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Clinical decision making of cardiologists regarding admission and treatment of suspected unstable angina or non-ST-elevation myocardial infarction patients: a study protocol of a clinical vignette study

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ABSTRACT

Introduction: Cardiologists face the difficult task of rapidly distinguishing cardiac related chest pain from other conditions, and to thoroughly consider whether invasive diagnostic procedures or treatments are indicated. The use of cardiac risk scoring instruments has been recommended in international cardiac guidelines. However, it is unknown to what degree cardiac risk scores and other clinical information influence cardiologists' decision making. This paper describes the development of a binary choice experiment using realistic descriptions of clinical cases. The study aims to determine the importance cardiologists put on different types of clinical information, including cardiac risk scores, when deciding on the management of patients suspected of unstable angina or non-ST-elevation myocardial infarction.

Methods and analysis: Cardiologists are asked, in a nationwide survey, to weigh different clinical factors in decision making regarding patient admission and treatment using realistic descriptions of patients in which specific characteristics are varied in a systematic way (e.g. web based clinical vignettes). These vignettes represent patients suspected of unstable angina or non-ST-elevation myocardial infarction. Associations between several clinical characteristics, with cardiologists' management decisions will be analyzed using generalized linear mixed models.

Ethics and dissemination: The study has received ethics approval and informed consent will be obtained from all participating cardiologists. The results of the study will provide insight into the relative importance of cardiac risk scores and other clinical information in cardiac decision making. Further, the results indicate cardiologists' adherence to the European Society of Cardiology guideline recommendations. In addition, the detailed description of the method of vignette development applied in this study could assist other researchers or clinicians in creating future choice experiments.

STRENGHTS AND LIMITATIONS OF THIS STUDY

Strengths

- This study provides insight in how cardiologists weigh clinical information in deciding on the admission and treatment of UA/NSTEMI patients.
- The clinical information presented to cardiologists is varied systematically and presented in clinical vignettes, reflecting clinical practice as closely as possible.
- Decision making is studied in a nationwide survey.

Limitations

- The decision cardiologists were asked to make is a complex decision which (sometimes) has to be made instantly. This was not simulated/taken into account in the clinical vignettes.
- The decision had to be made on the basis of seven or eight attributes while in clinical practice cardiologists may take into account other aspects in their decision making.

INTRODUCTION

About six percent of the emergency department presentations are due to chest pain.[1] Of these patients, a substantial number are diagnosed with an acute coronary syndrome, including unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI) and ST segment myocardial infarction (STEMI).[1, 2] Mortality after an acute coronary syndrome is substantial.[3, 4] To prevent cardiac damage or mortality, timely treatment is indicated. As a result, the attending physician has the difficult task to rapidly distinguish cardiac related chest pain from chest pain caused by other conditions. Patients presenting with chest pain to the emergency department should therefore be stratified according to their level of risk of having a cardiac condition.[5] Risk assessment is generally based on a patient's clinical history, physical examination, biomarkers and electrocardiogram findings.[6-9] The decision for hospital admission or type of treatment is dependent on a patients' risk of adverse cardiac events, such as re-infarction or mortality. The European Society of Cardiology guidelines on the management of UA or NSTEMI recommend to treat patients at high risk of re-infarction or death with invasive procedures or treatment (e.g. coronary angiography, Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG)).[7] To determine the patient's risk, several cardiac risk scores have been developed and validated i.e. the HEART,[5] GRACE-,[10, 11] TIMI-,[12] FRISC-,[13] and PURSUIT score.[14] Use of these instruments is recommended by professional guidelines.[7] Despite the availability of valid cardiac risk stratification tools and recommendations of their use, in previous studies, low risk patients were more likely to receive invasive procedures compared to high risk patients.[15-18] Such a treatment risk paradox implies low adherence rates with the guidelines, which possibly affects or even threatens patient safety on the one hand and results in suboptimal resource use on the other hand. Low guideline adherence might be explained by barriers affecting physicians' attitude towards guideline recommendations,[19] including

disagreement with the guidelines or unwillingness to adopt the guidelines. In addition, previous research indicates that physicians may consider evidence underlying the guidelines as unconvincing.[20] As a result, they may depend heavily on their own personal experience and seem to underestimate important risk factors.[21, 22] In this study we focus on cardiologists' decision making in the management of UA and NSTEMI. To our knowledge it is unknown to what degree cardiac risk scores and other clinical information influence their decisions about admission and choice of treatment. The objective of the present study is twofold. First, to determine the influence of a cardiac risk score upon cardiologists' decision on patient admission and treatment. Second, to determine the relative importance of different types of clinical information, in the presence or absence of a risk score, upon management decisions concerning suspected UA or NSTEMI patients.

METHODS AND ANALYSIS

Study design

To determine how cardiologists weigh different clinical factors (e.g. relative importance) in their decision to admit or to treat a patient, binary choice experiments are conducted using vignettes of clinical cases. Two decision moments were investigated, the decision to admit a patient to hospital and the decision to perform cardiac catheterization. In the vignettes the clinical factors are systematically varied according to a fractional factorial design.

Study population

Cardiologists working as a registered cardiologist in a Dutch hospital will be approached for participation in this study by email. They will be recruited through the Dutch directory of physicians.

Data collection

The data will be collected using a web-based survey, presenting cardiologists with clinical vignettes. The clinical vignettes describe patients by means of a set of attributes, reflecting characteristics of a patient or treatment.[23] Clinical vignettes are a frequently applied approach to study decision-making in health care as they closely reflect clinical practice.[24] In addition, clinical vignettes were shown to be a valid tool to measure the quality of care.[25, 26] Cardiologists will be asked to complete a web-based survey containing the clinical vignettes. Prior to completing the survey, cardiologists will be informed about the global study objective and asked to give consent for participation in the study. Cardiologists who initially fail to respond will be sent reminders one, three, eight and twelve weeks after first sending the survey. The completion time of the survey will be approximately 20 minutes and cardiologists are able to stop and continue completion of the survey at any time. The data will be processed anonymously.

Survey

The survey registers demographic characteristics, including year of birth, gender, current profession, years of cardiology care experience, whether cardiologists are still actively involved in the care for patients diagnosed with UA or NSTEMI and which risk score they apply in clinical practice. In addition, associated hospital characteristics such as type of hospital they work in and whether hospitals have revascularization facilities on site will be registered. After completing the section that registers demographic characteristics, cardiologists are presented with the vignettes. These are presented in two parts that differ in the decision that needs to be made. In the first part of the survey (A), the clinical vignettes describe patients who present themselves with chest pain to the emergency department. Cardiologists are asked to indicate on a binary scale (yes or no) whether he or she would

discharge the patient from the emergency department without any further diagnostic testing (e.g. no serial troponin testing or exercise testing). In addition, cardiologists are asked on a three point likert scale how certain they are of their decision (very sure, sure, somewhat sure). The clinical vignettes in the second part of the study (B) describe a patient's condition when the patient is already admitted to the hospital with a high suspicion of UA or NSTEMI. Cardiologists are asked to indicate whether he or she would advise an invasive procedure i.e. coronary angiography within 72 hours from admission and how certain they are of their decision (using the same three point likert scale). Cardiologists are asked to make decisions that reflect their actual clinical practice as closely as possible. The survey was pretested among two cardiology residents, not involved in the design of the study, and asked to provide feedback regarding the applicability of the survey. This provided insight in the comprehensiveness of the survey, and the time it takes to complete the survey.

Pre-selection of attributes

Potential attributes relevant for the management of UA and NSTEMI, regarding the decision to admit or treat a patient, were selected from clinical guidelines. It was assumed that these guidelines provided an integral overview of the published scientific evidence and therefore cover all relevant attributes.[6-9] Further, variables of validated risk scoring instruments,[5, 10-14] the website 'up-to-date',[27-29] and recently conducted interviews on the use of risk stratification instruments in practice (Engel et al. 2014 unpublished work),[30] were reviewed for additional relevant attributes. The website 'up-to-date' concerns an evidence-based resource that aims to support physicians in clinical decision making.

Initially, all aspects that can be taken into account when stratifying risk were selected from the aforementioned sources, which resulted in a pre-selection of 105 potential attributes. As Dutch cardiologists are most familiar with the European Society of Cardiology guidelines in

treating their patients, the pre-selection was subsequently reduced by selecting only those attributes that were mentioned in this guideline and in the validated risk scoring instruments. This left 56 attributes that were considered of importance for the present study (Table 1).

