Prognostic implications of left ventricular strain by speckle-tracking echocardiography in the general population: a meta-analysis

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Purpose: Left ventricular (LV) mechanics by speckle-tracking echocardiography (STE) is prognostic in patients with cardiovascular diseases, but evidence related to community-dwelling individuals is uncertain. We therefore performed a systematic review and meta-analysis of STE as a predictor of adverse outcomes in the general population.

Methods: PRISMA guidelines were followed and MEDLINE and EMBASE were searched to identify eligible studies. Primary outcome was all-cause mortality and secondary outcomes were composite cardiac and cardiovascular end-point. Random effects meta-analysis was performed, and a modified Newcastle-Ottawa Assessment Scale was used for quality assessment.

Results: Eight papers matched the predefined criteria (total number of individuals studied=11,744). All publications assessed global longitudinal strain (GLS) by two-dimensional speckle-tracking echocardiography (2D-STE), one assessed circumferential, radial and transverse strains, and one assessed GLS-derived post-systolic shortening. None assessed LV rotational measures in association with outcomes. Two studies reported associations between GLS and all-cause mortality and composite cardiovascular end-point. Six papers reported an association between GLS and composite cardiac end-point, three of which were from the same study. Four papers were suitable for meta-analysis. GLS predicted all-cause mortality (pooled minimally adjusted HR per unit strain (%)=1.07 [95% CI 1.03–1.11], p=0.001), and composite cardiovascular (pooled maximally adjusted HR=1.18 [1.09–1.28], p<0.0001) and cardiac (HR=1.08 [1.02–1.14], p=0.006) endpoints. GLS also predicted coronary heart disease (HR=1.15 [1.03–1.29], p=0.017) and heart failure (HR=1.07 [1.02–1.13], p=0.012). The quality of all studies was good.

Conclusions: This study provides some evidence that STE may have utility as a measure of cardiac function and risk in the general population. 2D-STE-based GLS predicts total mortality, major adverse cardiac and cardiovascular end-points in community-dwelling individuals in a limited number of studies. Despite this, this systematic review also highlights important knowledge gaps in the current literature and further evidence is needed regarding the prognostic value of LV mechanics in unselected older populations.

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Keywords: community-dwelling individuals, mortality, cardiovascular disease, left ventricular strain

Introduction

Left ventricular systolic dysfunction (LVSD), measured as a reduction in left ventricular (LV) ejection fraction (LVEF), is prognostic of adverse outcomes, including all-cause mortality and heart failure (HF) in the general population.¹
Nevertheless, LVEF has well-recognized limitations and LVSD may occur when LVEF is normal.\(^2\)

Speckle-tracking echocardiography (STE) is a comparatively new tool that quantifies myocardial mechanics,\(^3\) and may detect LVSD when LVEF is still preserved.\(^2\)

Alterations in STE-derived LV strain are associated with risk factors for cardiovascular disease (CVD), including diabetes mellitus (DM),\(^4\) hypertension\(^5\) and obesity,\(^6\) and lower global longitudinal strain (GLS) predicts unfavorable outcomes in aortic stenosis, HF and hypertrophic cardiomyopathy.\(^7\)\(^-\)\(^10\)

While systematic reviews and meta-analyses of STE-based LV strain as a predictor of adverse outcomes have previously been conducted based on studies of patients with established\(^11\)\(^,\)\(^12\) or established plus suspected CVD,\(^13\) a systemic review has not been performed for community-dwelling individuals, who were not selected on the basis of disease or clinical status. This is important, since selecting samples based on disease status can distort associations between risk factors and outcomes – termed index event bias (collider bias).\(^14\) Also, community-dwelling individuals are at lower risk of CVD compared with selected diseased populations, and the utility of STE in this setting is uncertain but potentially of value.

We therefore conducted a systematic review and meta-analysis to examine whether STE is associated with risk of total and cardiovascular mortality and morbidity independent of conventional risk factors in community-dwelling individuals (ie, in the general population).

**Materials and methods**

This systematic review and meta-analysis was conducted according to a previously published protocol\(^15\) and conforms to the PRISMA guidance.\(^16\) The protocol was registered with the PROSPERO database (CRD42018090302).

**Eligibility criteria**

All longitudinal studies (including placebo arms of population-based clinical trials) that assessed the prospective association of any STE-derived parameter with at least one of the pre-specified outcomes in community-dwelling individuals (>18 years), who were not selected on the basis of disease or clinical status were eligible. Studies were included if they were reported in English, published in peer-reviewed journals and adhered to appropriate ethical standards. Abstracts, reviews, conference proceedings or letters to the editor were excluded.

**Outcomes**

The primary outcome was all-cause mortality. Secondary outcomes were 1) a composite cardiac end-point, including any combination of cardiovascular mortality, coronary heart disease (CHD) events (myocardial infarction, unstable angina, angina/ ischemia requiring emergent hospitalization or revascularization), HF hospitalization, new-onset atrial fibrillation (AF), lifethreatening arrhythmia, recorded automatic implantable cardioverter defibrillator shocks, or 2) composite cardiovascular endpoints, including a composite cardiac end-point and stroke, transient-ischemic attacks or peripheral arterial disease with arterial revascularization procedure. Any individual secondary end-points included in composite cardiac or cardiovascular endpoints were considered as tertiary outcomes.

**Search strategy**

Literature was searched in MEDLINE and EMBASE via OvidSP interface. Search strategies are shown in the Supplementary materials and data to be extracted were predefined.\(^15\) The last search was carried out on February 28, 2018. Additional papers could be identified by searching the reference lists of relevant articles and their citation metrics using Web of Science Core Collection.

**Study selection and data extraction**

Search results from each database were combined and duplicates were removed before screening. Initial title and abstract screening were performed and full texts of selected articles were retrieved and double screened for eligibility using a predefined eligibility form,\(^15\) and data extracted using a predefined form.\(^15\) Screening and extraction was performed by two researchers working independently (L.A. and C.P.). Discrepancies were reviewed and resolved through consensus.

**Quality assessment**

A modified version of the Newcastle-Ottawa Quality Assessment Scale of cohort studies\(^17\) was used to assess the quality of included papers.\(^15\) The total quality score was reported as the average of the two researchers’ scores ranging from 0 (lowest quality score) to 7 (highest quality score). Papers were included irrespective of the quality assessment score.

