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Optimal dose and type of physical activity to improve functional capacity and minimise adverse events in acutely hospitalised older adults: A systematic review with dose-response network meta-analysis of randomised controlled trials

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Summary boxes

What is already known

- Hospitalised older adults spend most of their hospital time sedentary, usually in bed.
- Exposure to long periods of almost total inactivity during hospitalisation leads to post-hospital deconditioning, disability, morbidity, and mortality.
- Despite its potential benefits, the type and optimal dose of physical activity to counteract the adverse events of prolonged bed rest during hospitalisation remains unknown.

What are the new findings

- Bed rest is less safe than staying active for acute hospital stays
- A small amount of slow walking (~25 minutes / day) is sufficient to improve function during acute hospital stays
- Optimal improvements in function are provided by either ~50 minutes/day of slow walking or ~40 minutes/day spent in multicomponent interventions (e.g., ~20 minutes of resistance bands with ~20 minutes of aerobic activity)

Abstract

Objective To identify the optimal dose and type of physical activity to improve functional capacity and reduce adverse events in acutely hospitalised older adults.

Design Systematic review and Bayesian model-based network meta-analysis.

Data sources Four databases were searched from inception to June 20, 2022.

Eligibility criteria for selecting studies Randomised controlled trials that assessed the effectiveness of a physical activity-based intervention on at least one functional outcome in people aged 50 or over hospitalised due to an acute medical condition. Pooled effect estimates (i.e., standardised mean differences for functional capacity, and the ratio of means for adverse events) were calculated using random-treatment effects network meta-analysis models.

Results 19 studies (3498 participants) met the inclusion criteria. Approximately 100 METs-min/day (~40 min/day of light effort or ~25 min/day of moderate effort activities) was the minimal dose to improve the functional capacity of acute hospitalised older adults (SMD = 0.28, 95% CrI 0.01 to 0.55). The optimal dose was estimated at 159 METs-min/day (~70 min/day of light effort or ~40 min/day of moderate effort activities; SMD = 0.41, 95% CrI 0.08 to 0.72). Ambulation was deemed the most efficient intervention, and the optimal dose was reached at 143 METs-min/day (~50 min/day of slow-paced walking; SMD = 0.76, 95% CrI 0.35 to 1.16), showing a high evidential power (87.68%). The minimal effective ambulation dose was estimated at 74 METs-min/day (~25 min/day of slow-paced walking; SMD = 0.25, 95% CrI 0.01 to 0.41). Physical activity interventions demonstrated a decrease in the rate of adverse events compared with usual care at discharge (RoM = 0.96, 95% CrI 0.95 to 0.97; median time = 7 days).

Conclusions This meta-analysis yielded low-to-moderate evidence supporting the use of in-hospital supervised physical activity programmes in acutely hospitalised older adults. As low as ~25 min/day of slow-paced walking is sufficient to improve functional capacity and minimise adverse events in this population.

Trial registration PROSPERO CRD42021271999.

Introduction

Hospitalised older adults, including those who can walk independently, spend most of their hospital time sedentary, usually in bed [1]. A study found that older adults spend only 45 minutes/day out of their hospital bed, less than 5% of a 24-hour period [2]. Exposure to acute periods of almost total inactivity during hospitalisation plays a role in causing a condition known as post-hospital syndrome [3], a critical 30-day post-discharge period associated with a general deconditioning. If not managed, this period of increasing vulnerability may lead to hospital readmission, disability, nursing home placement, morbidity, and mortality [3]. These effects appear at least in part due to the admission itself, rather than the condition that caused the initial admission [4].