Table 1. Pre-selection of attributes (after removal of duplicates)

Category		Attribute	Source†
Demographics	1	Older age >75 years	ESC, RS
	2	Gender	ESC, RS
Risk factors	3	Presence of risk factors in general (including positive family history, peripheral artery disease, carotid stenosis, diabetes mellitus, kidney failure, smoking, hypertension, hypercholesterolemia, obesity)	ESC, RS
	4	Diabetes mellitus	ESC, RS
	5	Chronic kidney failure/ creatine level	ESC, RS
	6	Heart failure	ESC, RS
	7	Depressed left ventricular ejection fraction	ESC
	8	Killip-class classification	ESC, RS
	9	Anemia	ESC
	10	Obesity	ESC, RS
	11	Malnutrition	ESC
History	12	Known coronary artery disease	ESC, RS
	13	Previous myocardial infarction	ESC, RS
	14	Previous or recent percutaneous coronary intervention	ESC
	15	Previous or recent coronary artery bypass surgery	ESC
	16	Severity of coronary artery disease	ESC
	17	Cocaine use	ESC
	18	Aspirin use 7 days prior to admission	RS
Clinical presentation	19	Anamnesis suspicious for cardiac related chest pain	RS
	20	Persistent angina pectoris	ESC, RS
	21	Symptoms of angina pectoris in rest	ESC
	22	Reoccurring angina pectoris	ESC
	23	Several episodes of angina pectoris after event	ESC
	24	Tachycardia	ESC, RS
	25	Hypotensive	ESC, RS
	26	Hemodynamically instable	ESC
	27	Increased leucocytes at presentation	ESC
	28	Thrombocytopenia at presentation	ESC
	29	Increased bleeding risk	ESC
	30	Presence of bleeding	ESC
	31	Intermediate or high GRACE risk score	ESC
	32	Positive stress test	ESC
	33	Cardiac arrest at admission	ESC, RS
Electrocardiogram findings	34	ECG ST segment changes	ESC, RS
	35	ECG deviations at rest	ESC

	36	Dynamic ST/T changes	ESC
	37	Negative T waves	ESC
	38	ST depression	ESC
	39	ST elevation	ESC
	40	Ventricular arrhythmia	ESC
Laboratory results	41	Elevated troponine levels	ESC
	42	Elevated biomarkers	ESC, RS
	43	Hyperglycemia	ESC
	44	Elevated C-reactive protein	ESC
	45	Elevated B-type natriuretic peptide	ESC
Context information	46	Re-vascularization status	ESC
	47	Rest ischemia	ESC
	48	Severity of lesions	ESC
	49	Physical condition of patient	ESC
	50	Fragility of patient	ESC
	51	Cognitive decline	ESC
	52	Functional decline	ESC
	53	Physical dependence	ESC
	54	Quality of life	ESC
	55	Patient's wishes	ESC
	56	Risks versus benefits of re-vascularization	ESC

† Attributes are derived from the European Society of Cardiology guideline 2011 and from the GRACE-, TIMI-, FRISC-, PURSUIT- and/or HEART risk score. Abbreviations: ESC, European Society of Cardiology guideline; RS, risk score.

Final selection of attributes and attribute levels

As it is cognitively difficult for respondents to take into account large numbers of attributes, it is recommended – although there is no standard – to select between six to ten attributes in choice experiments.[31-33] This approach was followed in the present study. The final set of attributes was selected by a panel of three cardiologists in collaboration with the research team during a consensus meeting (1st of October 2013). These cardiologists were selected based on their affinity with research, and were chosen to reflect diversity in experience and type of hospital they work in. In preparing the consensus meeting, the cardiologists were asked to write down in order of importance the six to eight most important attributes when deciding to discharge a patient presenting with acute chest pain from the emergency department without further diagnostic testing (decision moment A). Equally, they listed attributes that were important in deciding on performing a coronary angiography within 72

hours in patients with a high suspicion of UA or NSTEMI (decision moment B). In case a cardiologist indicated that an attribute is essential in decision making, he had the option to select an additional attribute, on top of the six to eight that were already selected. The attributes selected by the cardiologists were the starting-point for the consensus meeting. The selected attributes were compared and discussed. Furthermore, the cardiologists reviewed and compared the pre-selection of potential attributes derived from the European Society of Cardiology guidelines and existing risk scoring instruments. After viewing this list, the cardiologists were given the opportunity to change their own attribute selection into a final selection. None of the cardiologists made any changes in their selection. Again, differences and similarities were discussed until consensus was reached over a final set of eight attributes for decision moment A and seven attributes for decision moment B (Table 2 and 3).

The arguments whether to select or remove a specific attribute were written down in a logbook. After determining the final set of attributes, the selection and description of attribute levels was discussed and confirmed / approved. In selecting attribute levels, we aimed to select levels that closely reflect the variety of presentations in clinical practice and will be easily understood by cardiologists. A secondary goal in selecting attribute levels was to keep the total number of possible vignettes i.e. the full factorial design, as small as possible. Therefore the number of levels within an attribute were kept to a minimum. The expert panel was re-approached by email to provide a further review of the selected attributes and attribute levels per decision moment on the basis of their initial feedback.

Table 2. Final selection of attributes and attribute levels of decision moment A	
Clinical setting: Patient presenting with acute chest pain at the emergency department. Decision: 'Would you send this patient home without any further diagnostic testing (e.g. no serial troponin testing or exercise testing)?'	
Attribute	**Attribute level**
Age	< 50 years 50-75 years > 75 years
Gender	Male Female
Known coronary artery disease	No Yes
Chest pain classification based on history taking	A-specific chest pain Atypical angina pectoris Typical angina pectoris
Symptoms of chest pain still present at presentation	No Yes
Risk factors†	No risk factors One risk factor More than one risk factor
ECG	Normal Atypical changes Typical ischemic changes
Troponin‡	Below reference level and representative Below reference level, not representative Above reference level
†Classic five: diabetes mellitus, hypertension, hypercholesterolemia, smoking and positive family history; ‡ According to cardiologists' own hospital standards.	

Table 3. Final selection of attributes and attribute levels decision moment B	
Clinical setting: Patient with suspicion of unstable angina or non-ST-elevation myocardial infarction is admitted for observation in the hospital. *Decision: 'Would you perform a coronary angiography within 72 hours in this patient?*	
Attribute	**Attribute level**
Age	< 70 years 70-80 years 80 years
Renal function	No renal dysfunction Mild to moderate renal dysfunction Severe renal dysfunction
Known coronary artery disease	No Yes
Persistent chest pain	No Yes
Risk factors†	No risk factors One risk factor More than one risk factor
ECG	Normal Atypical changes Typical ischemic changes
Troponin‡	Normal at repeated measures Significant rise and/or 'rise and fall'
† Classic five: diabetes mellitus, hypertension, hypercholesterolemia, smoking and positive family history; ‡ According to cardiologists' own hospital standards	

Cardiac risk score

In developing the clinical vignettes, initially cardiac risk score was considered as an attribute. However, this led to unrealistic vignettes and the attribute was therefore removed from the full factorial design. Additionally, by using the HEART risk score[5] (for decision moment A) and GRACE 2.0 risk score[34] (for decision moment B), cardiac risk was estimated for every vignette. This was accomplished by entering the values present in the vignette while holding the remaining parameters constant. The sample of cardiologists will, prior to completion of the survey, be divided in two groups. One group will complete vignettes without a cardiac risk score being present, while the other group completes the vignettes with a cardiac risk score present. Cardiologists will be instructed to consider the risk score as the one familiar from their own practice or knowledge.

Selection of clinical vignettes

The attributes and levels for decision moment A comprised $2^{3}*3^{5}$ = 1944 possible combinations in the full factorial design, where the base of the formula concerns the number of levels of an attribute and the exponent concerns the number of attributes with respectively two or three levels. For decision moment B, $2^{3}*3^{4}$ = 648 possible vignette combinations could be created. It is practically impossible to present respondents with such a vast amount of vignettes, therefore a fractional factorial design was created to reduce the number of vignettes for each decision moment. In selecting vignettes, the aim was to estimate the main effects of all attributes. The quality of the selection of vignettes was compared to a theoretical optimum by means of the G efficiency parameter which ranges between 0 (inefficient design) and 1 (efficient design). The G efficiency parameter is a useful guide when judging fractional factorial designs.[35] For both decision moments (i.e. discharge without further testing and prompt coronary angiography), the number of vignettes were reduced to 64. The vignettes selection showed substantial G efficiency of 0.94 for decision moment A and 0.95 for decision moment B. Per decision moment, the 64 scenarios were randomly allocated into eight blocks containing eight scenarios each. This is to ensure that all attribute levels will appear with equal frequency in each block.[36] Prior to sending the survey, cardiologists will be randomly assigned a block number in SPSS and being sent the corresponding questionnaire. Each survey comprises 16 scenarios in total (eight per decision moment).

Case description of clinical vignettes

Two members of the research team drafted the initial clinical case descriptions of the vignettes: one representing decision moment A and one representing decision moment B. Next, the clinical case descriptions were discussed and reviewed in a second consensus meeting (26th of February 2014), comprising four cardiologists and the research team. This

review process was undertaken to ensure accuracy, plausibility and clarity of the clinical event presentation in all of the vignettes. The vignettes were revised until both the research team as the panel of cardiologists agreed that the case descriptions represented clinical practice as closely as possible. An example of a vignette is presented in figure 1.

Study outcome

The study outcome is the relative importance cardiologists' put on different types of clinical information, both in the presence and absence of the risk score, when deciding on the management of suspected UA or NSTEMI patients.

Statistical considerations

Demographic characteristics will be presented using descriptive statistics. Associations of independent variables with the binary responses of cardiologists on the clinical vignettes in the survey will be studied with a generalized linear mixed model (GLMM), taking into account random effects for blocks and cardiologists. In total, 4 models will be created i.e. 2 for each decision moment taking into account the presence or absence of cardiac risk score information. In the analyses, cardiologists' responses (yes or no) are the binary outcome measure. Independent variables are the attributes, risk score (if present in the vignette) and the degree of certainty of respondents' answers. All independent variables will be simultaneously included in the analyses. A significance level of $p \leq 0.05$ will be used. The analysis with the GLMM will be performed by la Placian integration, conducted in R for windows (version 3.0.2) with package lme4.[37] The impact of the presence of the risk score on a cardiologist's decision will be studied by comparing results of the analyses with and without presenting risk score information in the vignettes.

