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Applicability and accuracy of pretest probability calculations implemented in the NICE clinical guideline for decision making about imaging in patients with chest pain of recent onset

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Abstract

Objectives To analyse the implementation, applicability and accuracy of the pretest probability calculation provided by NICE clinical guideline 95 for decision making about imaging in patients with chest pain of recent onset.

Methods The definitions for pretest probability calculation in the original Duke clinical score and the NICE guideline were compared. We also calculated the agreement and disagreement in pretest probability and the resulting imaging and management groups based on individual patient data from the Collaborative Meta-Analysis of Cardiac CT (CoMe-CCT).

Results 4,673 individual patient data from the CoMe-CCT Consortium were analysed. Major differences in definitions in the Duke clinical score and NICE guideline were found for the predictors age and number of risk factors. Pretest probability calculation using guideline criteria was only possible for 30.8 % (1,439/4,673) of patients despite availability of all required data due to ambiguity in guideline definitions for risk factors and age groups. Agreement regarding patient management groups was found in only 70 % (366/523) of patients in whom pretest probability calculation was possible according to both models.

Conclusions Our results suggest that pretest probability calculation for clinical decision making about cardiac imaging as implemented in the NICE clinical guideline for patients has relevant limitations.

Key Points

- *Duke clinical score is not implemented correctly in NICE guideline 95.*
- *Pretest probability assessment in NICE guideline 95 is impossible for most patients.*
- *Improved clinical decision making requires accurate pretest probability calculation.*
- *These refinements are essential for appropriate use of cardiac CT.*

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Keywords Coronary artery disease · Multidetector computed tomography · NICE clinical guideline · Duke clinical score · Pretest probability

Abbreviations

CACS	Coronary artery calcium score
CAD	Coronary artery disease
CoMe-CCT	Collaborative Meta-Analysis of Cardiac CT
CT	Computed tomography
CTA	Computed tomography angiography
ECG	Exercise electrocardiogram
ICA	Invasive coronary angiography
NICE	National Institute for Health and Care Excellence
PMG	Patient management group

Introduction

Due to its diagnostic accuracy and long-time experience with the method, invasive coronary angiography (ICA) [1] is considered the reference standard for diagnosing obstructive coronary artery disease (CAD), which is still the main cause of death worldwide [2, 3]. Nevertheless, in only 38–40 % of patients undergoing ICA, obstructive CAD is found [4, 5]. False-positive results by traditional tests, such as exercise electrocardiogram (ECG), stress echocardiography or myocardial scintigraphy are potential reasons for the low diagnostic yield of ICA [1, 6]. Over the last years coronary computed tomography angiography (CTA) developed into a non-invasive alternative to ICA with promising diagnostic accuracy for ruling-out CAD [7–10]. Previous analyses suggested that CTA could be appropriately used in patients with low to intermediate pretest probability for ruling out CAD [7, 11]. Thus, pretest probability estimation for presence of CAD is important for the choice of appropriate diagnostic tests and the avoidance of unneeded invasive examinations. The NICE clinical guideline 95 for assessment of patients presenting with recent onset chest pain of suspected cardiac region suggests using groups of pretest probability categories (<10 %, 10–29 %, 30–60 %, 61–90 %, >90 %) for patients presenting with stable chest pain and presence of typical or atypical angina [12] utilising an adaptation of the logistic regression model of Pryor and colleagues [13].

Since reliable pretest probability calculations are important for management of patients with suspected CAD, the aim of our study was to analyse the applicability, i.e. ease-of-use in a clinical context and correctness of the presented probability values of the clinical guideline for decision making about imaging and management [12], as well as to facilitate the use of pretest probability calculations for clinical practice by providing accurate methods to estimate such probability. For this purpose, we analysed the CoMe-CCT [14] cohort of >4,500 patients for pretest probability estimation defined in the clinical guideline [12] to verify its accuracy and clinical validity.

