
					>400 (70)	54 (77)	
Kaczmarek (2013)	N = 1132, 47 % men Age: 58.7 ± 11	First-generation DSCT	464 (41)	216 (47)	10–100 (221)	84 (38)	
					>100 (243)	132 (54)	
Intermediate and high pre-test probability							
Gottlieb (2010)	N = 291, 73 % men Age: 59 ± 10	64-slice MDCT	219 (75)	149 (68)	1–10 (24)	11 (46)	
					>10 (195)	138 (71)	
Dedic (2013)	N = 756, 51 % men Age: 56 ± 10	First-generation DSCT	475 (63)	n. r.	1–400	n. r.	
					>400	n. r.	
High pre-test probability							
LaMont (2002)	N = 153, 76 % men Age: 58 ± 9 Typical: 37 %, atypical: 39 %, non-anginal: 24 %	Electron beam CT	124 (81)	110 (89)			
Drosch (2010)	N = 500, 75 % men Age: 63 ± 10	16 or 64-slice MDCT	429 (86)	n. r.			

► Supplementary Table 2 (Continuation)

First author (year)	Population (N, % men, mean age, SD)	CT system	Total number of patients with CCS > 0 N (%) ^a	Total number of CCS > 0 patients with OCAD N (%)	Total number of patients per CCS > 0 category (N)	Total number of OCAD per CCS > 0 category N (%)
Type of symptoms						
Ho (2008)	N = 664, 84 % men Age: 62 ± 9 Atypical: 10 %	64-slice MDCT	572 (86)	86 (15)	1–100 (63)	5 (7.9)
Akram (2009)	N = 210, 47 % men Age: 57 ± 12 Typical/atypical: 64 %, non-anginal: 36 %	64-slice MDCT	140 (67)	34 (24)	101–400 (180)	15 (8.3)
Knez (2004)	N = 2115, 66 % men Age: 62 Typical/atypical: 80 %, non-anginal: 20 %	Electron beam CT	1789 (85)	1255 (71)	401–1000 (186)	27 (15)
Geluk (2008)	N = 304, 56 % men Age: 55 Typical: 19 %, atypical: 74 %, other ^b : 7 %	Electron beam CT	145 (48)	72 (50)	> 1000 (143)	39 (27)
Ueda (2012)	N = 753, 70 % men Age: 65 ± 11 Typical: 29 %, atypical: 20 %, asymptomatic ^c : 51 %	First-generation DSCT	389 (52)	149 (38)		
Pre-test probability or type of symptoms not reported						
Schmermund (2000)	N = 323, 77 % men Age: 55 ± 11	Electron beam CT	206 (64)***	162 (79)		
Feldman (2000)	N = 22, 82 % men Age: 60 ± 9.0	Helical CT: double layers of detectors	14 (65)	14 (100)		
Kiani (2020)	N = 219, 55 % men Age: 63 ± 12	192-slice MDCT	91 (42)****	61 (67)		

Note: SD = standard deviation. CT = computed tomography. CCS = coronary calcium score. CAD = coronary artery disease. MDCT = multi-detector CT. DSCT = dual-source CT. n.r. = not reported in the article.

^a percentage of patients with a CCS > 0 in relation to the total population of the study.

** CCS 0.1–0.9.

*** CCS > 15.

**** CCS > 100.

^a clinical suspicion of CAD based on prior testing (e.g., resting ECG, exercise ECG test).

^b arrhythmia, collapse, screening.

► **Supplementary Table 3** Prognostic value of CCS 0 in stable chest pain patients.