Sample size

In total, each cardiologist will complete 16 vignettes (8 for decision moment A and 8 for decision moment B). In calculating the minimum number of cardiologists needed, the following formula is followed: n = 500 * (c / (a * t)). In this formula, 'n' is the minimum number of cardiologists, 'c' is the largest number of levels for any of the attributes, 'a' is the number of alternative scenario's that cardiologists are presented with and 't' is the total number of choice scenarios per decision moment that each cardiologist is presented with.[38, 39] In this study a minimum sample size of, 500 * (3 / (1 * 8)), approximately 188 cardiologists are needed per group (with or without a cardiac risk score) to study main effects for decision moment A and B separately. The Dutch directory of physicians contains 963 cardiologists. If a response of 40% is assumed, 385 cardiologists will complete 16 vignettes in total, which will be sufficient for estimating main effects.

Ethics and dissemination

The study protocol was reviewed and approved by the medical ethical committee of the VU University Medical Center Amsterdam (protocol number: 2014008). A waiver of active informed consent was granted, as the study concerns completely anonymized data. A form of informed consent, however, will be conducted at the start of the survey when cardiologists are asked to consent that their answers will be used and stored for scientific purposes. Results are planned to be disseminated in two papers submitted to peer reviewed journals, and presentations at relevant conferences.

DISCUSSION

UA and NSTEMI are two conditions that are associated with high mortality rates. Correctly estimating patients' risk of re-infarction or death and taking into account this risk in selecting

a management strategy is of importance in preventing unnecessary deaths and optimal use of resources. Cardiac guidelines recommend the use of several sources of information to estimate the risk for an individual patient. However, it is unknown to what degree cardiologists take into account all these aspects in the management of patients suspected of UA or NSTEMI. As mentioned in the introduction several studies report a treatment risk paradox, i.e. low risk patients were more likely to receive invasive procedures compared to high risk patients. Implying that cardiac risk scores are not used or not of importance in decision making regarding admission or invasive treatment. The results of the present study will provide further insight in the complex decision regarding admission and treatment of UA and NSTEMI patients, and concern the degree of adherence to the European Society of Cardiology guideline recommendations. The results of this study could therefore be of interest for all practitioners applying these guidelines in the management of UA or NSTEMI patients. And are needed to reduce the variation in practice between cardiologists, hospitals and countries, and as a result find an optimal balance between correctly identifying UA or NSTEMI patients from the large pool of chest pain patients presenting at the emergency department who would benefit most from invasive treatment on the one hand and unnecessary admissions or resource use on the other. Also, this study provides other researchers or clinicians aiming to set up a clinical vignette study with a thorough methodological description of all research steps.

Potential limitations

In developing the study, several methodological limitations occurred which potentially affect interpretation of the findings. First, in this study the outcome measure concerns a complex decision to be made within a limited period of time in a sometimes hectic environment. The vignettes in this study are limited to respectively seven and eight attributes for each decision

moment while in clinical practice cardiologists may take into account other aspects in their decision making. Also cardiologists are not able to see the patient at hand which may influence decision making. However, clinical vignettes have proven to be a valid and valuable tool to measure the quality of care in previous studies.[25, 26]

Second, the pre-selection of attributes involved in UA/NSTEMI management was minimized to the European Society of Cardiology guidelines and to variables from existing risk scoring instruments, as it is cognitively impossible to take into account all attributes. Some attributes are therefore neglected. However, as Dutch cardiologists are most familiar with the European Society of Cardiology guidelines it was considered reasonable to derive attributes from these guidelines.

Finally, the calculated sample size was based on an assumption that every cardiologists reviews the same number of vignettes. In the present study however, every cardiologist reviews the same number of vignettes, but not all cardiologists will review the same vignettes due to the blocked design. The effect of ignoring this assumption may be limited as it is previous suggested that a minimum number of six assessments per scenario is sufficient.[40] With the present sample size calculation, this requirement is met.

CURRENT STATUS OF THE STUDY

The survey has been sent out by the 4th of June 2014. Results are expected by the end of 2014.

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AUTHORS' CONTRIBUTIONS

All authors provided intellectual input into conception and design, editing of the manuscript and preparation for publication. In addition, JE drafted the manuscript and IvdW designed the clinical vignettes (e.g. conduction of the fractional factorial and block design). All authors revised the manuscript for important intellectual content and gave their final approval for the version published.

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COMPETING INTERESTS

All authors declare that they have no competing interests.

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Figure 1. Example of clinical vignettes used in the web-based survey

Decision moment I (with risk score)

You see a 65 year or old woman with aspecific complaints of chest pain at the emergency department. At presentation the complaints are absent. The patient is known with coronary artery disease, but has no other risk factors [a]. The ECG is normal and the troponin at arrival is below the reference level and representative [b]. You calculate a risk score [c], which gives an intermediate risk.

1. Would you send this patient home without any further diagnostic testing (e.g. exercise testing)?

□ yes

□ no

2. How sure are you of your answer?

□ very sure

□ sure

□ somewhat sure

Decision moment II (with risk score)

You see a 65 year old patient, suspected of instable coronary artery disease (UA/NSTEMI), who stays in hospital for observation. Since presentation, the patient has persistent symptoms of chest pain. The patient has no history of coronary artery disease (CAD), but has more than one classical risk factors[a]. The ECG is normal and troponin levels are at repetition normal[b]. Further, the lab results show no presence of renal failure. You calculate a risk score [c], which gives a low risk .

1. Would you perform coronary angiography within 72 hours in this patient?

□ yes

□ no

2. How sure are you of your answer?

□ very sure

□ sure

□ somewhat sure

[a] risk factors: diabetes mellitus, hypertension, hypercholesterolemia, smoking and positive family history

[b] according to your hospital's standards

[c] calculated risk according to risk score applied in your own practice (for instance, GRACE, TIMI, FRISC, PURSUIT or HEART score.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Although we are aware of the SPIRIT checklist, the STROBE checklist seems most suited for this manuscript, as it describes the study design of a cross-sectional study. The SPIRIT checklist is specifically developed for reporting randomized trials and therefore its applicability to the contents of the present manuscript is limited. Also some parts of the STROBE checklist will not be applicable to our manuscript, these will be left empty.

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6 (setting, data collection) 17 (period of recruitment)
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	14
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Sources of data: survey p6-7 Method(s) of assessment: binary choice experiment/fractional factorial design p 5 + p 13

Bias	9	Describe any efforts to address potential sources of bias	16-17
Study size	10	Explain how the study size was arrived at	Sample size calculation: p15
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	14
		(*b*) Describe any methods used to examine subgroups and interactions	14
		(*c*) Explain how missing data were addressed	n.a.
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	15
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	15-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	

Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Clinical decision making of cardiologists regarding admission and treatment of suspected unstable angina or non-ST-elevation myocardial infarction patients: a study protocol of a clinical vignette study

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Clinical decision making of cardiologists regarding admission and treatment of suspected unstable angina or non-ST-elevation myocardial infarction patients: a study protocol of a clinical vignette study

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ABSTRACT

Introduction: Cardiologists face the difficult task of rapidly distinguishing cardiac related chest pain from other conditions, and to thoroughly consider whether invasive diagnostic procedures or treatments are indicated. The use of cardiac risk scoring instruments has been recommended in international cardiac guidelines. However, it is unknown to what degree cardiac risk scores and other clinical information influence cardiologists' decision making. This paper describes the development of a binary choice experiment using realistic descriptions of clinical cases. The study aims to determine the importance cardiologists put on different types of clinical information, including cardiac risk scores, when deciding on the management of patients suspected of unstable angina or non-ST-elevation myocardial infarction.

Methods and analysis: Cardiologists are asked, in a nationwide survey, to weigh different clinical factors in decision making regarding patient admission and treatment using realistic descriptions of patients in which specific characteristics are varied in a systematic way (e.g. web based clinical vignettes). These vignettes represent patients suspected of unstable angina or non-ST-elevation myocardial infarction. Associations between several clinical characteristics, with cardiologists' management decisions will be analyzed using generalized linear mixed models.

Ethics and dissemination: The study has received ethics approval and informed consent will be obtained from all participating cardiologists. The results of the study will provide insight into the relative importance of cardiac risk scores and other clinical information in cardiac decision making. Further, the results indicate cardiologists' adherence to the European Society of Cardiology guideline recommendations. In addition, the detailed description of the method of vignette development applied in this study could assist other researchers or clinicians in creating future choice experiments.

STRENGHTS AND LIMITATIONS OF THIS STUDY

Strengths

- This study provides insight in how cardiologists weigh clinical information in deciding on the admission and treatment of UA/NSTEMI patients.
- The clinical information presented to cardiologists is varied systematically and presented in clinical vignettes, reflecting clinical practice as closely as possible.
- Decision making is studied in a nationwide survey.

Limitations

- The decision cardiologists were asked to make is a complex decision which (sometimes) has to be made instantly. This was not simulated/taken into account in the clinical vignettes.
- The decision had to be made on the basis of seven or eight attributes while in clinical practice cardiologists may take into account other aspects in their decision making.

