Digital Predictors of Morbidity, Hospitalization, and Mortality Among Older Adults: A Systematic Review and Meta-Analysis

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The widespread adoption of digital health technologies such as smartphone-based mobile applications, wearable activity trackers and Internet of Things systems has rapidly enabled new opportunities for predictive health monitoring. Leveraging digital health tools to track parameters relevant to human health is particularly important for the older segments of the population as old age is associated with multimorbidity and higher care needs. In order to assess the potential of these digital health technologies to improve health outcomes, it is paramount to investigate which digitally measurable parameters can effectively improve health outcomes among the elderly population. Currently, there is a lack of systematic evidence on this topic due to the inherent heterogeneity of the digital health domain and the lack of clinical validation of both novel prototypes and marketed devices. For this reason, the aim of the current study is to synthesize and systematically analyse which digitally measurable data may be effectively collected through digital health devices to improve health outcomes for older people. Using a modified PICO process and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework, we provide the results of a systematic review and subsequent meta-analysis of digitally measurable predictors of morbidity, hospitalization, and mortality among older adults aged 65 or older. These findings can inform both technology developers and clinicians involved in the design, development and clinical implementation of digital health technologies for elderly citizens.

Keywords: digital health (eHealth), systematic (literature) review, meta-analysis, predictor, hospitalization-, mortality, elderly

INTRODUCTION

The growing field of digital health attests that digital technologies are increasingly converging with human health and the delivery of healthcare services. In the last decade, the widespread adoption of, among others, smartphone-based mobile applications, wearable activity trackers, and Internet of Things (IoT) systems, have fuelled a socio-technical trend known as the Quantified Self,
i.e., the use of digital technology (broadly defined) for self-tracking purposes (1). Tracking parameters relevant to human health, aiming at improving health outcomes (in short, tracking for health) is a primary justification of self-tracking. The first generation of wearable devices and mobile tools could collect data, and provide insights only related to a small portion of human health and physiology, chiefly mobility reports (e.g., daily steps, physical position). Novel applications have expanded their data sources and can now record a broader variety of health-related parameters and underlying processes. This is due to a four-fold technological transformation. First, self-quantification technologies have expanded in variety as to include data sources that previously could only be collected exclusively via medical devices such as heartbeat rate and electroencephalography (2).

Second, smartphone-sensing methods have improved in quality and reliability, now permitting fine-grained, continuous and unobtrusive collection of novel health-related data such as sleep patterns and voice records (3). Third, advances in Artificial Intelligence (AI)-driven software, especially deep learning (4), are increasingly allowing to generate insights about human health from digitally measured data. For example, smartphone apps can be used to predict a person’s cognitive status from their responses to gamified cognitive tasks such as 3D virtual navigation (5).

Leveraging digital health to track parameters relevant to human health is particularly important for the older segments of the population as old age is associated with multimorbidity (6) and higher care needs. Given the rapid erosion of the old age dependency ratio (reduction in share of working-age people vs. older people) and the often-stated wish of older adults to age in place, these digital technologies can enable novel and more continuous autonomy-preserving tools for health monitoring, prevention and telemedicine. In countries like Italy (34.3%), Switzerland (33.3%), and Germany (32%) this dependency ratio has already shrunk to only three working-age people for every person aged 65 and older (7). Personal digital technologies enable continuous and environment-sensitive collection of clinically relevant data which could be used to improve preventative, diagnostic, and therapeutic outcomes. For example, hypertension, systolic, and diastolic blood pressure can be measured by digital sphygmodynamometers and blood pressure monitors. Handheld echo-cardiography can be used for the assessment of a variety of hemodynamic parameters, such as right and left ventricular dimension and function, left ventricular ejection fraction (LVEF), valvulopathies, pulmonary hypertension and arrhythmias. Arrhythmias can also be detected using pulse oximeters, smartwatches, sensors, or contact free electric sensors. ABI can also be measured using portable or digital ABI systems, or automated blood pressure monitors. Diabetes can be measured using a variety of digital blood glucose meters in form of wireless monitors, wearable sensors, or mobile applications. Digital measurements of BMI include digital electronic scales, weight monitors, or smart fat calculators. Respiratory parameters such as respiratory rate, pulmonary ventilation, or oxygen saturation can be measured by pulse oximeters, pressure sensors spirometers, microphones, humidity sensors, accelerometers, or resistive sensors. Finally, physical activity as any other kinematic and cardiovascular factor can be assessed using sensors like patches or necklaces, accelerometers, pedometers, heart rate monitors, or armbands. Balance parameters such as standing, lying, and sitting can be assessed using a variety of sensors, sensitive to capture a wide range of movements in a specific time range. Handgrip strength and muscle strength can be measured using a digital dynamometer. Handgrip strength is also a marker for frailty. Also, a variety of sensors are being used for the diagnosis of fatigue. They are sensitive in detecting circadian variations, electrodermal activity and cardiovascular parameters in fatigue.

Furthermore, digital pressure algometers and other devices such as dolorimeters are being used to measure the pressure pain threshold in humans. Finally, for the measurement of fever, new technologies such as wearable thermometers and/or non-contact thermometers have also emerged.

In order to assess the potential of these digital health technologies to improve health outcomes, it is paramount to ground the analysis on solid scientific evidence (8). In particular, it is necessary to investigate which digitally measurable parameters—defined as parameters that are measured or can be measured using personal digital devices—can effectively improve health outcomes among the elderly population. Currently, there is a lack of systematic evidence on this topic due to the inherent heterogeneity of the digital health domain and the lack of clinical validation of both novel prototypes and marketed devices. Our study aims at producing systematic and generalizable knowledge on which digitally measurable data may be effectively collected by future digital health devices to improve health outcomes in certain patient groups. Using a modified PICO process and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework (9), we provide the results of a systematic review and subsequent meta-analysis of digitally measurable predictors of morbidity, hospitalization and mortality among older adults aged 65 or older. These findings can inform both technology developers and clinicians involved in the design, development, and clinical implementation of digital health technologies for elderly citizens.

**METHODOLOGY**

**Search Strategy and Study Selection**

We searched MEDLINE/Pubmed, Embase, Web of Science and PsycInfo on the 30th of March 2020. We searched the databases for eligible peer-reviewed articles on digitally measurable parameters of hospitalization, morbidity, and mortality published in one of the four languages spoken by the authors, namely English, Italian, Greek, or German. After extensive pilot-testing and validation of the search string, we searched the title, abstract, and keywords using a modified PICO process for studies published from 1995 to 2020 (see Annex 1). We set limitations regarding study type excluding secondary studies (e.g., reviews), theoretical studies and studies with no proof of concept. A full description of the search terms is available as Supplementary Material. A total of 4,266 entries were retrieved using this string. The systematic search was performed by the first author (SD) and inspected for validation by the last author (MI). Query logic was adapted to each search database to optimize retrieval. Following the recommendations by (10), the study selection process was conducted and presented...
using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (http://prisma-statement.org/) as a guide (see Figure 1). The PRISMA study selection process entails four phases: identification, screening, eligibility, and final synthesis.

In the screening phase, duplicates were removed both automatically using the Endnote tool for duplicate detection and manually based on abstract screening. A total of 343 articles was removed at this stage. The remaining 2,187 entries were screened manually to remove entries whose ineligibility could be detected via abstract assessments. Thousand eight hundred and eighty-eight records were excluded at this stage. Subsequently, full-text screening was performed on the remaining 299 records. Uncertainties and diverging inclusion choices between the two reviewers were discussed among the research team with documented reasons and re-evaluated until a consensus was reached.
Studies included in the synthesis had the features described in Table 1.

### Data Extraction and Coding

We created three different spreadsheets in Microsoft Excel, one for each of the outcomes reported. Each spreadsheet included information on the study and outcome characteristics (Supplementary Material). Study characteristics included year of publication, study type, sample size, proportion of male participants, mean age, age range, and population diagnoses. For mortality events, we extracted the digitally measurable predictors, the devices used for these measurements and the duration of follow-up period when mortality was measured. For morbidity events, information included all the digitally measurable predictors, all the digital devices used for these measurements and all the adverse health conditions observed after the investigation period. For hospitalization events, coded information included, apart from the digitally measurable predictors and the used devices, the hospital admission and readmission rates. For the estimation of the outcomes we collected all the hazard ratios (HRs), odds ratios (ORs), and 95% Confidence Intervals (CIs) reported for mortality, morbidity, and hospitalization events. In cases where the ORs, HRs, and CIs were not provided as primary data by the studies, we calculated them by extracting for each predictor the number of patients with the outcome and the total number of patients for each predictor assigned to each study group (11). For consistency reasons, crude values were preferred over adjusted. We combined HRs and ORs reported separately across studies per gender, per age groups of older people or per quartile of the same predictor across studies, since the aim was an overall outcome assessment without subgroup differentiations (12–17). We also calculated inverse HRs for specific comparisons (18–21).

### Data Analysis

Random-effects meta-analysis was performed using the Knapp-Hartung-Sidik-Jonkman estimator (22, 23). Pooled estimates are presented using odds ratios or hazard ratios. Heterogeneity was assessed using tau2, which defines the variance of the true effects sizes and determines the weight assigned to each of the included studies in the meta-analysis model. In addition, the $I^2$ statistic which describes the magnitude of heterogeneity across studies that is attributable to the true differences of the results rather than chance or sampling error was also examined (23). Heterogeneity can be interpreted as low, when $I^2 = 0–40\%$, as moderate, when $I^2 = 30–60\%$, as substantial, when $I^2 = 50–90\%$ and as considerable when $I^2 = 75–100\%$ (24). Meta-regression was performed to examine whether the results differ based on the diagnosis of the participants. The presence of publication bias was assessed using a funnel plot (23, 25). All analyses were performed using Stata 16.1 (StataCorp, TX, USA).