**Statistical methods**

All analyses were performed using Stata 15.1 (StataCorp LLC, USA). We used random effects meta-analysis to pool
effect estimates and calculated the 95% CIs of the relevant HRs based on the expectation of heterogeneity between different studies. All HRs were rescaled to per unit strain (%). Results were presented graphically as forest plots and heterogeneity was assessed using Higgins Thompson I^2 test and Cochran’s Q test.\textsuperscript{15}

We planned to carry out a meta-analysis on a minimally adjusted model (ie, age, sex and ethnicity [if relevant]) and a maximally adjusted model, including cardiovascular risk factors and conventional echocardiographic measures. Meta-analyses were only possible for GLS. Endocardial strain was used for primary analyses, but we performed sensitivity analysis by repeating analyses replacing endocardial with midwall or epicardial strains when available.

We planned to assess potential sources of heterogeneity,\textsuperscript{15} but were unable to perform any subgroup analysis or meta-regression due to the limited number of identified studies per analysis. Similarly, it proved impossible to compare different software for STE analysis due to lack of relevant data.

**Results**

**Search results and study selection**

A PRISMA diagram is shown in Figure 1. A total of 7040 records were identified. After removing duplicates, 6222 records of 6235 were excluded by title and abstract. Thirteen full text articles were assessed for eligibility. Five did not meet the inclusion criteria (n=1: ineligible outcome;\textsuperscript{18} n=4: same cohort, deemed not population representative due to selection criteria\textsuperscript{19–22}), the other eight papers from five studies were eligible (n=2 from Cardiovascular Abnormalities and Brain Lesion study,\textsuperscript{23,24} n=3 from Copenhagen City Heart Study\textsuperscript{25–27}, and n=1 from

![Figure 1 PRISMA flow diagram illustrates different stages of this systematic review.](https://www.dovepress.com/)

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Flemish Study on Environment, Genes and Health Outcomes [FLEMENGHO], and Atherosclerosis Risk in Communities.

Characteristics of included papers
Characteristics of included papers are shown in Table 1 (additional information regarding the studies is included in Table S1). Most (4/8) were based on US samples (two papers from the same study). The remainder included one paper from Belgium and three papers (from the same study) from Denmark. The total number of participants was 11,744, participants in the five studies reported in the eight identified papers ranged between 675 and 6118. Follow-up ranged between 608 days (469–761) (median; IQR) and 12.5 years (9.4–12.8). One study recruited participants free of CVD at baseline, while others included participants with known CVD.

Exposures and outcomes of included papers
Exposures and outcomes from included papers are shown in Table 2. All used two-dimensional speckle-tracking echocardiography (2D-STE). Two used Philips QLAB 8.1, two used TomTec CPA and four used EchoPac. All studies (n=8) assessed GLS. One study also assessed circumferential, radial and transverse strains and another assessed GLS-derived post-systolic shortening measures. None assessed LV rotational measures in association with the chosen outcomes. All papers except one provided data on exposure reliability (intra-observer, inter-observer reproducibility or both).

GLS and all-cause mortality
Two studies found associations between 2D-STE-derived measures and all-cause mortality (Table 3). GLS was reported in both studies; however, only one provided both minimally and maximally adjusted estimates. Consequently, meta-analysis was only performed on the two minimally adjusted estimates; pooled HR=1.07 (1.03–1.11), p=0.001 (Figure 2A).

GLS and composite cardiovascular end-point
Two studies reported associations between GLS and a composite cardiovascular end-point, but neither provided a minimally adjusted estimate (Table 3). Random effect meta-analysis indicated that lower 2D-STE-based GLS was associated with higher risk of a composite cardiovascular end-point; pooled maximally adjusted HR=1.18 (1.09–1.28), p=0.0001 (Figure 2C). Substituting mid-wall or epicardial-wall strains for endocardial strain did not alter this finding (Figure S1).

GLS and composite cardiac end-point
Among six papers which assessed different 2D-STE-derived measures, only GLS or a GLS-derived measure (post-systolic index) was associated with a composite cardiac end-point (Table 3). Three of these papers were from the same study population; one study was not suitable for quantitative synthesis because the estimates provided combined GLS and LVEF, and were available only for a selected high-risk subset of the population (stage A and B HF). Therefore, data from three papers were used for meta-analysis. Low GLS predicted higher HR of a composite cardiac end-point; pooled maximally adjusted HR=1.08 (1.02–1.14), p=0.006 (Figure 2B). A sensitivity analysis showed that replacing the endocardial with mid- or epicardial-wall strains had minimal effect (Figure S3). Analysis of minimally adjusted estimates is shown in Figure S2.

GLS and tertiary outcomes
Four papers provided data on GLS in association with tertiary outcomes, one of which assessed circumferential, radial and transverse strains (Table 4). Three papers reported CHD, two HF, one AF and one cardiovascular death. GLS was associated with CHD, AF and HF, whereas circumferential strain was only associated with HF although this was assessed in only one study (Table 4). Meta-analysis showed that GLS was a predictor of CHD and HF (CHD maximally adjusted HR=1.15 [1.03–1.29], p=0.017; HF HR=1.07 [1.01–1.13], p=0.012; Figure 3). Meta-analysis based on minimally adjusted estimates is shown in Figure S4, and further sensitivity analysis was performed for CHD replacing the endocardial with mid- or epicardial-wall strains and results were hardly altered (Figure S5). Additional information from studies that reported Kaplan–Meier data related to various outcomes is shown in Table S1.