INTRODUCTION

About six percent of the emergency department presentations are due to chest pain.[1] Of these patients, a substantial number are diagnosed with an acute coronary syndrome, including unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI) and ST segment myocardial infarction (STEMI).[1, 2] Mortality after an acute coronary syndrome is substantial.[3, 4] To prevent cardiac damage or mortality, timely treatment is indicated. As a result, the attending physician has the difficult task to rapidly distinguish cardiac related chest pain from chest pain caused by other conditions. Patients presenting with chest pain to the emergency department should therefore be stratified according to their level of risk of having a cardiac condition.[5] Risk assessment is generally based on a patient's clinical history, physical examination, biomarkers and electrocardiogram findings.[6-9] The decision for hospital admission or type of treatment is dependent on a patients' risk of adverse cardiac events, such as re-infarction or mortality. The European Society of Cardiology guidelines on the management of UA or NSTEMI recommend to treat patients at high risk of re-infarction or death with invasive procedures or treatment (e.g. coronary angiography, Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG)).[7] To determine the patient's risk, several cardiac risk scores have been developed and validated i.e. the HEART,[5] GRACE-,[10, 11] TIMI-,[12] FRISC-,[13] and PURSUIT score.[14] Use of these instruments is recommended by professional guidelines.[7] Despite the availability of valid cardiac risk stratification tools and recommendations of their use, in previous studies, low risk patients were more likely to receive invasive procedures compared to high risk patients.[15-18] Such a treatment risk paradox implies low adherence rates with the guidelines, which possibly affects or even threatens patient safety on the one hand and results in suboptimal resource use on the other hand. Low guideline adherence might be explained by barriers affecting physicians' attitude towards guideline recommendations,[19] including

disagreement with the guidelines or unwillingness to adopt the guidelines. In addition, previous research indicates that physicians may consider evidence underlying the guidelines as unconvincing.[20] As a result, they may depend heavily on their own personal experience and seem to underestimate important risk factors.[21, 22] In this study we focus on cardiologists' decision making in the management of UA and NSTEMI. To our knowledge it is unknown to what degree cardiac risk scores and other clinical information influence their decisions about admission and choice of treatment. The objective of the present study is twofold. First, to determine the influence of a cardiac risk score upon cardiologists' decision on patient admission and treatment. Second, to determine the relative importance of different types of clinical information, in the presence or absence of a risk score, upon management decisions concerning suspected UA or NSTEMI patients.

METHODS AND ANALYSIS

Study design

To determine how cardiologists weigh different clinical factors (e.g. relative importance) in their decision to admit or to treat a patient, binary choice experiments are conducted using vignettes of clinical cases. Two decision moments were investigated, the decision to admit a patient to hospital and the decision to perform cardiac catheterization. In the vignettes the clinical factors are systematically varied according to a fractional factorial design.

Study population

Cardiologists working as a registered cardiologist in a Dutch hospital will be approached for participation in this study by email. They will be recruited through the Dutch directory of physicians.

Data collection

The data will be collected using a web-based survey, presenting cardiologists with clinical vignettes. The clinical vignettes describe patients by means of a set of attributes, reflecting characteristics of a patient or treatment.[23] Clinical vignettes are a frequently applied approach to study decision-making in health care as they closely reflect clinical practice.[24] In addition, clinical vignettes were shown to be a valid tool to measure the quality of care.[25, 26] Cardiologists will be asked to complete a web-based survey containing the clinical vignettes. Prior to completing the survey, cardiologists will be informed about the global study objective and asked to give consent for participation in the study. Cardiologists who initially fail to respond will be sent reminders one, three, eight and twelve weeks after first sending the survey. The completion time of the survey will be approximately 20 minutes and cardiologists are able to stop and continue completion of the survey at any time. The data will be processed anonymously.

Survey

The survey registers demographic characteristics, including year of birth, gender, current profession, years of cardiology care experience, whether cardiologists are still actively involved in the care for patients diagnosed with UA or NSTEMI and which risk score they apply in clinical practice. In addition, associated hospital characteristics such as type of hospital they work in and whether hospitals have revascularization facilities on site will be registered. After completing the section that registers demographic characteristics, cardiologists are presented with the vignettes. These are presented in two parts that differ in the decision that needs to be made. In the first part of the survey (A), the clinical vignettes describe patients who present themselves with chest pain to the emergency department. Cardiologists are asked to indicate on a binary scale (yes or no) whether he or she would

discharge the patient from the emergency department without any further diagnostic testing (e.g. no serial troponin testing or exercise testing). In addition, cardiologists are asked on a three point likert scale how certain they are of their decision (very sure, sure, somewhat sure). The clinical vignettes in the second part of the study (B) describe a patient's condition when the patient is already admitted to the hospital with a high suspicion of UA or NSTEMI. Cardiologists are asked to indicate whether he or she would advise an invasive procedure i.e. coronary angiography within 72 hours from admission and how certain they are of their decision (using the same three point likert scale). Cardiologists are asked to make decisions that reflect their actual clinical practice as closely as possible. The survey was pretested among two cardiology residents, not involved in the design of the study, and asked to provide feedback regarding the applicability of the survey. This provided insight in the comprehensiveness of the survey, and the time it takes to complete the survey.

Pre-selection of attributes

Potential attributes relevant for the management of UA and NSTEMI, regarding the decision to admit or treat a patient, were selected from clinical guidelines. It was assumed that these guidelines provided an integral overview of the published scientific evidence and therefore cover all relevant attributes.[6-9] Further, variables of validated risk scoring instruments,[5, 10-14] the website 'up-to-date',[27-29] and recently conducted interviews on the use of risk stratification instruments in practice,[30] were reviewed for additional relevant attributes. The website 'up-to-date' concerns an evidence-based resource that aims to support physicians in clinical decision making.

Initially, all aspects that can be taken into account when stratifying risk were selected from the aforementioned sources, which resulted in a pre-selection of 105 potential attributes. As Dutch cardiologists are most familiar with the European Society of Cardiology guidelines in

treating their patients, the pre-selection was subsequently reduced by selecting only those attributes that were mentioned in this guideline and in the validated risk scoring instruments. This left 56 attributes that were considered of importance for the present study (Table 1).

Table 1. Pre-selection of attributes (after removal of duplicates)

Category		Attribute	Source†
Demographics	1	Older age >75 years	ESC, RS
	2	Gender	ESC, RS
Risk factors	3	Presence of risk factors in general (including positive family history, peripheral artery disease, carotid stenosis, diabetes mellitus, kidney failure, smoking, hypertension, hypercholesterolemia, obesity)	ESC, RS
	4	Diabetes mellitus	ESC, RS
	5	Chronic kidney failure/ creatine level	ESC, RS
	6	Heart failure	ESC, RS
	7	Depressed left ventricular ejection fraction	ESC
	8	Killip-class classification	ESC, RS
	9	Anemia	ESC
	10	Obesity	ESC, RS
	11	Malnutrition	ESC
History	12	Known coronary artery disease	ESC, RS
	13	Previous myocardial infarction	ESC, RS
	14	Previous or recent percutaneous coronary intervention	ESC
	15	Previous or recent coronary artery bypass surgery	ESC
	16	Severity of coronary artery disease	ESC
	17	Cocaine use	ESC
	18	Aspirin use 7 days prior to admission	RS
Clinical presentation	19	Anamnesis suspicious for cardiac related chest pain	RS
	20	Persistent angina pectoris	ESC, RS
	21	Symptoms of angina pectoris in rest	ESC
	22	Reoccurring angina pectoris	ESC
	23	Several episodes of angina pectoris after event	ESC
	24	Tachycardia	ESC, RS
	25	Hypotensive	ESC, RS
	26	Hemodynamically instable	ESC
	27	Increased leucocytes at presentation	ESC
	28	Thrombocytopenia at presentation	ESC
	29	Increased bleeding risk	ESC
	30	Presence of bleeding	ESC
	31	Intermediate or high GRACE risk score	ESC
	32	Positive stress test	ESC
	33	Cardiac arrest at admission	ESC, RS
Electrocardiogram findings	34	ECG ST segment changes	ESC, RS
	35	ECG deviations at rest	ESC

	36	Dynamic ST/T changes	ESC
	37	Negative T waves	ESC
	38	ST depression	ESC
	39	ST elevation	ESC
	40	Ventricular arrhythmia	ESC
Laboratory results	41	Elevated troponin levels	ESC
	42	Elevated biomarkers	ESC, RS
	43	Hyperglycemia	ESC
	44	Elevated C-reactive protein	ESC
	45	Elevated B-type natriuretic peptide	ESC
Context information	46	Re-vascularization status	ESC
	47	Rest ischemia	ESC
	48	Severity of lesions	ESC
	49	Physical condition of patient	ESC
	50	Fragility of patient	ESC
	51	Cognitive decline	ESC
	52	Functional decline	ESC
	53	Physical dependence	ESC
	54	Quality of life	ESC
	55	Patient's wishes	ESC
	56	Risks versus benefits of re-vascularization	ESC

† Attributes are derived from the European Society of Cardiology guideline 2011 and from the GRACE-, TIMI-, FRISC-, PURSUIT- and/or HEART risk score. Abbreviations: ESC, European Society of Cardiology guideline; ECG, electrocardiogram; GRACE, Global Registry of Acute Coronary Events; RS, risk score.

