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Psychological and cognitive factors related to prehospital delay in acute coronary syndrome: A systematic review

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ABSTRACT

Background: In acute coronary syndrome the time elapsed between the start of symptoms and the moment the patient receives treatment is an important determinant of survival and subsequent recovery. However, many patients do not receive treatment as quickly as recommended, mostly due to substantial prehospital delays such as waiting to seek medical attention after symptoms have started.
Objective: To conduct a systematic review with meta-analysis of the relationship between nine frequently investigated psychological and cognitive factors and prehospital delay.
Design: A protocol was preregistered in PROSPERO [CRD42018094198] and a systematic review was conducted following PRISMA guidelines.
Data sources: The following databases were searched for quantitative articles published between 1997 and 2019: Medline (PubMed), Web of Science, Scopus, Psych Info, PAIS, and Open grey.
Review methods: Study risk of bias was assessed with the NIH Quality Assessment Tool for Observational, Cohort, and Cross-Sectional Studies. A best evidence synthesis was performed to summarize the findings of the included studies.
Results: Forty-eight articles, reporting on 57 studies from 23 countries met the inclusion criteria. Studies used very diverse definitions of prehospital delay and analytical practices, which precluded meta-analysis. The best evidence synthesis indicated that there was evidence that patients who attributed their symptoms to a cardiac event ($n = 37$), perceived symptoms as serious ($n = 24$), or felt anxiety in response to symptoms ($n = 15$) reported shorter prehospital delay, with effect sizes indicating important clinical differences (e.g., 1.5–2 h shorter prehospital delay). In contrast, there was limited evidence for a relationship between prehospital delay and knowledge of symptoms ($n = 18$), concern for troubling others ($n = 18$), fear ($n = 17$), or embarrassment in asking for help ($n = 14$).
Conclusions: The current review shows that symptom attribution to cardiac events and some degree of perceived threat are fundamental to speed up help-seeking. In contrast, social concerns and barriers in seeking medical attention (embarrassment or concern for troubling others) may not be as important as initially thought. The current review also shows that the use of very diverse methodological practices strongly limits the integration of evidence into meaningful recommendations. We conclude that there is urgent need for common guidelines for prehospital delay study design and reporting.

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What is already known about the topic?

- Prehospital delay is an important determinant of survival and subsequent recovery of acute coronary syndrome patients.
- Many studies have investigated what psychological or cognitive factors are related to prehospital delay, showing mixed results.

What this paper adds

- This systematic review showed that patients who attributed their symptoms to a cardiac event, perceived symptoms as serious, or felt anxiety reported shorter prehospital delay.
- In contrast, prehospital delay was not consistently related to knowledge of symptoms, concern for troubling others, fear of potential consequences, or embarrassment to seek help.
- Research on prehospital delay uses very diverse methodological practices. There is urgent need for common guidelines for study design and reporting.

Acute coronary syndrome is the greatest single cause of mortality and loss of disability-adjusted life years (DALYs) worldwide, accounting for roughly 7 million deaths and 129 million DALYs annually (Naghavi et al., 2017; Vedanthan et al., 2014). Acute coronary syndromes are often caused by the abrupt occlusion of a coronary artery, and are treated with thrombolytic therapy or percutaneous coronary intervention to restore blood flow. When the occlusion of a coronary artery lasts more than 20–30 min, myocardial necrosis begins to occur, with serious consequences for the patient's health. However, mortality and the associated complications can be substantially reduced if treatment is administered soon after symptom onset (e.g., within one or two hours) (Moser et al., 2006; Ibanez et al., 2018). Therefore, the time elapsed between the start of the symptoms and the moment the patient receives treatment is an important determinant of survival and subsequent recovery (Moser et al., 2006). Research shows that the large majority of patients do not receive treatment within the "golden time window" (one or two hours) and this delay is mostly due to patients waiting to seek medical attention after the symptoms have started (Wechkunanukul et al., 2017). To illustrate, a recent worldwide review of studies showed that mean times to seeking medical care ranged from 1.6 to 12.9 h and they were always greater than the recommended timeframes in the available studies (Wechkunanukul et al., 2017).

Research has identified several determinants of prehospital delay. The majority of studies have focused on socio-demographic, clinical, and social/situational factors. For instance, socio-demographic characteristics related to longer prehospital delays include female gender, older age, lower educational level, lower socioeconomic status, and belonging to a minority ethnic group (Moser et al., 2006; Wechkunanukul et al., 2017; Khraim and Carey, 2009). Clinical factors that characterize patients with longer delays include history of myocardial infarction, angina, or other chronic diseases such as diabetes (Moser et al., 2006; Wechkunanukul et al., 2017). Finally, social/situational factors related to longer delays include living alone or being alone at symptom onset, not calling an ambulance, consulting with a physician, and suffering the cardiac episode during daytime (Moser et al., 2006; Wechkunanukul et al., 2017). In contrast, the presence or advice of family members or co-workers seems to help decrease delays, although results are mixed (Moser et al., 2006; Wechkunanukul et al., 2017; Khraim and Carey, 2009).

Research has also explored how psychological or cognitive factors affect prehospital delay in patients with symptoms of acute coronary syndrome (Dracup and Moser, 1997). This research can be especially useful because it may reveal the psychological mechanisms that drive delays. In addition, many psychological and cognitive factors are actionable and can be addressed in campaigns and interventions aiming to reduce prehospital delay. For instance, several studies have found that patients who interpret their symptoms as potential cardiac events–as opposed to stemming from anxiety, musculoskeletal pain, or other less serious conditions–wait about an hour less before seeking medical attention (Abed et al., 2015; McKee et al., 2013; McKinley et al., 2004). In contrast, worrying about troubling others by asking for help could double the odds of hospital arrival later than one hour after symptom onset (Dracup and Moser, 1997), and even later than 2 h (Bray et al., 2015). Such large differences in the time taken to receive medical attention can have strong effects on patient outcomes because each half an hour of delay in administering treatment could reduce patients' life-expectancy by a year (Rawles, 1997) and delays in general increase the risk of recurrent cardiac events or death (Cullen et al., 2016; De Luca et al., 2004).

However, results from research on psychological and cognitive factors tend to be mixed. For instance, studies suggest that anxiety, perceived seriousness of symptoms, embarrassment or concern for troubling others might affect prehospital delay, yet results have not always been consistent (Moser et al., 2006; Wechkunanukul et al., 2017; Khraim and Carey, 2009). Knowledge of the symptoms of acute coronary syndrome has also been only occasionally associated with prehospital delay (McKee et al., 2013; Albarqouni et al., 2016; Maeso-Madronero, 2000). In addition, extensive and costly information campaigns and interventions that aimed to reduce prehospital delay by focusing on some of these factors were only occasionally effective (Farquharson et al., 2019; Mooney et al., 2012; Mooney et al., 2014). The majority of these interventions employed mass media campaigns emphasizing the symptoms of acute coronary syndrome and the importance of rapid action, but their effectiveness was limited and it was not clear what factors differentiated effective and ineffective interventions (Farquharson et al., 2019; Mooney et al., 2012). Finally, almost all these interventions have put a lot of emphasis on knowledge of acute coronary syndrome warning signs, benefits of treatment, and instructions about what to do, but only a small number of them directly addressed potential perceived psychological barriers to seeking help (Farquharson et al., 2019; Mooney et al., 2012; Mooney et al., 2014)–an aspect that might affect their effectiveness.