### Risk of Bias

For RCTs we used the revised Cochrane tool (RoB 2) to assess risk of bias in randomized trials. (26) This tool includes seven items that cover six bias domains; (i) selection bias (2 items); (ii) performance bias; (iii) detection bias; (iv) attrition bias; (v) reporting bias; and (vi) other bias. This tool has three grading levels: (i) low, (ii) moderate, and (iii) high risk of bias. The worst grading in individual items define the overall risk of bias for each single study. For the cohort studies we used the Cochrane Risk Of Bias In Non-randomized Studies—of Interventions (ROBINS-I tool) (27) and also the Newcastle-Ottawa quality assessment scale (NOS) for Cohort Studies. (28) Main domains for risk of the ROBINS-I bias assessment here are: (i) bias due to confounding; (ii) bias in selection of participants into the study; (iii) bias in classification of interventions, (iv) bias due to deviations from intended interventions, (v) bias due to missing data, (vi) bias in measurement of outcomes, and (vii) bias in selection of the reported result. Grading of this scale includes four levels: (i) low, (ii) moderate, (iii) serious, and (iv) critical. Again, the worst grading in any of these items define the overall risk of bias for every single study. The Ottawa scale consists of nine items that cover three dimensions: (i) patient selection (4 items); (ii) comparability of cohorts (2 items); and (iii) assessment of outcome (three items). A point is assigned to each item that is satisfied by the study. The total score therefore ranges from zero to nine, with higher scores indicating higher quality. A total score $\geq 7$ represents high quality.

### Results

A PRISMA flowchart summarizing the article selection process is presented in Figure 1. After the initial database search, 43 studies were considered relevant according to the inclusion criteria and were included in the analysis.

A full description of the included studies is depicted in Tables 2A, 2B. Two of the included studies were RCTs (41,
| References          | Study design | Participants N (%males), mean age, age range | Diagnosis                        | Intervention                                      |
|---------------------|--------------|---------------------------------------------|----------------------------------|--------------------------------------------------|
| Aboyans et al. (29) | Retrospective cohort | 387 (78%), mean age: 68.22 (12.24) | Peripheral arterial disease      | Digital Subtraction Angiography                   |
| Afilalo et al. (30) | Prospective cohort | 131 (66%), mean age: 75.8 (4.4)   | Scheduled to undergo cardiac surgery | Cardiac Surgery                                   |
| Amar et al. (31)    | Prospective cohort | 100 (74%), mean age: 63.78 (8.48) | No diagnosis                      | Esophagectomy                                     |
| Arboix et al. (32)  | Retrospective cohort | 47 (57%), mean age: 71.55 (10.82) | Thalamic hemorrhage               | –                                                |
| Barnett et al. (33) | Retrospective cohort | 8,361 (74.1%), mean age: 63.0 (11.4) | Open heart procedure             | Cardiovascular Surgery                             |
| Baumert et al. (12) | Retrospective cohort | 3,092 (86.9%), mean age: 77.1 (5.65) | No diagnosis/Osteoporosis         | –                                                |
| Berton et al. (34)  | Prospective cohort | 505 (71.5%), mean age: 68.01 | Acute myocardial infarction      | Intensive Care Unit                               |
| Buch et al. (35)    | Prospective cohort | 946 (48.8%), age range: 60–80 | Age-related macular degeneration | –                                                |
| Buchman et al. (18) | Prospective cohort | 1,249 (23%), mean age: 80.0 (7.72) | No diagnosis                      | –                                                |
| Casella et al. (36) | Prospective cohort | 1,959 (70%) mean age: 67 (12) | Acute myocardial infarction      | Coronary Care Unit                                |
| Ferrer et al. (37)  | Prospective cohort | 328 (38.4%), mean age: 85 | No diagnosis                      | –                                                |
| Fisher et al. (13)  | Prospective cohort | 4,910 (43.10%), mean age: 79.4 (6.6) | Age-related macular degeneration | –                                                |
| Fujishima et al. (38) | Prospective cohort | 187 (61%), mean age: 71 (10) | Coronary artery disease          | –                                                |
| Fukumoto et al. (39) | Prospective cohort | 1,786 (65.5%), mean age: 66 (10) | Cardiac catheterization          | Left-heart Catheterization                        |
| Ho et al. (40)      | Prospective cohort | 1,483 (50.44%), age: >70 | No diagnosis                      | –                                                |
| Inoue et al. (14)   | Prospective cohort | 4,373 (38%), mean age: 68.1 (6.6) | No diagnosis                      | –                                                |
| Jones et al. (41)   | RCT            | 988 (59%), mean age: 67 (10) | Heart failure                     | Digitalis vs. Placebo plus Diuretics and Angiotensin-converting–enzyme Inhibitors |
| Joseph et al., (59) | Prospective cohort | 101 (46.5%), mean age: 79 (9) | Patients with ground level fall-injuries | Hospitalized for ground-level falls               |
| Jotheeswaran et al. (10) | Prospective cohort | 12,373 (37.7%), mean age: 74.1 (7.0) | Dementia                         | –                                                |
| Law et al. (42)     | Retrospective cohort | 168 (75.6%), mean age: 83.5 (2.5) | Aortic aneurysm                  | Open and endovascular repair of abdominal aortic aneurysm |
| Lee et al. (43)     | Prospective cohort | 1,147 (60.2%), mean age: 64.5 (12.32) | Ischemic stroke                  | Robotic totally endoscopic coronary artery bypass grafting |
| Lion et al., (63)   | Prospective cohort | 61 (0%), mean age: 71.68 (4.28) | No diagnosis                      | –                                                |
| Lyra et al. (15)    | Prospective cohort | 295 (35.3%), mean age: 75 | No diagnosis                      | –                                                |
| Matsuzawa et al. (44) | Prospective cohort | 140 (0%), mean age: 68.12 (10.58) | Chest pain                       | Cardiac catheterization                            |
| Missouri et al. (45) | Prospective cohort | 110 (60%), mean age: 70.8 (9.99) | Peripheral vascular disease      | –                                                |
| Mujib et al. (46)   | RCT            | 7,788 (75%), mean age: 64 (11)   | Chronic heart failure            | Digoxin or placebo                                |
| Oberman et al. (47) | Prospective cohort | 3,613 (0%), age range: 50–79  | No diagnosis                      | –                                                |
| Palmisano et al. (16) | Prospective cohort | 770 (66.4%), mean age: 65.5 (14)  | No diagnosis                      | –                                                |
| Park et al. (48)    | Prospective cohort | 498 (60%), mean age: 82.8 (5.3)  | 30 days phone intervention post hospital discharge | Care transition quality improvement program |
| Philbert et al. (49) | Retrospective cohort | 2,278 (46%), mean age: 66 (9) | No diagnosis                      | –                                                |
| Pinto et al. (50)   | Prospective cohort | 2,968 (48.6), age range: 57–85  | Global sensory impairment         | –                                                |
| Plakht et al. (51)  | Retrospective cohort | 2,763 (67.8%), mean age: 66.6 (13.3) | Acute myocardial infarction      | Hospitalization after atrial myocardial infarction |
| Radhakrishnan et al. (52) | Prospective cohort | 403 (45%), age range: <60->94 | No diagnosis                      | Telehealth                                        |
| Rolland et al. (47) | Prospective cohort | 7,250 (0%), mean age: 80.5 (3.76) | Hip fracture                      | –                                                |
| Sheng et al. (53)   | Prospective cohort | 4,055 (44.5%), mean age: 68.5 (7.5) | Peripheral arterial disease      | –                                                |
| Smirnova et al. (54) | Retrospective cohort | 2,978 (51%), mean age: 65.9 (9.8)  | No diagnosis                      | –                                                |
| Stein et al. (19)   | Prospective cohort | 1,655 (82%), mean age: 66.81 (11.69) | ICD implantation                 | Implantable cardioverter defibrillator            |
TABLE 2A | Continued

| References                  | Study design      | Participants N (%males), mean age, age range | Diagnosis                      | Intervention          |
|------------------------------|-------------------|---------------------------------------------|--------------------------------|-----------------------|
| Tateishi et al. (55)         | Retrospective cohort | 164 (53%), median age: 76                 | Acute ischemic stroke        | Thrombolysis.        |
| van Vugt et al. (56)         | Retrospective cohort | 1,614 (55.5%), mean age: 68.6 (10.8)   | Colorectal cancer            | Colorectal cancer surgery |
| Ward et al. (57)             | Retrospective cohort | 309 (43.3%), mean age: 65.7 age range: 34-94 | Peripheral arterial disease   | –                     |
| Wilson et al. (58)           | Prospective cohort  | 5,630 (56.1%), age: ≥70              | No diagnosis                  | –                     |
| Zeitzer et al. (20)          | Prospective cohort  | 2,976 (100%), mean age: 76.4 (5.53)    | Osteoporosis                  | –                     |
| Zhu et al. (21)              | Retrospective cohort | 186 (84.4%), mean age: 65             | Bladder cancer                | Robot-assisted radical cystectomy |

46), 28 prospective (10, 13–20, 30, 31, 34–40, 43–45, 47, 48, 50, 53, 58–60) and 13 retrospective cohort studies (12, 21, 29, 32, 33, 42, 49, 51, 52, 54–57). The total number of older participants (≥65 years) included in the analysis was 92,994, of whom, 48% (n = 44,461) were males and 52% (n = 48,533) females. Of the 43 studies, 18 studies included cardiovascular patients, 13 studies included patients with other diagnoses, and in 12 studies the participants had no specific diagnosis. Twenty-nine of the included studies reported results about mortality events, 18 about morbidity and five studies reported results about nine of the included studies reported results about mortality. Of the 43 studies, 18 studies included cardiovascular patients, 13 studies included patients with other diagnoses, and in 12 studies the participants had no specific diagnosis. Twenty-nine of the included studies reported results about mortality events, 18 about morbidity and five studies reported results about nine of the included studies reported results about mortality.