Final selection of attributes and attribute levels

As it is cognitively difficult for respondents to take into account large numbers of attributes, it is recommended – although there is no standard – to select between six to ten attributes in choice experiments.[31-33] This approach was followed in the present study. The final set of attributes was selected by a panel of three cardiologists in collaboration with the research team during a consensus meeting (1st of October 2013). These cardiologists were selected based on their affinity with research, and were chosen to reflect diversity in experience and type of hospital they work in. In preparing the consensus meeting, the cardiologists were asked to write down in order of importance the six to eight most important attributes when deciding to discharge a patient presenting with acute chest pain from the emergency department without further diagnostic testing (decision moment A). Equally, they listed

attributes that were important in deciding on performing a coronary angiography within 72 hours in patients with a high suspicion of UA or NSTEMI (decision moment B). In case a cardiologist indicated that an attribute is essential in decision making, he had the option to select an additional attribute, on top of the six to eight that were already selected. The attributes selected by the cardiologists were the starting-point for the consensus meeting. The selected attributes were compared and discussed. Furthermore, the cardiologists reviewed and compared the pre-selection of potential attributes derived from the European Society of Cardiology guidelines and existing risk scoring instruments. After viewing this list, the cardiologists were given the opportunity to change their own attribute selection into a final selection. None of the cardiologists made any changes in their selection. Again, differences and similarities were discussed until consensus was reached over a final set of eight attributes for decision moment A and seven attributes for decision moment B (Table 2 and 3).

The arguments whether to select or remove a specific attribute were written down in a logbook. After determining the final set of attributes, the selection and description of attribute levels was discussed and confirmed / approved. In selecting attribute levels, we aimed to select levels that closely reflect the variety of presentations in clinical practice and will be easily understood by cardiologists. A secondary goal in selecting attribute levels was to keep the total number of possible vignettes i.e. the full factorial design, as small as possible. Therefore the number of levels within an attribute were kept to a minimum. The expert panel was re-approached by email to provide a further review of the selected attributes and attribute levels per decision moment on the basis of their initial feedback.

Table 2. Final selection of attributes and attribute levels of decision moment A	
Clinical setting: Patient presenting with acute chest pain at the emergency department. Decision: 'Would you send this patient home without any further diagnostic testing (e.g. no serial troponin testing or exercise testing)?'	
Attribute	**Attribute level**
Age	< 50 years 50-75 years > 75 years
Gender	Male Female
Known coronary artery disease	No Yes
Chest pain classification based on history taking	A-specific chest pain Atypical angina pectoris Typical angina pectoris
Symptoms of chest pain still present at presentation	No Yes
Risk factors†	No risk factors One risk factor More than one risk factor
ECG	Normal Atypical changes Typical ischemic changes
Troponin‡	Below reference level and representative Below reference level, not representative Above reference level
†Classic five: diabetes mellitus, hypertension, hypercholesterolemia, smoking and positive family history; ‡ According to cardiologists' own hospital standards.	

Table 3. Final selection of attributes and attribute levels decision moment B	
Clinical setting: Patient with suspicion of unstable angina or non-ST-elevation myocardial infarction is admitted for observation in the hospital. *Decision: 'Would you perform a coronary angiography within 72 hours in this patient?*	
Attribute	**Attribute level**
Age	< 70 years 70-80 years 80 years
Renal function	No renal dysfunction Mild to moderate renal dysfunction Severe renal dysfunction
Known coronary artery disease	No Yes
Persistent chest pain	No Yes
Risk factors†	No risk factors One risk factor More than one risk factor
ECG	Normal Atypical changes Typical ischemic changes
Troponin‡	Normal at repeated measures Significant rise and/or 'rise and fall'
† Classic five: diabetes mellitus, hypertension, hypercholesterolemia, smoking and positive family history; ‡ According to cardiologists' own hospital standards	

Cardiac risk score

In developing the clinical vignettes, initially cardiac risk score was considered as an attribute. However, this led to unrealistic vignettes and the attribute was therefore removed from the full factorial design. Additionally, by using the HEART risk score[5] (for decision moment A) and GRACE 2.0 risk score[34] (for decision moment B), cardiac risk was estimated for every vignette. This was accomplished by entering the values present in the vignette while holding the remaining parameters constant. The sample of cardiologists will, prior to completion of the survey, be divided in two groups. One group will complete vignettes without a cardiac risk score being present, while the other group completes the vignettes with

a cardiac risk score present. Cardiologists will be instructed to consider the risk score as the one familiar from their own practice or knowledge.

Selection of clinical vignettes

The attributes and levels for decision moment A comprised $2^{3}*3^{5}$ = 1944 possible combinations in the full factorial design, where the base of the formula concerns the number of levels of an attribute and the exponent concerns the number of attributes with respectively two or three levels. For decision moment B, $2^{3}*3^{4}$ = 648 possible vignette combinations could be created. It is practically impossible to present respondents with such a vast amount of vignettes, therefore a fractional factorial design was created to reduce the number of vignettes for each decision moment. In selecting vignettes, the aim was to estimate the main effects of all attributes. The quality of the selection of vignettes was compared to a theoretical optimum by means of the G efficiency parameter which ranges between 0 (inefficient design) and 1 (efficient design). The G efficiency parameter is a useful guide when judging fractional factorial designs.[35] For both decision moments (i.e. discharge without further testing and prompt coronary angiography), the number of vignettes were reduced to 64. The vignettes selection showed substantial G efficiency of 0.94 for decision moment A and 0.95 for decision moment B. Per decision moment, the 64 scenarios were randomly allocated into eight blocks containing eight scenarios each. This is to ensure that all attribute levels will appear with equal frequency in each block.[36] Prior to sending the survey, cardiologists will be randomly assigned a block number in SPSS and being sent the corresponding questionnaire. Each survey comprises 16 scenarios in total (eight per decision moment).

Case description of clinical vignettes

Two members of the research team drafted the initial clinical case descriptions of the vignettes: one representing decision moment A and one representing decision moment B. Next, the clinical case descriptions were discussed and reviewed in a second consensus meeting (26th of February 2014), comprising four cardiologists and the research team. This review process was undertaken to ensure accuracy, plausibility and clarity of the clinical event presentation in all of the vignettes. The vignettes were revised until both the research team as the panel of cardiologists agreed that the case descriptions represented clinical practice as closely as possible. An example of a vignette is presented in figure 1.

Study outcome

The study outcome is the relative importance cardiologists' put on different types of clinical information, both in the presence and absence of the risk score, when deciding on the management of suspected UA or NSTEMI patients.

Statistical considerations

Demographic characteristics will be presented using descriptive statistics. Associations of independent variables with the binary responses of cardiologists on the clinical vignettes in the survey will be studied with a generalized linear mixed model (GLMM), taking into account random effects for blocks and cardiologists. In total, 4 models will be created i.e. 2 for each decision moment taking into account the presence or absence of cardiac risk score information. In the analyses, cardiologists' responses (yes or no) are the binary outcome measure. Independent variables are the attributes, risk score (if present in the vignette) and the degree of certainty of respondents' answers. All independent variables will be simultaneously included in the analyses. A significance level of $p \leq 0.05$ will be used. The analysis with the

GLMM will be performed by la Placian integration, conducted in R for windows (version 3.0.2) with package lme4.[37] The impact of the presence of the risk score on a cardiologist's decision will be studied by comparing results of the analyses with and without presenting risk score information in the vignettes.

Sample size

In total, each cardiologist will complete 16 vignettes (8 for decision moment A and 8 for decision moment B). In calculating the minimum number of cardiologists needed, the following formula is followed: n = 500 * (c / (a * t)). In this formula, 'n' is the minimum number of cardiologists, 'c' is the largest number of levels for any of the attributes, 'a' is the number of alternative scenario's that cardiologists are presented with and 't' is the total number of choice scenarios per decision moment that each cardiologist is presented with.[38, 39] In this study a minimum sample size of, 500 * (3 / (1 * 8)), approximately 188 cardiologists are needed per group (with or without a cardiac risk score) to study main effects for decision moment A and B separately. The Dutch directory of physicians contains 963 cardiologists. If a response of 40% is assumed, 385 cardiologists will complete 16 vignettes in total, which will be sufficient for estimating main effects.

Ethics and dissemination

The study protocol was reviewed and approved by the medical ethical committee of the VU University Medical Center Amsterdam (protocol number: 2014008). A waiver of active informed consent was granted, as the study concerns completely anonymized data. A form of informed consent, however, will be conducted at the start of the survey when cardiologists are asked to consent that their answers will be used and stored for scientific purposes. Results are

planned to be disseminated in two papers submitted to peer reviewed journals, and presentations at relevant conferences.

DISCUSSION

UA and NSTEMI are two conditions that are associated with high mortality rates. Correctly estimating patients' risk of re-infarction or death and taking into account this risk in selecting a management strategy is of importance in preventing unnecessary deaths and optimal use of resources. Cardiac guidelines recommend the use of several sources of information to estimate the risk for an individual patient. However, it is unknown to what degree cardiologists take into account all these aspects in the management of patients suspected of UA or NSTEMI. As mentioned in the introduction several studies report a treatment risk paradox, i.e. low risk patients were more likely to receive invasive procedures compared to high risk patients. Implying that cardiac risk scores are not used or not of importance in decision making regarding admission or invasive treatment. The results of the present study will provide further insight in the complex decision regarding admission and treatment of UA and NSTEMI patients, and concern the degree of adherence to the European Society of Cardiology guideline recommendations. The results of this study could therefore be of interest for all practitioners applying these guidelines in the management of UA or NSTEMI patients. And are needed to reduce the variation in practice between cardiologists, hospitals and countries, and as a result find an optimal balance between correctly identifying UA or NSTEMI patients from the large pool of chest pain patients presenting at the emergency department who would benefit most from invasive treatment on the one hand and unnecessary admissions or resource use on the other. Also, this study provides other researchers or clinicians aiming to set up a clinical vignette study with a thorough methodological description of all research steps.