Materials and methods

Implementation of pretest probability calculation in the clinical guideline

The NICE clinical guideline 95 and resulting patient management groups are based on an adaptation [12] of the Duke clinical score developed by Pryor et al. [13]: By evaluating 3,627 patients with chest pain referred for ICA, Pryor et al. found the parameters age, sex, chest pain type (typical angina, atypical angina, non-anginal chest pain), history of myocardial infarction, ECG Q-waves, ECG ST-T wave changes, smoking status, diabetes and hyperlipidaemia to be clinically important when predicting the probability of significant CAD defined as ≥75 % luminal diameter narrowing in at least one major coronary artery [15]. Identified characteristics were finally validated in an outpatient cohort with 1,030 patients [13]. Since the clinical guideline uses its own adaptation of this model [12], we systematically compared the definitions used for pretest probability calculation in the Duke clinical score [13] and in the guideline's implementation [12].

Applicability of pretest probability calculation in the guideline

For further analyses, individual patient data of the Collaborative Meta-Analysis of Cardiac CT (CoMe-CCT) were used including information on 7,455 patients from 68 studies [14]. Eligible studies for CoMe-CCT were identified using results of the meta-analysis of Schuetz et al. [8] followed by search updates in order to include most recent studies. A detailed description of the methodological procedure of CoMe-CCT can be found elsewhere [14].

Patients with suspected and not known CAD were included for analysis. Thus, patients with unstable angina were excluded, since the NICE guideline is intended for patients with stable chest pain [12]. Patients with missing information on the presence of coronary bypasses, stents or unstable angina remained in the analysis if exclusion was not indicated based on the available information (632, nine and 1,153 patients, respectively, had missing information on one, two and all three parameters). After further exclusion of patients with missing information, 4,673 patients were eligible for analysis

of the pretest probability calculation suggested by the NICE guideline (Fig. 1).

To assess the applicability, defined as operability of the guideline in a clinical context (i.e. calculating pretest probability and choosing patient management groups), we assigned CoMe-CCT patients to the recommended management group using pretest probability values according to the guideline [12] and the Duke