Campaigns and interventions will be more effective when they properly address the main reasons for prehospital delay in the target population, which so far seem to be unclear. A systematic review of the existing literature would shed light on this issue as it would help integrate the existing knowledge. Such a review can also help develop an integrated theoretical model of the factors influencing prehospital delay and help design successful, theoretically-driven interventions. In this paper, we aimed to conduct a systematic review with meta-analysis of the relationship between several frequently investigated psychological and cognitive factors and prehospital delay.

Method

When designing the study, we followed PRISMA guidelines for conducting and reporting systematic reviews (Moher et al., 2010). All data, detailed results, and PRISMA and MOOSE checklists are available on the Open Science Framework (OSF): 10.17605/OSF.IO/4MB3D. As per protocol, we searched the following databases: Medline (PubMed), Web of Science, Scopus, and Psych Info, and considered articles published between 1997 (date of publication of the modified Response to Symptoms Questionnaire–the first instrument to systematically measure psychological and cognitive factors in relation to prehospital delay (Dracup and Moser, 1997)) and March 2019. In addition, we searched two databases that contain grey literature: PAIS and Open grey. The search terms used are provided in the registration protocol in PROSPERO [CRD42018094198]. The bibliographic search was conducted by a researcher with methodological training in systematic reviews.

Selection of psychological and cognitive factors that might affect prehospital delay

The selection of the variables was based on factors categorized as psychological and/or cognitive in previous related reviews of broad scope (Moser et al., 2006; Khraim and Carey, 2009). To identify existing narrative reviews, systematic reviews, or other similar articles that could guide us in the selection process, we conducted a preliminary exploratory study of the literature in PubMed and PsychInfo. We identified three reviews (Moser et al., 2006; Wechkunanukul et al., 2017; Khraim and Carey, 2009), and we searched for additional articles not included in the reference list of the reviews, which resulted in 14 additional articles. From these, we aimed to identify factors that were frequently measured in previous studies. Because we aimed to conduct meta-analyses, we restricted the search to those psychological or cognitive factors where there was indication that a meta-analytic synthesis would be meaningful (i.e., availability of multiple studies and indications for relatively homogenous measures). The final list of factors contained variables measured by the frequently used (modified) Response to Symptoms Questionnaire (Dracup and Moser, 1997), whereas other psychological factors such as personality traits were discarded for potential lack of accumulated evidence.

The psychological and cognitive factors selected for the review were the following: a) objective knowledge of the symptoms of acute coronary syndrome (patients' correct recognition of the symptoms in a test-like questionnaire: e.g., "Is chest pain a symptom of a heart attack?"); b) subjective knowledge of the symptoms of acute coronary syndrome (patients' self-reported knowledge of the symptoms before the cardiac event, e.g., "Did you know the symptoms of a heart attack?"); c) attribution of the symptoms to a cardiac vs. another event; d) anxiety in response to symptoms; e) perceived seriousness of the symptoms; f) concern/worry for troubling others; g) fear in response to symptoms; h) fear from the potential consequences of the symptoms or disease; i) embarrassment/shame in asking for help.

Inclusion criteria

We included quantitative studies with adult participants that measured prehospital delay and reported its relationship with any of the psychological/cognitive factors listed above. We did not select studies based on the exact definition of the prehospital delay interval but instead we followed previous work (Mackay et al., 2014), and recorded and analyzed the definition used in each study. During the process of review, we came across studies that reported several prehospital delay intervals. In these cases, we decided to extract the decision delay interval if available (time elapsed from symptom onset to the decision to seek medical attention) or the interval closest to it, because it is the interval that should be most influenced by psychological/cognitive and not external (e.g., transportation) factors.

There were no restrictions regarding the specific study design or language in which the paper was written. Cross-sectional, longitudinal, and experimental/intervention research was considered as long as the relationships of interest were reported. We considered for inclusion both studies with patients who retrospectively reported on their prehospital delay and studies with healthy populations who reported hypothetical prehospital delay in a hypothetical scenario (e.g., participants had to think about how they would feel and react). Abstracts in languages not spoken by the research team were screened using translate.google.com.

Exclusion criteria

We excluded reviews, qualitative studies, editorials, opinion articles, conference proceedings or similar publications not reporting data from original empirical studies.

Article selection

The citations were managed in the software Refworks (www.refworks.com). After removing duplicates, the titles of all publications identified in the search were screened by one author who discarded publications when the title clearly suggested that the article would not meet inclusion criteria (e.g., a publication on an unrelated topic or a systematic review). Subsequently, the abstracts of the remaining publications were independently screened by two reviewers who resolved disagreements through discussion or revision of the full text. Two reviewers independently reviewed the full texts of the selected abstracts. After an initial sample of articles was identified for inclusion, their reference lists were thoroughly reviewed to identify additional articles of relevance. The review procedure was repeated with the studies identified from the reference lists.

Data extraction

One researcher extracted the data from the selected studies using a predefined data sheet according to the review preregistration protocol in PROSPERO and another author thoroughly checked it. Disagreements were resolved through discussion. Information was extracted about study and publication characteristics and regarding the relationships of interest (see Table 1 and OSF:10.17605/OSF.IO/4MB3D). Regarding the relationships of interest, we recorded the definitions and scales/items used to measure the variables, the statistical result reported (and its effect size when available), whether it was reported as significant, and whether the statistical results were extracted from simple or adjusted (for covariates) analyses. Whenever necessary we contacted authors to request additional information.

Study risk of bias

The risk of bias for each study was assessed with the NIH Quality Assessment Tool for Observational, Cohort, and Cross-Sectional Studies (National Institutes of Health 2015). We chose this tool because of its suitability for cross-sectional studies, which we expected to form the majority of the study sample. In addition, four items were added to the NIH tool to evaluate the quality of the prehospital delay measurement, following similar procedures for research on early cancer diagnosis (Weller et al., 2012). These items were: (a) Whether prehospital delay was clearly defined and measured according to the definition stated by the authors; (b) Whether the time elapsed between the diagnosis of acute coronary syndrome and participation in the study/interview was reported, and if yes, if it was reasonable according to our expert judgment (e.g., a reasonable time would be two weeks or fewer after the cardiac event (i.e., when memory is fresh) vs. one year or more after the cardiac event); (c) Whether patient-reported data on prehospital delay was cross-checked with other sources (e.g., hospital records, family members, etc.); (d) Whether data analysis was described in full, including how and why data are categorized, how missing and incomplete data were managed, and how outliers at both ends of the spectrum were accounted for.

The highest possible score in the quality assessment was 18 (14 NIH items + 4 prehospital delay items). We defined cut-offs regarding what was considered low, medium, and high risk based on our judgment regarding the relative and not absolute risk of bias

Table 1
Best evidence synthesis procedure.

Study inclusion criteria:

- Studies that measure the relationships of interest as per study protocol.