Digital measurements were reported in 15 studies for a wide range of physical and physiological functions. Wearable sensors and stopwatches were used for the measurement of walking speed and other kinematic factors, such as balance parameters. Balance parameters such as standing posture and switches between sitting and standing were also measured by body fixed sensors and stopwatches. Also, a wrist-worn accelerometer and an implantable defibrillator were used for the assessment of physical activity. A triaxial wearable gyroscope sensor was used for the measurement of the arterial stiffness and frailty among older people. A digital standing scale was used for the measurement of Body Mass Index (BMI) and an inhome polysomnography for the measurement of respiratory rate. Other devices that were used comprised an automatic device for the Ankle Brachial Index (ABI), an electronic spirometry for the vital capacity, an electric counter for the tapping rate and a digital reactive hyperaemia peripheral arterial tonometry (RH-PAT) for the assessment of the reactive hyperaemia peripheral arterial tonometry index. The remaining 28 studies involved measurements that were not collected using personal digital devices but could have been obtained using commercially available digital devices (e.g., hypertension, systolic and diastolic blood pressure, and arrhythmias as they can be measured via, respectively, digital sphygmodynamometers, blood pressure monitors, and pulse oximeters or smartwatches.

Risk of Bias Assessment
Risk of bias assessment was performed independently by two authors (Tables 3–5). Disagreements were solved through discussion and re-evaluation of the differently evaluated points until a consensus was reached. According to RoB and ROBINS-I scales, 17 studies were assessed as being of serious risk of bias, 16 studies were assessed of moderate risk of bias and only 10 studies were assessed as being of low risk of bias. According to the Newcastle Ottawa Scale, only six studies had a total score ≥ 7.

RESULTS

Mortality
Meta-analysis of all the digitally measurable predictors of mortality identified by the search, indicated six statistically significant predictors (Figure 2). These included diabetes (HR 1.70; CI 1.37, 2.10; 8 studies; OR 1.64; CI 1.06, 2.51; 6 studies), decreased BMI (HR 1.24; CI 1.06, 1.45; 6 studies), arrhythmias (HR 1.77; CI 1.33, 2.35; 5 studies), slow walking speed (HR 1.69; CI 1.32, 2.16; 4 studies), not being physically active (HR 1.97; CI 1.20, 3.24; 3 studies) and LVEF < 40 (OR 2.17; CI 1.63, 2.90; 3 studies). Hypertension results were marginally insignificant for mortality (HR 1.22; CI: 0.94, 1.58; 5 studies; OR 1.49; CI: 0.89, 2.50; 4 studies). Being physically active, having increased BMI and obesity were significantly associated with survival (HR 0.42; CI 0.20, 0.88; 2 studies, HR 0.77; CI 0.61, 0.96; 5 studies and OR 0.71; CI 0.50, 0.99; 6 studies, respectively), whereas the results related to systolic blood pressure ≤90 (HR 1.91; CI 0.88, 4.13; 2 studies) were neither for mortality nor for survival statistically significant.

The description of four balance parameters was based on two studies on standing posture [HR 1.23; CI 1.11, 1.36; (18) and (17)] and sit-to-stand ability [HR 1.06; CI 0.72, 1.56; (18) and (17)] while measurements of the other two variables were reported only in one study (18). Since these multiple balance measurements were originating from the same samples, we did not estimate a common effect size for all the balance parameters to avoid the unit of analysis error (23). In contrast, we created a forest plot visual representation of the outcomes which indicates that the only significant predictor of mortality was pooled standing posture (HR 1.23; CI 1.11, 1.36; 2 studies).

Table 3 summarizes additional predictors of mortality identified only once across the included studies. According to these results, a respiratory rate ≥16 breaths-min⁻¹ (HR 1.44; CI 1.29, 1.62), arterial stiffness (HR 2.98; CI 2.08, 4.27), ABI >90 (HR 2.33; CI 1.24, 4.39) severe left ventricular dysfunction (HR 2.12; CI 1.75; 2.57) significant left ventricular hypertrophy (HR 1.96; CI 1.49; 2.57), left ventricular dilatation (HR 1.79; CI 1.3; 2.47), left ventricular filling pressure (HR 1.17; CI
| References          | Predictor type (digitally measurable) | Digital device used          | Outcome             | Time spectrum for mortality | Morbidity severity                  | Hospital admission               |
|---------------------|--------------------------------------|------------------------------|---------------------|-----------------------------|------------------------------------|----------------------------------|
| Aboyans et al. (29) | Hypertension, diabetes               | No digital device mentioned  | Mortality, morbidity | 62 months                  | Renal artery stenosis              | Intensive Care Unit admission    |
| Afilalo et al. (30) | Slow walking speed                   | Stopwatch                    | Mortality           | –                           | Morbidity                         | –                                |
| Amar et al. (31)    | Supraventricular tachydysrhythmias   | No digital device mentioned  | Mortality           | 30 days                     | Supraventricular tachydysrhythm-ias| –                                |
| Arboix et al. (32)  | Respiratory events, obesity          | No digital device mentioned  | Mortality           | Not mentioned               | –                                  | –                                |
| Barnett et al. (33) | Hypertension, diabetes, ejection fraction > 40, obesity | No digital device mentioned | Mortality           | 30 days                     | –                                  | –                                |
| Baumert et al. (12) | Respiratory rate ≥ 16 breaths·min⁻¹ | Overnight in-home polysomnography | Mortality           | 6.4 (1.6) years /8.9 (2.6) years | –                                  | –                                |
| Berton et al. (34)  | Diabetes                              | No digital device mentioned  | Mortality, morbidity| –                           | Atrial fibrillation/flutter        | –                                |
| Buch et al. (35)    | Hypertension, diabetes               | No digital device mentioned  | Mortality           | 14 years                    | –                                  | –                                |
| Buchman et al. (18) | Standing posture, Timed Up and Go (TUG) stand, TUG sit to stand, TUG stand to sit, 32-ft. Slow walking speed | Body-fixed sensor | Mortality, morbidity | 3.6 years                   | Mild cognitive impairment, Dementia | –                                |
| Casella et al. (38) | Systolic blood pressure ≤ 90, diabetes, heart rate > 100 b/min | No digital device mentioned | Mortality           | 30 days                     | –                                  | –                                |
| Ferrer et al. (37)  | Atrial fibrillation                  | No digital device mentioned  | Mortality           | 3 years                     | –                                  | –                                |
| Fisher et al. (13)  | Decreased BMI, increased BMI, hypertension, diabetes | No digital device mentioned | Mortality           | 4.8 years                   | –                                  | –                                |
| Fujishima et al. (38)| Hypertension, diabetes, diastolic blood pressure, increased BMI | No digital device mentioned | Morbidity           | –                           | Ischemia                           | –                                |
| Fukumoto et al. (39)| Hypertension, diabetes, atrial fibrillation, left ventricular ejection fraction < 45 | No digital device mentioned | Morbidity           | –                           | Cholesterol embolization syndrome   | –                                |
| Ho et al. (40)      | Hypertension, diabetes               | No digital device mentioned  | Morbidity           | –                           | Mobility decline                  | –                                |
| Inoue et al. (14)   | Arterial stiffness                   | Triaxial wearable gyroscope sensor | Mortality           | 9 years                     | –                                  | –                                |

(Continued)
| References       | Predictor type (digitally measurable)                                                                 | Digital device used                                      | Outcome                        | Time spectrum for mortality | Morbidity severity | Hospital admission                  |
|------------------|------------------------------------------------------------------------------------------------------|----------------------------------------------------------|-------------------------------|-----------------------------|--------------------|-------------------------------------|
| Jones et al. (41) | Decreased BMI, increased BMI, diabetes, ejection fraction                                             | No digital device mentioned                               | Mortality                     | 3.5 years                   | –                  | –                                   |
| Joseph et al., (59) | Upper-extremity function-frailty                                                                  | Triaxial wearable gyroscope sensor                        | Hospitalization               | –                           | –                  | Institutionalization, readmissions  |
| Jotheeswaran et al. (10) | Weight loss, decreased physical activity, slow walking speed                                       | Standard timed walking test for walking speed             | Mortality                     | 2.8–5 years                 | Incident dependence | –                                   |
| Law et al. (42)   | Hypertension, diabetes                                                                             | No digital device mentioned                               | Mortality                     | 30 days                     | –                  | –                                   |
| Lee et al. (43)   | Abnormal ABI <0.90                                                                                  | Automatic device                                          | Mortality                     | 30 days                     | –                  | –                                   |
| Lion et al., (60) | Systolic blood pressure                                                                             | No digital device mentioned                               | Morbidity                     | –                           | Dizziness          | –                                   |
| Lyra et al. (15)  | Vital capacity                                                                                      | Electronic spirometer                                     | Mortality                     | 10 years                    | –                  | –                                   |
| Matsuzawa et al. (44) | Reactive hyperaemia peripheral arterial tonometry index                                               | Digital reactive hyperaemia peripheral arterial tonometry (RH-PAT) | Morbidity                     | –                           | Ischemic heart disease | –                                   |
| Misouris et al. (45) | Hypertension, diabetes                                                                             | Semi-automated ultrasound sphygmomanometer               | Mortality                     | 6.1 years                   | –                  | –                                   |
| Mujib et al. (46) | Hypertension, diabetes, ejection fraction <35                                                       | No digital device mentioned                               | Morbidity                     | –                           | Stroke/neurological deficit | –                                   |
| Oberman et al. (47) | Hypertension, diabetes, systolic blood pressure                                                      | No digital device mentioned                               | Morbidity                     | –                           | Hypertrophied left ventricular mass | –                                   |
| Palmisano et al. (16) | Decreased physical activity                                                                        | Implantable cardioverter defibrillator                    | Morbidity                     | –                           | Atrial arrhythmias     | –                                   |
| Park et al. (48)  | Weakness, pain, palpitations, fatigue, fever, weight gain, difficulty breathing                    | No digital device mentioned                               | Hospitalization               | –                           | –                  | 30-day readmissions                |
| Philibert et al. (49) | Systolic blood pressure, diastolic blood pressure, diabetes                                         | No digital device mentioned                               | Mortality                     | Not mentioned               | –                  | –                                   |
| Pinto et al. (50) | Hypertension, diabetes, increased BMI, decreased BMI, obesity                                      | No digital device mentioned                               | Morbidity                     | –                           | Impaired mobility      | –                                   |
| References               | Predictor type (digitally measurable)                                                                 | Digital device used          | Outcome | Time spectrum for mortality | Morbidity severity | Hospital admission |
|--------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------|---------|-----------------------------|--------------------|-------------------|
| Plakht et al. (51)       | Hypertension, obesity, atrial fibrillation, severe left ventricular dysfunction, significant left ventricular hypertrophy, left ventricular dilatation, left ventricular filling pressure, moderate or severe mitral valve regurgitation pulmonary hypertension, left atrial dilatation, right ventricular dysfunction, moderate or severe tricuspid regurgitation | No digital device mentioned  | Mortality | 8.2 years                   |                    |                   |
| Radhakrishnan et al. (52)| Pulmonary and arrhythmia comorbidity, obesity                                                        | No digital device mentioned  | Hospitalization | –                          | –                  | Admission        |
| Rolland et al. (17)      | Slow walking speed, repeated chair stands, balance test                                              | Stopwatch                    | Mortality | 3.8 years                   | –                  | –                |
| Sheng et al. (53)        | Hypertension, diabetes                                                                               | Blood pressure monitor       | Mortality | 5.9 years                   | –                  | –                |
| Smirnova et al. (54)     | Obesity, diabetes                                                                                    | No digital device mentioned  | Mortality | 5 years                     | –                  | –                |
| Stern et al. (19)        | Atrial fibrillation, diabetes, decreased BMI, obesity, left ventricular ejection fraction <40, increased physical activity, decreased physical activity | No digital device mentioned  | Mortality | 1 year                      | –                  | –                |
| Tateishi et al. (55)     | Hypertension, diabetes                                                                               | No digital device mentioned  | Mortality, morbidity | 90 days                    | Unfavorable outcome | –                |
| van Vught et al. (56)    | Atrial fibrillation                                                                                  | No digital device mentioned  | Morbidity | –                           | –                  | LOS, readmission |
| Ward et al. (57)         | Hypertension, diabetes, abnormal ABI <0.90                                                           | No digital device mentioned  | Morbidity | –                           | Left ventricular ejection fraction <35 | –                |
| Wilson et al. (58)       | Hypertension, increased BMI, decreased BMI, walking difficulty/slow walking speed                     | No digital device mentioned  | Morbidity | –                           | Hip fracture       | –                |
| Zeitzer et al. (20)      | Increased physical activity, decreased physical activity                                               | Wrist-worn accelerometer     | Mortality | 6.5 years                   | –                  | –                |
| Zhu et al. (21)          | Increased BMI                                                                                        | No digital device mentioned  | Mortality | Not mentioned               | –                  | –                |
TABLE 3 | Additional predictors of Mortality.