Publication bias and study quality
Assessment of publication bias was not possible due to the small number of identified studies.
| Reference            | Study name                                      | Study design   | Region            | n      | Age (years) | Female (%) | Ethnicity                                                                 | F/U     | HTN (%)  | DM (%) | Dyslipidemia (%) | Smoking status | Known CVD (%) |
|----------------------|-------------------------------------------------|----------------|-------------------|--------|-------------|------------|---------------------------------------------------------------------------|---------|-----------|--------|-----------------|----------------|----------------|
| Russo et al (2014)   | Cardiovascular Abnormalities and Brain Lesion   | Longitudinal   | Manhattan, USA     | 708    | 71±9        | 431 (61)   | 66.8% Hispanics, 17.1% blacks, 14.1% whites, and 2% of other race-ethnicities | 4.8±1.5  | 548 (77.4) | 197 (27.8) | Hypercholesterolemia: 462 (65.2) | Smoking history: 374 (53) | CAD: 36 (5.08) AF: 41 (5.79) |
| Cheng et al (2015)   | The Framingham Offspring Study and the Framingham Omnibus Study | Longitudinal   | Framingham, Massachusetts, USA | 2831   | 66±9        | 1613 (57)  | 259 (9) non-white ethnicity                                               | 6.0±1.2 years | 1679 (59) | 365 (13) | N/A                                         | Current smoker: 236 (8) | 0 |
| Russo et al (2015)   | CABL study                                       | Longitudinal   | Manhattan, USA     | 675    | 71±9        | 408 (60)   | N/A                                                         | 63.6±18.7 months | 521 (77) | 187 (27.7) | Hypercholesterolemia: 443 (65.6) | N/A                                         | CAD: 39 (5.7) Hx HF: 19 (2.8) |
| Kuznetsova et al (2016) | Flemish Study on Environment, Genes and Health Outcomes (FLEMENGHO) | Cross-sectional | Northern Belgium  | 791    | 50.8±15.5   | 410 (51.8) | White Europeans                                                   | Median (5th–95th percentile): 7.9 years (3.7–9.6) | 326 (41.2) | 34 (4.3) | N/A                                         | Current smokers: 167 (21.1) | 43 (5.4) |
| Biering-Sorensen et al (2017) | Copenhagen City Heart Study                     | Longitudinal   | Copenhagen, Denmark | 1296   | 57.0±16.2   | 747 (57.6) | Almost all white                                                     | Median (IQR): 110 years (9.9–112) | 489 (37.8) | 122 (9.4) | N/A                                         | Never: 428 (33.3) Previous: 426 (33.2) Current: 430 (33.5) | Previous IHD: 64 (4.9) |
| Brainin et al (2018) | Copenhagen City Heart Study                     | Cross-sectional | Copenhagen, Denmark | 1296   | 56.9±16.2   | 747 (57.6) | Almost all white                                                     | Median (IQR): 110 years (9.9–112) | 489 (37.7) | 122 (9.4) | 186 (14.3)                                         | Never: 380 (29.3) Previous: 394 (30.4) Current: 401 (30.9) | Previous IHD: 64 (4.9) |
| Reference       | Study name                                      | Study design               | Region          | n    | Age (years) | Female (%) | Ethnicity | F/U    | HTN (%) | DM (%) | Dyslipidemia (%) | Smoking status (%) | Known CVD (%) |
|-----------------|------------------------------------------------|----------------------------|-----------------|------|-------------|------------|-----------|--------|---------|--------|------------------|--------------------|---------------|
| Modin et al     | Copenhagen City Heart Study                  | Copenhagen, Denmark        | 1294            | 570±16.2 | 744 (57.5)  | N/A        | Median (IQR): 12.5 years (9.4–12.8) | 489 (38.3) | 123 (9.5) | N/A | 406 (33.4) | IHD: 63 (4.9)     | Ischemic stroke: 25 (1.9) |
| Shah et al      | Atherosclerosis Risk in Communities (ARIC)    | USA                        | 6118            | Median (IQR): 75.3 (71.7–79.7) | 3548 (58) | 22% black  | Median (IQR): 608 days (469–761) | 5078 (83) | 2325 (38) | N/A | Ever: 3793 (62) | Current smoker: 367 (6) | CAD: 10 (17) |

Notes: 1Studies are from the same cohort (CABL study). 2Studies are from the same cohort (Copenhagen City Heart Study).
Abbreviations: AF, atrial fibrillation; CAD, coronary artery disease; CVD, cardiovascular disease; DM, diabetes mellitus; F/U, follow up; HTN, hypertension; HF, heart failure; Hx, history of; IHD, ischemic heart disease; MI, myocardial infarction; N/A, not reported; PAD, peripheral arterial disease.
| References                  | Hardware      | Software     | Procedure | Measured parameter | Images obtained from | Number of segments involved | Provided data on exposure reliability | Primary outcome (All-cause mortality) | Secondary outcomes | Tertiary outcomes |
|-----------------------------|---------------|--------------|-----------|--------------------|----------------------|--------------------------|---------------------------------------|--------------------------------------|-------------------|-------------------|
| Russo et al (2014)²³        | E 33, Philips | Philips QLAB | 2D-STE    | Longitudinal strain| N/A                  | N/A                      | Intra-observer reproducibility: ICC 0.82 (95% CI: 0.60–0.93, <0.01), mean difference (0.07 ±2.3%), and COV (SD/mean) 8.4%. Inter-observer reproducibility: ICC 0.85, mean difference (0.08 ±2.4%) and COV 9.2%. | n=58 (included ischemic stroke [n=16], MI [n=10], and vascular death [n=32]) |                      |                   |
|                             |               |             |           |                    |                      |                          |                                      |                                      |                   |                   |
| Cheng et al (2015)²⁸        | Hewlett-Packard 5500, Philips | Cardiac Performance Analysis [CPA] v1.1; TomTec Imaging Systems | 2D-STE | Longitudinal strain | N/A                  | 1 sonographer per specific view | Intra-observer reproducibility: Average COV: <6% for global longitudinal and circumferential strain. <9% for global transvers and radial strain. Inter-observer reproducibility: Average COV: ≤4% for global longitudinal and circumferential strain. <8% for global transvers and radial strain. | n=199 14= CHD, 8= cerebrovascular disease, and 13= other CVD causes. 164 death not attributable to a CVD cause. | New-onset CHD: n=69 (comprising fatal or nonfatal MI, coronary insufficiency, and angina pectoris) | New-onset CHD: n=69 (comprising fatal or nonfatal MI, coronary insufficiency, and angina pectoris) | HF: n=71              |
|                             |               |             |           |                    |                      |                           |                                      |                                      |                   |                   |
| References                        | Exposure characteristics | Outcome characteristics |
|----------------------------------|--------------------------|-------------------------|
| Russo et al (2015)               | 43, Philips              | Inter-observer reproducibility: ICC 0.85, mean difference (0.08 ±2.4%), and COV 0.09. |
|                                  | Philips QLAB 8.1          |                         |
|                                  | 2D-STE                   |                         |
|                                  | Longitudinal strain      |                         |
|                                  | Apical 4- and 2-chamber views |                     |
|                                  | 12 segments               |                         |
|                                  | N/A                      |                         |
| Kuznetsova et al (2016)          | Vivid 7 Pro, GE          | Intra-observer reproducibility: Absolute bias 0.47±0.55% and absolute limit of agreement ranged from 0.62% to 1.55% (reproducibility =1.1%). Relative bias –2.51±3.02% and the limits of agreement ranged from 8.44% to 3.41% (reproducibility=6.1%). |
|                                  | EchoPac, BT113, GE       |                         |
|                                  | 2D-STE                   |                         |
|                                  | Longitudinal strain      |                         |
|                                  | Apical 4-chamber view    |                         |
|                                  | N/A                      |                         |
|                                  | 1                        |                         |
| Biering-Sorensen et al (2017)    | Vivid 5, GE              | Intra-observer reproducibility: Mean difference ±1.96 SD (0.1 ±1.6%). Inter-observer reproducibility: Mean difference ±1.96 SD (−0.08 ±2.0%). |
|                                  | EchoPac, 2008, GE        |                         |
|                                  | 2D-STE                   |                         |
|                                  | Longitudinal strain      |                         |
|                                  | Apical 4-, 3- and 2-chamber views |                     |
|                                  | when possible            |                         |
|                                  | N/A                      |                         |
|                                  | 1                        |                         |
| Russo et al (2015)               | iE 33, Philips           | n=96 (comprised cardiac endpoints, stroke, transient ischemic attack, aortic aneurysm, arterial embolism, and revascularization of peripheral arteries) |
|                                  | Philips QLAB 8.1          |                         |
|                                  | 2D-STE                   |                         |
|                                  | Longitudinal strain      |                         |
|                                  | Images obtained from     |                         |
|                                  | Number of segments       |                         |
| Kuznetsova et al (2016)          | Vivid 7 Pro, GE          | n=68 (Included coronary events, fatal and nonfatal HF, pulmonary heart disease, new-onset AF, and life-threatening arrhythmias) |
|                                  | EchoPac, BT113, GE       |                         |
|                                  | 2D-STE                   |                         |
| Biering-Sorensen et al (2017)    | Vivid 5, GE              | Coronary events: n=34 [Included fatal and nonfatal MI, coronary revascularization, and new-onset angina (stable or unstable)] |
|                                  | EchoPac, 2008, GE        |                         |
|                                  | 2D-STE                   |                         |