Recent meta-analytic evidence [5] has demonstrated the effectiveness of active interventions to prevent functional declines in older adults admitted to hospital. Martinez-Velilla et al. [6] showed the benefits of an individualised multicomponent intervention to reverse the functional decline associated with acute hospitalisation in very elderly patients. Other studies have shown the feasibility of increasing mobilisation in hospitalised older adults, with positive outcomes such as improved functionality [7]. The world-first consensus-based statements from expert and stakeholder consultation recommends that hospitalised older adults should '*be as physically active as their abilities and condition allows*' [8]. The same group of experts, however, flagged some key knowledge gaps that impede the effective application of physical activity as a critical clinical tool to prevent functional declines and adverse outcomes amongst hospitalised older adults. First, the most efficient type of physical activity intervention has not yet been identified. Second, the optimal dosage, which may be physical activity-type dependent, remains unknown. Finally, there is a common perception that physical activity may increase falls and other negative events (fostering the culture of '*bed rest*' while in hospital) [7,9]. Physical activity interventions often report no [6] or few adverse events [7]. Yet, there is no meta-analytic evidence assessing the number of adverse events from active interventions amongst hospitalised patients.

Capitalising on novel meta-analytic techniques (i.e., model-based dose-response network meta-analysis under a Bayesian framework) and evidence from existing RCTs, the current report aimed to identify the optimal dose and type of physical activity to improve functional capacity and reduce adverse event outcomes in acutely hospitalised older adults. We also examined the time-course relationship of physical activity with functional capacity and adverse events.

Methods

This pre-registered systematic review and meta-analysis (PROSPERO CRD42021271999) was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for network meta-analyses of health care interventions [10]. The methodological development of this work was guided by the technical support documents provided by the Decision Support Unit (DSU) of the National Institute for Health and Care Excellence (NICE) [11].

Search strategy

A systematic search was conducted in PubMed, Web of Science (WoS), Scopus, and Embase databases from inception to June 2022. The specific search strategy for each database including search terms, dates, and process, are shown in Supplementary File 1. The reference lists of relevant articles and systematic reviews were also screened for additional studies. Two reviewers (DGG and BdPC) independently screened title/abstract and full texts, with disagreements resolved by discussion or adjudication by a third author (JdPC).

Eligibility criteria

We included (1) randomised controlled trials that involved (2) individuals aged 50 years or over [12] admitted to either Intensive Care Units or general wards due to an acute medical condition; and that (3) used any form of physical activity as an intervention. Studies had to (4) use a control group receiving usual care or another type of physical activity intervention as comparison. Studies also had to (5) report on any assessment of functional capacity (i.e., ability to perform daily-living activities independently and safely [5]) at baseline and, at least, at discharge. The number and type of adverse events (i.e., functional decline, hospital re-admission, fall, or death) at discharge or at any follow-up time point available were also recorded. We excluded studies with individuals admitted for reasons where acute physical activity is contraindicated: orthopaedic surgery wards, those admitted for a knee/hip replacement, with a stroke, or with injuries (e.g., fractures), and those who were admitted for long-term conditions. We also excluded studies detailing interventions that did not require a physically active involvement of participants (e.g., blood flow restriction or electrostimulation), or those that combined multiple treatments and for which the effects of physical activity could not be isolated.

Data extraction

Two authors independently extracted data from the included studies (DGG and JdPC) and disagreements were resolved by consensus between all authors. From each of the included studies, we extracted data on functional capacity and adverse events at the different available time points. We also extracted the parameters of the intervention (i.e., frequency, duration, intensity, and type), key characteristics of included participants (i.e., sex, age, body mass index, and admission cause), functional capacity assessment tool, and any data that could be used to calculate effect sizes of interest based on the Cochrane Handbook for Systematic Reviews of Interventions [13]. When the minimally required data to conduct dose-response or time-course meta-analyses could not be retrieved from the published reports [14–16], we contacted the authors and invited them to provide additional data. Out of 3 studies for which further information was requested [14–16], we could retrieve the required data from 2 studies [15,16].