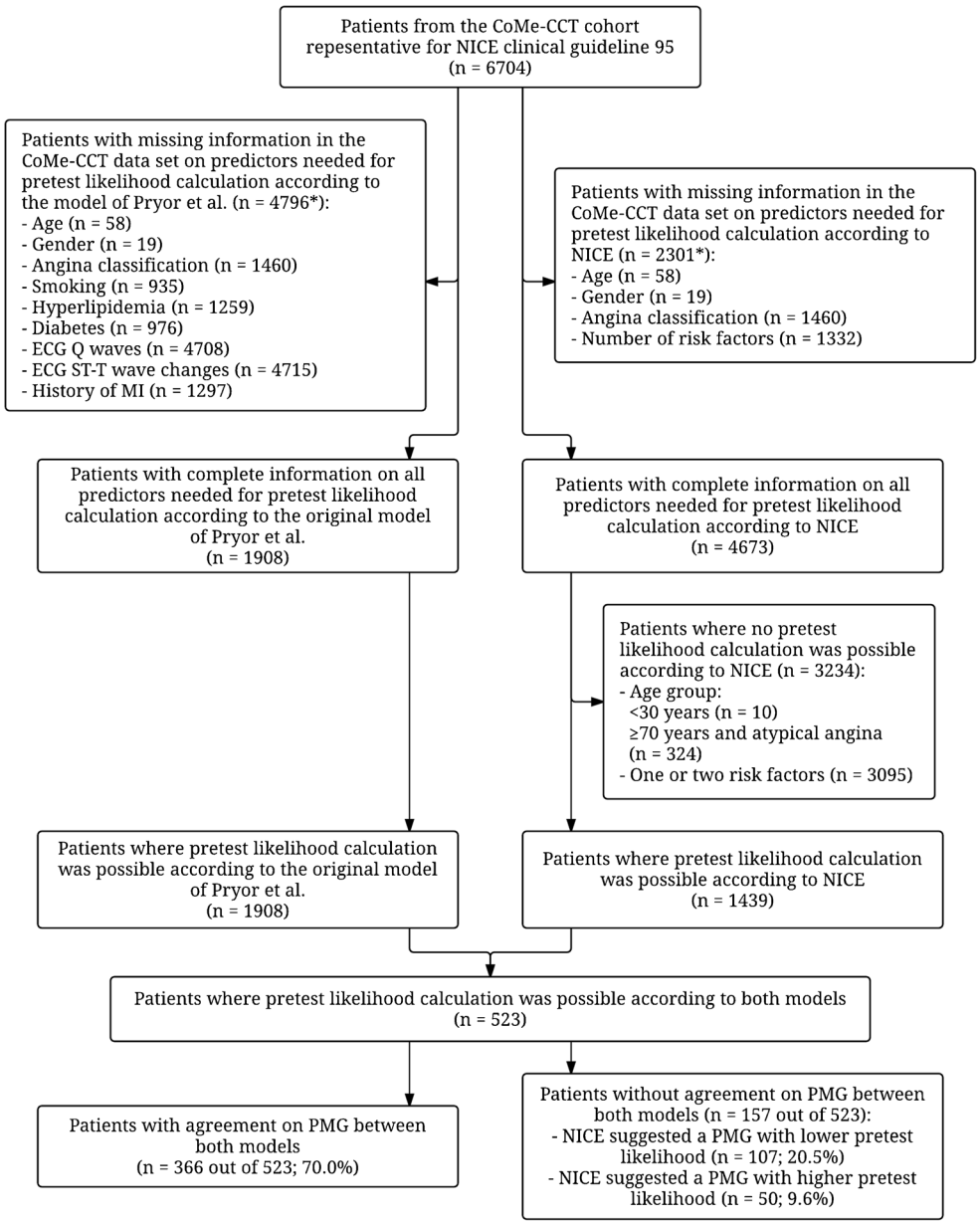

Fig. 1 Flow-chart of the analysis. 6,704 patients were eligible for the analysis. Complete information on all predictors needed for the pretest probability calculation in the original Duke clinical score [13] was available for 1,908 patients (28.5 %) patients. Assigning pretest probability was possible for all 1,908 patients. Complete information on all predictors needed for the pretest probability classification of the NICE clinical guideline [12] was available for 4,673 patients (69.7 %). Out of these, assigning pretest probability values was possible for only 1,439 patients (30.8 %). The number of risk factors (i.e. patients with one or two risk factors for which the guideline does not provide pretest probability values) was the main reason for not being able to estimate pretest probability using the adapted guideline model (95.7 %), while age (i.e. patients younger than 30 years, or older than 70 years presenting with non-anginal chest pain) was subordinated. In total, calculation of pretest probability values according to the original Duke clinical score [13] and according to the implementation of the guideline [12] was possible simultaneously for 523 patients. Agreement between both models [12, 13] in assigning patient management groups was found in 366 patients (70.0 %) out of 523 patients, where the guideline's classification [12] suggested a higher patient management group (i.e. a patient management group with higher pretest probability) in 50 patients (9.6 %) and a lower patient management group (i.e. a patient management group with lower pretest probability) in 107 patients (20.5 %). * Overall sum is not equal to sum of subcategories due to overlap. *PMG* Patient Management Group

clinical score [13]. Due to the guideline's adaptation of the Duke clinical score [12], we first calculated the proportion of patients in which pretest probability calculation was possible in the guideline's model. No pretest probability values were given for patients with one or two risk factors. Therefore, all patients with one or two risk factors cannot be assigned a pretest probability in this analysis. Second, we compared differences in the choice of management groups for all patients where an allocation could be made. Patients with non-anginal chest pain were included in the analysis although the clinical guideline recommends investigating other causes of chest pain first [12]. The reasoning for this approach was that for these patients pretest probability values can actually be calculated by using the original Duke clinical score [13] and this patient group does have a low to intermediate probability of CAD.

Correctness of pretest probability provided in the NICE guideline

In order to verify the correctness of the pretest probability calculations provided in the NICE guideline, we recalculated the values of the given pretest table [12] for each cell by using the original Duke clinical score [13] and examined agreement of the results. Moreover, we implemented the Duke clinical score [13] in an easy-to-use and downloadable EXCEL sheet (online Supplementary Material).

Statistical analysis

Since this work is supposed to be a straightforward evaluation of the NICE guideline, descriptive methods (i.e. absolute and relative frequencies) and the original logistic regression model by Pryor et al. [13] were used to carry out the aforementioned examinations.