(Continued)
## Table 2 (Continued).

| References                  | Exposure characteristics | Outcome characteristics |
|-----------------------------|--------------------------|-------------------------|
|                            | Hardware, Software, Procedure | Number of sonographers involved | Provided data on exposure reliability | Primary outcome (All-cause mortality) | Secondary outcomes | Tertiary outcomes |
| Brainin et al (2018)        | Vivid S, GE, EchoPac, 2008, GE, 2D-STE | Longitudinal strain, Post-systolic index, post-systolic strain, peak post-systolic time and, post-systolic shortening, Apical 4-, 3- and 2-chamber views when possible, 18 (6 per view) | 1 | Intra-observer reproducibility: PSS: mean difference ±1.96 SD (0.2±0.95) PSI: mean difference ±1.96 SD (0.25±0.74) Inter-observer reproducibility: PSS: mean difference ±1.96 SD (-0.04±0.73) PSI: mean difference ±1.96 SD (0.06±0.56) | n=236 (18.1%) | n=149 (11.5%) (composite of HF [n=78], MI [n=43], and CV death [n=74]) |
| Modin et al (2018)          | Vivid S, GE, EchoPac, 2008, GE, 2D-STE | Longitudinal strain, Apical 4-, 3- and 2-chamber views when possible, GLS was calculated as the average of strain values from available views | N/A | No | n=222 (17.2%) (Composite outcome of either IHD or HF) n=145 (65%) in hypertensive participants and n=77 (35%) in non-hypertensive individuals | (Continued) |
Table 2 (Continued).

| References | Exposure characteristics | Outcome characteristics |
|------------|--------------------------|-------------------------|
|            | ● Hardware                | ● Primary outcome       |
|            | ● Software                | (All-cause mortality)   |
|            | ● Procedure               | ● Secondary outcomes    |
|            |● Measured parameter      |● Composite CV end point |
|            |● Images obtained from     |● Composite cardiac end point |
|            |● Number of sonographers perform the analysis |                        |
|            |● Number of segments involved |                         |
| Shah et al (2017)\(^{10}\) |● iE 33, Philips TomTec CPA package 2D-STE |● Multiple (4) |
|            |● Longitudinal strain     |● Intra-observer reproducibility:  |
|            |● Apical 4- and 2-chamber views |Mean difference±SD (0.2±1.4% for LS in apical 4-chamber view; and 0.8±1.2% in apical 2-chamber view) and COV 7.7% for LS in apical 4-chamber view and 6.4% in apical 2-chamber view. |
|            |● 6 in each view          |                          |
|            |● Multiple (4)            |                          |
|            |                           |● n=194 (composite of deaths [n=145] and HF [n=113]) |

Abbreviations: AF, atrial fibrillation; CV, cardiovascular; CVD, cardiovascular disease; CHD, coronary heart disease; COV, coefficient of variation; GLS, global longitudinal strain; HF, heart failure; ICC, intra-class correlation coefficient; IHD, ischemic heart disease; MI, myocardial infarction; PSI, post-systolic index; PSS, post-systolic shortening; 2D-STE, two-dimensional speckle-tracking echocardiography.
Table 3 Results of studies assessed the association between two-dimensional speckle-tracking echocardiographic-derived measures and all-cause mortality, composite cardiovascular and cardiac end-points

| Citation          | Exposure                              | Primary outcome | Secondary outcomes | Unit |
|-------------------|---------------------------------------|----------------|--------------------|------|
|                   |                                       | All-cause mortality | Composite CV end point | Composite cardiac end point |
|                   |                                       | HRs, 95% CI, P  | n (events) Adjustments, | HRs, 95% CI, P  | n (events) Adjustments, |
| Russo et al       | Global longitudinal strain (GLS)      | • N/A           | • N/A              | 1.24 (1.12, 1.37), <0.001 | 1.15 (1.03, 1.28), 0.012 |
|                   |                                       |                |                    | None | Model 1 + LVEF |
|                   |                                       |                |                    | Age, sex, SBP, DBP, HTN, anti-hypertensive medications, DM, LVMi, relative wall thickness, LAVi, diastolic dysfunction, and AF (Model 1) | |
|                   |                                       |                |                    | 1.15 (1.03, 1.28), 0.012 | |
| Cheng et al, (2015) | Global average longitudinal strain | 1.31 (1.14, 1.52), 0.0002 | Age, sex and ethnicity (Model 1) | 1.37 (1.06, 1.76), 0.01 | Model 1 |
|                   |                                       | 1.24 (1.05, 1.46), 0.01 | Age, sex, ethnicity, BMI, SBP, DBP, anti-hypertensive treatment, total/HDL cholesterol, DM, smoking status, and HR (Model 2) | 1.36 (1.03, 1.79), 0.03 | Model 2 |
|                   |                                       | 1.21 (1.02, 1.44), 0.03 | age, sex, ethnicity, BMI, SBP, DBP, anti-hypertensive treatment, total/HDL cholesterol, DM, smoking status, LV mass, LV fractional shortening, and HR (Model 3) | 1.29 (0.96, 1.74), 0.09 | Model 3 |