First author/ (year)	Population (N, % men, mean age, SD)	CT system	Follow-up duration (mean, SD; median, IQR)	Endpoints	Total number of CCS 0 patients N (%*)	Total number of CCS patients with MACE (N, %)
Low pre-test probability						
Kwon (2011)	N = 3979, 44% men Age: 60 ± 10	64-slice MDCT	2.3 ± 1 years	<ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP Revascularization 	2406 (61)	2 (0.1)
Wang (2019)	N = 1753, 46% men Age: 57 ± 12	Second-generation DSCT	2.2 years (IQR 1.8–3.7)	<ul style="list-style-type: none"> Cardiac death Non-fatal MI Revascularization 	915 (52)	5 (0.6)
Low and intermediate pre-test probability						
van Werkhoven (2009)	N = 432, 59% men Age: 58 ± 11	64-slice MDCT	2 years (IQR 1.2–2.5)	<ul style="list-style-type: none"> All-cause mortality Non-fatal MI Revascularization 	147 (34)	2 (1.1)
Nappi (2018)	N = 155, 67% men Age: 63 ± 11 Typical: 15%, atypical: 30%	64-slice MDCT	6.8 ± 2.8 years	<ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP & revascularization 	42 (27)	0 (0)
Villines (2011)	N = 10037, 56% men Age: 57 ± 11 Typical: 13%	64-slice MDCT	2.1 years (IQR 2.0)	<ul style="list-style-type: none"> All-cause mortality Non-fatal MI Revascularization 	4738 (47)	44 (0.9)
Kim (2012)	N = 2088, 49% men Age: 59 ± 0 Typical: 16%, atypical: 44%, non-anginal: 40%	64-slice MDCT	2.8 ± 0.4 years	<ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP Revascularization 	1114 (53)	14 (1.3)
Bom (2016)	N = 1551, 38% men Age: 58 ± 10	64-slice MDCT	1.7 years (IQR n.r.)	<ul style="list-style-type: none"> All-cause mortality MI Revascularization 	739 (47)	2 (0.3)
Budoff (2017)	N = 4209, 49% men Age: 61 ± 8 Typical: 11.2%, atypical: 78%, non-anginal: 10.6%	64-slice MDCT	2.1 years (IQR 1.5–2.8)	<ul style="list-style-type: none"> Cardiac death MI 	1457 (35)	21 (1.4)
Dedic (2011)	N = 471, 52% men Age: 56 ± 10 Typical: 32%, atypical: 52%, non-anginal: 16%	First-generation DSCT	2.6 years (IQR 2.1–3.2)	<ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP Revascularization 	151 (32)	2 (1.3)
Senoner (2020)	N = 1451, 49% men Age: 53 ± 11 Symptomatic: 66%, asymptomatic: 34%	Second-generation DSCT	6.6 ± 4.2 years	<ul style="list-style-type: none"> All-cause and cardiac mortality Composite of non-fatal and fatal MACE 	1289 (90)	7 (0.6) [†]
Intermediate pre-test probability						

▶ Supplementary Table 3 (Continuation)

First author/ (year)	Population (N, % men, mean age, SD)	CT system	Follow-up duration (mean, SD; median, IQR)	Endpoints	Total number of CCS 0 patients N (%)	Total number of CCS patients with MACE (N, %)
Petretta (2012)	N = 326, 67% men Age: 62 ± 12 Typical: 32%, atypical: 63%, non-anginal: 5%	64-slice MDCT	2.2 ± 1.0 years	<ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP 	106 (33)	0 (0)
Hulten (2014)	N = 1145, 63% men Age: 55 ± 12	64-slice MDCT	2.4 years (IQR 1.5–3.5)	<ul style="list-style-type: none"> Death MI UAP Late revascularization 	483 (42)	2 (0.5)
Parma (2016)	N = 588, 36% men Age: 61 ± 10	64-slice MDCT	1.9 years (IQR 1.6–2.3)	<ul style="list-style-type: none"> Cardiac death Non-fatal MI Revascularization 	239 (41)	0 (0)
Intermediate and high pre-test probability						
Mittal (2017)	N = 3914, 50% men Age: 57 ± 12 Typical: 19%, atypical: 42%, non-anginal: 25%, dyspnea: 15%	64-slice MDCT	5.2 ± 2.8 years total follow-up 13 years	<ul style="list-style-type: none"> All-cause death 	1978 (51)	28 (1.4)**
Type of symptoms						
Geluk (2008)	N = 304, 56% men Age: 55 Typical: 19%, atypical: 74%, other [†] : 7%	Electron beam CT	1.0 ± 0.3 years	<ul style="list-style-type: none"> Coronary death MI Revascularization 	159 (52)***	0 (0)
Hou (2012)	N = 4425, 62% men Age: 60 ± 11 Typical: 6%, atypical: 16%, non-anginal: 47%	64-slice MDCT	3 years (IQR 2.6–3.3)	<ul style="list-style-type: none"> Cardiac death MI Revascularization 	2785 (63)	56 (2.1)
Pre-test probability or type of symptoms not reported						
Schmermund (2004)	N = 255, 71% men Age: 55 ± 11	Electron beam CT	3.1 years (range 0.2–3.5 years)	<ul style="list-style-type: none"> Cardiac death MI Revascularization 	150 (59)****	5 (3.4)
Rijlaardam- Hermesen (2011)	N = 134, 19% men Age: 57 ± 9	16-slice MDCT	3.7 years (IQR 2.9–4.5)	<ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP & revascularization 	134 (100)	0 (0)
Marfei (2011)	N = 722, 66% men Age: 63 ± 11	64-slice MDCT	1.6 ± 0.3 years	<ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP Revascularization 	n.r.	n.r. (6)
Versteylen (2013)	N = 283, 51% men Age: 54 ± 10	64-slice MDCT	2.1 years (IQR 1.8–2.8)	<ul style="list-style-type: none"> ACS Revascularization 	149 (53)	1 (0.7)