Best evidence synthesis exclusion criteria:

- Studies with high risk of bias: ≤9 points on the methodological quality assessment (per pre-registered protocol).
- Studies with very small sample sizes (<73) able to detect only effect sizes>R^2 = 0.10, based on analyses with G*power, assuming alpha = 0.05, power = 0.80 (post hoc).

Best evidence synthesis conclusion criteria:

- Strong evidence: Consistent evidence provided by 70% or more of the low risk studies, provided that a sufficient number of studies is available.
- Moderate evidence: Consistent evidence provided by 60% or more of the medium and low risk studies, provided that a sufficient number of studies is available.
- Limited evidence: Consistent evidence provided by less than 60% of the medium and low risk studies available, or a very small number of studies available.
- Conflicting evidence: Inconsistent findings in multiple studies.
- No evidence: No studies of low or medium risk were located.

Clinical significance:

- In case of moderate or strong evidence: Description (e.g., median difference in minutes of prehospital delay) and categorization (low, medium, strong) of effect sizes whenever possible for the low risk studies with positive findings.

of the studies. In particular, we considered a wide range of scores as low risk because all studies meeting the inclusion criteria were cross-sectional and thus no study received more than 14 points. In contrast, we considered a conservative threshold regarding what is considered high risk because all studies were of low evidence level. Thus, we considered a score of 12 (highest quartile) or more as low risk of bias, a score of 10 or 11 (2nd and 3rd quartiles) as medium risk, and a score of 9 or less (lowest quartile) as high risk. Two reviewers evaluated the studies independently and the disagreements were resolved by discussion with a third reviewer.

Analysis

We aimed to conduct a meta-analysis of the relationships of interest. However, despite the relatively high homogeneity of the measures used across studies and the large number of studies available, the very diverse analytical and reporting practices of authors precluded any meaningful quantitative synthesis (see more details in the results section). Even considering studies separately as a function of whether prehospital delay was dichotomized for analysis or not, authors reported very diverse statistics that could not be meaningfully combined (e.g., differences in means, in log-transformed means, in medians, in geometric means, standardized beta coefficients, unstandardized B coefficients, ORs, etc.) and often no sufficient detail regarding transformations was provided.

Instead, we conducted a qualitative "best evidence synthesis" (Slavin, 1995). This method is recommended for cases where meta-analysis is not meaningful and constitutes a critical qualitative summary of the available evidence, taking into account strict inclusion criteria, the methodological quality of the evidence, and the effect sizes. Following recent applications of the method (Slavin, 1995; van Deutekom et al., 2017; de Vries et al., 2018; Asker et al., 2018), we adapted the best evidence synthesis procedure to the current research and developed a procedure for evidence evaluation described in Table 1. The evidence for each relationship of interest was classified as strong, moderate, limited, conflicting, or no evidence based on criteria specified in Table 1. In case of moderate or strong evidence, the clinical significance of the effects was determined from the effects sizes and/or the practical significance of the documented differences (e.g., median difference in minutes of prehospital delay).

In addition, we conducted sensitivity analysis exploring how conclusions would change if we considered whether the effects were obtained from simple (unadjusted) analyses or from analyses adjusted for important covariates (e.g., demographics, other psychological factors). This is important to consider because some of the effects of interest may be mediated by other more proximal predictors and thus could be significant in unadjusted but not in adjusted analyses.

Finally, we also explored how the results vary according to the definition of prehospital delay and the continent where the study was conducted. We considered whether authors measured prehospital decision delay (i.e., the time elapsed from symptom onset to the decision to seek medical attention, the interval most likely to be influenced by psychological or cognitive factors) or another definition of prehospital delay (e.g., the time elapsed from symptom onset to arrival at the hospital, to first medical contact, or to first treatment). The grouping by continent was done based on cultural and socio-economic similarity and the available number of studies. The three groups created were: Asia/Africa (there was only one study from Africa, in particular Egypt), America/Australia, and Europe.

Results

Fig. 1 shows a flow diagram of the selection process and Table 2 presents the basic characteristics of the included studies. In some of the included publications, the relationships of interest were examined only by separating the total study sample in several groups (e.g., based on demographics such as country or gender of the participants) and the relationships of interest were not reported in the whole sample. This was the case for five publications that separated the total study sample based on gender, one based on race, and one based on country. To be able to summarize the evidence in accordance with the pre-planned procedure, and to increase homogeneity of the results keeping up with the common one-country-per-study pattern, we have considered each sub-sample as a separate study (a result that is indicated in the first column of Table 2).

A total of 48 publications were eligible according to the criteria. After considering samples separated by country, gender, or race as different studies, these 48 publications resulted in 57 studies from 23 different countries. All studies were cross-sectional studies with patients in which prehospital delay and the psychological/cognitive factors were measured retrospectively after the cardiac event had taken place. No longitudinal, experimental, or cross-sectional studies with healthy samples fulfilled the inclusion criteria. The studies included 17,501 participants overall; 46 studies (81%) included pa-

Table 2
Basic characteristics of the included studies.

First author	Pub. year	Country	Patients' diagnosis	Sample size	% females	Average age	Definition of prehospital delay	Was delay dichotomized?	Cutoff in minutes	Psychological /cognitive measures	Risk of bias	
											NIH+additional items	TOTAL score
Dracup et al. (1997)	1997	Australia	Both	317	Not speci-fied	63	to arrival at the hospital	Yes	120	**A, PS, W, FC, E**	(9 + 4) Low risk	13
Bray et al. (2015)	1997	USA	STEMI	277	28	58	to arrival at the hospital	Yes	60	KS, A, PS, W, FC, E	(8 + 4) Low risk	12
McKinley et al. (2000)	2000	Australia	Both	147	34	62	to arrival at the hospital	No		KS, A, PS, W, FC, E	(7 + 4) Medium risk	11
O'Carroll et al. (2001)	2001	UK	Both	72	31	63	to arrival at the hospital	Yes	240	**A**	(7 + 4) Medium risk	11
Carney et al. (2002)	2002	UK	Both	62	11%	57	to the decision to seek medical attention	Yes	60	**A**	(7 + 3) Medium risk	10
Kentsch et al. (2002)	2002	Germany	STEMI	739	30	65	to the decision to seek medical attention	Yes	60	**A, ANX, PS, W, FS**	(9 + 2) Medium risk	11
Johansson et al. (2004)	2004	Sweden	Both	381	43	62	to the decision to seek medical attention	Yes	60	A, PS	(9 + 2) Medium risk	11
McKinley et al. (2004)	2004	USA	Both	191	50	61	to arrival at the hospital	No		**KO, A, ANX, PS**, W, FC, E	(8 + 4) Low risk	12
McKinley et al. (2004)	2004	South Korea	Both	127	23	60	to arrival at the hospital	No		**KO**, A, ANX, PS, W, FC, E	(8 + 4) Low risk	12
McKinley et al. (2004)	2004	Japan	Both	136	20	61	to arrival at the hospital	No		KO, A, ANX, PS, W, FC, E	(8 + 4) Low risk	12
McKinley et al. (2004)	2004	UK	Both	141	23	61	to arrival at the hospital	No		KO, A, ANX, PS, W, FC, E	(8 + 4) Low risk	12
Ottesen et al. (2004)	2004	Denmark	Both	240	31	68	time from symptom onset to hospital presentation	No		A	(8 + 49 Low risk	12
Walsh et al. (2004)	2004	Ireland	Both	61	28	62	to arrival at the hospital (doctor's estimate)	No		**ANX**	(8 + 4) Low risk	12
Wu et al. (2004)	2004	China	Both	102	23,5	62	to the decision to seek medical attention	No		**A**	(8 + 2) Medium risk	10
Al-Hassan and Omran (2005)	2005	Jordan	Both	79	31	52	to the decision to seek medical attention	Yes	60	A	(9 + 2) Medium risk	11
Fukuoka et al. (2005)	2005	Japan	Both	145	13	62	to arrival at the hospital	No		**KS, A**, ANX, PS, W, FC, E	(9 + 4) Low risk	13
Morgan (2005)	2005	USA	Both	98	37	63	to the decision to seek medical attention	No		**ANX, PS**	(9 + 3) Low risk	12
Moser et al. (2005)	2005	USA	Both	194	49	60	to arrival at the hospital	No		KO, A, ANX, PS, W, FC, E	(7 + 4) Medium risk	11
Quinn (2005)	2005	USA	Both	100	41	64	to the decision to seek medical attention	No		**A**	(9 + 4) Low risk	13
Taylor et al. (2005)	2005	Australia	diverse diagnoses (chest pain)	150	40	52	to the decision to seek medical attention	Yes	180	KS, A, PS, W, FC, E	(10+4) Low risk	14
Noureddine et al. (2006)	2006	Lebanon	Both	204	28	62	to arrival at the hospital	No		KO, A, PS, W, FC	(9 + 3) Low risk	12
Khan et al. (2007)	2007	Pakistan	Both	720	22	54	to arrival at the hospital	Yes	360	**KO**	(7 + 3) Medium risk	10