Table 1 Comparison of definitions of variables used in the original model of the Duke clinical score [13] and the current adaptation of the Duke clinical score in the clinical guideline [12]

Variable	Original Duke clinical score [13]	Current adaptation in the clinical guideline [12]
CAD definition	≥75 % luminal diameter narrowing of at least one major coronary artery	≥70 % diameter stenosis of at least one major epicardial artery segment or ≥50 % diameter stenosis in the left main coronary artery
Age	Age is included as a continuous predictor. Pretest probability calculation is possible for every age individually. However, the model was developed in a patient cohort ranging from 20 to 80 years. Thus, estimation outside this region should be made with caution.	Grouped for all decades from 30 to 70 years. All patients within one age group get the pretest probability of a patient at the midpoint of the decade. For example, all patient between 30 and 39 get the pretest probability value of a 35-year-old patient. For patients older than 70 years with typical or atypical angina, minimum pretest probability is suggested. Probability estimations for patients older than 70 years with non-anginal chest pain are not provided, as other causes of chest pain would be routinely investigated first. Pretest probability values for patients younger than 30 are not provided
Gender	Male and female	Male and female
Angina classification	Non-anginal chest pain, atypical chest pain and typical chest pain according to Diamond and Forrester [16]	Non-anginal chest pain, atypical chest pain and typical chest pain according to Diamond & Forrester [16]
Diabetes	Present or not	Risk groups are defined by diabetes, smoking, and hyperlipidaemia: Patients presenting with all three risk factors are classified into high risk group, patients showing none of the risk factors into the low risk group. For patients presenting with one or two risk factors no pretest probability values are provided by the NICE guideline [12]
Smoking status	Current smoker or not	
Hyperlipidaemia	Present or not	
Resting 12-lead ECG Q-waves	Present or not	Patients are treated as if they were not presenting with resting 12-lead ECG Q waves or ST-T wave changes. Nevertheless, it has been stated that probability is higher if at least one of the mentioned ECG changes occurs
Resting 12-lead ECG ST-T wave changes	Present or not	
Prior myocardial infarction	Present or not	Prior myocardial infarction is regarded as confirmed CAD as well as a factor making stable angina more likely

Results

Implementation of pretest probability calculation in the guideline

For detailed description of the different definitions used in the original Duke clinical score [13] and the clinical guideline [12] see Table 1. The biggest differences were found for the risk factors diabetes, smoking, hyperlipidaemia and age: Diabetes, smoking and hyperlipidaemia were combined into a low-risk group (if no risk factors were present) and a high-risk group (all three risk factors present) by the guideline. The continuous predictor age in the Duke clinical score [13] was categorized in