Potential limitations

In developing the study, several methodological limitations occurred which potentially affect interpretation of the findings. First, in this study the outcome measure concerns a complex decision to be made within a limited period of time in a sometimes hectic environment. The vignettes in this study are limited to respectively seven and eight attributes for each decision moment while in clinical practice cardiologists may take into account other aspects in their decision making, for instance bleeding risk scores in deciding on coronary angiography. Also cardiologists are not able to see the patient at hand which may influence decision making. However, clinical vignettes have proven to be a valid and valuable tool to measure the quality of care in previous studies.[25, 26]

Second, the pre-selection of attributes involved in UA/NSTEMI management was minimized to the European Society of Cardiology guidelines and to variables from existing risk scoring instruments, as it is cognitively impossible to take into account all attributes. Some attributes are therefore neglected. However, as Dutch cardiologists are most familiar with the European Society of Cardiology guidelines it was considered reasonable to derive attributes from these guidelines.

Finally, the calculated sample size was based on an assumption that every cardiologists reviews the same number of vignettes. In the present study however, every cardiologist reviews the same number of vignettes, but not all cardiologists will review the same vignettes due to the blocked design. The effect of ignoring this assumption may be limited as it is previous suggested that a minimum number of six assessments per scenario is sufficient.[40] With the present sample size calculation, this requirement is met.

CURRENT STATUS OF THE STUDY

The survey has been sent out by the 4th of June 2014. Results are expected by the end of 2014.

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AUTHORS' CONTRIBUTIONS

All authors provided intellectual input into conception and design, editing of the manuscript and preparation for publication. In addition, JE drafted the manuscript and IvdW designed the clinical vignettes (e.g. conduction of the fractional factorial and block design). All authors revised the manuscript for important intellectual content and gave their final approval for the version published.

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COMPETING INTERESTS

All authors declare that they have no competing interests.

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Figure 1. Example of clinical vignettes used in the web-based survey

Clinical decision making of cardiologists regarding admission and treatment of suspected unstable angina or non-ST-elevation myocardial infarction patients: a study protocol of a clinical vignette study

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ABSTRACT

Introduction: Cardiologists face the difficult task of rapidly distinguishing cardiac related chest pain from other conditions, and to thoroughly consider whether invasive diagnostic procedures or treatments are indicated. The use of cardiac risk scoring instruments has been recommended in international cardiac guidelines. However, it is unknown to what degree cardiac risk scores and other clinical information influence cardiologists' decision making. This paper describes the development of a binary choice experiment using realistic descriptions of clinical cases. The study aims to determine the importance cardiologists put on different types of clinical information, including cardiac risk scores, when deciding on the management of patients suspected of unstable angina or non-ST-elevation myocardial infarction.

Methods and analysis: Cardiologists are asked, in a nationwide survey, to weigh different clinical factors in decision making regarding patient admission and treatment using realistic descriptions of patients in which specific characteristics are varied in a systematic way (e.g. web based clinical vignettes). These vignettes represent patients suspected of unstable angina or non-ST-elevation myocardial infarction. Associations between several clinical characteristics, with cardiologists' management decisions will be analyzed using generalized linear mixed models.

Ethics and dissemination: The study has received ethics approval and informed consent will be obtained from all participating cardiologists. The results of the study will provide insight into the relative importance of cardiac risk scores and other clinical information in cardiac decision making. Further, the results indicate cardiologists' adherence to the European Society of Cardiology guideline recommendations. In addition, the detailed description of the method of vignette development applied in this study could assist other researchers or clinicians in creating future choice experiments.

STRENGHTS AND LIMITATIONS OF THIS STUDY

Strengths

- This study provides insight in how cardiologists weigh clinical information in deciding on the admission and treatment of UA/NSTEMI patients.
- The clinical information presented to cardiologists is varied systematically and presented in clinical vignettes, reflecting clinical practice as closely as possible.
- Decision making is studied in a nationwide survey.

Limitations

- The decision cardiologists were asked to make is a complex decision which (sometimes) has to be made instantly. This was not simulated/taken into account in the clinical vignettes.
- The decision had to be made on the basis of seven or eight attributes while in clinical practice cardiologists may take into account other aspects in their decision making.

INTRODUCTION

About six percent of the emergency department presentations are due to chest pain.[1] Of these patients, a substantial number are diagnosed with an acute coronary syndrome, including unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI) and ST segment myocardial infarction (STEMI).[1, 2] Mortality after an acute coronary syndrome is substantial.[3, 4] To prevent cardiac damage or mortality, timely treatment is indicated. As a result, the attending physician has the difficult task to rapidly distinguish cardiac related chest pain from chest pain caused by other conditions. Patients presenting with chest pain to the emergency department should therefore be stratified according to their level of risk of having a cardiac condition.[5] Risk assessment is generally based on a patient's clinical history, physical examination, biomarkers and electrocardiogram findings.[6-9] The decision for hospital admission or type of treatment is dependent on a patients' risk of adverse cardiac events, such as re-infarction or mortality. The European Society of Cardiology guidelines on the management of UA or NSTEMI recommend to treat patients at high risk of re-infarction or death with invasive procedures or treatment (e.g. coronary angiography, Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG)).[7] To determine the patient's risk, several cardiac risk scores have been developed and validated i.e. the HEART,[5] GRACE-,[10, 11] TIMI-,[12] FRISC-,[13] and PURSUIT score.[14] Use of these instruments is recommended by professional guidelines.[7] Despite the availability of valid cardiac risk stratification tools and recommendations of their use, in previous studies, low risk patients were more likely to receive invasive procedures compared to high risk patients.[15-18] Such a treatment risk paradox implies low adherence rates with the guidelines, which possibly affects or even threatens patient safety on the one hand and results in suboptimal resource use on the other hand. Low guideline adherence might be explained by barriers affecting physicians' attitude towards guideline recommendations,[19] including

disagreement with the guidelines or unwillingness to adopt the guidelines. In addition, previous research indicates that physicians may consider evidence underlying the guidelines as unconvincing.[20] As a result, they may depend heavily on their own personal experience and seem to underestimate important risk factors.[21, 22] In this study we focus on cardiologists' decision making in the management of UA and NSTEMI. To our knowledge it is unknown to what degree cardiac risk scores and other clinical information influence their decisions about admission and choice of treatment. The objective of the present study is twofold. First, to determine the influence of a cardiac risk score upon cardiologists' decision on patient admission and treatment. Second, to determine the relative importance of different types of clinical information, in the presence or absence of a risk score, upon management decisions concerning suspected UA or NSTEMI patients.

METHODS AND ANALYSIS

Study design

To determine how cardiologists weigh different clinical factors (e.g. relative importance) in their decision to admit or to treat a patient, binary choice experiments are conducted using vignettes of clinical cases. Two decision moments were investigated, the decision to admit a patient to hospital and the decision to perform cardiac catheterization. In the vignettes the clinical factors are systematically varied according to a fractional factorial design.

Study population

Cardiologists working as a registered cardiologist in a Dutch hospital will be approached for participation in this study by email. They will be recruited through the Dutch directory of physicians.

Data collection

The data will be collected using a web-based survey, presenting cardiologists with clinical vignettes. The clinical vignettes describe patients by means of a set of attributes, reflecting characteristics of a patient or treatment.[23] Clinical vignettes are a frequently applied approach to study decision-making in health care as they closely reflect clinical practice.[24] In addition, clinical vignettes were shown to be a valid tool to measure the quality of care.[25, 26] Cardiologists will be asked to complete a web-based survey containing the clinical vignettes. Prior to completing the survey, cardiologists will be informed about the global study objective and asked to give consent for participation in the study. Cardiologists who initially fail to respond will be sent reminders one, three, eight and twelve weeks after first sending the survey. The completion time of the survey will be approximately 20 minutes and cardiologists are able to stop and continue completion of the survey at any time. The data will be processed anonymously.

Survey

The survey registers demographic characteristics, including year of birth, gender, current profession, years of cardiology care experience, whether cardiologists are still actively involved in the care for patients diagnosed with UA or NSTEMI and which risk score they apply in clinical practice. In addition, associated hospital characteristics such as type of hospital they work in and whether hospitals have revascularization facilities on site will be registered. After completing the section that registers demographic characteristics, cardiologists are presented with the vignettes. These are presented in two parts that differ in the decision that needs to be made. In the first part of the survey (A), the clinical vignettes describe patients who present themselves with chest pain to the emergency department. Cardiologists are asked to indicate on a binary scale (yes or no) whether he or she would

discharge the patient from the emergency department without any further diagnostic testing (e.g. no serial troponin testing or exercise testing). In addition, cardiologists are asked on a three point likert scale how certain they are of their decision (very sure, sure, somewhat sure). The clinical vignettes in the second part of the study (B) describe a patient's condition when the patient is already admitted to the hospital with a high suspicion of UA or NSTEMI. Cardiologists are asked to indicate whether he or she would advise an invasive procedure i.e. coronary angiography within 72 hours from admission and how certain they are of their decision (using the same three point likert scale). Cardiologists are asked to make decisions that reflect their actual clinical practice as closely as possible. The survey was pretested among two cardiology residents, not involved in the design of the study, and asked to provide feedback regarding the applicability of the survey. This provided insight in the comprehensiveness of the survey, and the time it takes to complete the survey.