(*Continued on next page*)

Table 2 (*Continued*).

First author	Pub. year	Country	Patients' diagnosis	Sample size	% females	Average age	Definition of prehospital delay	Was delay dichotomized?	Cutoff in minutes	Psychological /cognitive measures	Risk of bias	
											NIH+additional items	TOTAL score
Lovlien et al. (2007) (Female sample)	2007	Norway	Both	149	100	61	to the decision to seek medical attention	Yes	60	A	(9 + 2) Medium risk	11
Lovlien et al. (2007) (Male sample)	2007	Norway	Both	384	0%	59	to the decision to seek medical attention	Yes	60	**A**	(9 + 2) Medium risk	11
McSweeney et al. (2007)(Female sample)		USA	Both	509	100	63	to receiving treatment	Yes	120	**A**	(8 + 2) Medium risk	10
McSweeney et al. (2007) (Male sample)	2007	USA	Both	500	100	67	to receiving treatment	Yes	120	**A**	(8 + 2) Medium risk	10
Perkins-Porras et al. (2008)	2008	UK	Both	177	22	60	to arrival at the hospital	Yes	130	**A**	(9 + 4) Low risk	13
Khraim et al. (2009) (Female sample)	2009	Jordan	Both	24	100	about 55	to the decision to seek medical attention	No		KS, A, ANX, PS, W, E	(10+3) Low risk	13
Khraim et al. (2009)(Male sample)	2009	Jordan	Both	110	0	about 55	to the decision to seek medical attention	No		**KS, A, ANX, PS, W, E**	(10+3) Low risk	13
Perkins-Porras et al. (2009)	2009	UK	Both	228	22	59	to the decision to seek medical attention	Yes	60	**A**	(8 + 2) Medium risk	10
Zegrean et al. (2009)	2009	USA and Canada	Both	135	28	60	to the decision to seek medical attention	No		**PS**	(7 + 3) Medium risk	10
Herlitz et al. (2010)	2010	Sweden	Both	1879	25	about 65	to the decision to seek medical attention	Yes	60	**A, ANX, FS**	(9 + 4) Low risk	13
Lesneski (2010)	2010	USA	Both	105	31	64	to arrival at the hospital	No		KS, A, ANX, PS, W, FC, E	(10+4) Low risk	14
Gouveia Vde et al. (2011)	2011	Brasil	STEMI	115	31	the majority above 60	to admission at the hospital	Yes	720	A	(5 + 2) High risk	7
Damasceno et al. (2012)	2012	Brasil	Both	100	29	59	to the decision to seek medical attention	No		A, PS	(8 + 2) Medium risk	10
Hwang and Jeong (2012)	2012	South Korea	Both	165	43	74	to arrival at the hospital	Yes	360	**A**	(7 + 3) Medium risk	10
Kirchberger et al. (2012)	2012	Germany	Both	2243	25	61	to first examination by a physician	Yes	120	**A**	(8 + 3) Medium risk	11
Momeni et al. (2012)	2012	Iran	STEMI	162	35	60	to arrival at the hospital	Yes	120	**A**, ANX, PS	(7 + 3) Medium risk	10
Gao and Zhang (2013)	2013	China	Both	119	28	64	to initiation of treatment	Yes	360	**KS**, A	(5 + 1) High risk	6
McKee et al. (2013)	2013	Ireland	Both	1894	28	63	to arrival at the hospital	No		KO, A	(10+3) Low risk	13
Vidotto et al. (2013)	2013	Italy	Both	929	0	about 60, NR	to the decision to seek medical attention	No		A	(8 + 2) Medium risk	10

(*Continued on next page*)

Table 2 (*Continued*).

First author	Pub. year	Country	Patients' diagnosis	Sample size	% females	Average age	Definition of prehospital delay	Was delay dichotomized?	Cutoff in minutes	Psychological /cognitive measures	Risk of bias	
											NIH+additional items	TOTAL score
Al-Hassan (2014)	2014	Oman	Both	112	18	59	to arrival at the hospital	Yes	180	**A, FC**	(8 + 2) Medium risk	10
Abed et al. (2015)	2015	Jordan	Both	299	20	about 55	to arrival at the hospital	No		**A, ANX, PS**	(8 + 4) Low risk	12
Allana et al. (2015) (Female sample)	2015	Pakistan	Both	116	100	56	"prehospital delay" undefined	No		**KS**, A, ANX, PS, W, FS	(8 + 1) High risk	9
Allana et al, (2015) (Male sample)	2015	Pakistan	Both	133	0	56	"prehospital delay" undefined	No		**KS, A, ANX**, PS, W, FS	(8 + 1) High risk	9
Bray et al. (2015)	2015	Australia	Both	199	32	62	to arrival at the hospital	Yes	120	**A, ANX, PS, W**, FC, E	(9 + 3) Low risk	12
Ghazawy et al. 2015)	2015	Egypt	Both	207	25	about 58	to arrival at the hospital	Yes	120	**A**	(7 + 2) High risk	9
Albarqouni et al. (2016)	2016	Germany	STEMI	486	25	62	to first ECG in the clinic	No		**KO**	(8 + 2) Medium risk	10
Darawad et al. (2016)	2016	Jordan	Both	160	53	53	to arrival at the hospital	No		KO	(9 + 1) Medium risk	10
Kim et al. (2017) (Female sample)	2017	South Korea	STEMI	64	100	71	to arrival at the hospital	Yes	120	KS	(7 + 4) Medium risk	11
Kim et al. (2017) (Male sample)	2017	South Korea	STEMI	286	0	59	to arrival at the hospital	Yes	120	KS	(7 + 4) Medium risk	11
Petrova et al. (2017)	2017	Spain	Both	102	16	58	to the decision to seek medical attention	Yes	60	KO, A, ANX, PS, W, FC, E	(10+4) Low risk	14
Mesas et al. (2018)	2018	Brazil	STEMI	50	36	59	first medical contact	Yes	60	PS	(8 + 3) Medium risk	11
Sederholm Lawesson et al. (2018) (Female sample)	2018	Sweden	STEMI	109	100	70	to first medical contact	No		**PS, W**	(7 + 4) Medium risk	11
Sederholm Lawesson et al. (2018) (Male sample)	2018	Sweden	STEMI	340	0	65	to first medical contact	No		**PS, W**	(7 + 4) Medium risk	11
Venkatesan et al. (2018)	2018	India	Both	93	14	>65% above 50	time from symptom onset to arrival at the hospital	Yes	120	**K, PS**	(6 + 2) High risk	8