Table 2 Characteristics of the patient cohorts

Characteristic		Complete Info NICE (N=4,673)	Complete Info Pryor (N=1,908)	Complete Info both models (N=523)
Age, y	n (%)	4,673 (100)	1,908 (100)	523 (100)
	Mean (SD)	61.52 (10.37)	62.93 (10.38)	60.66 (10.2)
	Median (IQR)	61.3 (54.8; 69)	63 (56; 70)	60.8 (54; 68)
	Range	19; 96.8	30.6; 96.8	33.3; 86.1
Age category, y	n (%)	4,673 (100)	1,908 (100)	523 (100)
	<30	10 (0.2)	0 (0)	0 (0)
	30-70	3,614 (77.3)	1,397 (73.2)	433 (82.8)
	> 70	1,049 (22.4)	511 (26.8)	90 (17.2)
Gender	n (%)	4,673 (100)	1,908 (100)	523 (100)
	Female	1,600 (34.2)	708 (37.1)	197 (37.7)
	Male	3,073 (65.8)	1,200 (62.9)	326 (62.3)
Chest pain symptoms	n (%)	4,673 (100)	1,908 (100)	523 (100)
	Typical angina	1,656 (35.4)	581 (30.5)	140 (26.8)
	Atypical angina	1,353 (29)	635 (33.3)	195 (37.3)
	Non-anginal chest discomfort	736 (15.8)	353 (18.5)	88 (16.8)
	Other chest discomfort or no pain	928 (19.9)	339 (17.8)	100 (19.1)
Number of risk factors*	n (%)	4,673 (100)	1,908 (100)	523 (100)
	0	1,420 (30.4)	529 (27.7)	463 (88.5)
	1	2,120 (45.4)	889 (46.6)	0 (0)
	2	975 (20.9)	423 (22.2)	0 (0)
	3	158 (3.4)	67 (3.5)	60 (11.5)
Hypertension	n (%)	4,658 (99.7)	1,908 (100)	523 (100)
	No	2,147 (46.1)	769 (40.3)	279 (53.3)
	Yes	2,511 (53.9)	1,139 (59.7)	244 (46.7)
Diabetes	n (%)	4,673 (100)	1,908 (100)	523 (100)
	No	3,841 (82.2)	1,563 (81.9)	463 (88.5)
	Yes	832 (17.8)	345 (18.1)	60 (11.5)
Hyperlipidaemia	n (%)	4,673 (100)	1,908 (100)	523 (100)
	No	2,201 (47.1)	810 (42.5)	463 (88.5)
	Yes	2,472 (52.9)	1,098 (57.5)	60 (11.5)
Smoker	n (%)	4,673 (100)	1,908 (100)	523 (100)
	No	3,433 (73.5)	1,415 (74.2)	463 (88.5)
	Yes	1,240 (26.5)	493 (25.8)	60 (11.5)
Former smoker	n (%)	3,610 (77.3)	1,898 (99.5)	520 (99.4)
	No	2,742 (76)	1,391 (73.3)	404 (77.7)
	Yes	868 (24)	507 (26.7)	116 (22.3)
Positive family history	n (%)	4,334 (92.7)	1,771 (92.8)	482 (92.2)
	No	2,688 (62)	1,156 (65.3)	352 (73)
	Yes	1,646 (38)	615 (34.7)	130 (27)

*Diabetes, hyperlipidaemia and smoking

the guideline using pretest probability of a patient at the midpoint of a decade for all patients (Table 1).

Applicability of pretest probability calculation as implemented in the guideline

A summary of the analysis of the applicability of the guideline is shown in Fig. 1. Characteristics of the analysed patients are shown in Table 2. Complete information on all predictors needed for the pretest probability classification of the NICE guideline [12] was available for 4,673 out of the 6,704 patients with suspected CAD included in CoMe-CCT (69.7 %, Fig. 1). Assigning pretest probability values to these 4,673 patients was possible for 30.8 % (1,439 patients). For the other 3,234 patients (69.2 %) no calculation was possible due to number of risk factors (n = 3,095) or age group (n = 334; see Fig. 1)

In total, simultaneous calculation of pretest probability values according to the Duke clinical score [13] and the implementation in the guideline [12] was possible for 523 patients (Fig. 1). The results of patient classification into management groups using both models [12, 13] are given in Table 3. Agreement between the two models [12, 13] was found in 366 patients (70.0 %) out of 523 patients, whereas the guideline's classification [12] suggested a higher-risk patient management group (i.e. a patient management group with higher pretest probability) in 50 patients (9.6 %) and lower-risk patient management group (i.e. a patient management group with lower pretest probability) in 107 patients (20.5 %).

We additionally analysed how the three reasonable approaches of regrouping patients with one or two risk factors (one risk factor into low risk and two risk factors into high risk, both into low-risk, both into high-risk group) would influence the results: When regrouping those patients into low- or high-risk group, simultaneous calculation of pretest probability was possible for 1,710 patients. Depending on the regrouping, an agreement between 56.6 % (both low-risk group) and 66.6 % (division into low- and high-risk group) was achieved.

Correctness of pretest probability provided in the guideline

The pretest probability values obtained using definitions implemented in the guideline [12] are given in Supplementary Material Table 1. Recalculations of these pretest probability values using the original Duke clinical score [13] are given in Table 4. About 10% (5/48) of the pretest probability in the guideline's table [12] could not be reproduced when comparing Table 4 and Supplementary Material Table 1. Using the CoMe-CCT cohort, 53 patients (3.7 %) out of 1,439 patients where pretest probability calculation was possible according to the guideline [12] would have been assigned to false pretest probability due to wrong entries in the clinical guideline's table.