(Continued)
Table 3 (Continued).

| Citation             | Exposure                        | Primary outcome                  | Secondary outcomes                   | Unit                  |
|----------------------|---------------------------------|----------------------------------|--------------------------------------|-----------------------|
|                      |                                 | All-cause mortality              | Composite CV end point               | Composite cardiac end point |
|                      |                                 | HRs, 95% CI, P (n events)        | HRs, 95% CI, P (n events)            | HRs, 95% CI, P (n events) |
|                      |                                 | Adjustments,                      | Adjustments,                         | Adjustments,          |
|                      |                                 |                                  |                                      |                       |
|                      | Global average                  | 1.3 (1.12, 1.52), 0.0007 Model 1 | 1.1 (0.85, 1.42), 0.48 Model 1        | Per 1 SD change       |
|                      | circumferential                 | 1.21 (1.04, 1.42), 0.02 Model 2  | 1.14 (0.87, 1.48), 0.34 Model 2        | (SD=5.8%)             |
|                      | strain                           | 1.11 (0.92, 1.34), 0.27 Model 3  | 1.11 (0.81, 1.51), 0.53 Model 3        |                       |
|                      | Global average                  | 0.73 (0.61, 0.87), 0.0003 Model 1| 0.87 (0.67, 1.13), 0.3 Model 1        | Per 1 SD change       |
|                      | radial strain                   | 0.76 (0.64, 0.91), 0.002 Model 2 | 0.9 (0.68, 1.17), 0.43 Model 2        | (SD=16.8%)            |
|                      | Global average                  | 0.82 (0.68, 0.98), 0.03 Model 3  | 0.95 (0.72, 1.26), 0.72 Model 3        |                       |
|                      | average                         | 0.93 (0.81, 1.07), 0.32 Model 1  | 1.02 (0.80, 1.29), 0.89 Model 1        | Per 1 SD change       |
|                      | transvers strain                | 0.99 (0.85, 1.14), 0.85 Model 2  | 1.02 (0.81, 1.29), 0.87 Model 2        | (SD=7.1%)             |
|                      | transvers                       | 1 (0.85, 1.17), 0.97 Model 3     | 1.04 (0.81, 1.34), 0.75 Model 3        |                       |
| Kuznetsova et al     | GLS                             |                                  |                                      |                       |
| (2016)²              | • Mid-wall                      |                                  |                                      |                       |
|                      | • N/A                           |                                  |                                      |                       |
|                      | • N/A                           | 1.75 (1.39, 2.20), <0.0001       | 1.54 (1.21, 1.96), 0.0005 Clinical model = Family clusters, sex, age, BMI, SBP, serum cholesterol, smoking, antihypertensive treatment, DM, and a history of cardiac disease. |
|                      |                                 | 1.75 (1.36, 2.20), <0.0001       | 1.54 (1.21, 2.0), 0.0005 Clinical model = LVMi |
|                      |                                 | 1.61 (1.27, 2.08), <0.0001       | 1.54 (1.13, 1.85), 0.0045 Clinical model + LVMi |
|                      |                                 | 1.61 (1.27, 2.08), <0.0001       | 1.45 (1.13, 1.89), 0.0041 Clinical model + LVMi + TDI e’ |

(Continued)
| Citation                  | Exposure | Primary outcome | Secondary outcomes | Unit |
|--------------------------|----------|-----------------|--------------------|------|
|                          |          | All-cause mortality | Composite CV end point | Composite cardiac end point |
|                          |          | HRs, 95% CI, P n (events) | HRs, 95% CI, P n (events) | HRs, 95% CI, P n (events) |
|                          |          | Adjustments, | Adjustments, | Adjustments, |
| All-cause mortality      |          |                |                |                |
| Biering-Sørensen et al (2017)

| Endocardial ● | ● N/A | ● N/A | 1.74 (1.35, 2.19), <0.0001 | 1.74 (1.35, 2.19), <0.0001 |
|               |       |       | Clinical model | Clinical model |
|               |       |       | + LVMi | + LVMi |
|               |       |       | 1.62 (1.25, 2.05), <0.0001 | 1.62 (1.25, 2.05), <0.0001 |
|               |       |       | Clinical model + TDI e′ | Clinical model + TDI e′ |
|               |       |       | 1.62 (1.25, 2.05), 0.0001 | 1.62 (1.25, 2.05), 0.0001 |
|               |       |       | Clinical model + LVMi + TDI e′ | Clinical model + LVMi + TDI e′ |
| Epicardial ● | ● N/A | ● N/A | 1.66 (1.33, 2.10), <0.0001 | 1.66 (1.33, 2.10), <0.0001 |
|               |       |       | Clinical model | Clinical model |
|               |       |       | + LVMi | + LVMi |
|               |       |       | 1.55 (1.23, 1.97), 0.0002 | 1.55 (1.23, 1.97), 0.0002 |
|               |       |       | Clinical model + TDI e′ | Clinical model + TDI e′ |
|               |       |       | 1.55 (1.23, 1.97), 0.0002 | 1.55 (1.23, 1.97), 0.0002 |
|               |       |       | Clinical model + LVMi + TDI e′ | Clinical model + LVMi + TDI e′ |
| GLS ●         | ● N/A | ● N/A | 1.12 (1.08, 1.17), <0.001 | 1.12 (1.08, 1.17), <0.001 |
|               |       |       | None | None |
|               |       |       | Age and sex | Age and sex |
|               |       |       | Clinical model = | Clinical model = |
|               |       |       | Age, sex, HR, | Age, sex, HR, |
|               |       |       | HTN, DM, previous ischemic heart disease, SBP, and pro-BNP (>150 pmol/L) | HTN, DM, previous ischemic heart disease, SBP, and pro-BNP (>150 pmol/L) |
|               |       |       | 1.08 (1.04, 1.13), <0.001 | 1.08 (1.04, 1.13), <0.001 |
|               |       |       | 1.07 (1.01, 1.11), 0.013 | 1.07 (1.01, 1.11), 0.013 |
|               |       |       | 1.05 (1.0, 1.11), 0.045 | 1.05 (1.0, 1.11), 0.045 |

(Continued)
Table 3 (Continued).