Note: The design of all studies is cross-sectional. KO= knowledge of symptoms-objective measure, KS= knowledge of symptoms-subjective measure, *A*=Attribution of symptoms to a cardiac event, ANX=anxiety in response to symptoms, PS=Perceives seriousness of symptoms, *W*=Worry about disturbing others, FS=Fear of symptoms, FC= Fear of consequences, *E*=Embarrassed to seek help. ***In bold, those that reached statistical significance according to the original study authors (*p* < 0.05)**. STEMI=ST-elevation myocardial infarction. Both=both STEMI and non-STEMI. In the article by Ottesen et al. (2004) (Ottesen et al., 2004) decision delay was available for a much smaller sample, so time to arrival at the hospital was extracted instead.

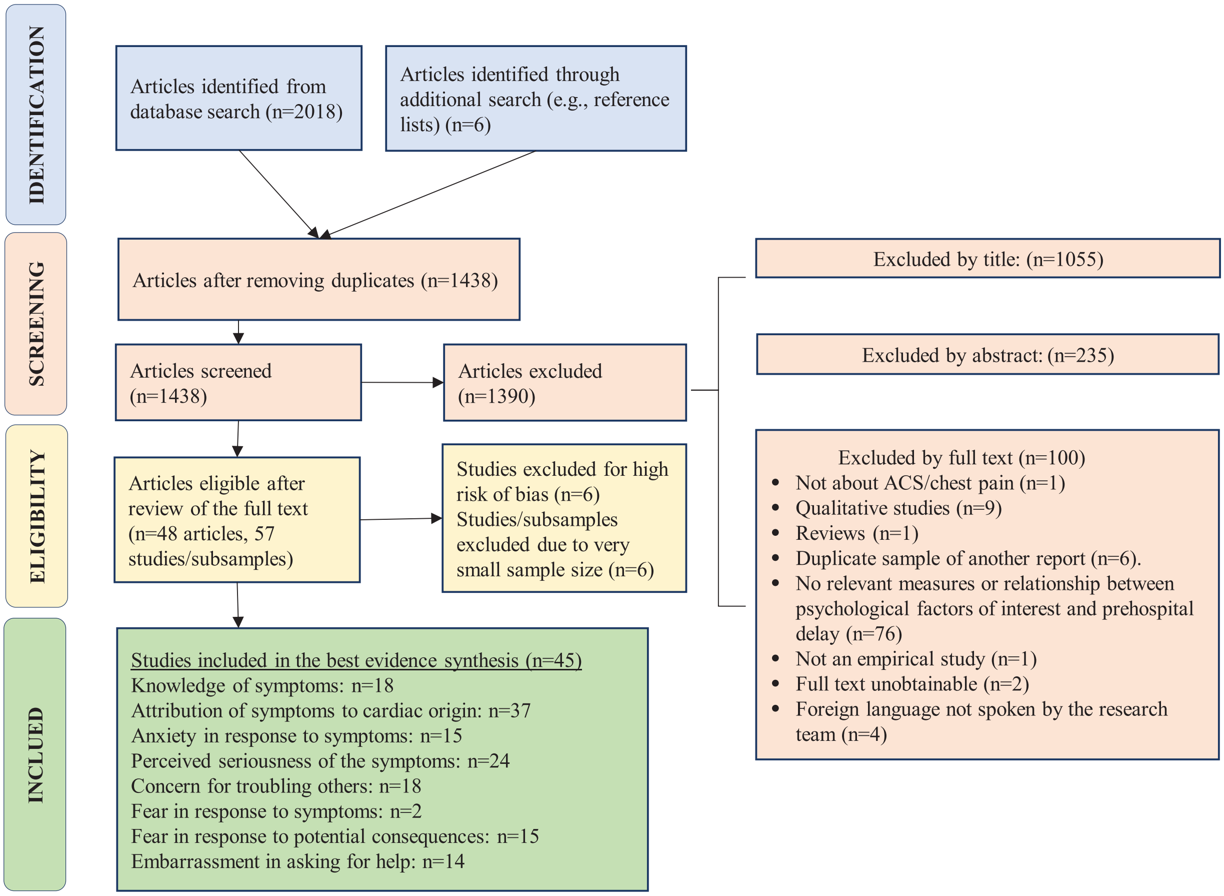

Fig. 1. Flow diagram of the search process.

tients with both STEMI (i.e., ST-elevation myocardial infarction) and non-STEMI; 10 studies (17%) included patients with STEMI only; and 1 study (2%) included patients with chest pain regardless of final diagnosis. Seventeen studies (30%) were conducted in countries in America or Australia, 21 (37%) in Asia/Africa, and 19 (33%) in Europe. The countries most often represented were USA (9 studies), Jordan (5 studies), UK (5 studies), South Korea (4 studies), and Sweden (4 studies). Regarding methodological quality, 6 studies (11%) received high risk of bias rating, 28 (49%) medium, and 23 (40%) low.

In all the studies, the starting point for the prehospital delay interval was defined as the moment of symptom onset. In most studies the end point of the prehospital delay interval was arrival at the hospital as estimated by the patient, $n = 24$ (42%), or the decision to seek medical attention $n = 19$ (33%). The remaining studies, $n = 14$ (25%), used other very diverse definitions included in Table 2. In 51% ($n = 29$) of the studies the measure of prehospital delay was dichotomized for analysis (delay vs. no delay group). Among the most frequent cut-offs used to define delay were 60 min ($n = 10$, 34%) or 120 min. ($n = 10$, 34%). The rest of studies ($n = 28$, 49%) analyzed prehospital delay as a continuous variable, and the majority ($n = 22$, 78%) employed some transformation to eliminate the typical positive skew of the variable.

