Reporting and Quality of Patient Preference Studies: A Systematic Literature Review in the Cardiovascular Domain

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Objective

- Although patient preference studies are gaining interest from drug developers, regulatory agencies and reimbursement decision makers, there is a lack of standards for study design and reporting.
- The aim of this literature review was to systematically assess reporting standards and quality of patient preference studies in the cardiovascular domain.

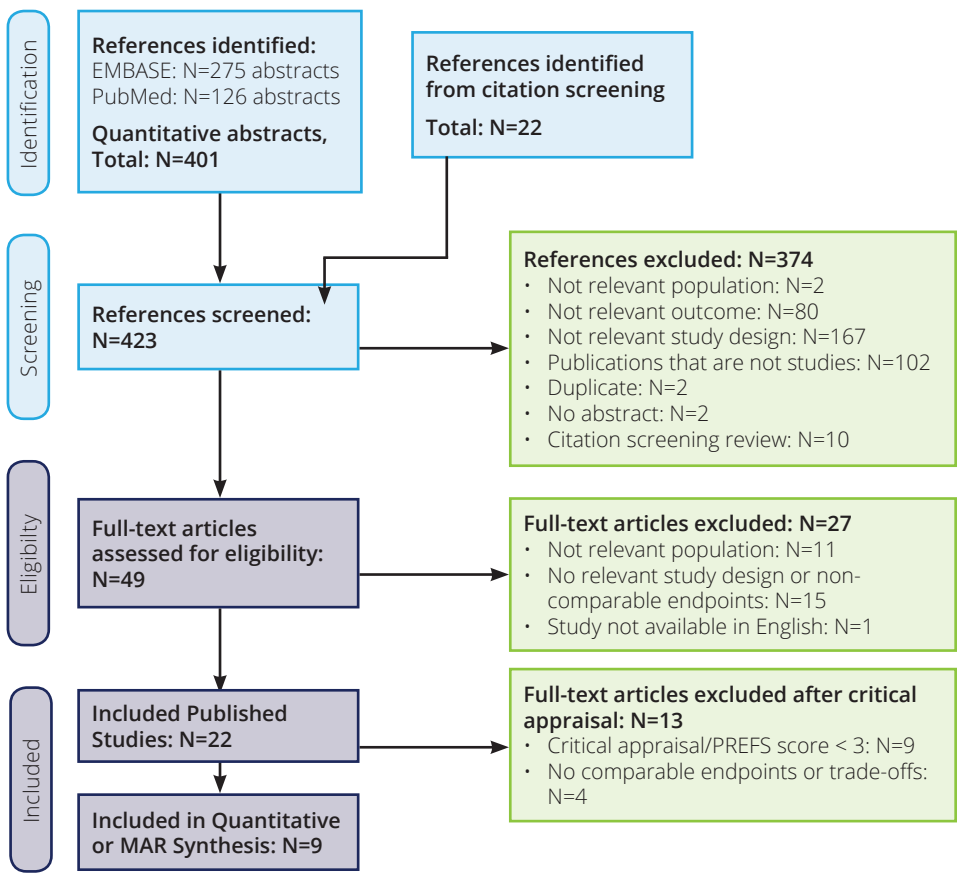
Methods

- Patient preference studies in cardiovascular indications were identified from PubMed and Embase databases (final search completed on September 7th, 2018) and backward citation screening, screened by title and abstract, and selected on pre-defined inclusion/exclusion criteria, followed by data extraction.
- Eligible studies were scored on a 5-point scale with a critical appraisal method developed for patient preference studies to assess the purpose of study, respondent sampling, explanation of methods, findings reported, and significance testing (PREFS).[1]
- Studies with a PREFS score ≥3 were reviewed for appropriateness for quantitative synthesis, where preferences on safety and efficacy endpoints were normalized to measure maximum acceptable risk (MAR).

Results

- 423 studies were screened and 22 studies met all inclusion/exclusion criteria (Figure 1).

Figure 1. PRISMA Diagram



- Attribute definitions varied between the studies. Seven studies reported cognitive interviews to assess patient understanding of the preference elicitation task. Fourteen studies reported internal consistency testing.
- The average PREFS was 2.5 in the 22 studies and 3.25 in 9 studies selected for MAR synthesis (Table 1).
  - Seven of these studies included major stroke/major bleeding attributes with varying MAR (2.20% to 7.62%) (Figure 2).
  - The MAR also varied across three studies with major stroke/MI attributes (Figure 3), with the highest MAR (7.62%; 11.00%) in a best-worst scaling (BWS) study and the lowest MAR (2.20%; 2.52%) in two discrete choice experiments (DCE).
  - MAR values were more similar for non-major stroke/major bleeding (0.23% to 1.07%; n=2 studies) and for moderate stroke/major bleeding (1.04% to 3.17%; n=5 studies) (Figure 2).