| No. | References | Predictor | HR/OR (95% CI) | p       |
|-----|------------|-----------|----------------|---------|
| 1.  | Arboix et al. (32) | Respiratory events | OR 3.30; CI 0.62, 17.62 | 0.081   |
| 2.  | Baumert et al. (12) | Respiratory rate \( \geq 16 \) breaths/min\(^{-1}\) | HR 1.44; CI 1.29, 1.62 | \(<0.00001\) |
| 3.  | Inoue et al. (14) | Arterial stiffness | HR 2.98; CI 2.08, 4.27 | \(<0.00001\) |
| 4.  | Lee, (43) | ABI \(>90\) | HR 2.33; CI 1.24, 4.39 | 0.009   |
| 5.  | Lyra (15) | Vital capacity | HR 0.97; CI 0.03, 0.19 | \(<0.00001\) |
| 6.  | Lyra (15) | Tapping rate | HR 0.04; CI 0.77, 0.91 | \(<0.00001\) |
| 7.  | Lyra (15) | Muscle strength | HR 0.73; CI 0.58, 0.92 | 0.007   |
| 8.  | Philibert et al. (49) | Diastolic Blood Pressure | HR 0.67; CI 0.60, 0.75 | \(<0.00001\) |
| 9.  | Ptakht et al. (51) | Severe Left ventricular dysfunction | HR 2.12; CI 1.75; 2.57 | 0.002   |
| 10. | Ptakht et al. (51) | Constrictive or significant left ventricular hypertrophy | HR 1.96; CI 1.49; 2.57 | 0.788   |
| 11. | Ptakht et al. (51) | Left ventricular dilatation | HR 1.79; CI 1.3; 2.47 | 0.003   |
| 12. | Ptakht et al. (51) | Left ventricular filling pressure | HR 1.17; CI 1.09; 1.24 | 0.152   |
| 13. | Ptakht et al. (51) | Moderate or severe mitral valve regurgitation | HR 1.47; CI 1.14; 1.9 | \(<0.001\) |
| 14. | Ptakht et al. (51) | Moderate or severe pulmonary hypertension | HR 1.88; CI 1.48; 2.39 | 0.001   |
| 15. | Ptakht et al. (51) | Left atrial dilatation | HR 1.24; CI 1.14; 1.35 | 0.929   |
| 16. | Ptakht et al. (51) | Right ventricular dysfunction | HR 1.22; CI 1.1; 1.36 | 0.159   |
| 17. | Ptakht et al. (51) | Moderate or severe tricuspid regurgitation | HR 1.65; CI 1.29; 2.1 | \(<0.001\) |
| 18. | Rolland et al. (17) | Low handgrip strength | HR 1.47; CI 1.18, 1.83 | 0.0006  |

TABLE 4 | Additional predictors of Morbidity.

| No. | References | Predictor | OR/HR; (95% CI) | p       |
|-----|------------|-----------|----------------|---------|
| 1.  | Buchman et al. (18) | Slow walking speed for MCI | HR 1.15; CI 0.93, 1.42 | 0.08    |
| 2.  | Buchman et al. (18) | Slow walking speed for Dementia | HR 1.62; CI 1.23, 2.14 | 0.0006  |
| 3.  | Jotheeswaran et al. (10) | Slow walking speed | IRR 1.28; CI 1.12, 1.47 | 0.003   |
| 4.  | Matsuzawa et al. (44) | Reactive hyperemia peripheral arterial tonometry index | OR 0.51; CI 0.38, 0.66 | \(<0.00001\) |
| 5.  | Palmisano et al. (18) | Decreased physical activity | OR 5.56; CI 2.45, 12.64 | \(<0.0001\) |
| 6.  | Pinto et al. (50) | BMI obesity | OR 1.12; CI 0.76, 1.63 | 0.57    |
| 7.  | Ward et al. (57) | ABI \(<0.90\) | OR 2.48; CI 1.22, 5.07 | 0.01    |

1.09; 1.24), moderate or severe mitral valve regurgitation (HR 1.47; CI 1.14; 1.9), pulmonary hypertension (HR 1.88; CI 1.48; 2.39), left atrial dilatation (HR 1.24; CI 1.14; 1.35) right ventricular dysfunction (HR 1.22; CI 1.1; 1.36), moderate or severe tricuspid regurgitation (HR 1.65; CI 1.29; 2.1), and low handgrip strength (HR 1.47; CI 1.18, 1.83) were significantly associated to mortality. Vital capacity (HR 0.07; CI 0.03, 0.19), high tapping rate (HR 0.04; CI 0.77, 0.91), and muscle strength (HR 0.73; CI 0.58, 0.92), were significant predictors of longer survival.

Current analysis represents a synthesis of the digitally measurable predictors of mortality. The analysis indicates that a variety of crucial health-related survival parameters, such as hemodynamic, respiratory, kinetic measurements, BMI and diabetes, can be measured and managed remotely. Digital technologies such as blood pressure monitors, pulse oximeters, and sensors for the measurement of heart and respiratory rate, blood glucose meters for diabetes, height-weight monitors for BMI, movement sensors, accelerometers, pedometers for physical activity parameters,
TABLE 5 | Predictors of hospitalization.

| No. | References          | Predictor type (digitally measurable) | OR (95% CI)     | p   |
|-----|---------------------|----------------------------------------|-----------------|-----|
|     |                     |                                         |                 |     |
|     | Hospital admission  |                                         |                 |     |
| 1.  | Joseph, (59)        | Upper-Extremity Function-Frailty         | OR 4.14; CI 1.63, 10.51 | 0.000 |
| 2.  | Radhakrishnan et al. (52) | Pulmonary comorbidity | OR 3.43; CI 1.12, 10.5 | 0.031 |
|     |                     |                                         |                 |     |
|     | Hospital readmission |                                         |                 |     |
| 1.  | Joseph, (59)        | Upper-Extremity Function-Frailty         | OR 2.12; CI 0.89, 5.16 | 0.045 |
| 2.  | Park et al. (48)    | Upper-Extremity Function-Frailty         | OR 2.37; CI 1.05, 5.33 | 0.019 |
| 3.  |                     | Weakness                                | OR 0.68; CI 0.42, 1.09 | 0.065 |
| 4.  |                     | Pain                                    | OR 0.42; CI 0.21, 0.85 | 0.008 |
| 5.  |                     | Palpitations                            | OR 1.62; CI 0.6, 4.38 | 0.172 |
| 6.  |                     | Fatigue                                 | OR 3.04; CI 1.15, 8.03 | 0.013 |
| 7.  |                     | Fever                                   | OR 1.15; CI 0.14, 9.33 | 0.045 |
| 8.  |                     | Weight gain                             | OR 3.83; CI 1.30, 11.27 | 0.007 |
| 9.  |                     | Difficulty breathing                    | OR 1.58; CI 0.68, 3.64 | 0.144 |
| 10. | van Vugt et al. (56) | Increased BMI                           | OR 0.91; CI 0.66, 1.26 | 0.291 |
| 11. |                     | Decreased BMI                           | OR 0.95; CI 0.46, 1.97 | 0.441 |
| 12. |                     | Obesity                                 | OR 1.03; CI 0.68, 1.58 | 0.044 |

Dynamometers for muscle strength, spirometers, and hand-held echocardiogram can be efficiently incorporated in routine-care of older people, since they are correlated with survival or mortality, respectively.