► **Supplementary Table 3** (Continuation)

First author/ (year)	Population (N, % men, mean age, SD)	CT system	Follow-up duration (mean, SD; median, IQR)	Endpoints	Total number of CCS 0 patients N (%*)	Total number of CCS patients with MACE (N, %)
Shah (2014)	N = 7078, 49% men Age: n. r.	64-slice MDCT	2.1 years (IQR 1.5–3.2)	<ul style="list-style-type: none"> ▪ Overall mortality 	4047 (57)	471 (1.1)
Yamamoto (2018)	N = 736, 62% men Age: 65 ± 10	64-slice MDCT	6.5 years (IQR 1.0–12)	Composite of: <ul style="list-style-type: none"> ▪ Cardiac death ▪ Non-fatal MI ▪ Non-fatal stroke 	270 (37)	3.9†
Shiga (2020)	N = 502, 50% men Age: 65 ± 10	64-slice MDCT	3.5 ± 0.6 years total follow-up 5 years	<ul style="list-style-type: none"> ▪ Cardiac death ▪ MI ▪ Revascularization ▪ Ischemic stroke 	202 (40)	9 (4.5)

Note: description of patients with major adverse cardiac events (MACE) with a negative and positive coronary calcium score (CCS) in articles that described the pre-test probability and/or typicality of angina pectoris symptoms. IQR = interquartile range. ACS = acute coronary syndrome.

* percentages of total CCS 0 patients of the total populations.

† all-cause mortality not included.

** non-cardiac related deaths.

*** CCS < 10.

**** CCS < 100

‡ arrhythmia, collapse, screening.

† cumulative rate at 10 years.

► **Supplementary Table 4** Prognostic value of CCS > 0 in stable chest pain patients.