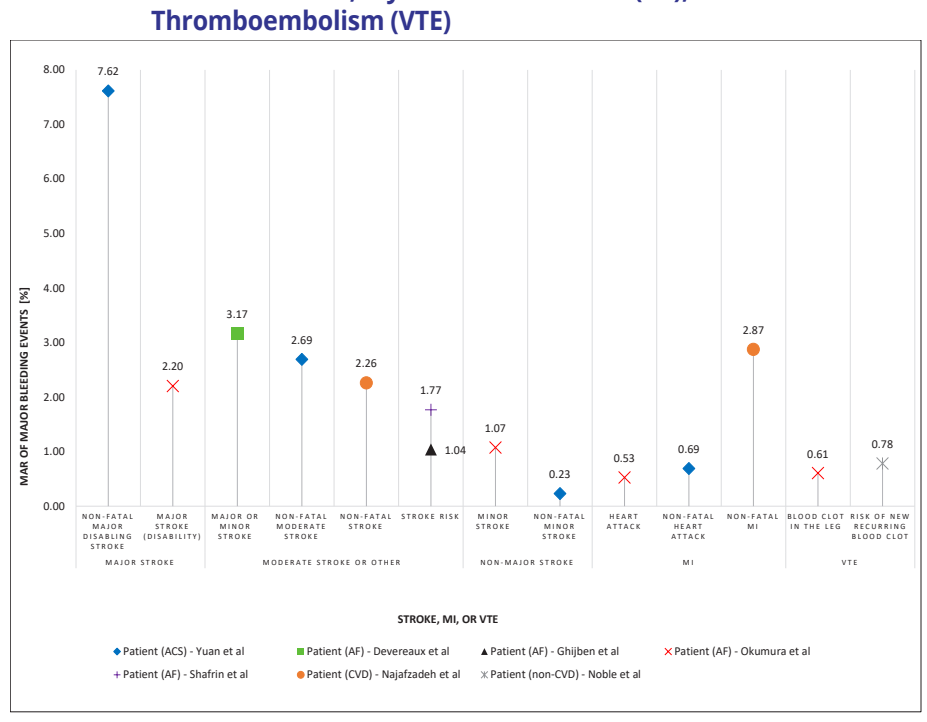
Table 1. Summary of Studies Included in Quantitative Synthesis

Study	Design	Population/ Indication/ Mean Age	Measurement Type	CVD Attributes	Description of Endpoints
Devereaux et al. 2001[2,*]	Probability tradeoff	Patients; AF N=124; mean age=53.3	MAR; MAB	• Maj. stroke • Maj. bleeding	• Maj. or min. stroke • Excess bleeding
Ghijben et al. 2014[3]	DCE	Patients; AF; N=76; mean age=47.9	MNL utility	• Min. bleeding • Maj. stroke	• Bleed risk • Stroke risk
Mühlbacher and Bethge 2015[4]	DCE	Patients; ACS; N=683; age not reported	MNL utility	• Death • MI	• Mortality risk • Risk of new MI
Noble et al. 2015[5]	DCE	Patients; VTE; N=100; mean age=53 GER; 61 UK	MNL utility	• VTE • Maj. bleeding • Min. bleeding	• Risk of new/recurrent blood clot • Risk of maj. blood clot (transfusion/hospitalization) • Risk of min. bleeding (bruising/ nose bleed)
Najafzadeh et al. 2014[6]	DCE	Patients; CVD; N=341; mean age=51.5	MNL utility: MAR	• Non-maj. stroke • Min. bleeding • Maj. bleeding • MI • Death • Death	• Non-fatal stroke • Min. bleeding • Maj. bleeding • Non-fatal MI • Cardiovascular death • Bleeding death
Okumura et al. 2015[7,*]	DCE	Patients; AF; N=609; mean age=63.3 (JPN); 65.6 (US)	Relative importance; MAR	• Minor stroke • Major stroke • Mod. bleeding • Maj. bleeding • VTE • All-cause-death	• Non-maj. stroke • Maj. stroke (disability) • Mod. bleeding (non-maj.) • Non-fatal maj. bleeding; non-fatal maj. bleeding (extracranial) • Blood clot in the leg (non-CNS, systemic embolism) • Death
Shafrin et al. 2016[8,*]	DCE	Patients; AF; N=401; mean age not reported	MNL utility	• Maj. stroke • Maj. bleeding	• Stroke risk • Maj. bleeding risk
Wanishayakorn et al. 2016[9]	DCE	Patients; CVD; N=370; mean age=51.2	MNL utility	• Stroke • MI	• Stroke reduction • MI reduction
Yuan et al. 2014[10]	BWS	Patients; ACS; N=479; mean age=65.1	Normalized importance	• Maj. stroke Non-maj. stroke • Maj. bleeding • Mod. bleeding • Non-fatal • Death	• Non-fatal maj. disabling stroke • Non-fatal maj. or mod. stroke; non-fatal maj. or min. stroke • Non-fatal maj. bleeding (with transfusion); non-fatal maj. bleeding (without transfusion) • Non-fatal mod. bleeding • Non-fatal severe HCP • Death