Discussion

We analysed the implementation of pretest probability calculation by the NICE guideline 95 for imaging and management decisions in patients with chest pain of recent onset [12]. We found pretest probability calculation using guideline criteria was only possible for 30.8 % of patients due to ambiguity in guideline definitions for risk factors and age groups. Moreover, agreement regarding patient management groups was found in only 70 % of patients in whom pretest probability calculation was possible. This indicates relevant clinical shortcomings of the implementation of pretest probability assessment and the need to improve

Table 3 Assignment of patients to management groups (pretest probability ranges in %) defined by the NICE guideline according to the original Duke clinical score [13] and the current adaptation of the Duke clinical score in this clinical guideline [12]

		Current adaptation in the clinical guideline[12]				
	Patient management group*	<10%	10% – <30%	30% – 60%	>60% – 90%	>90%
Original Duke clinical score[13]	<10%	74	4			
	10% – <30%	36	55		3	
	30% – 60%		23	79	23	
	>60% – 90%	1	3	29	95	20
	>90%			5	10	63

All values represent absolute numbers. Empty cells mean that no patient was in this category. Calculation of pretest probability values according to the original Duke clinical score [13] and according to its implementation in the NICE guideline 95 [12] simultaneously was possible for 523 patients. Green cells (diagonal cells, 366 patients, 70.0 %) indicate agreement between both models, whereas red cells (above diagonal cells) indicate a higher patient management group suggested by the guideline (50 patients, 9.6 %) and yellow cells (below diagonal cells) indicate a lower patient management group suggested by the guideline (107 patients, 20.5 %)

*The patient management groups suggested by the clinical guideline are as follows: <10 %, 10–29 % and 30–60 %, 61–90 % and >90 % [12]. The groups in the present table were readjusted so that no gaps between the categories were present because in the Duke clinical score [13], for example, a pretest probability of 29.5 % can occur

Table 4 Recalculated pretest probability (in %) of significant CAD based on the original Duke clinical score [13] and differences to the NICE clinical guideline [12]

	Non-anginal chest pain				Atypical chest pain				Typical chest pain			
	Men		Women		Men		Women		Men		Women	
Age, y	Low risk	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk
35	3	36*	1	19	8	59	2	39	30	88	10	76*
45	9	47	2	22	21	70	5	43	57**	92	20	79
55	23	59	4	25	45	79	10	47	80	95	36*	82
65	49	69	9	29	71	86	20	52*	93	97	56	84
>70§	≥62	≥74	≥13	≥30	≥81	≥88	≥28	≥54	≥96	≥97	≥66	≥85

About 10 % (5/48) of the given pretest probability in the cells of the pretest probability table given in the NICE guideline [12] (Supplementary Material Table 1) could not be reproduced. Patients >70 years were excluded from this comparison as the values presented by the clinical guideline are proposals for assigning patients to one of the management groups (see Supplementary Material Table 1) [12]

*Values deviate up to 2 % from the values given in the clinical guideline (see Supplementary Material Table 1)

**Values deviate ≥ 2 % from the values given in the clinical guideline (see Supplementary Material Table 1). The biggest deviation was 6 % for 40- to 49-year-old male patients with typical chest pain in the low-risk group.

§ Values for patients >70 years are not comparable to the clinical guideline because these patients are assigned to one of the management groups without an exact pretest probability (see Supplementary Material Table 1)

clarity of definitions as well as appreciation for the complexity of the underlying statistical model.

The different assumptions made by the guideline in order to generate its pretest probability table [12] leave room for ambiguity as well as approximations, which can result in inappropriate patient management group assignment: For patients within the same age decade (e.g. 30–39 years) only one patient management group is suggested by the guideline, although the real pretest probability values according to the Duke clinical score [13] might recommend different management groups. Assigning patients with one or two risk factors to either low- or high-risk group as recommended in the guideline often leaves room for at least two possible patient management groups. In contrast, history of myocardial infarction is equivalent to an increase between 10 and 39 years of patient age depending on the combination of risk factors in the Duke clinical score [13] (see details in Table 5).