First author/ (year)	Population (N, % men, mean age, SD)	CT system	Follow-up duration and endpoints (mean, SD; median, IQR)	Total number of patients with CCS > 0 N (%*)	Total number of CCS > 0 patients with MACE N (%)	Total number of patients per CCS > 0 category (N)	Total number of MACE per CCS > 0 category N (%)
Low pre-test probability							
Kwon (2011)	N = 3979, 44% men Age: 60 ± 10	64-slice MDCT	2.3 ± 1 years <ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP Revascularization 	1573 (39)	103 (5.4)		
Wang (2019)	N = 1753, 46% men Age: 57 ± 12	Second-generation DSCT	2.2 years (IQR 1.8–3.7) <ul style="list-style-type: none"> Cardiac death Non-fatal MI Revascularization 	838 (48)	17 (2.1)		
Low and intermediate pre-test probability							
van Werkhoven (2009)	N = 432, 59% men Age: 58 ± 11	64-slice MDCT	2 years (IQR 1.2–2.5) <ul style="list-style-type: none"> All-cause mortality Non-fatal MI Revascularization 	285 (66)	26 (9.2)	1–99 (122) 100–399 (75) 400–999 (56) >1000 (32)	n.r. (1.4%) n.r. (3.7%) n.r. (4.8%) n.r. (8.5%)
Nappi (2018)	N = 155, 67% men Age: 63 ± 11 Typical: 15%, atypical: 30%	64-slice MDCT	6.8 ± 2.8 years <ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP & revascularization 	114 (74)	22 (19)	1–300 (98) >300 (16)	14 (15) 8 (50)
Villines (2011)	N = 10 037, 56% men Age: 57 ± 11 Typical: 13%	64-slice MDCT	2.1 years (IQR 2.0) <ul style="list-style-type: none"> All-cause mortality Non-fatal MI Revascularization 	4169 (42)	191 (4.6)		
Kim (2012)	N = 2088, 49% men Age: 59 ± 10 Typical: 16%, atypical: 44%, non-anginal: 40%	64-slice MDCT	2.8 ± 0.4 years <ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP Revascularization 	974 (47)	46 (4.8)		
Born (2016)	N = 1551, 38% men Age: 58 ± 10	64-slice MDCT	1.7 years (IQR n.r.) <ul style="list-style-type: none"> All-cause mortality MI Revascularization 	812 (52)	21 (2.6)	0.1–100 (498) 100–400 (215) >400 (99)	5 (1) 9 (4.2) 7 (7.1)

► Supplementary Table 4 (Continuation)

First author/ (year)	Population (N, % men, mean age, SD)	CT system	Follow-up duration and endpoints (mean, SD; median, IQR)	Total number of patients with CCS > 0 N (%)	Total number of CCS > 0 patients with MACE N (%)	Total number of patients per CCS > 0 category (N)	Total number of MACE per CCS > 0 category N (%)
Budoff (2017)	N = 4209, 49 % men Age: 61 ± 8 Typical: 11.2 %, atypical: 78 %, non-anginal: 10.6 %	64-slice MDCT	2.1 years (IQR 1.5–2.8) <ul style="list-style-type: none"> Cardiac death MI 	2752 (65)	133 (4.8)		
Dedic (2011)	N = 471, 52 % men Age: 56 ± 10 Typical: 32 %, atypical: 52 %, non-anginal: 16 %	First-generation DSCT	2.6 years (IQR 2.1–3.2) <ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP Revascularization 	272 (58)	28 (10)	1–10 (51) 10–100 (92) 100–400 (66) >400 (63)	2 (4) 10 (11) 7 (11) 9 (14)
Senoner (2020)	N = 1451, 49 % men Age: 53 ± 11 Symptomatic: 66 %, asymptomatic: 34 %	Second-generation DSCT	6.6 ± 4.2 years <ul style="list-style-type: none"> All-cause and cardiac mortality Composite of non-fatal and fatal MACE 	162 (11)**	1 (0.6)†		
Intermediate pre-test probability							
Petretta (2012)	N = 326, 67 % men Age: 62 ± 12 Typical: 32 %, atypical: 63 %, non-anginal: 5 %	64-slice MDCT	2.2 ± 1.0 years <ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP 	220 (68)	34 (16)	1–100 (138) 101–400 (70) >400 (12)	9 (6.7) 19 (27) 6 (50)
Hulten (2014)	N = 1145, 63 % men Age: 55 ± 12	64-slice MDCT	2.4 years (IQR 1.5–3.5) <ul style="list-style-type: none"> Death MI UAP Late revascularization 	662 (58)	14 (2.1)		
Parma (2016)	N = 588, 36 % men Age: 61 ± 10	64-slice MDCT	1.9 years (IQR 1.6–2.3) <ul style="list-style-type: none"> Cardiac death Non-fatal MI Revascularization 	349 (59)	119 (34)		
Intermediate and high pre-test probability							
Mittal (2017)	N = 3914, 50 % men Age: 57 ± 12 Typical: 19 %, atypical: 42 %, non-anginal: 25 %, dyspnea: 15 %	64-slice MDCT	5.2 ± 2.8 years <ul style="list-style-type: none"> All-cause death 	1936 (39)	119 (6.1)		

Supplementary Table 4 (Continuation)