| Citation            | Exposure | Primary outcome | All-cause mortality | Composite CV end point | Composite cardiac end point | Unit                      |
|---------------------|----------|----------------|---------------------|------------------------|-----------------------------|---------------------------|
|                     |          |                | HRs, 95% CI, P      | n (events) Adjustments | HRs, 95% CI, P              | n (events) Adjustments,   |
| Brainin et al       | GLS      |                | 1.05 (1.02, 1.09), 0.004 | None                   | None                        | None                      |
|                     |          |                | n = 236             |                        | n = 149                     |                           |
|                     | Post systolic index | 1.33 (1.21, 1.47), <0.001 | None | 1.12 (1.08, 1.17), <0.001 | None | Per unit (1%) decrease |
|                     |          |                | 1.14 (1.0, 1.30), 0.044 | Age, sex, HTN, HR, LVMi, LVEF, GLS, pro-B-type natriuretic peptide, previous ischemic heart disease, SBP, LAVi, e', estimated glomerular filtration rate, and E/A | 1.36 (1.20, 1.54), <0.001 | None | Per 1% increase |
| Modin et al         | GLS      |                | 1.67 (1.41, 1.99), <0.001 | None                   | None                        | None                      |
|                     |          |                | 1.37 (1.14, 1.65), 0.001 | Clinical model = Age, sex, SBP, smoking status, DM and total cholesterol and HTN | 1.23 (0.99, 1.52), 0.06 | Per 5% decrease |
|                     |          |                | n = 222             |                         |                             |                           |

(Continued)
studies was good. Seven scored a maximum 23–26,28–30 and one scored 627 (Table S2). The degree of heterogeneity indicated by I-square was small in most of the meta-analyses and was only large in two analyses.

**Discussion**

This systematic review and meta-analysis summarizes current evidence about the prognostic value of STE-derived measures in the general population. 2D-STE-derived GLS was the most studied measure and it predicted total mortality, major adverse cardiac and cardiovascular end-points in community-dwelling individuals in a limited number of studies that included a total of 11,744 participants. Although information on potential confounders was limited and inconsistent, there was some evidence that this was independent of conventional cardiovascular risk factors and other echocardiographic measures. There was insufficient evidence in relation to other myocardial deformation indices or 3D-STE-derived indices to draw conclusions with respect to outcomes. Therefore, this systematic review also highlights important knowledge gaps in the current literature regarding the possible utility of myocardial deformation indices in unselected older populations, and further evidence is still required, particularly regarding 3D-STE.

Risk assessment and management of patients with CVD are guided by the measurement of LV global systolic function.2 LVEF is considered the cornerstone in assessing LV systolic function,1 but LV strain imaging is attracting interest as an additional tool to improve risk assessment and guide management in diseased populations.2,12 Nevertheless, the evidence on the utility of STE as a measure of cardiac function and risk in community-dwelling individuals has been limited. We provide a synthesis of current evidence that provides some support for GLS as a useful risk measure but also highlights the need for more information regarding the utility of STE for risk assessment and diagnosis. Based on limited numbers of identified studies, GLS was a prognostic marker of cardiovascular mortality and morbidity independent of conventional risk factors. This is important because risk factors which potentially lead to CVDs such as aging, hypertension and DM are common characteristics of longitudinal population-based samples of elderly23–30 and are known to be associated with alterations in GLS even when LVEF is still normal.4,5,31,32

According to the disease progression, the layers of the myocardium as well as the various other contributors to cardiac mechanics can be affected differently.33 Disease affecting the subendocardial layer such as ischemia,
hypertension or DM tends to impair longitudinal mechanics, while circumferential and twist mechanics remain preserved or even enhanced to preserve the overall LV systolic performance and LVEF. With more involvement of the mid-myocardial and subepicardial layers, both circumferential and twist mechanics will deteriorate leading to a reduction in LVEF. In unselected population without overt cardiac diseases, Russo et al characterized the relationship between multidirectional myocardial mechanics with radial thickening and LVEF. Radial strain was more influenced by circumferential strain than longitudinal strain explaining why radial thickening, and hence LVEF, is less sensitive than longitudinal function in detecting subclinical LVSD. This may contribute to the added prognostic value of GLS over LVEF especially when LVEF is still normal or mildly impaired.

STE-based LV strain imaging allows comprehensive quantification of complex myocardial mechanics. While STE is increasingly used in clinical practice, it suffers from inherent technical limitations. High-quality images and adequate frame rates are crucial for accurate tracking. For 2D-STE, multiple views are required which is time-consuming to