Data coding and management

We followed the principles described by Pedder et al. [17,18] and prepared two datasets, one for dose-response analyses and another dataset for time-course analyses. The dataset used in the dose-response analyses included only data corresponding to admission (i.e., baseline) and discharge time points. The time-course analysis dataset included additional data for all available follow-up time points. In both datasets, interventions were coded into three hierarchical levels [19]: first, we coded interventions as “Physical activity” or “Control”

("overall" level); second, interventions were coded considering the specific type of the intervention performed as "Range of motion", "Ambulation", "Multicomponent", or "Usual care" ("agent" level). We classified interventions as range of motion when participants, bedridden or not, performed assisted or independent exercises aimed to provide joints with a full range of motion movements. Ambulation was based on walking but could additionally include daily-living activities such as sit-to-standing or stepping on the site. Multicomponent intervention was based on various physical activity components applied during the same session (e.g., resistance, aerobic, and balance physical activities). Third, interventions were coded at the intersection of the specific type of intervention and dose ("treatment" level). For instance, the "Ambulation_50" code indicates 50 METs-min/day of ambulation intervention.

The term dose used in this meta-analysis refers to energy expenditure (EE), expressed as Metabolic Equivalents of Task per day (METs-min/day). We followed the validated approach by Ainsworth et al. [20] to calculate the different doses associated with each of the included interventions in this meta-analysis. Next, we clustered the interventions into six pre-specified different groups by approximating the estimated METs-min/day to the closest convenient pre-specified grouping categories of 0 (control group, i.e., usual care and no intervention), 50, 100, 150, 200, and 250 METs-min/day. This approximation was done to facilitate the network connectivity, a necessary step to conduct a network meta-analysis [21].

Data synthesis

Functional capacity

We used a random-effects Bayesian Model-Based Network Meta-Analysis (MBNMA) [22] to summarise the dose-response and time-course relationships between physical activity and functional capacity. No indication of violation of key assumptions for network meta-analysis (i.e., connectivity [23], consistency in the data, transitivity, and homogeneity [24,25]) was found (Supplementary File 2). Functional capacity was modelled using a normal likelihood with an identity link function. Predicted responses were calculated as pre-post change score for dose-response models to estimate the effects of physical activity at discharge time point, and as pre-follow up change score for time-course models to explore the physical activity effects at multiple follow-up times across the critical post-discharge period for this population; they were then standardised using the baseline standard deviation of each study [11], and reported as standardised mean differences (SMD; Hedges' g form [26]); posterior medians are reported with 95% credible intervals (CrI) to assess the certainty of our estimates [27]. In addition, the 95% prediction interval (PI) was calculated to inform about potential effects to be expected in future trials. Finally, the statistical power of each treatment effect estimate was calculated to detect their evidential value (Supplementary File 3).

Dose-response models

First, we plotted the observed effects of different interventions on functional capacity to detect a potential dose-response functional pattern. Based on the observed shapes, a range of recommended non-linear functions (i.e., log-linear, quadratic, Emax, and splines [28]) were used to model the data. Next, we derived and compared different fit indices [29] (i.e., Deviance Information Criterion [DIC], residual deviance and the number of data points, deviance of the

model, and number of estimated parameters) as well as corresponding deviance plots [29] across all estimated models (Supplementary File 4). For dose-response, natural cubic splines yielded the best fit at all levels (i.e., fitted at overall and agent levels) and were therefore used to assess the non-linear dose-response associations (Supplementary File 4). Implementation parameters of the fitted models (i.e., prior knowledge, Markov Chain Monte-Carlo iterations, and convergence analysis) are also detailed in the Supplementary File 4. Selecting for the model with the best fit and biological plausibility [28], we placed knots at overall level (i.e., 20^{th} and 75^{th} percentile) and at intervention-specific level (i.e., different knots location for each intervention: 20^{th} and 75^{th} for usual care and ambulation, 50^{th} for range of motion, and 20^{th} and 60^{th} for multicomponent) whenever data was available [30]. Beta coefficients from the splines models were used to estimate the physical activity dose at which the predicted maximal significant effect on functional capacity was achieved (referred herein as the 'optimal dose'). This information was used to rank the analysed treatments (i.e., type of intervention at a specific dose) based on their probability to enhance functional capacity, from worst to best. We also estimated the minimal dose associated with significant changes in the outcome of interest. Additionally, the maximal tolerated dose (i.e., the dose from which there were null/worsening effects on our outcome of interest) was also calculated.

To assess the robustness of our estimates, we also conducted dose-response meta-analytic models (1) including only studies with a low risk of bias, and (2) using other dose-response functions that also fitted the data well as sensitivity analyses.