First author/ (year)	Population (N, % men, mean age, SD)	CT system	Follow-up duration and endpoints (mean, SD; median, IQR)	Total number of patients with CCS > 0 N (%*)	Total number of CCS > 0 patients with MACE N (%)	Total number of patients per CCS > 0 category (N)	Total number of MACE per CCS > 0 category N (%)
Type of symptoms							
Geluk (2008)	N = 304, 56% men Age: 55 Typical: 19%, atypical: 74%, other ^a : 7%	Electron beam CT	1.0 ± 0.3 years <ul style="list-style-type: none"> Coronary death MI Revascularization 	145 (48)	52 (36)	10–399 (103) ≥ 400 (42)	11 (11) 17 (41)
Hou (2012)	N = 4425, 62% men Age: 60 ± 11 Typical: 6%, atypical: 16%, non-anginal: 47%	64-slice MDCT	3 years (IQR 2.6–3.3) <ul style="list-style-type: none"> Cardiac death MI Revascularization 	1640 (37)	290 (18)	1–100 (813) 101–400 (483) > 400 (344)	103 (13) 74 (16) 113 (34)
Pre-test probability or type of symptoms not reported							
Schmermund (2004)	N = 255, 71% men Age: 55 ± 11	Electron beam CT	3.1 (range 0.2–3.5 years) <ul style="list-style-type: none"> Cardiac death MI Revascularization 	105 (41)***	35 (34)		
Rijlaardam- Hermesen (2011)	N = 134, 19% men Age: 57 ± 9	16-slice MDCT	3.7 years (IQR 2.9–4.5) <ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP & revascularization 	n. r.	n. r.	n. r.	n. r.
Maffei (2011)	N = 722, 66% men Age: 63 ± 11	64-slice MDCT	1.6 ± 0.3 years <ul style="list-style-type: none"> Cardiac death Non-fatal MI UAP Revascularization 			11–100 (n. r.) 101–400 (21) 401–1000 (n. r.) > 1000 (n. r.)	n. r. (10) 3 (15) n. r. (23) n. r. (34)
Versteylen (2013)	N = 283, 51% men Age: 54 ± 10	64-slice MDCT	2.1 years (IQR 1.8–2.8) <ul style="list-style-type: none"> ACS revascularization 	134 (48)	5 (3.8)		
Shah (2014)	N = 7078, 49% men Age: n. r.	64-slice MDCT	2.1 years (IQR 1.5–3.2) <ul style="list-style-type: none"> Overall mortality 	3031 (43)	165 (5.4)	1–10 (524) 11–99 (1300) 100–399 (823) ≥ 400 (384)	41 (1.5) 86 (2.4) 29 (4.1) 9 (10)

► Supplementary Table 4 (Continuation)

First author/ (year)	Population (N, % men, mean age, SD)	CT system	Follow-up duration and endpoints (mean, SD; median, IQR)	Total number of patients with CCS > 0 N (%)*	Total number of CCS > 0 patients with MACE N (%)	Total number of patients per CCS > 0 category (N)	Total number of MACE per CCS > 0 category N (%)
Yamamoto (2018)	N = 736, 62% men Age: 65 ± 10	64-slice MDCT	6.5 years (IQR 1.0–12) Composite of: ■ Cardiac death ■ Non-fatal MI ■ Non-fatal stroke	470 (64)	39 (8.3)	1–199 (228) 100–399 (162) ≥400 (80)	9.2 [‡] 12 [‡] 18 [‡]
Shiga (2020)	N = 502, 50% men Age: 65 ± 10	64-slice MDCT	3.5 ± 0.6 years ■ Cardiac death ■ MI ■ Revascularization ■ Ischemic stroke	300 (60)	35 (12)		

Note: description of patients with major adverse cardiac events (MACE) with a negative and positive coronary calcium score (CCS) in articles that described the pre-test probability and/or typicality of angina pectoris symptoms. IQR = interquartile range. ACS = acute coronary syndrome.

* percentages of total CCS 0 patients of the total populations.

† event rate.

** CCS 0.1–0.9

†† all-cause mortality not included.

*** CCS > 100.

‡ arrhythmia, collapse, screening.

‡ cumulative rate at 10 years.