The guideline defines significant CAD as ≥70 % diameter stenosis of at least one major epicardial artery segment or ≥50 % diameter stenosis in the left main coronary artery [12], which slightly differs from the definition in the Duke clinical score (≥75 % luminal diameter narrowing of at least one major coronary artery) [13]. Finally, the CAD Consortium [17] and Cheng et al. [18] found the Duke clinical score [13] overestimating the probability of severe CAD (≥70 % stenosis or ≥50 % left main stenosis).

Taking the aforementioned aspects into account, the implementation of the Duke clinical score [12] in the guideline has relevant clinical limitations. In order to overcome such issues, a downloadable and easy-to-use calculator for pretest probability incorporating the Duke clinical score [13] was introduced with this analysis (online Supplementary Material). Using this tool, calculations can be done individually for patients in order to aid the physician in choosing the best diagnostic pathway.

Previously published studies

There is conflicting data on the economic implications of the guideline. Some studies found a decrease in costs by 9–43 % [19, 20] by implementing the guideline, whereas others found an increase in costs for examinations by 24–93 % [21, 22]. Due to exclusion of patients from further diagnostic testing using the guideline's approach, Patterson et al. showed that the presence of CAD could be underestimated in up to 10 % of patients presenting with recent onset chest pain, which would influence patient care enormously [23]. Our study analysed a sufficiently high number of patients from the CoMe-CCT consortium and thus, we could exclude all patients in whom no pretest probability assignment by the guideline was possible. Interestingly, McKavanagh et al. [24] showed pretest probability estimation of the guideline to be less accurate in predicting CAD compared to the calcium score, and overestimated the presence of CAD. Nevertheless, Pavitt et al. [25] developed an accurate method that allows replacing traditional CACS with conversion of CTA results in order to assess coronary artery pathology while reducing radiation exposure. Thus, the study supports potential guideline changes. To the best of our knowledge no previous study evaluated the applicability and correctness of pretest probability calculation implemented in the guideline.

Table 5 Clinical case examples of variation in pretest probability estimation according to the Duke clinical score [13] that would be missed by the current adaptation of the Duke clinical score in the clinical guideline [12] due to assignment to patient management groups

	Patient 1	Pretest probability patient 1*	Patient 2	Pretest probability patient 2*	Difference of pretest probability between patient 1 and patient 2
Case 1: Age group	**50 years old** Female Typical angina Low risk group	27 %	**59 years old** Female Typical angina Low risk group	44 %	17 %
Case 2: Risk group	35 years old Female Typical angina **Low risk group**	10 %	35 years old Female Typical angina **High risk group**	76 %	66 %
Case 3: Rest ECG Q wave and ST-T wave changes	45 years old Male Atypical angina Low risk group **No Q waves and no ST-T wave changes**	21 %	45 years old Male Atypical angina Low risk group **Q waves and ST-T wave changes**	63 %	42 %
Case 4: Prior myocardial infarction	38 years old Male Atypical chest pain Low risk group Q waves **No prior myocardial infarction**	29 %	38 years old Male Atypical chest pain Low risk group Q waves **Prior myocardial infarction**	72 %	43 %

Due to the adaptation of the Duke clinical score [13] in the NICE clinical guideline, several patients with very different original pretest probability are grouped together in the same patient management group or cannot be classified at all. Some examples are summarized here: Patients within the same age decade (e.g. 50–59 years) are assigned to the same management group, although the real pretest probability values according to the Duke clinical score [13] might recommend different groups. An allocation to one of the management groups for patients with one or two risk factors is hardly possible, since the difference between the low- and high-risk groups often leaves room for at least two possible patient management groups. The amount of increase in pretest probability in patients with Q waves and ST-T wave changes is not included in the guideline [12] as it is recommended by the Duke clinical score [13]. Prior myocardial infarction is regarded proven CAD by the guideline. In contrast, a history of myocardial infarction is equivalent to an increase between 10 and 39 years of patient age depending on the combination of risk factors in the Duke clinical score [13]

*Pretest probability values were calculated with the original Duke clinical score [13]

Limitations of the study

The CoMe-CCT cohort may not be representative of the worldwide population as our database, while relatively large, comprises 7,455 patients from only 19 European, North American and Asian countries. A further limitation of this analysis is that we included studies that may have used different approaches to clinical angina and risk factor classification. Nevertheless, we tried to minimise potential heterogeneity by defining respective items in advance. The different structure of diagnostic accuracy studies may introduce an inclusion bias, since these patients may not be representative for the routine patient cohort that the guideline was intended for.