Pre-selection of attributes

Potential attributes relevant for the management of UA and NSTEMI, regarding the decision to admit or treat a patient, were selected from clinical guidelines. It was assumed that these guidelines provided an integral overview of the published scientific evidence and therefore cover all relevant attributes.[6-9] Further, variables of validated risk scoring instruments,[5, 10-14] the website 'up-to-date',[27-29] and recently conducted interviews on the use of risk stratification instruments in practice ~~(Engel et al. 2014 unpublished work)~~,[30] were reviewed for additional relevant attributes. The website 'up-to-date' concerns an evidence-based resource that aims to support physicians in clinical decision making.

Initially, all aspects that can be taken into account when stratifying risk were selected from the aforementioned sources, which resulted in a pre-selection of 105 potential attributes. As Dutch cardiologists are most familiar with the European Society of Cardiology guidelines in

treating their patients, the pre-selection was subsequently reduced by selecting only those attributes that were mentioned in this guideline and in the validated risk scoring instruments. This left 56 attributes that were considered of importance for the present study (Table 1).

Table 1. Pre-selection of attributes (after removal of duplicates)

Category		Attribute	Source†
Demographics	1	Older age >75 years	ESC, RS
	2	Gender	ESC, RS
Risk factors	3	Presence of risk factors in general (including positive family history, peripheral artery disease, carotid stenosis, diabetes mellitus, kidney failure, smoking, hypertension, hypercholesterolemia, obesity)	ESC, RS
	4	Diabetes mellitus	ESC, RS
	5	Chronic kidney failure/ creatine level	ESC, RS
	6	Heart failure	ESC, RS
	7	Depressed left ventricular ejection fraction	ESC
	8	Killip-class classification	ESC, RS
	9	Anemia	ESC
	10	Obesity	ESC, RS
	11	Malnutrition	ESC
History	12	Known coronary artery disease	ESC, RS
	13	Previous myocardial infarction	ESC, RS
	14	Previous or recent percutaneous coronary intervention	ESC
	15	Previous or recent coronary artery bypass surgery	ESC
	16	Severity of coronary artery disease	ESC
	17	Cocaine use	ESC
	18	Aspirin use 7 days prior to admission	RS
Clinical presentation	19	Anamnesis suspicious for cardiac related chest pain	RS
	20	Persistent angina pectoris	ESC, RS
	21	Symptoms of angina pectoris in rest	ESC
	22	Reoccurring angina pectoris	ESC
	23	Several episodes of angina pectoris after event	ESC
	24	Tachycardia	ESC, RS
	25	Hypotensive	ESC, RS
	26	Hemodynamically instable	ESC
	27	Increased leucocytes at presentation	ESC
	28	Thrombocytopenia at presentation	ESC
	29	Increased bleeding risk	ESC
	30	Presence of bleeding	ESC
	31	Intermediate or high GRACE risk score	ESC
	32	Positive stress test	ESC
	33	Cardiac arrest at admission	ESC, RS
Electrocardiogram findings	34	ECG ST segment changes	ESC, RS
	35	ECG deviations at rest	ESC

	36	Dynamic ST/T changes	ESC
	37	Negative T waves	ESC
	38	ST depression	ESC
	39	ST elevation	ESC
	40	Ventricular arrhythmia	ESC
Laboratory results	41	Elevated troponin levels	ESC
	42	Elevated biomarkers	ESC, RS
	43	Hyperglycemia	ESC
	44	Elevated C-reactive protein	ESC
	45	Elevated B-type natriuretic peptide	ESC
Context information	46	Re-vascularization status	ESC
	47	Rest ischemia	ESC
	48	Severity of lesions	ESC
	49	Physical condition of patient	ESC
	50	Fragility of patient	ESC
	51	Cognitive decline	ESC
	52	Functional decline	ESC
	53	Physical dependence	ESC
	54	Quality of life	ESC
	55	Patient's wishes	ESC
	56	Risks versus benefits of re-vascularization	ESC

† Attributes are derived from the European Society of Cardiology guideline 2011 and from the GRACE-, TIMI-, FRISC-, PURSUIT- and/or HEART risk score. Abbreviations: ESC, European Society of Cardiology guideline; ECG, electrocardiogram; GRACE, Global Registry of Acute Coronary Events; RS, risk score.

Final selection of attributes and attribute levels

As it is cognitively difficult for respondents to take into account large numbers of attributes, it is recommended – although there is no standard – to select between six to ten attributes in choice experiments.[31-33] This approach was followed in the present study. The final set of attributes was selected by a panel of three cardiologists in collaboration with the research team during a consensus meeting (1st of October 2013). These cardiologists were selected based on their affinity with research, and were chosen to reflect diversity in experience and type of hospital they work in. In preparing the consensus meeting, the cardiologists were asked to write down in order of importance the six to eight most important attributes when deciding to discharge a patient presenting with acute chest pain from the emergency department without further diagnostic testing (decision moment A). Equally, they listed

attributes that were important in deciding on performing a coronary angiography within 72 hours in patients with a high suspicion of UA or NSTEMI (decision moment B). In case a cardiologist indicated that an attribute is essential in decision making, he had the option to select an additional attribute, on top of the six to eight that were already selected. The attributes selected by the cardiologists were the starting-point for the consensus meeting. The selected attributes were compared and discussed. Furthermore, the cardiologists reviewed and compared the pre-selection of potential attributes derived from the European Society of Cardiology guidelines and existing risk scoring instruments. After viewing this list, the cardiologists were given the opportunity to change their own attribute selection into a final selection. None of the cardiologists made any changes in their selection. Again, differences and similarities were discussed until consensus was reached over a final set of eight attributes for decision moment A and seven attributes for decision moment B (Table 2 and 3).

The arguments whether to select or remove a specific attribute were written down in a logbook. After determining the final set of attributes, the selection and description of attribute levels was discussed and confirmed / approved. In selecting attribute levels, we aimed to select levels that closely reflect the variety of presentations in clinical practice and will be easily understood by cardiologists. A secondary goal in selecting attribute levels was to keep the total number of possible vignettes i.e. the full factorial design, as small as possible. Therefore the number of levels within an attribute were kept to a minimum. The expert panel was re-approached by email to provide a further review of the selected attributes and attribute levels per decision moment on the basis of their initial feedback.

Table 2. Final selection of attributes and attribute levels of decision moment A	
Clinical setting: Patient presenting with acute chest pain at the emergency department. Decision: 'Would you send this patient home without any further diagnostic testing (e.g. no serial troponin testing or exercise testing)?'	
Attribute	**Attribute level**
Age	< 50 years 50-75 years > 75 years
Gender	Male Female
Known coronary artery disease	No Yes
Chest pain classification based on history taking	A-specific chest pain Atypical angina pectoris Typical angina pectoris
Symptoms of chest pain still present at presentation	No Yes
Risk factors†	No risk factors One risk factor More than one risk factor
ECG	Normal Atypical changes Typical ischemic changes
Troponin‡	Below reference level and representative Below reference level, not representative Above reference level
†Classic five: diabetes mellitus, hypertension, hypercholesterolemia, smoking and positive family history; ‡ According to cardiologists' own hospital standards.	

Table 3. Final selection of attributes and attribute levels decision moment B	
Clinical setting: Patient with suspicion of unstable angina or non-ST-elevation myocardial infarction is admitted for observation in the hospital. *Decision: 'Would you perform a coronary angiography within 72 hours in this patient?*	
Attribute	**Attribute level**
Age	< 70 years 70-80 years 80 years
Renal function	No renal dysfunction Mild to moderate renal dysfunction Severe renal dysfunction
Known coronary artery disease	No Yes
Persistent chest pain	No Yes
Risk factors†	No risk factors One risk factor More than one risk factor
ECG	Normal Atypical changes Typical ischemic changes
Troponin‡	Normal at repeated measures Significant rise and/or 'rise and fall'
† Classic five: diabetes mellitus, hypertension, hypercholesterolemia, smoking and positive family history; ‡ According to cardiologists' own hospital standards	

Cardiac risk score

In developing the clinical vignettes, initially cardiac risk score was considered as an attribute. However, this led to unrealistic vignettes and the attribute was therefore removed from the full factorial design. Additionally, by using the HEART risk score[5] (for decision moment A) and GRACE 2.0 risk score[34] (for decision moment B), cardiac risk was estimated for every vignette. This was accomplished by entering the values present in the vignette while holding the remaining parameters constant. The sample of cardiologists will, prior to completion of the survey, be divided in two groups. One group will complete vignettes without a cardiac risk score being present, while the other group completes the vignettes with

a cardiac risk score present. Cardiologists will be instructed to consider the risk score as the one familiar from their own practice or knowledge.