Subgroup analyses comparing participants with cardiovascular diseases to those with no cardiovascular diagnoses were performed on three of the statistically significant predictors of mortality. Subgroup analysis for diabetes (HR 1.69; CI 1.43, 2.00 for cardiovascular vs. HR 1.62; CI 0.95, 2.75 for other diagnoses) and decreased BMI (HR 1.24; CI 1.08, 1.42 for cardiovascular patients vs. HR 1.24; CI 0.96, 1.61 for other diagnoses) indicated that diabetes and decreased BMI are significant predictors of mortality only for cardiovascular patients, whereas arrhythmias (HR 1.61; CI 1.35, 1.93 for cardiovascular vs. HR 2.63; CI 1.46, 4.74 for other diagnoses) did not differentiate across diagnoses regarding their association with mortality.

We did not perform a subgroup analysis for slow walking speed, not being physically active and LVEF<40 and since, in the first case none of the studies included cardiovascular patients, and in the two last cases the number of studies included was not sufficient for a subgroup analysis.

Some of the previous analyses were based on a small number of studies and the instability of these results should be considered. The 95% Confidence Intervals of the included studies are very narrow, and although estimates are close to each other suggesting homogeneity, the $I^2$ is relatively high (23, 24). Non-significant heterogeneity tests for Hypertension in ORs ($I^2 = 59$, $p = 0.06$) and systolic blood pressure ($I^2 = 92$, $p = 0.11$) possibly occurred due to low power, since the number of studies included in these analyses was small (23).

**Morbidity**

Predictors of morbidity are depicted in Figure 3. Hypertension (OR 1.32; CI 1.06, 1.64; 13 studies), and decreased BMI (OR 1.50; CI 1.11, 2.01; 3 studies) were identified as significant predictors of morbidity. Meta-analysis of outcomes reporting results for arrhythmias (OR 1.44; CI 0.73, 2.84; 3 studies), LVEF < 45 (OR 1.04; CI 0.71, 1.52; 4 studies) and diastolic blood pressure (OR 1.45; CI 0.60, 3.47; 2 studies) did not provide any statistically significant result, whereas results regarding diabetes (OR; CI 1.26 0.96, 1.65; 13 studies), slow walking speed (HR 1.57; CI 0.91, 2.68; 3 studies) increased BMI (OR 1.03; CI 0.89, 1.19; 5 studies) and systolic blood pressure (OR 1.06; CI 0.97, 1.16; 3 studies) were marginally insignificant.

Figure 3 also provides a visualization of the contribution of each of the four balance parameters to morbidity, based on the combined outcomes of two independent groups originating from the same study (18). Results indicate that none of them was associated to dementia and/or mild cognitive impairment or to being healthy.

Other statistically important predictors of morbidity identified only once through the literature search (Table 4), were slow walking speed reported as HR for dementia (HR 1.62; 1.23, 2.14) and as incidence rate ratio IRR (IRR 1.28; 1.12, 1.47). Other statistically important predictors of morbidity were decreased physical activity (OR 5.56; CI 2.45, 12.64) and an abnormal ABI <90 (OR 2.48; CI 1.22, 5.07).
### Diabetes HR

| Study       | Hazard ratio with 95% CI | Weight (%) |
|-------------|-------------------------|------------|
| Aboyans 2017 | 1.64 [1.14, 2.36]       | 13.68      |
| Casella 2005 | 3.02 [1.39, 6.59]       | 5.60       |
| Fisher 2015  | 1.25 [1.07, 1.46]       | 20.32      |
| Jones 2004   | 1.45 [1.06, 1.98]       | 15.24      |
| Missouri 2004| 1.48 [0.82, 2.67]       | 8.25       |
| Philibert 2019| 2.15 [1.63, 2.84]      | 16.43      |
| Sheng 2016   | 2.81 [1.15, 6.87]       | 4.53       |
| Stein 2009   | 1.78 [1.33, 2.38]       | 15.95      |
| **Overall**  | 1.70 [1.37, 2.10]       |            |

Heterogeneity: $I^2 = 64.83\%$, $H^2 = 2.84$
Test of $\theta = \theta$: $Q(7) = 18.32$, $p = 0.01$
Test of $\theta = 0$: $z = 4.88$, $p = 0.00$

Random-effects Sidik-Jonkman model

### Diabetes OR

| Study       | Odds ratio with 95% CI | Weight (%) |
|-------------|------------------------|------------|
| Barnett 2003 | 1.37 [1.02, 1.84]     | 24.41      |
| Berton 2009  | 1.70 [1.30, 2.22]     | 24.90      |
| Buch 2005    | 5.54 [1.95, 15.74]    | 10.50      |
| Law 2018     | 1.73 [0.45, 6.65]     | 7.44       |
| Smimova 2019 | 1.15 [0.88, 1.50]     | 24.92      |
| Tateishi 2016| 1.43 [0.39, 5.24]     | 7.83       |
| **Overall**  | 1.64 [1.06, 2.51]     |            |

Heterogeneity: $I^2 = 79.42\%$, $H^2 = 4.86$
Test of $\theta = \theta$: $Q(5) = 10.76$, $p = 0.06$
Test of $\theta = 0$: $z = 2.25$, $p = 0.02$

Random-effects Sidik-Jonkman model

### Decreased BMI

| Study       | Hazard ratio with 95% CI | Weight (%) |
|-------------|-------------------------|------------|
| Fisher 2015 | 1.05 [1.02, 1.08]       | 33.30      |
| Jones 2004  | 1.22 [1.06, 1.40]       | 26.78      |
| Jotheeswaran 2015 | 1.40 [1.19, 1.65] | 25.04      |
| Stein 2009  | 1.44 [0.92, 2.26]       | 9.15       |
| van Vugt 2015| 0.95 [0.24, 3.74]      | 1.31       |
| Zhu 2019    | 1.85 [0.91, 3.76]       | 4.42       |
| **Overall** | 1.24 [1.06, 1.45]       |            |

Heterogeneity: $I^2 = 73.13\%$, $H^2 = 3.72$
Test of $\theta = \theta$: $Q(5) = 19.16$, $p = 0.00$
Test of $\theta = 0$: $z = 2.62$, $p = 0.01$

Random-effects Sidik-Jonkman model

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**FIGURE 2** Continued
FIGURE 2 | Continued

Arrhythmias

| Study         | Hazard ratio with 95% CI | Weight (%) |
|---------------|--------------------------|------------|
| Amar 1996     | 4.46 [0.33, 60.45]       | 1.15       |
| Casella 2005  | 1.49 [1.03, 2.16]        | 23.14      |
| Ferrer 2017   | 2.56 [1.40, 4.68]        | 13.98      |
| Plakht 2015   | 1.50 [1.30, 1.73]        | 34.73      |
| Stein 2009    | 2.00 [1.49, 2.68]        | 27.01      |

**Overall**
Heterogeneity: $\tau^2 = 0.05$, $I^2 = 64.26\%$, $H^2 = 2.80$
Test of $\theta = \theta_0$: $Q(4) = 6.05$, $p = 0.20$
Test of $\theta = 0$: $z = 3.93$, $p = 0.00$

Random-effects Sidik-Jonkman model

Slow Walking Speed

| Study         | Hazard ratio with 95% CI | Weight (%) |
|---------------|--------------------------|------------|
| Buchman 2019  | 1.85 [1.58, 2.17]        | 35.30      |
| Jotheeswaran 2015 | 1.36 [1.21, 1.53]    | 37.77      |
| Lyra 2005     | 2.75 [1.18, 6.41]        | 7.03       |
| Rolland 2006  | 1.83 [1.23, 2.72]        | 19.90      |

**Overall**
Heterogeneity: $\tau^2 = 0.04$, $I^2 = 75.56\%$, $H^2 = 4.09$
Test of $\theta = \theta_0$: $Q(3) = 12.07$, $p = 0.01$
Test of $\theta = 0$: $z = 4.18$, $p = 0.00$

Random-effects Sidik-Jonkman model

Decreased physical activity

| Study         | Hazard ratio with 95% CI | Weight (%) |
|---------------|--------------------------|------------|
| Jotheeswaran 2015 | 1.53 [1.32, 1.77]    | 37.01      |
| Stein 2009    | 3.57 [2.13, 5.98]        | 27.01      |
| Zeitzer 2018  | 1.64 [1.34, 2.01]        | 35.98      |

**Overall**
Heterogeneity: $\tau^2 = 0.17$, $I^2 = 92.30\%$, $H^2 = 12.98$
Test of $\theta = \theta_0$: $Q(2) = 9.56$, $p = 0.01$
Test of $\theta = 0$: $z = 2.69$, $p = 0.01$

Random-effects Sidik-Jonkman model
**FIGURE 2** Continued

### LVEF > 40

| Study     | Odds ratio with 95% CI | Weight (%) |
|-----------|------------------------|------------|
| Afiallo 2010 | 2.17 [0.67, 7.03] | 5.88 |
| Barnett 2003 | 2.48 [1.73, 3.55] | 53.52 |
| Stein 2009     | 1.83 [1.20, 2.79] | 40.60 |

Overall: Heterogeneity: $\tau^2 = 0.01$, $I^2 = 8.50\%$, $H^2 = 1.09$

Test of $\theta = \theta$: $Q(2) = 1.15$, $p = 0.56$

Test of $\theta = 0$: $z = 5.30$, $p = 0.00$

Random-effects Sidik-Jonkman model

### Hypertension HR

| Study     | Hazard ratio with 95% CI | Weight (%) |
|-----------|--------------------------|------------|
| Aboyans 2017 | 1.07 [0.78, 1.47] | 19.18 |
| Fisher 2015   | 1.27 [1.12, 1.44] | 25.02 |
| Missouri 2014 | 1.21 [0.73, 2.01] | 13.29 |
| Plakht 2015   | 0.91 [0.80, 1.04] | 24.88 |
| Sheng 2016    | 2.02 [1.41, 2.89] | 17.63 |