Best evidence synthesis

Table 3 provides a summary of the best evidence synthesis results and Table 4 displays the results as a function of type of analysis, prehospital delay definition, and continent. Despite a large number of available studies, we found limited evidence for a relationship between prehospital delay and symptom knowledge, concern for troubling others, and being embarrassed to seek help. Two available studies suggest that fear in response to symptoms is related to shorter prehospital delay. However, the evidence was judged as limited due to the small number of studies. Evidence regarding the relationship between fear in response to the potential consequences of the disease and prehospital delay was limited and conflicting (see Table 3).

In contrast, we found strong evidence that patients who attribute their symptoms to a cardiac event have shorter prehospital delay (70% of low risk studies finding a significant relationship). Effect sizes from the low risk studies suggest an important clinical difference (e.g., a difference of 2 h in prehospital delay between those who attribute symptoms correctly vs. incorrectly, and halved odds of delay in studies using a cut-off for prehospital delay, see Table 3 for details). However, 32% of good-quality (medium and low risk) studies did not demonstrate a significant relationship so true effect sizes are likely smaller. Overall, 15 studies investigated decision delay and 22 studies used other definitions of prehospital delay (see Table 4). A similar number of studies was conducted in America/Australia (13 studies), Asia/Africa (11 studies), and Europe (13 studies), and the percentage showing significant results was similar.

In addition, we found evidence that patients who were more anxious when symptoms started had shorter prehospital delay, again with effect sizes of clinical importance, (e.g., a difference of about 2 h in prehospital delay between those who report anxiety vs. no anxiety, and halved odds of delay in studies using a cut-off for prehospital delay, see Table 3 for details). However, 40% of good-quality (medium and low risk) studies did not demonstrate a significant relationship, so the strength of the evidence was judged as borderline moderate, and true effect sizes are very

Table 3
Summary of results: Number and percentage of significant studies and conclusions.

	Study selection				Study synthesis				
	Number of studies excluded		Studies included		Studies reporting a significant relationship			Conclusion	Effect sizes
	High risk of bias	Low sample size	Number	Sample size:mean, median (min, max)	Total	Low risk only	Direction of relationship		
Knowledge of symptoms (objective)	1 Venkatesan et al. (2018)	0	5	672, 486 (102, 1894)	2/5 (40%)	0	Better knowledge, shorter prehospital delay.	Limited evidence	–
Knowledge of symptoms (subjective)	3 Allana et al. (2015) (F.) Allana et al. (2015) (M.) Kirchberger et al. (2012)	2 Khraim et al. (2009) Kim et al. (2017)	13	170, 147 (105, 286)	4/13 (31%)	4/10 (40%)	Better knowledge, shorter prehospital delay	Limited evidence	–
Knowledge of symptoms (objective OR subjective)	4 Allana et al. (2015) (F.) Al-Hassan (2014)(M.) Momeni et al. (2012) Sederholm Lawesson et al. (2018)	2 Khraim et al. (2009) Kim et al. (2017)	18	309, 150 (102, 1894)	6/18 (33%)	4/11 (36%)	Better knowledge, shorter prehospital delay.	Limited evidence	–
Attribution of symptoms to cardiac event	6 Allana et al. (2015) (F.) Allana et al. (2015) (M.) Hwang and Jeong (2012) Ghazawy et al. (2015) Gouveia Vde et al. (2011) Mesas et al. (2018)	3 Khraim et al. (2009) Kentsch et al. (2002) O'Carroll et al. (2001)	37	378, 177 (79, 2243)	25/37 (68%)	14/20 (70%)	Attributed to a cardiac event, shorter prehospital delay.	Strong evidence	Mean standardized beta coefficient 0.33 (based on 4 studies); a median difference of 2 h (7 studies); mean OR for delay of 0.45 (3 studies).

(*Continued on next page*)

Table 3 (*Continued*).

	Study selection				Study synthesis				
	Number of studies excluded		Studies included		Studies reporting a significant relationship			Conclusion	Effect sizes
	High risk of bias	Low sample size	Number	Sample size:mean, median (min, max)	Total	Low risk only	Direction of relationship		
Anxiety in response to symptoms	2 Allana et al. (2015) (F.) Allana et al., (2015) (M.)	2 Khraim et al. (2009) Wu et al. (2004)	15	308, 145 (98, 1879)	9/15 (60%)	7/13 (54%)	Stronger anxiety, shorter prehospital delay.	Moderate evidence	Standardized beta coefficient of 0.29 (1 study); a median difference of 1.85 h (2 studies); mean OR for delay 0.53 (2 studies); F value of 3.57 (1 study); Spearman rho of 0.23 (1 study).
Perceived seriousness of symptoms	3 Allana et al. (2015) (F.) Allana et al. (2015) (M.) Venkatesan et al. (2018)	2 Khraim et al. (2009) (Mesas et al. (2018)	24	204, 147 (98, 739)	18/24 (75%)	9/15 (60%)	More perceived seriousness, shorter prehospital delay.	Moderate evidence	Standardized beta coefficient of 0.39 (2 studies); a median difference of 2.1 h (4 studies); mean OR for delay 0.56 (3 studies); mean correlation 0.27 (2 studies).
Concern for troubling others	2 Allana et al. (2015) (F.) Allana et al. (2015) (M.)	1 Khraim et al. (2009)	18	207, 147 (102, 739)	9/18 (50%)	6/13 (46%)	More concern for troubling others, longer prehospital delay.	Limited evidence	–
Fear in response to symptoms	2 Allana et al. (2015) (F.) Allana et al. (2015) (M.)	0	2	NA, NA (739, 1897)	2/2 (100%)	1/1 (100%)	More fear, shorter prehospital delay.	Limited evidence (small number of studies)	–
Fear in response to potential consequences	0	0	15	170, 147 (102, 317)	3/15 (20%)	2/12 (17%)	One study: more fear, shorter prehospital delay. Three studies: more fear, longer prehospital delay.	Limited and conflictive evidence	–
Embarrassment in asking for help	0	1 Khraim et al. (2009)	14	167, 145 (102, 317)	5/14 (36%)	4/12 (33%)	More embarrassment/ shame, longer prehospital delay.	Limited evidence	–

Note: Conclusions are based on the criteria in Table 1. Study risk refers to the results of the methodological quality assessment. Effect size are from low risk studies reporting significant effects. F.=female sample. M.=male sample.

Table 4
Sensitivity analyses: number and percentage of significant results according to study characteristics.