Selection of clinical vignettes

The attributes and levels for decision moment A comprised $2^{3}*3^{5}$ = 1944 possible combinations in the full factorial design, where the base of the formula concerns the number of levels of an attribute and the exponent concerns the number of attributes with respectively two or three levels. For decision moment B, $2^{3}*3^{4}$ = 648 possible vignette combinations could be created. It is practically impossible to present respondents with such a vast amount of vignettes, therefore a fractional factorial design was created to reduce the number of vignettes for each decision moment. In selecting vignettes, the aim was to estimate the main effects of all attributes. The quality of the selection of vignettes was compared to a theoretical optimum by means of the G efficiency parameter which ranges between 0 (inefficient design) and 1 (efficient design). The G efficiency parameter is a useful guide when judging fractional factorial designs.[35] For both decision moments (i.e. discharge without further testing and prompt coronary angiography), the number of vignettes were reduced to 64. The vignettes selection showed substantial G efficiency of 0.94 for decision moment A and 0.95 for decision moment B. Per decision moment, the 64 scenarios were randomly allocated into eight blocks containing eight scenarios each. This is to ensure that all attribute levels will appear with equal frequency in each block.[36] Prior to sending the survey, cardiologists will be randomly assigned a block number in SPSS and being sent the corresponding questionnaire. Each survey comprises 16 scenarios in total (eight per decision moment).

Case description of clinical vignettes

Two members of the research team drafted the initial clinical case descriptions of the vignettes: one representing decision moment A and one representing decision moment B. Next, the clinical case descriptions were discussed and reviewed in a second consensus meeting (26th of February 2014), comprising four cardiologists and the research team. This review process was undertaken to ensure accuracy, plausibility and clarity of the clinical event presentation in all of the vignettes. The vignettes were revised until both the research team as the panel of cardiologists agreed that the case descriptions represented clinical practice as closely as possible. An example of a vignette is presented in figure 1.

Study outcome

The study outcome is the relative importance cardiologists' put on different types of clinical information, both in the presence and absence of the risk score, when deciding on the management of suspected UA or NSTEMI patients.

Statistical considerations

Demographic characteristics will be presented using descriptive statistics. Associations of independent variables with the binary responses of cardiologists on the clinical vignettes in the survey will be studied with a generalized linear mixed model (GLMM), taking into account random effects for blocks and cardiologists. In total, 4 models will be created i.e. 2 for each decision moment taking into account the presence or absence of cardiac risk score information. In the analyses, cardiologists' responses (yes or no) are the binary outcome measure. Independent variables are the attributes, risk score (if present in the vignette) and the degree of certainty of respondents' answers. All independent variables will be simultaneously included in the analyses. A significance level of $p \leq 0.05$ will be used. The analysis with the

GLMM will be performed by la Placian integration, conducted in R for windows (version 3.0.2) with package lme4.[37] The impact of the presence of the risk score on a cardiologist's decision will be studied by comparing results of the analyses with and without presenting risk score information in the vignettes.

Sample size

In total, each cardiologist will complete 16 vignettes (8 for decision moment A and 8 for decision moment B). In calculating the minimum number of cardiologists needed, the following formula is followed: n = 500 * (c / (a * t)). In this formula, 'n' is the minimum number of cardiologists, 'c' is the largest number of levels for any of the attributes, 'a' is the number of alternative scenario's that cardiologists are presented with and 't' is the total number of choice scenarios per decision moment that each cardiologist is presented with.[38, 39] In this study a minimum sample size of, 500 * (3 / (1 * 8)), approximately 188 cardiologists are needed per group (with or without a cardiac risk score) to study main effects for decision moment A and B separately. The Dutch directory of physicians contains 963 cardiologists. If a response of 40% is assumed, 385 cardiologists will complete 16 vignettes in total, which will be sufficient for estimating main effects.

Ethics and dissemination

The study protocol was reviewed and approved by the medical ethical committee of the VU University Medical Center Amsterdam (protocol number: 2014008). A waiver of active informed consent was granted, as the study concerns completely anonymized data. A form of informed consent, however, will be conducted at the start of the survey when cardiologists are asked to consent that their answers will be used and stored for scientific purposes. Results are

planned to be disseminated in two papers submitted to peer reviewed journals, and presentations at relevant conferences.

DISCUSSION

UA and NSTEMI are two conditions that are associated with high mortality rates. Correctly estimating patients' risk of re-infarction or death and taking into account this risk in selecting a management strategy is of importance in preventing unnecessary deaths and optimal use of resources. Cardiac guidelines recommend the use of several sources of information to estimate the risk for an individual patient. However, it is unknown to what degree cardiologists take into account all these aspects in the management of patients suspected of UA or NSTEMI. As mentioned in the introduction several studies report a treatment risk paradox, i.e. low risk patients were more likely to receive invasive procedures compared to high risk patients. Implying that cardiac risk scores are not used or not of importance in decision making regarding admission or invasive treatment. The results of the present study will provide further insight in the complex decision regarding admission and treatment of UA and NSTEMI patients, and concern the degree of adherence to the European Society of Cardiology guideline recommendations. The results of this study could therefore be of interest for all practitioners applying these guidelines in the management of UA or NSTEMI patients. And are needed to reduce the variation in practice between cardiologists, hospitals and countries, and as a result find an optimal balance between correctly identifying UA or NSTEMI patients from the large pool of chest pain patients presenting at the emergency department who would benefit most from invasive treatment on the one hand and unnecessary admissions or resource use on the other. Also, this study provides other researchers or clinicians aiming to set up a clinical vignette study with a thorough methodological description of all research steps.

Potential limitations

In developing the study, several methodological limitations occurred which potentially affect interpretation of the findings. First, in this study the outcome measure concerns a complex decision to be made within a limited period of time in a sometimes hectic environment. The vignettes in this study are limited to respectively seven and eight attributes for each decision moment while in clinical practice cardiologists may take into account other aspects in their decision making, for instance bleeding risk scores in deciding on coronary angiography. Also cardiologists are not able to see the patient at hand which may influence decision making. However, clinical vignettes have proven to be a valid and valuable tool to measure the quality of care in previous studies.[25, 26]

Second, the pre-selection of attributes involved in UA/NSTEMI management was minimized to the European Society of Cardiology guidelines and to variables from existing risk scoring instruments, as it is cognitively impossible to take into account all attributes. Some attributes are therefore neglected. However, as Dutch cardiologists are most familiar with the European Society of Cardiology guidelines it was considered reasonable to derive attributes from these guidelines.

Finally, the calculated sample size was based on an assumption that every cardiologists reviews the same number of vignettes. In the present study however, every cardiologist reviews the same number of vignettes, but not all cardiologists will review the same vignettes due to the blocked design. The effect of ignoring this assumption may be limited as it is previous suggested that a minimum number of six assessments per scenario is sufficient.[40] With the present sample size calculation, this requirement is met.

CURRENT STATUS OF THE STUDY

The survey has been sent out by the 4th of June 2014. Results are expected by the end of 2014.

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AUTHORS' CONTRIBUTIONS

All authors provided intellectual input into conception and design, editing of the manuscript and preparation for publication. In addition, JE drafted the manuscript and IvdW designed the clinical vignettes (e.g. conduction of the fractional factorial and block design). All authors revised the manuscript for important intellectual content and gave their final approval for the version published.

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COMPETING INTERESTS

All authors declare that they have no competing interests.

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Figure 1. Example of clinical vignettes used in the web-based survey

Decision moment I (with risk score)

You see a 65 year or old woman with aspecific complaints of chest pain at the emergency department. At presentation the complaints are absent. The patient is known with coronary artery disease, but has no other risk factors [a]. The ECG is normal and the troponin at arrival is below the reference level and representative [b]. You calculate a risk score [c], which gives an intermediate risk.

1. Would you send this patient home without any further diagnostic testing (e.g. exercise testing)?

□ yes

□ no

2. How sure are you of your answer?

□ very sure

□ sure

□ somewhat sure

Decision moment II (with risk score)

You see a 65 year old patient, suspected of instable coronary artery disease (UA/NSTEMI), who stays in hospital for observation. Since presentation, the patient has persistent symptoms of chest pain. The patient has no history of coronary artery disease (CAD), but has more than one classical risk factors[a]. The ECG is normal and troponin levels are at repetition normal[b]. Further, the lab results show no presence of renal failure. You calculate a risk score [c], which gives a low risk .

1. Would you perform coronary angiography within 72 hours in this patient?

□ yes

□ no

2. How sure are you of your answer?

□ very sure

□ sure

□ somewhat sure

[a] risk factors: diabetes mellitus, hypertension, hypercholesterolemia, smoking and positive family history

[b] according to your hospital's standards

[c] calculated risk according to risk score applied in your own practice (for instance, GRACE, TIMI, FRISC, PURSUIT or HEART score.

165x227mm (200 x 200 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Although we are aware of the SPIRIT checklist, the STROBE checklist seems most suited for this manuscript, as it describes the study design of a cross-sectional study. The SPIRIT checklist is specifically developed for reporting randomized trials and therefore its applicability to the contents of the present manuscript is limited. Also some parts of the STROBE checklist will not be applicable to our manuscript, these will be left empty.

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6 (setting, data collection) 17 (period of recruitment)
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	14
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Sources of data: survey p6-7 Method(s) of assessment: binary choice experiment/fractional factorial design p 5 + p 13

Bias	9	Describe any efforts to address potential sources of bias	16-17
Study size	10	Explain how the study size was arrived at	Sample size calculation: p15
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	14
		(*b*) Describe any methods used to examine subgroups and interactions	14
		(*c*) Explain how missing data were addressed	n.a.
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	15
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	15-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	

Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.