Overall: Heterogeneity: $\tau^2 = 6.98$

Test of $\theta = \theta$: $Q(4) = 24.51$, $p = 0.00$

Test of $\theta = 0$: $z = 1.49$, $p = 0.14$

Random-effects Sidik-Jonkman model

### Hypertension OR

| Study     | Odds ratio with 95% CI | Weight (%) |
|-----------|------------------------|------------|
| Barnett 2003 | 1.25 [0.94, 1.66] | 40.08 |
| Buck 2005   | 2.03 [1.50, 2.75] | 39.48 |
| Law 2018    | 0.78 [0.26, 2.34] | 14.98 |
| Tateishi 2016 | 3.38 [0.42, 27.20] | 5.45 |

Overall: Heterogeneity: $\tau^2 = 0.15$, $I^2 = 72.07\%$, $H^2 = 3.58$

Test of $\theta = \theta$: $Q(3) = 7.28$, $p = 0.06$

Test of $\theta = 0$: $z = 1.50$, $p = 0.13$

Random-effects Sidik-Jonkman model
**FIGURE 2 | Continued**

### Increased physical activity

| Study          | Hazard ratio with 95% CI | Weight (%) |
|----------------|-------------------------|------------|
| Stein 2009     | 0.28 [0.17, 0.46]       | 46.74      |
| Zeitzer 2018   | 0.61 [0.44, 0.85]       | 53.26      |

**Overall**

- Heterogeneity: $\chi^2 = 0.23$, $I^2 = 83.25\%$, $H^2 = 5.97$
- Test of $\theta = \theta_0$: $Q(1) = 6.50$, $p = 0.01$
- Test of $\theta = 0$: $z = -2.30$, $p = 0.02$

Random-effects Sidik-Jonkman model

### Increased BMI

| Study          | Hazard ratio with 95% CI | Weight (%) |
|----------------|-------------------------|------------|
| Fisher 2015    | 0.95 [0.92, 0.98]       | 35.98      |
| Jones 2004     | 0.81 [0.71, 0.92]       | 32.27      |
| Stein 2009     | 0.56 [0.36, 0.87]       | 15.20      |
| van Vugt 2015  | 0.60 [0.31, 1.18]       | 8.60       |
| Zhu 2019       | 0.54 [0.27, 1.10]       | 7.95       |

**Overall**

- Heterogeneity: $\chi^2 = 0.04$, $I^2 = 81.66\%$, $H^2 = 5.45$
- Test of $\theta = \theta_0$: $Q(4) = 14.60$, $p = 0.01$
- Test of $\theta = 0$: $z = -2.32$, $p = 0.02$

Random-effects Sidik-Jonkman model

### Obesity

| Study          | Odds ratio with 95% CI | Weight (%) |
|----------------|------------------------|------------|
| Arboix 2007    | 2.57 [0.20, 32.41]     | 1.67       |
| Barnett 2003   | 0.91 [0.66, 1.25]      | 23.30      |
| Plakht 2015    | 0.66 [0.50, 0.88]      | 24.45      |
| Smirnova 2019  | 0.66 [0.45, 0.97]      | 21.39      |
| Stein 2009     | 0.47 [0.30, 0.74]      | 19.28      |
| van Vugt 2015  | 0.95 [0.40, 2.27]      | 9.90       |

**Overall**

- Heterogeneity: $\chi^2 = 0.10$, $I^2 = 66.77\%$, $H^2 = 3.01$
- Test of $\theta = \theta_0$: $Q(5) = 7.28$, $p = 0.20$
- Test of $\theta = 0$: $z = -2.02$, $p = 0.04$

Random-effects Sidik-Jonkman model
Subgroup analysis indicated that hypertension was a significant predictor of morbidity for cardiovascular patients, compared to people with other diagnoses (OR 1.55; CI 1.19, 2.00 vs. OR 1.12; CI 0.88, 1.43), while diabetes was a significant predictor of morbidity only for non-cardiovascular patients (OR 1.23; CI 0.95, 1.59; for cardiovascular vs. OR 1.57; CI 1.22, 2.00 for other diagnoses).

Heterogeneity was moderate for hypertension ($I^2 = 45$, $p = 0.006$) and diabetes ($I^2 = 47$, $p = 0.004$), and no heterogeneity was evident for decreased BMI studies ($I^2 = 0$, $p = 0.006$). The small number of studies included in the remaining analyses, could account for the non-significant heterogeneity values, indicating limiting power for estimating the true effect (23).

**Hospitalization**

Two studies reported results about predictors of hospitalization, three about predictors of hospital readmission and one study provided a ratio for the Intensive Care Unit (ICU) admission. Identified predictors of the included studies are presented in Table 5. The odds for hospitalization were higher for people with ground-level fall injuries diagnosed as frail compared to those who were not diagnosed as frail (OR 4.14; CI 1.63, 10.51). Obesity (OR 2.69; CI 1.0, 7.19) and pulmonary problems (OR 3.43; CI 1.12, 10.5) were significant predictors of hospitalization for people with colorectal cancer. Frailty (OR 2.37; CI 1.05, 5.33) was reported as a significant predictor of 60-day readmission for people with fall injuries, while fatigue (OR 3.04; CI 1.15, 8.03) and weight gain (OR 3.83; CI 1.30, 11.27) were reported as significant predictors of 30-day readmissions for people with a history of hospitalization followed for 30 days after the last hospital admission. Finally, supraventricular tachydysrhythmias seem to be an important predictor of ICU admission (OR 18.9; CI 4.59, 77.87) for people that have undergone esophageal operation. Although hospitalization outcomes did not provide us with an adequate number of studies to proceed to an analysis with multiple predictors, we succeeded however to find associations between additional technologies and health management of older people. These technologies include digital dynamometers for the assessment of frailty and weakness in older people, sensors, sensitive in identifying fatigue symptoms and, digital pressure algometers and dolorimeters for the measurement of pain.

**Limitations**

This study presents several limitations mostly due to the high heterogeneity of the study population. A first limitation is the relatively small number of studies included in the synthesis
### Hypertension

![Hypertension](image)

**Odds ratio with 95% CI**
- Aboyans 2017: 1.92 [1.01, 3.65]
- Amar 1996: 1.10 [0.31, 3.91]
- Berton 2009: 2.61 [1.50, 4.54]
- Fujishima 2013: 1.70 [0.85, 3.38]
- Fukumoto 2003: 1.04 [0.14, 7.80]
- Ho 1997: 1.10 [0.80, 1.51]
- Mujib 2010 N. Deficit: 0.89 [0.51, 1.55]
- Mujib 2010 Stroke: 1.52 [1.16, 1.99]
- Oberman 2006: 1.61 [1.16, 2.23]
- Pinto 2017: 0.92 [0.64, 1.32]
- Tateishi 2016: 0.97 [0.45, 2.11]
- Ward 2005: 2.20 [0.83, 5.83]
- Wilson 2006: 0.90 [0.59, 1.37]

**Weight (%)**
- Aboyans 2017: 6.77
- Amar 1996: 2.52
- Berton 2009: 7.95
- Fujishima 2013: 6.20
- Fukumoto 2003: 1.09
- Ho 1997: 12.10
- Mujib 2010 N. Deficit: 7.91
- Mujib 2010 Stroke: 13.03
- Oberman 2006: 11.91
- Pinto 2017: 11.23
- Tateishi 2016: 5.32
- Ward 2005: 3.84
- Wilson 2006: 10.13

**Random-effects Sidik-Jonkman model**

**Heterogeneity:** $i^2 = 0.08$, $I^2 = 56.18\%$, $H^2 = 2.28$

Test of $\theta = 0$: $Q(12) = 21.97$, $p = 0.04$

Test of $\theta = 0$: $z = 2.49$, $p = 0.01$

### Decreased BMI

![Decreased BMI](image)

**Odds ratio with 95% CI**
- Ho 1997: 1.60 [1.10, 2.33]
- Pinto 2017: 1.58 [0.59, 4.23]
- Wilson 2006: 1.30 [0.77, 2.19]

**Weight (%)**
- Ho 1997: 59.78
- Pinto 2017: 8.97
- Wilson 2006: 31.25

**Random-effects Sidik-Jonkman model**

**Heterogeneity:** $i^2 = 0.00$, $I^2 = 1.90\%$, $H^2 = 1.02$

Test of $\theta = 0$: $Q(2) = 0.41$, $p = 0.81$

Test of $\theta = 0$: $z = 2.67$, $p = 0.01$

### Arrhythmias

![Arrhythmias](image)

**Odds ratio with 95% CI**
- Berton 2009: 0.96 [0.53, 1.71]
- Fukumoto 2003: 1.04 [0.14, 7.80]
- Tateishi 2016: 2.51 [1.24, 5.06]

**Weight (%)**
- Berton 2009: 48.43
- Fukumoto 2003: 9.79
- Tateishi 2016: 41.77

**Random-effects Sidik-Jonkman model**

**Heterogeneity:** $i^2 = 0.16$, $I^2 = 45.51\%$, $H^2 = 1.84$

Test of $\theta = 0$: $Q(2) = 4.38$, $p = 0.11$

Test of $\theta = 0$: $z = 1.06$, $p = 0.29$

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FIGURE 3 | Continued
FIGURE 3 | Continued
given the large number of variables examined. Some of our analyses were based on a small (<5) number of studies, which is typically considered the minimal threshold for random-effects meta-analyses to maintain statistical power. In particular, the quantification of hospital admissions could not be continued because the meta-analysis showed that too few studies shed light on the topic of “hospitalizations” to quantify them in a statistically significant way. Secondly, no review protocol was published prior to the start of our analysis. Thirdly, we included in the synthesis only studies written in one of the languages spoken by the research team. This limitation had no effect on the final synthesis as all retrieved studies were written in English. Finally, some of the studies we analyzed appeared to be subject to a risk of bias. To minimize this risk, we implemented several bias assessments, especially a risk of bias and publication bias assessment. The results indicate that most studies under review (39) were assessed as being of high and moderate risk of bias, while 10 studies were assessed as having a low risk of bias. Publication bias assessment was conducted to assess small study effects via funnel plot (61, 62). In case of publication bias, the results of smaller studies are spread widely, due to lower precision, and asymmetrically around the average estimate compared to the results of larger studies. This asymmetry is suggestive of missing studies. In the absence of publication bias, individual study results are more evenly distributed around the pooled estimate (23, 62, 63). However, caution should be exercised when interpreting funnel plots especially when the number of included studies is smaller than 10 (25). In our cases, the funnel plots for diabetes related mortality and morbidity (Figures 4, 5, respectively) are hard to interpret.