		Significant results according to:						
		Analysis:		Prehospital delay definition:		Continent:		
	Number of studies included	Unadjusted	Adjusted	Decision delay	Other	Americas/Australia	Asia/Africa	Europe
Knowledge of symptoms (objective)	5	1/1 (100%)	1/4 (25%)	0/1 (0%)	2/4 (50%)	0	1/2 (50%)	1/3 (33%)
Knowledge of symptoms (subjective)	13	3/10 (30%)	1/3 (33%)	2/4(50%)	3/11 (27%)	1/6 (17%)	3/6 (50%)	0/1 (0%)
Knowledge of symptoms (objective OR subjective)	18	4/11 (36%)	2/7 (29%)	1/3 (33%)	5/15 (33%)	1/6 (17%)	4/8 (50%)	1/4 (25%)
Attribution of symptoms to cardiac event	37	9/16 (56%)	16/21 (76%)	8/15 (53%)	17/22 (77%)	9/13 (69%)	7/11 (64%)	9/13 (69%)
Anxiety in response to symptoms	15	9/13 (69%)	0/2 (0%)	4/5 (80%)	5/10 (50%)	4/5 (80%)	2/6 (33%)	3/4 (75%)
Perceived seriousness of symptoms	24	9/13 (69%)	9/11 (82%)	7/8 (88%)	11/16 (69%)	9/11 (82%)	4/7 (57%)	5/6 (83%)
Concern for troubling others	18	3/11 (27%)	6/7 (86%)	3/4 (75%)	6/14 (43%)	4/8 (50%)	2/5 (40%)	3/5 (60%)
Fear in response to symptoms	2	1/1 (100%)	1/1 (100%)	2/2 (100%)	0	0	0	2/2 (100%)
Fear in response to potential consequences	15	3/14 (21%)	0/1 (0%)	0/2 (0%)	3/13 (23%)	2/8 (25%)	1/5 (20%)	0/2 (0%)
Embarrassment in asking for help	14	4/12 (33%)	1/2 (50%)	2/3 (66%)	3/11 (27%)	3/8 (38%)	2/4 (50%)	0/2 (0%)

likely smaller. Overall, 5 studies investigated decision delay and 10 studies used other definitions of prehospital delay (see Table 4). A similar number of studies was conducted in Asia/Africa (5 studies), America/Australia (6 studies), and Europe (4 studies). The proportion reporting significant results was lowest for Asia/Africa (Table 4).

Finally, there was moderate evidence that patients who perceived their symptoms as serious had shorter prehospital delay, with effect sizes of clinical importance similar to those of the other factors, (e.g., a difference of about 2 h in prehospital delay between those who perceive symptoms as serious vs not, and halved odds of delay in studies using a cut-off for prehospital delay, see Table 3 for details). In this case, 25% of good-quality (medium and low risk) studies did not report a significant relationship, so the evidence was judged as moderate and true effect sizes are likely smaller. Overall, 8 studies investigated decision delay and 16 studies used other definitions of prehospital delay (see Table 4). The majority of studies investigating the relationship between symptom attribution and prehospital delay were conducted in America/Australia (11 studies), with fewer studies from Asia/Africa (7 studies) and Europe (6 studies). The proportion reporting significant results was lowest for Asia/Africa (Table 4).

The sensitivity analysis showed that the majority of results were based on unadjusted analysis but the analysis did not show further differences in the significance of the effects as a function of covariate adjustment (Table 4). There were no other notable differences in the results as a function of prehospital delay definition or continent (Table 4).

Discussion

Summary of findings. This is the first systematic review focused on the relationship between psychological and cognitive factors and prehospital delay in the context of acute coronary syndrome. This review builds on previous reviews of from 10 or more years ago (Moser et al., 2006; Khraim and Carey, 2009) and offers updated evidence based on a systematic pre-registered protocol to examine the relationships between nine factors and prehospital delay. Prehospital delay is associated with higher risk of mortality and health complications (Moser et al., 2006; Cullen et al., 2016; De Luca et al., 2004). Multiple studies from around the world have identified several demographic, clinical, and situational predictors of longer prehospital delay, such as female gender, older age, or history of chronic disease (Moser et al., 2006; Wechkunanukul et al., 2017; Khraim and Carey, 2009). However, the psychological or cognitive determinants of prehospital delay are crucial and add to this body or research because they can shed light on the mechanisms behind long delays that can be addressed in interventions and campaigns aiming to reduce prehospital delay. Unfortunately, with a few exceptions, the interventions conducted so far have had little success overall and it is not clear what differentiates successful from unsuccessful interventions (Farquharson et al., 2019; Mooney et al., 2012). This review aimed to shed light on what psychological or cognitive factors may be worth addressing in intervention design or further research aiming to reduce prehospital delay.

We found strong evidence that patients who attributed their symptoms to a cardiac event reported shorter prehospital delay. We also found moderate evidence that those patients who perceived symptoms as serious and felt anxiety reported shorter prehospital delay. The effect sizes reported speak of clinically significant differences in prehospital delay that could have a strong effect on treatment success and patient outcomes (e.g., a median difference of up to 1.5–2 h between patients who correctly attribute symptoms to a cardiac event vs. those who do not).

In contrast, we found no support for the relationships between prehospital delay and knowledge of symptoms, concern for troubling others, fear of the potential consequences, or embarrassment in seeking help. These factors have been suggested as potential barriers or facilitators to timely help-seeking in previous narrative reviews (Moser et al., 2006; Khraim and Carey, 2009). However, a systematic examination of the recent evidence taking into account study quality shows that these factors do not consistently show significant relationships with prehospital delay. In addition, fear of the potential consequences showed conflictive evidence. The contradictory findings are in line with the previously documented ambivalent role of fear in help-seeking behavior: it can act as a motivator for action and decrease time to help-seeking but it can also delay help-seeking due to denial or not wanting to face the consequences (Dubayova et al., 2010).

Implications for intervention design. The current results do not suggest addressing perceived social barriers to help-seeking as a promising strategy, because concerns for troubling others and feeling embarrassed to seek help have not shown consistent relationships with prehospital delay. Instead, the results show that those patients who attribute the experienced symptoms to a cardiac event, recognize that they are serious, and have an adequate emotional response to a threatening situation (i.e., anxiety) are those who delay less. Hence, results suggest that interventions should focus on helping patients recognize cardiac symptoms and raising awareness of the serious consequences of acute coronary syndrome. However, virtually all previous interventions provided education about symptoms but only a limited number of those were successful (Farquharson et al., 2019; Mooney et al., 2012). In addition, education about the serious consequences of acute coronary syndrome instead of the benefit of timely treatment could easily backfire by generating fear and inadequate coping strategies instead of timely action. Thus, we suggest that symptom attribution to a cardiac event and the perception of some level of threat (i.e., seriousness, anxiety) are the most important facilitators of timely help-seeking identified to date.

Finally, the importance of the attribution of symptoms to a cardiac event stands at odds with the results showing that symptom knowledge was largely unrelated to prehospital delay. On one hand, this suggests that knowing the symptoms of acute coronary syndrome may not guarantee correct attribution of symptoms when one is experiencing them. This could be because other factors mediate the relationship between knowledge and attribution (e.g., perceived risk: if patients do not perceive they are at risk of a heart condition, they may fail to attribute their symptoms to a cardiac event). On the other hand, it is important to keep in mind that all studies in this review were retrospective and the variables were reported only after the cardiac event had occurred. It is likely that patients learn about their condition during hospitalization or at least learn from their experience, thus retrospective studies are not adequate to examine the relationship between knowledge of symptoms and prehospital delay (e.g., due to memory biases). In the next section we give methodological recommendations regarding how this and other shortcomings in the study of prehospital delay could be overcome.