*Studies included results with HCPs

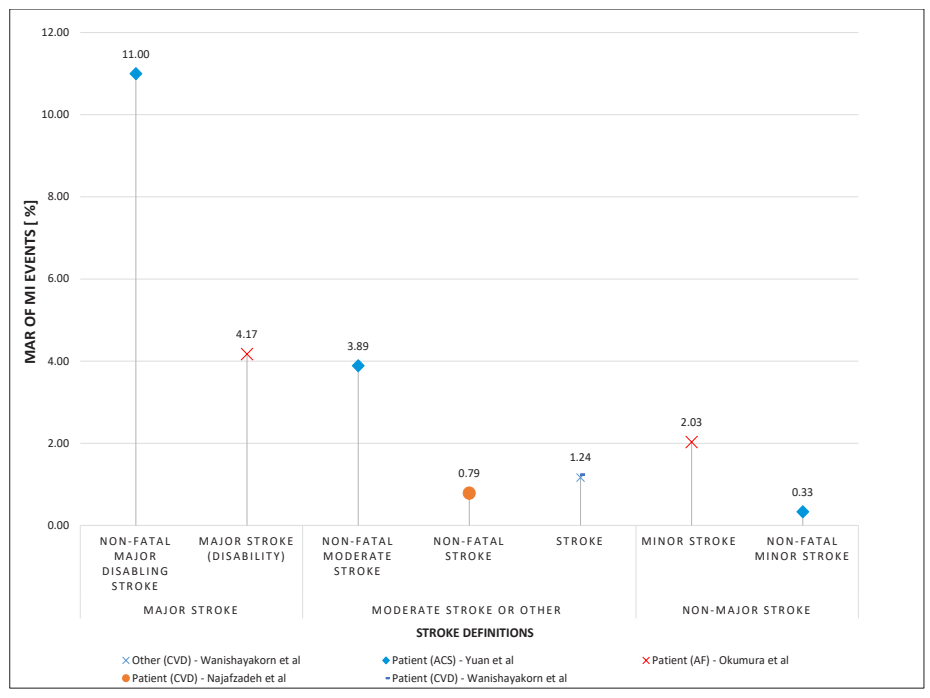
Results (Cont'd)

Figure 2. Maximum Acceptable Risk of Major Bleedings for 1% Decrease in Risk of Stroke, Myocardial Infarction (MI), or Venous Thromboembolism



Stroke, MI and VTE event definitions from each study were extracted in the analysis. All classifications were based on the descriptions reported from each listed article in this figure. Major bleeding for Shafrin et al. 2016[8] and Yuan et al. 2014[10] was defined as need for blood transfusion; Devereaux et al. 2001[2] Ghijben et al. 2014[3], and Najafzadeh et al. 2015[6] also described a possible major bleeding event with transfusion or need for hospitalization, although the endpoints were not distinct to major bleeding only; Yuan et al. 2014[10] also included fatal or critical site bleeding. Okumura et al. 2015[7] defined major bleeding as extracranial major bleeding (non-fatal event). Stroke definitions were classified as major stroke (i.e., disability), moderate or other (i.e., not specified as major stoke, moderate or minor stroke, or unclear or provided definitions for major or minor stroke), or minor stroke (i.e., non-fatal). MI events refer to heart attack, non-fatal heart attack, or non-fatal MI; and VTE was described as a risk of new recurring blood clot or a blood clot in the leg.

Figure 3. Maximum Acceptable Risk of Myocardial Infarction (MIs) for 1% Decrease in Risk of Stroke



MI and stroke event definitions from each study were extracted in the analysis. MI events refer to heart attack, non-fatal heart attack, or non-fatal MI. Stroke definitions were classified as major stroke (i.e., disability), moderate or other (i.e., not specified as major stoke, moderate or minor stroke, or unclear or provided definitions for both major or minor stroke), or minor stroke (i.e., non-fatal).

Conclusions

- Patient preference studies in the cardiovascular domain vary in reporting, endpoint (attribute) definitions, and methods used for preference elicitation. Differences in study design and attribute definition may explain some differences in the observed MAR values.
- This review highlights inconsistency of reporting within patient preference studies in the cardiovascular domain, with more than half of the studies that met inclusion criteria having a low quality criteria score. The availability of estimates of precision or magnitude of standard errors is important to develop methods aimed to synthesize patient preference data.
- Future patient preference research should focus on quality reporting and transparency of study results, as this will help build a stronger evidence base needed to conduct systematic reviews.

Abbreviations

Abbreviations: AF = atrial fibrullation; ACS = acute coronary syndrome; BWS = best-worst scaling; CNS = central nervous system; CVD = cardiovascular disease; DCE = discrete choice experiment; HCP = healthcare professional; JPN = Japan; MAB = minimum acceptable benefit; MAR = maximum acceptable risk; MI = myocardial infarction; MNL = multinomial logit; PREFS = purpose of study, respondent sampling, explanation of methods, findings reported, and significance testing; US = United States; VTE = venous thromboembolism

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