Figure 2 GLS as a predictor of all-cause mortality (A), composite cardiac end-point (B) and cardiovascular end-point (C). All-cause mortality HR estimates are from minimally adjusted (Cheng et al) and unadjusted (Brainin et al) models. Composite cardiovascular and cardiac end-points are based on maximally adjusted models (listed in the Supplementary materials). For Kuznetsova et al, endocardial-wall strain is shown. Hazard ratios are per unit change in strain value. The heterogeneity assessment including the $I^2$ statistics and p-value of Q test is shown.
| References       | Tertiary outcomes (n)                                                                 | Exposure                  | HRs, 95% CI, P | Results                                                                 | Unit                                                                 |
|------------------|--------------------------------------------------------------------------------------|---------------------------|----------------|-------------------------------------------------------------------------|----------------------------------------------------------------------|
| Cheng et al      | 1. Coronary heart disease (69) (comprising fatal or non-fatal myocardial infarction, coronary insufficiency, and angina pectoris) | Global average longitudinal strain | 1.37 (1.06, 1.76), 0.01 | Age, sex and ethnicity (Model 1)                                        | Per 1 SD change (SD=3.3%)                                            |
|                  |                                                                                      |                           | 1.36 (1.03, 1.79), 0.03 | Age, sex, ethnicity, BMI, SBP, DBP, anti-hypertensive treatment, total/HDL cholesterol, DM, smoking status, and HR (Model 2) |                                                                    |
|                  |                                                                                      |                           | 1.29 (0.96, 1.74), 0.09 | Age, sex, ethnicity, BMI, SBP, DBP, anti-hypertensive treatment, total/ HDL cholesterol, DM, smoking status, LV mass, LV fractional shortening, and HR (Model 3) |                                                                    |
|                  |                                                                                      | Global average circumferential strain | 1.1 (0.85, 1.42), 0.48 | Model 1                                                                 | Per 1 SD change (SD=5.8%)                                            |
|                  |                                                                                      |                           | 1.14 (0.87, 1.48), 0.34 | Model 2                                                                 |                                                                     |
|                  |                                                                                      |                           | 1.11 (0.81, 1.51), 0.53 | Model 3                                                                 |                                                                     |
|                  |                                                                                      | Global average radial strain | 0.87 (0.67, 1.13), 0.3 | Model 1                                                                 | Per 1 SD change (SD=16.8%)                                            |
|                  |                                                                                      |                           | 0.9 (0.68, 1.17), 0.43 | Model 2                                                                 |                                                                     |
|                  |                                                                                      |                           | 0.95 (0.72, 1.26), 0.72 | Model 3                                                                 |                                                                     |
|                  |                                                                                      | Global average transvers strain | 1.02 (0.80, 1.29), 0.89 | Model 1                                                                 | Per 1 SD change (SD=7.1%)                                            |
|                  |                                                                                      |                           | 1.02 (0.81, 1.29), 0.87 | Model 2                                                                 |                                                                     |
|                  |                                                                                      |                           | 1.04 (0.81, 1.34), 0.75 | Model 3                                                                 |                                                                     |
|                  |                                                                                      | 2. Heart failure (71)                                                                 |                                |                                                                         |                                                                      |
|                  |                                                                                      | Global average longitudinal strain | 1.45 (1.14, 1.84), 0.003 | Model 1                                                                 | Per 1 SD change (SD=3.3%)                                            |
|                  |                                                                                      |                           | 1.29 (0.99, 1.69), 0.06 | Model 2                                                                 |                                                                     |
|                  |                                                                                      |                           | 1.14 (0.86, 1.50), 0.37 | Model 3                                                                 |                                                                     |
|                  |                                                                                      | Global average circumferential strain | 1.7 (1.29, 2.25), 0.0002 | Model 1                                                                 | Per 1 SD change (SD=5.8%)                                            |
|                  |                                                                                      |                           | 1.59 (1.18, 2.14), 0.002 | Model 2                                                                 |                                                                     |
|                  |                                                                                      |                           | 1.41 (1.0, 2.0), 0.05  | Model 3                                                                 |                                                                     |
|                  |                                                                                      | Global average radial strain | 0.64 (0.46, 0.88), 0.007 | Model 1                                                                 | Per 1 SD change (SD=16.8%)                                            |
|                  |                                                                                      |                           | 0.82 (0.59, 1.13), 0.22 | Model 2                                                                 |                                                                     |
|                  |                                                                                      |                           | 0.98 (0.72, 1.34), 0.92 | Model 3                                                                 |                                                                     |
|                  |                                                                                      | Global average transvers strain | 0.73 (0.57, 0.93), 0.01 | Model 1                                                                 | Per 1 SD change (SD=7.1%)                                            |
|                  |                                                                                      |                           | 0.79 (0.61, 1.02), 0.07 | Model 2                                                                 |                                                                     |
|                  |                                                                                      |                           | 0.84 (0.65, 1.1), 0.21 | Model 3                                                                 |                                                                     |
|                  |                                                                                      | 2. Heart failure (71)                                                                 |                                |                                                                         |                                                                      |
|                  |                                                                                      | (Continued)                                                             |                                |                                                                         |                                                                      |
Table 4 (Continued).

| References            | Tertiary outcomes (n)                                                                                               | Exposure                          | Results                        | Adjustments                                                                 | Unit                                |
|-----------------------|---------------------------------------------------------------------------------------------------------------------|-----------------------------------|-------------------------------|----------------------------------------------------------------------------|-------------------------------------|
| Russo et al, (2015)   | Atrial fibrillation (32)                                                                                           | Global average longitudinal strain| HRs, 95% CI, P                | None                                                                       | Per unit (1%) decrease Death as a Competing Risk |
|                       |                                                                                                                    | 1.2 (1.08, 1.34), 0.001           |                               | Age, obesity, HTN, antihypertensive treatment, coronary artery disease, LVMi, relative wall thickness. |                                      |
|                       |                                                                                                                    | 1.22 (1.04, 1.43), 0.015          |                               |                                                                            |                                      |
| Kuznetsova et al (2016) | Coronary heart disease (34) Comprising fatal and nonfatal myocardial infarction, coronary revascularization, and new-onset angina (stable or unstable) | Global longitudinal strain        |                               | Clinical model = Family clusters, sex, age, BMI, SBP, serum cholesterol, smoking, antihypertensive treatment, DM, and a history of cardiac disease. | Per 1 SD decrease (SD= 2.5%)       |
|                       | • Mid-wall                                                                                                        | 2.45 (1.61, 3.66), <0.0001        |                               | Clinical model + LVMi                                                      |                                      |
|                       |                                                                                                                    | 2.53 (1.68, 3.82), <0.0001        |                               | Clinical model + TDI e’                                                    |                                      |
|                       |                                                                                                                    | 2.32 (1.51, 3.55), <0.0001        |                               | Clinical model + LVMi + TDI e’                                            |                                      |
|                       |                                                                                                                    | 2.4 (1.54, 3.71), <0.0001         |                               |                                                                            |                                      |
|                       | • Endocardial                                                                                                     | 2.34 (1.58, 3.50), <0.0001        |                               | Clinical model                                                            | Per 1 SD decrease (SD= 2.9%)        |
|                       |                                                                                                                    | 2.44 (1.62, 3.77), <0.0001        |                               | Clinical model + LVMi                                                      |                                      |
|                       |                                                                                                                    | 2.24 (1.46, 3.43), 0.0002         |                               | Clinical model + TDI e’                                                    |                                      |
|                       |                                                                                                                    | 2.29 (1.50, 3.56), 0.0002         |                               | Clinical model + LVMi + TDI e’                                            |                                      |
|                       | • Epicardial                                                                                                      | 2.3 (1.58, 3.38), <0.0001         |                               | Clinical model                                                            | Per 1 SD decrease (SD= 2.2%)        |
|                       |                                                                                                                    | 2.4 (1.61, 3.56), <0.0001         |                               | Clinical model + LVMi                                                      |                                      |
|                       |                                                                                                                    | 2.2 (1.47, 3.30), <0.0001         |                               | Clinical model + TDI e’                                                    |                                      |
|                       |                                                                                                                    | 2.26 (1.49, 3.38), <0.0001        |                               | Clinical model + LVMi + TDI e’                                            |                                      |

(Continued)
Table 4 (Continued).