In spite of these limitations, our study provided a systematic synthesis of digital measurements that can be predictive of mortality, morbidity, and hospitalizations among older adults. Our findings identify a number of digitally measurable physiological parameters that can serve as proxies for the worsening of an older person’s health. This is information is critical to evaluate the current promises and challenges of digital health technologies in the care and health promising of older people, especially in the context of telemedicine and assisted living. Furthermore, this information can inform evidence-based decision making in the context of digital health and gerontechnology.

**DISCUSSION**

Our results identified the following predictors of mortality: diabetes, decreased BMI, arrhythmias, slower walking speed, and insufficient physical activity. Hypertension, diabetes and decreased BMI were also identified as significant predictors of morbidity, while frailty, pulmonary comorbidity, obesity, pain, fatigue, and fever were identified as significant predictors of hospital admission or readmission. Overall, our results show that personal digital health technologies that can adequately measure the above parameters have the potential to improve health outcomes for older people. This investigation is a prerequisite for the design, development, and deployment of personal digital health technologies that can effectively measure the most informative parameters and thereby leverage that information to enhance health outcomes within the older population segment. Our analysis indicates that a variety of health parameters, such as hemodynamic, respiratory, kinetic parameters, BMI, and diabetes, which are potentially collectable using personal digital technologies can be effectively used to predict and improve the health outcomes of older people aged 65 or older. Further, digital technologies such as blood pressure monitors, pulse oximeters and sensors for the measurement of heart and respiratory rate, blood glucose meters for diabetes, height-weight monitors for BMI, movement sensors, accelerometers, pedometers for physical activity parameters, dynamometers for muscle strength, spirometers and hand-held echocardiogram can be efficiently incorporated in routine-care of older people, since they are correlated with survival or mortality, respectively. All the digitally measurable predictors of morbidity pertained to parameters that can be managed remotely using personal digital health technology. Our results
suggest that the incorporation of blood pressure monitors, of blood glucose monitors, of digital height-weight monitors, of movement sensors and stopwatches aiming to measure physical activity and gait speed as well as the incorporation of hand-held echocardiogram in routine care of older people can efficiently contribute to health maintenance and to the protection from adverse health conditions. Since the purpose of the current research was to provide a synthesis of the new technologies that can be used to measure risk factors of morbidity, we did not distinguish morbid conditions regarding their pathogenesis.

These results are consistent with previous studies that revealed positive correlations between specific technologies and health outcomes. For example, the use of remote digital arrhythmia monitoring has been observed to have an impact on medical care regarding hospitalization rates and effects on morbidity and mortality (64, 65). The systematic and meta-analytic nature of our study, however, allows contextualizing this evidence against a broader technological and medical context, comparing different data sources and thereby achieving more solid and generalizable knowledge. Some of the associations revealed by our study may appear prima facie counter-intuitive. One of them is the fact that obesity is positively associated with survival (OR 0.70; CI 0.56, 0.87; 6 studies) in older adults. However, this so-called “obesity paradox” appears to be well-known. Among others, Abramowitz et al. (66). report that numerous studies over the past two decades have shown a body-mass index (BMI) in the normal range is associated with the lowest risk of death. Other large cohort studies in various populations have reached different conclusions, demonstrating a survival benefit for overweight or even obesity, which has been interpreted by many as a causal relationship (66). Although obesity has been associated with a higher risk for cardiovascular and peripheral diseases and also for different types of cancer, previous studies have found that, in cases of acute decompensation or chronic hypertensive disease, type 2 diabetes, chronic kidney disease, or metastatic cancer, obese people in the older population segments tend to live longer (67–69), suggesting that obesity-induced health outcomes depend on variables such as age (68). Although for younger patients obesity is a risk factor for a higher mortality, in older patients it can become protective due to greater reserve for the fight against a disease. In the elderly, recent studies indicate that obesity is associated with a lower mortality risk (70, 71). These findings could be possibly explained by the fact that many previous studies were retrospective analyses which did not examine obesity as primary outcome and did not control for potential confounders that could influence the outcome, such as the presence of specific chronic conditions (69, 72). Further, current data are compatible with the view that not obesity but BMI changes are the primary factor which requires continuous monitoring in the old age as losing weight with age is generally associated with worse outcomes. Nonetheless, the possibility of this “obesity paradox” continues to be debated in the literature and is of great public health importance, not least because of the message communicated to the public (66). Another counter-intuitive result is that hypertension does not appear to be a significant predictor of mortality of people aged 65+. However, the little effect of blood pressure values on mortality risk is not surprising. As part of their treatment for stroke and CHD, many of the individuals were under treatment with agents to decrease triglyceride or lipid levels. It is possible that inclusion of categorical diagnostic information for hypertension and lipid treatment could have improved the prediction model. Unfortunately, these data are not currently available to us. However, we will note that hypertension exerts its deadly effects through CHD and stroke, so it is possible that some if not most of all the variance with respect to death are being captured by those variables (49).

CONCLUSIONS

Our meta-analysis has systematically reviewed and compared 43 studies. Our results identified the following predictors of mortality for people aged 65 years or older: diabetes, reduced BMI, arrhythmias, slower walking speed, and insufficient physical activity. Hypertension, diabetes and decreased BMI were also identified as significant predictors of morbidity. Overall, our
results show that digital health technologies that can adequately measure the above parameters have the potential to improve health outcomes for older people. This information is essential to develop digital health technologies for older people that could improve their overall health and well-being.

**DATA AVAILABILITY STATEMENT**

The original contributions presented in the study are included in the article/Supplementary Materials, further inquiries can be directed to the corresponding author/s.

**AUTHOR CONTRIBUTIONS**

SD developed the methodology, collected and analyzed the data, and drafted the manuscript. ARAs conceived of the study, reviewed the data, and contributed to the manuscript. CH and MW reviewed the data, and contributed to the manuscript. MI obtained funding, conceived of the study, and contributed to the manuscript. AS and NP contributed to the study design and to the manuscript. RK contributed to the study design and to the manuscript. ARU obtained funding, conceived of the study, and contributed to the manuscript. All authors approve the final version of this manuscript.

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**SUPPLEMENTARY MATERIAL**

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fdgh.2020.602093/full#supplementary-material

**REFERENCES**

1. Lupton D. The Quantified Self. Cambridge: John Wiley & Sons (2016).
2. Iero R, Haselager P, Emanuel EJ. Brain leaks and consumer neurotechnology. Nat Biotechnol. (2018) 36:805–10. doi: 10.1038/ntbt.4240
3. Harari GM, Lane ND, Wang R, Crosier BS, Campbell AT, Gosling SD. Using smartphones to collect behavioral data in psychological science: opportunities, practical considerations, and challenges. Perspect Psychol Sci. (2016) 11:838–54. doi: 10.1177/1745691616650285
4. LeCun Y, Bengio Y, Hinton G. Deep learning. Nature. (2015) 521:436–44. doi: 10.1038/nature14539
5. Morgan J, Gaming for dementia research: a quest to save the brain. Lancet Neurol. (2016) 15:1313. doi: 10.1016/s1474-4422(16)30123-5
6. Banerjee S. Multimorbidity—older adults need health care that can count past one. Lancet. (2015) 385:587–9. doi: 10.1016/S0140-6736(14)61596-8
7. Eurostat, Population structure and ageing, European Commission Luxembourg (2017).
8. Vayena E, Lenca M. Digital medicine and ethics: rooting for evidence. Am J Bioethics. (2018) 18:49–51. doi: 10.1080/15265161.2018.1498955
9. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. (2009) 6:e1000100. doi: 10.1371/journal.pmed.1000100
10. Jotheeswaran AT, Bryce R, Prina M, Acosta D, Ferri CP, Guerra M, et al. Frailty and the prediction of dependence and mortality in low- and middle-income countries: a 10/66 population-based cohort study. BMC Med. (2015) 13:4. doi: 10.1186/s12116-015-0378-4
11. Higgins JPT, Li T, Deeks JJ. Chapter 6: choosing effect measures and computing estimates of effect. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 6.1. Cochrane (2020). Available online at: www.training.cochrane.org/handbook
12. Baumert M, Linz D, Stone K, McEvoy RD, Cummins S, Redline S, et al. Mean nocturnal respiratory rate predicts cardiovascular and all-cause mortality in community-dwelling older men and women. Eur J Epidemiol. (2019) 34:117. doi: 10.1007/s10654-018-05641-1
13. Fisher DE, Jonasson F, Eiriksdottir G, Sigurdsson S, Klein R, Launer LJ, et al. Age-related macular degeneration and mortality in community-dwelling elders the age, gene/environment susceptibility reykjavik study. Ophthalmology. (2015) 122:382–90. doi: 10.1016/j.ophtha.2014.08.006
14. Inoue N, Kawakami H, Yamamoto H, Ito C, Fujiiwara S, Sasaki H, et al. Second derivative of the finger photoplethysmogram and cardiovascular mortality in middle-aged and elderly Japanese women. Hypertens Res. (2017) 40:207–11. doi: 10.1007/hr.2016.123
15. Lyrra TM, Leskinen E, Heikkinen E. A cohort study found good respiratory, sensory and motor functions decreased mortality risk in older people. J Clin Epidemiol. (2005) 58:509–16. doi: 10.1016/j.jclinepi.2004.08.015
16. Palmisano P, Guerra F, Ammedolla E, Ziacchi M, Luigi Pisano EC, Dell’Era G, et al. Physical activity measured by implanted devices predicts atrial arrhythmias and patient outcome: results of IMPLANTED (Italian multisite observational registry on patients with implantable devices remotely monitored). J Am Heart Assoc. (2018) 7:e008146. doi: 10.1161/JAHA.117.008146
17. Rolland Y, Lauwers-Cances V, Cesarini M, Vellas B, Pahor M, Grandjean H. Physical performance measures as predictors of mortality in a cohort of community-dwelling older French women. Eur J Epidemiol. (2006) 21:113–22. doi: 10.1007/s10654-005-5458-x
18. Buchman AS, Dawe RJ, Leurgans SE, Curran TA, Truty T, Yu L, et al. Different combinations of mobility metrics derived from a wearable sensor are associated with distinct health outcomes in older adults. J Gerontol A Biol Sci Med Sci. (2019) 74:1176–83. doi: 10.1093/gerona/gly030
19. Stein KM, Mittal S, Gilliam FR, Gilligan DM, Zhong Q, Kraus SM, et al. Predictors of early mortality in implantable cardioverter-defibrillator recipients. Europace. (2009) 11:734–40. doi: 10.1093/eurheartj/epp055
20. Zeitzer JM, Blackwell T, Hoffan AR, Cummings S, Ancoli-Israel S, Stone K, et al. Osteoporotic fractures men nr, daily patterns of accelerometer activity predict changes in sleep, cognition, and mortality in older men. J Gerontol A Biol Sci Med Sci. (2018) 73:682–7. doi: 10.1093/gerona/gly160
21. Zhu ZW, Wang XJ, Wang JG, Wang SZ, Fan YF, Fu TL, et al. Preoperative predictors of early death risk in bladder cancer patients treated with robotassisted radical cystectomy. Cancer Med. (2019) 8:344–52. doi: 10.1002/cam4.2237
22. Sidik K, Jonkman JN. A simple confidence interval for meta-analysis. Stat Med. (2002) 21:3153–9. doi: 10.1002/sim.1262
23. Borenstein M, Hedges LV, Higgins J, Rothstein HR. Introduction to Meta-Analyses. Cambridge: John Wiley & Sons (2011).
24. Higgins J, Thompson SG, Deeks JJ, Altman DG. Cambridge: Measuring inconsistency in metaanalyses. BMJ. (2003) 327:557–60. doi: 10.1136/bmj.327.7414.557
25. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane Handbook for Systematic Reviews of Interventions. Cambridge: John Wiley & Sons (2019). doi: 10.1002/9781119536604