The variation of agreement between the original Duke clinical score and its implementation in the guideline was not fully determined. We focused on the evaluation of the number of risk factors and thus, no further analyses of specific approaches for patient classification with missing pretest probability given by the clinical guideline were done. However, approximations of pretest probability for patients with missing pretest probability values were not done, because any general approach of approximating pretest probability between the risk groups, does not represent the underlying logistic regression model of the Duke clinical score [13] appropriately. Nevertheless, such simulations were not necessary, since ambiguities during assignment of pretest probability values can be easily avoided by using a model that only takes into account age, gender and angina classification [26] or by using our provided calculator for the original Duke clinical score [13].

We were able to check the patient management group agreement for 523/1,439 (36.3 %) patients with available data and possible pretest likelihood calculation of the NICE guideline, which may introduce a potential selection bias. Despite the low percentage, our aim was to show whether the implementation of the model of Pryor et al. introduces changes to the management groups. Since we found substantial differences in the analysed subset, our concern was fortified. The inclusion of patients with unknown status of coronary bypass, stents or unstable angina may lead to a potential selection bias

but it can be assumed that only a small percentage of these patients would be excluded if all information was available.

In daily clinical routine, decisions are not solely based on given numbers or statistics. Diagnostic management of patients always involves personal experience, patient preferences and behaviour, further characteristics and symptoms. Patients are individual persons and cannot exclusively be diagnosed by values alone [27].

Alternative models to the Duke clinical score [13] include those proposed by Diamond and Forrester [16] or recently in 2011 and 2012 by the CAD Consortium [17, 26]. The suggested models may be more convenient than the Duke clinical score [13] to estimate pretest probability, since they are based on age, gender, angina classification [16, 17, 26], and additionally, risk factor and calcium scoring (CAD Consortium [17]). Nevertheless, it has to be pointed out that these models use a different definition of CAD (at least one vessel with ≥50 % stenosis) than the clinical guideline [12] whereas the definition used in the Duke clinical score [13] most closely resembles the intention of the NICE guideline. Moreover, the data of Diamond and Forrester [16] date from 1979, and the CAD Consortium found that the model of Diamond and Forrester overestimates the presence of CAD in more recent patient cohorts and may thus not be preferable [26].

Clinical implications

In accordance to the guideline, only 31 % of patients from the analysed CoMe-CCT cohort subset can be assigned to one of the imaging and management groups defined in the NICE guideline 95 [12]. As a result, many assumptions need to be made by physicians when applying the table of pretest probability presented in the clinical guideline. Therefore, we provide an Excel document based on the original Duke clinical score [13] that allows accurate calculation of pretest probability for all patients within the framework of the clinical guideline for patients with chest pain of recent onset.

Future aspects

As far as we know, our study is the first to investigate the validity and accuracy of pretest probability calculation as implemented in the NICE clinical guideline 95 [12] for the assessment of appropriate imaging tests in patients presenting with recent onset chest pain of suspected cardiac origin. The recent discussion [28, 29] concerning the new American College of Cardiology/American Heart Association guideline on the assessment of cardiovascular risk [30] showed that clinical guideline decisions are of great public interest and that appropriate estimations are very important. Thus, an improved model of pretest probability calculation avoiding approximations would ease the use of the NICE guideline 95 on the management of patients with recent onset chest pain of suspected cardiac region. The provided Excel document in the Supplementary Material might be a pragmatic approach in this regard to more accurately assess pretest probability and increase the appropriate use of cardiac imaging tests in patients with suspected CAD.

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Compliance with ethical standards

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Methodology
- diagnostic study
- individual patient data meta-analysis
- multicentre study

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