Methodological recommendations. This review confirms previous findings that the study of factors related to prehospital delay lacks a “consistent operational definition of prehospital delay duration, rendering comparisons and conclusions tenuous” (Mackay et al., 2014). The studies used diverse definitions of prehospital delay and the majority of them did not measure the different intervals within the total delay period (e.g., decision delay, health system delay). Exact definitions of what is considered as “symptom onset” were also rare. In order to better understand the causes for delays and make reliable comparisons across studies and populations (e.g., based on age or gender), it is vital that definitions and measurements in the literature are standardized (e.g., a standard cut-off of 60 min). In addition, in our opinion the decision delay interval offers the most sensitive and logical measure when it comes to studying the influence of psychological or cognitive factors, because patient decision making is unlikely to influence health system delays. A standardized definition and measurement would also help make valid comparisons across studies to identify how age, gender, or culture may influence the role of different psychological factors.

All studies meeting the inclusion criteria in this review were cross-sectional studies with patients who had recently experienced a cardiac event. Whereas these studies are certainly useful to study determinants of prehospital delay, they have major shortcomings that limit their validity. For instance, mild cognitive impairment and hence memory biases may be an issue (Saczynski et al., 2017), in addition to the fact that only survivors are included. This leaves out the most vulnerable population (i.e., those who may have waited too long and did not survive) and hence some important barriers to help-seeking may never come to light using this methodology. We believe that the study of prehospital delay in acute coronary syndrome could borrow insight from the study of early diagnosis in cancer, where recent advances have been made using hypothetical studies with healthy populations (Petrova et al., 2019; Donnelly et al., 2017). In this methodology, healthy persons are recruited and report how long they would wait to seek medical attention if they were experiencing certain symptoms, and this waiting time is investigated in relation to a number of psychological factors or perceived barriers. For instance, using such a methodology the relationship between symptom knowledge and prehospital delay could be investigated producing useful results. Another methodology that has been previously proposed includes the use of surrogates (e.g., family members) to represent the experiences of non-surviving patients (Khraim and Carey, 2009) but that is also rarely used. Although practically more difficult, prospective studies may also be feasible with populations at high risk of acute coronary syndrome, where psychological factors are measured at baseline and prehospital delay is assessed after a cardiac event occurs.

Limitations and future directions. The heterogeneity of reporting practices prevented us from conducting meta-analyses and exploring potentially important moderators of the relationships of interest (e.g., definition of prehospital delay, gender composition of the sample, age, country or health system characteristics, measurement properties, etc.). To overcome this limitation, we adapted an evidence synthesis procedure for which we needed to make a number of decisions regarding evidence quality. We conducted sensitivity analyses to explore the impact of these decisions; nevertheless, the used methodology relied on statistical significance, which can produce spurious results especially when studies are underpowered. We have made all data and results (including effect sizes where available) accessible to researchers who wish to consult specific information: OSF 10.17605/OSF.IO/4MB3D.

The sample of studies was highly international. Given the multitude of cultural and economic differences between the 23 countries represented, it would be interesting to explore cross-cultural differences in the influence of the different psychological factors on prehospital delay. Unfortunately, the current analytical approach was limited: a meta-regression analysis would have been better suited and more sensitive to detect cross-cultural differences. Nevertheless, the current results do suggest that anxiety in response to symptoms and perceived symptom seriousness could be less reliable predictors of delay in patients from Asian/African countries (there was overall a smaller proportion of studies reporting significant relationships in this group). Culture, and in particular the independent vs. interdependent self-construal could explain these findings. A more independent self-construal with a focus on individualism and autonomy is characteristic of Northern American and European countries, whereas a more interdependent self-construal with a focus on group goals is characteristic of Asian and African countries. Fukuoka and colleagues (Fukuoka et al., 2005) found that patients with more interdependent self-construal had longer prehospital delay times. One reason proposed by the authors to explain these differences was that individuals with more interdependent self-construal may be more likely to stay in their social roles and continue with their work or family obligations after symptoms have started. Such a tendency would explain why anxiety and perceived seriousness of symptoms may be less reliable predictors of prehospital delay in countries where a more interdependent self-construal is predominant. Future studies should investigate how culture shapes decision making during a cardiac event and how intervention strategies should take into account such cultural influences.

A limitation was that in several publications the effects of interest were reported separately for men and women, whereas in the majority of publications this was not the case. Gender comparisons were not among the goals of the current review but they would be essential to address in future research given the general differences in prehospital delay between men and women, and their potential causes. In particular, a review of 42 studies showed that women consistently had longer prehospital delays and that, unfortunately, these differences did not decrease over time (Nguyen et al., 2010). However, there are several differences in the factors related to prehospital delay between men and women. Perhaps the most often explored reason for this gender gap has been symptom presentation: women often report different or more “atypical” symptoms, although findings have been mixed (Chen et al., 2005). In addition, whereas in men longer prehospital delays were related to low education, symptom onset at home, not asking for help, having early musculoskeletal pain, or lack of consistency between expected and experienced symptoms, in women longer prehospital delay were related to older age, being single, having a history of MI, being alone during symptom onset, and not wanting to trouble anyone (Nguyen et al., 2010). Age is another factor consistently related to prehospital delay with older persons reporting longer prehospital delays; however, few studies have investigated the reasons behind these differences (Nguyen et al., 2010). In the current review, the study samples were relatively homogeneous in terms of age and only a few studies reported the relationships of interest as a function of gender; for this reason we could not reliably investigate if gender or age influenced the relationships studied. Given that women and older patients consistently report longer prehospital delays, it would be important to do more research on the possible psychological, cognitive, and social reasons for these differences.

All studies that met the inclusion criteria were cross-sectional and no studies of higher evidence category (e.g., longitudinal) or alternative designs (e.g., surveys with healthy populations measuring hypothetical prehospital decision delays) reported the relationships of interest. Thus, it is not possible to make any causal inferences. Although all studies were of the same evidence category (cross-sectional), we found that an independent evaluation of the risk of bias was essential. In particular, several publications had high risk of bias (due mostly to lack of detail). Finally, this review examined a pre-defined list of frequently investigated psychological and cognitive factors and did not cover all such factors or barriers of potential relevance, thus it is not an exhaustive examination of all psychological factors in relation to prehospital delay. Future research should continue to explore psychological determinants beyond those included in this review (e.g., individual differences in personality and cognitive traits (Petrova et al., 2017)).

Conclusion. This review was based on evidence from 23 countries, including both high and low income countries. We conclude that prehospital delay is consistently related to attribution of symptoms to a cardiac event, perceiving symptoms as serious, and feeling anxiety in response to symptoms. In contrast, prehospital delay was not consistently related to knowledge of symptoms, concern for troubling others, fear of the potential consequences, or embarrassment in seeking help. Despite the high homogeneity in the measures used, the variety of analytical and reporting practices prevented meta-analysis. Given the inconclusive and inconsistent findings of interventions aiming to reduce prehospital delay (Farquharson et al., 2019; Mooney et al., 2012), there is urgent need for a higher quality, methodologically-consistent research on psychological factors and barriers influencing prehospital delay. This could be achieved by agreeing on common guidelines for study design, procedure, and reporting (see an example on delays in cancer diagnosis (Weller et al., 2012)), that guide the choice of definition of prehospital delay and the analysis and reporting of results, among others. Such guidelines can help produce higher quality studies that would be informative for intervention design and theory advancement in the field of prehospital delay.

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