| References                   | Tertiary outcomes (n) | Exposure               | Results HRs, 95% CI, P | Adjustments                                                                 | Unit                      |
|------------------------------|-----------------------|------------------------|------------------------|-----------------------------------------------------------------------------|---------------------------|
| Biering-Sorensen et al (2017) | 1. Heart failure (78) | Global longitudinal strain | 1.6 (1.09, 1.23), <0.001 | None                                                                            | Per unit (1%) decrease    |
|                              |                       |                        | 1.12 (1.05, 1.18), <0.001 | Age and sex (Model 1)                                                        |
|                              |                       |                        | 1.1 (1.03, 1.17), 0.003  | Age, sex, HR, HTN, DM, previous IHD, SBP, and pro-BNP (>150 pmol/L) (Model 2) |
|                              |                       |                        | 1.09 (1.02, 1.17), 0.016 | Age, sex, HR, HTN, DM, previous IHD, SBP, pro-BNP (>150 pmol/L), LVEF (<50%), LVMi, LV dimension, deceleration time, LA dimension, and E/e' (Model 3) |
|                              | 2. Acute myocardial infarction (43) |                        | 1.16 (1.08, 1.26), <0.001 | None                                                                            | Per unit (1%) decrease    |
|                              |                       |                        | 1.13 (1.04, 1.22), 0.003 | Model 1                                                                        |
|                              |                       |                        | 1.1 (1.01, 1.19), 0.022  | Model 2                                                                        |
|                              |                       |                        | 1.11 (1.01, 1.22), 0.024 | Model 3                                                                        |
|                              | 3. Cardiovascular death (74) |                        | 1.06 (1.0, 1.13), 0.059  | None                                                                            | Per unit (1%) decrease    |
|                              |                       |                        | 1.02 (0.96, 1.08), 0.54  | Model 1                                                                        |
|                              |                       |                        | 0.99 (0.93, 1.06), 0.85  | Model 2                                                                        |
|                              |                       |                        | 0.98 (0.91, 1.06), 0.59  | Model 3                                                                        |

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; HTN, hypertension; HRs, hazard ratios; HR, heart rate; IHD, ischemic heart disease; LA, left atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; LVMi, left ventricular mass index; SBP, systolic blood pressure; SD, standard deviation; TDI, tissue Doppler imaging.
A Coronary heart disease

| Author/s (Total no; No of events) | HR (95% CI) | Weight % |
|----------------------------------|-------------|-----------|
| Cheng et al (2015) (2311; 64)    | 1.09 (0.99, 1.22) | 39.77 |
| Kuznetsova et al (2016) (791; 34) | 1.44 (1.17, 1.88) | 17.17 |
| Biering-Sorensen et al (2017) (1296; 43) | 1.11 (1.01, 1.22) | 43.06 |
| Overall (I-squared=57.8%, \( p = 0.093 \)) | 1.15 (1.03, 1.29) | 100.00 |

Weights are from random effects analysis

B Heart failure

| Author/s (Total no; No of events) | HR (95% CI) | Weight % |
|----------------------------------|-------------|-----------|
| Cheng et al (2015) (2410; 62)    | 1.04 (0.96, 1.15) | 35.63 |
| Biering-Sorensen et al (2017) (1296; 78) | 1.09 (1.02, 1.17) | 64.37 |
| Overall (I-squared=0.0%, \( p = 0.447 \)) | 1.07 (1.02, 1.13) | 100.00 |

Weights are from random effects analysis

Figure 3 GLS as a predictor of coronary heart disease (A) and heart failure (B) on maximally adjusted models (listed in the Supplementary materials). For Kuznetsova et al, endocardial-strain is shown. Hazard ratios are per unit change in strain value. The heterogeneity assessment including the \( I^2 \) statistics and \( p \)-value of Q test is shown.

apply in large population-based studies. Indeed, among identified studies, only one study measured circumferential, radial and transverse strains, while none measured LV rotation. This could be due to analysis time required or the limited feasibility and reproducibility of these measurements. Nevertheless, circumferential strain, both MRI-based and 2D-STE based, was an independent prognostic marker for incident HF over and beyond traditional risk factors and conventional measures in subjects free of CVDs of community-dwelling individuals. Further, Cheng et al have suggested that distinct components of LV mechanics (ie, GLS, circumferential strain, etc.) are differently associated with individual CVD outcomes, but it was not possible to answer this question due to the limited number of studies. In the future, 3D imaging methods may overcome some of the limitations of 2D-STE and provide additional insight to the different relationship between individual components of LV mechanics and CVD outcomes.

**Study limitations**

A number of limitations of this study ought to be acknowledged. This systematic review was limited to English language publications, which may have introduced a selection bias. We identified only eight papers based on five
different studies; all identified studies used 2D-STE and no study examined additive the prognostic value of 3D-STE-derived LV deformation indices in a general population. Once multiple publications from the same study were accounted for, meta-analyses were based on either two or three studies limiting the precision of estimates of between-study variance which could result in an underestimate of the width of the confidence intervals. Further, meta-analysis should be performed when results of at least ten relevant studies are available. The small number of studies also precluded sub-group analysis and meta-regression to explore sources of heterogeneity between studies. We assumed a priori that there would be heterogeneity between the various observational studies and consequently used random effects modeling, although there was not strong evidence of heterogeneity in the identified studies. Since estimates from random effects models behave like the fixed effect estimate as heterogeneity decreases, it is not likely that this will have introduced substantial error. The small number of studies also prevented us from employing formal assessment of publication bias (e.g. funnel plots), but this bias cannot be excluded. Analyses employed different vendor-specific software and possibly different software versions; both are factors which may introduce systematic differences between studies. For this reason, GLS analysis including LV segmentation is different between studies included in this meta-analysis (e.g. endocardial analysis of GLS from 12 LV-segments, transmural analysis of GLS from 18 LV-segments, or GLS from only 6 LV-segments). However, since we examined associations with outcomes in relation to a continuous exposure (GLS) the impact of this source of heterogeneity is likely to be small, consistent with our sensitivity analysis.

Conclusion
This study synthesized current evidence regarding STE-derived measures as prognostic indicators of mortality and cardiovascular events in community-dwelling individuals. Despite limited number of studies in this meta-analysis, LV GLS by 2D-STE showed prognostic value in this population and may add to conventional cardiovascular risk factors and other echocardiographic measures. However, our findings also highlight the limitations of the existing evidence base and identify important knowledge gaps in the current literature regarding the possible utility of myocardial deformation indices and 3D-STE in unselected older populations – these are issues where further evidence is needed.

Abbreviation list
AF, atrial fibrillation; CHD, coronary heart disease; CVD, cardiovascular disease; DM, diabetes mellitus; GLS, global longitudinal strain; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction; MI, myocardial infarction; STE, speckle-tracking echocardiography.

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