26. Sterne JA, Savovici J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. Rob 2: a revised tool for assessing risk of bias in randomised trials. BMJ. (2019) 366:l4898. doi: 10.1136/bmj.l4898

27. Sterne JA, Hernán MA, Reeves BC, Savovici J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. (2016) 355:i4919. doi: 10.1136/bmj.i4919

28. Wells GA, Tugwell P, O’Connell D, Welch V, Peterson J, Shea B, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses (2015).

29. Aboyans V, Desormais I, Magne J, Morange G, Mohty D, Lacroix P. Renal artery stenosis in patients with peripheral artery disease: prevalence, risk factors and long-term prognosis. Eur J Vasc Endovasc Surg. (2017) 53:380–5. doi: 10.1016/j.ejvs.2016.10.029

30. Afilalo J, Eisenberg MJ, Morin J-F, Bergman H, Monette J, Noiseux N, et al. Predictors of mortality in patients with peripheral vascular disease. A prospective follow-up study. Br J Surg. (2004) 91:196–200. doi: 10.1002/bjs.48004030901

31. Amar D, Burt ME, Bains MS, Leung DHY. Symptomatic tachydysrhythmias after esophagectomy: Incidence and outcome measures. Ann Thorac Surg. (1996) 61:1506–9. doi: 10.1016/0003-4975(96)00111-7

32. Arboix A, Rodríguez-Aguilar R, Oliveres M, Comes E, García-Eroles L, Massons J. Thalamic haemorrhage vs internal capsule-basal ganglia haemorrhage: clinical profile and predictors of in-hospital mortality. BMC Neurol. (2007) 7:7. doi: 10.1186/1471-2377-7-32

33. Barnett SD, Halpin LS, Speir AM, Albus RA, Akl BF, Massimiano J, et al. Factors influencing hospital length of stay after robotic totally endoscopic coronary artery bypass grafting. Ann Thorac Surg. (2014) 97:512–9. doi: 10.1016/j.athoracsur.2012.10.087

34. Berton G, Cordiano R, Cucchini F, Cavuto F, Pellegrinet M, Palatini P. Atrial fibrillation during acute myocardial infarction: association with all-cause mortality and sudden death after 7-year of follow-up. Int J Clin Practice. (2009) 63:712–21. doi: 10.1111/j.1742-1241.2009.02023.x

35. Buch H, T. Vinding, la Cour M, Jensen GB, Prause JU, Nielsen NV. Age-related maculopathy: a risk indicator for poorer survival in women - The Copenhagen city eye study. Ophthalmology. (2005) 112:305–12. doi: 10.1016/j.ophtha.2004.08.025

36. Casella G, Savonitto S, Chiarella F, Gonzalez L, Di Chiara A, Bolognese L, et al. Clinical characteristics and outcome of diabetic patients with acute myocardial infarction. Data from the BLITZ-T study. Ital Heart J. (2005) 6:374–83.

37. Ferrer A, Formiga F, Sanz H, Almeda J, Padros G. Multimorbidity as specific disease combinations, an important predictor factor for mortality in octogenarians: the Octabaix study. J Interv Aging. (2017) 12:223–31. doi: 10.2147/CIA.S123173

38. Fujishima S, Murakami N, Haga Y, Nyuta E, Nakate Y, Ishihara S, et al. Low sinuses rhythm: findings from the DIG stroke sub-study. Int J Cardiol. (2010) 144:389–93. doi: 10.1016/j.ijcard.2009.04.035

39. Fujishima S, Murakami N, Haga Y, Nyuta E, Nakate Y, Ishihara S, et al. Digital assessment of endothelial function and ischemic heart disease in women. J Am Coll Cardiol. (2010) 55:1688–96. doi: 10.1016/j.jacc.2009.10.073

40. Fujishima S, Nyuta E, Nakate Y, Ishihara S, et al. Digital assessment of endothelial function and ischemic heart disease in women. J Am Coll Cardiol. (2010) 55:1688–96. doi: 10.1016/j.jacc.2009.10.073

41. Fujishima S, Nyuta E, Nakate Y, Ishihara S, et al. Digital assessment of endothelial function and ischemic heart disease in women. J Am Coll Cardiol. (2010) 55:1688–96. doi: 10.1016/j.jacc.2009.10.073

42. Fujishima S, Nyuta E, Nakate Y, Ishihara S, et al. Digital assessment of endothelial function and ischemic heart disease in women. J Am Coll Cardiol. (2010) 55:1688–96. doi: 10.1016/j.jacc.2009.10.073

43. Fujishima S, Nyuta E, Nakate Y, Ishihara S, et al. Digital assessment of endothelial function and ischemic heart disease in women. J Am Coll Cardiol. (2010) 55:1688–96. doi: 10.1016/j.jacc.2009.10.073

44. Fujishima S, Nyuta E, Nakate Y, Ishihara S, et al. Digital assessment of endothelial function and ischemic heart disease in women. J Am Coll Cardiol. (2010) 55:1688–96. doi: 10.1016/j.jacc.2009.10.073
60. Lion A, Spada RS, Gauchard GC, Anello G, Bosco P, et al. Biological determinants of postural disorders in elderly women. *Int J Neurosci.* (2013) 123:24–30. doi: 10.3109/00207454.2012.722570

61. Hussain R, Hassali MA, Patel M, Babar ZUD. Publication Bias, *Encyclopedia of Pharmacy Practice and Clinical Pharmacy.* Oxford: Elsevier (2019).

62. Song F, Hooper L, Loke Y. Publication bias: what is it? How do we measure it? How do we avoid it? *Open Access J Clin Trials.* (2013) 2013:71–81. doi: 10.2147/OAICT.S34419

63. Wilson DB, Lipsy M. *Practical Meta-Analysis.* Thousand Oaks, CA: Sage (2001).

64. Akar JG, Bao H, Jones PW, Wang Y, Varosy PD, Masoudi FA, et al.-Normand LT, Curtis JP. Use of remote monitoring is associated with lower risk of adverse outcomes among patients with implanted cardiac defibrillators. *Circulation.* (2015) 8:1173–80. doi: 10.1161/CIRCEP.114.003030

65. Shinbane JS, Saxon LA. Digital monitoring and care: virtual medicine. *Trends Cardiovasc Med.* (2016) 26:722–30. doi: 10.1016/j.tcm.2016.05.007

66. Abramowitz MK, Hall CB, Amodu A, Sharma D, Androga L, Hawkins M. Muscle mass, BMI, and mortality among adults in the United States: a population-based cohort study. *PLoS ONE.* (2018) 13:e0194697. doi: 10.1371/journal.pone.0194697

67. Tsang NM, Pai PC, Chuang CC, Chuang WC, Tseng CK, Chang KP, et al. Overweight and obesity predict better overall survival rates in cancer patients with distant metastases. *Cancer Med.* (2016) 5:665–75. doi: 10.1002/cam4.634

68. Amundson DE, Djurkovic S, Matviyoff GN. The obesity paradox. *Crit Care Clin.* (2010) 26:583–96. doi: 10.1016/j.ccc.2010.06.004

69. Ades PA, Savage PD. The obesity paradox: perception vs knowledge. In: *Mayo Clinic Proceedings.* Rochester: Mayo Foundation (2010). doi: 10.4065/mcp.2009.0777

70. Oreopoulos A, Kalantar-Zadeh K, Sharma AM, Fonarow GC. The obesity paradox in the elderly: potential mechanisms and clinical implications. *Clin Geriatr Med.* (2009) 25:643–59. doi: 10.1016/j.cger.2009.07.005

71. Dorner TE, Rieder A. Obesity paradox in elderly patients with cardiovascular diseases. *Int J Cardiol.* (2012) 155:56–65. doi: 10.1016/j.ijcard.2011.01.076

72. Lechi A, The obesity paradox: is it really a paradox? *Hypertension.* (2017) 22:43–8. doi: 10.1007/s40519-016-0330-4

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