Time-course models

First, we plotted the observed responses in each arm of each study over time to consider which functional forms were appropriate for modelling the time-course relationship [28]. Based on the available data, we used log-linear, quadratic, and splines functions. A common-treatment effects spline time-course model was deemed optimal and was therefore used to model the time-course effects of physical activity interventions on functional capacity. Despite plans to explore these separately, intervention-level time-course models could not be conducted considering the paucity of available time-course data on some type-specific interventions.

Adverse events

We used a common-treatment effects MBNMA for modelling the time-course relationship between adverse events and overall physical activity using usual care as reference treatment. Adverse event counts were assumed to be negatively binomially distributed and were modelled using a log link. The predicted responses were therefore expressed as a ratio of means (RoM), which has demonstrated similar treatment effects and no large differences in heterogeneity compared with difference-based methods [31]. This effect measure can be interpreted as the coefficient between adverse events in the intervention arm and the control arm (i.e., a RoM below 1 favours the intervention, and vice versa).

We originally planned to conduct similar analyses combining time-course and dose-response at deeper levels of intervention description (i.e., type and dose of physical activity) but the paucity of data available (n = 32 data points in total) prevented us from conducting such analyses. Instead, we carried out qualitative analyses to explore the distribution of adverse

events across different types of interventions (i.e., usual care, ambulation, or multicomponent training). As an exploratory analysis, we plotted the number of adverse events in each study arm by dose and fitted a natural spline model to explore the potential dose-outcome trend association in an arm-based analysis that did not allow for between-study heterogeneity. Compared to contrast-based MBNMA, arm-based analyses such as this assume that prognostic factors and effect modifiers are the same across studies, and results may therefore be affected by differences in prognostic factors between studies [32]. As sensitivity analysis, we used other smoothing techniques (i.e., beta spline and locally weighted least squares regression [loess] functions) to assess the robustness of the estimated trend.

All analyses were performed in R 4.0.3 [33]. We used the '*MBNMAdose*' package [17] to perform Bayesian dose-response MBNMA models; the *'MBNMAtime'* package [18] to perform Bayesian time-course MBNMA models; the '*metameta'* package [34] to perform power analysis; and the *'ggplot2'* package [35] for plotting and visualisation. The code and data necessary to reproduce the results presented in this manuscript are available through a public repository (link: https://github.com/dgalgom).

Risk of bias and certainty of evidence

Three reviewers (DGG, JRM, and FAB) assessed and rated the risk of bias in the included studies according to the Cochrane Risk of Bias tool criteria (Cochrane ROB tool) [36]. The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) system was used to rate the certainty in estimates from our network meta-analysis [37].

Equity, diversity, and inclusion statement

Our research team included junior, mid-career, and senior researchers from different disciplines (i.e., physical therapy, physiology, and biostatistics) and countries (i.e., Spain, United Kingdom, and Australia). Our study population included both male and female hospitalised older adults on an equivalent basis; however, in discussing the generalizability of our results and limitations of the findings, we acknowledge we did not examine the gender effect on our outcome of interest.

Results

Overall, 2905 records were identified through the initial electronic searches. After removing duplicates, 1601 records were screened for titles and abstracts, and 44 full-text articles were screened for eligibility. In total, 19 studies [6,14–16,38–52] involving 3498 participants were included in the review. For the dose-response analyses, 39 data points [i.e., effect sizes] were retrieved. For the time-course analyses, 49 data points were considered. The full screening and selection process is shown in Figure 1.

Characteristics of included studies

The characteristics of included studies are shown in Supplementary File 4. The year of publication ranged from 2000 to 2022. A total of 3,842 participants were analysed, of which 2,087 (54.32%) were female. The median reported age was 78 (range = 55 to 87) years. Participants were admitted to an Intensive Care Unit (ICU) (758; 21.67%) [6,16,51] or general wards [14,15,37–49,51]. The median reported body mass index (BMI) was 27 (range = 24.5 to

33). The median length of stay of included participants was 7 days (range = 4 to 42 days). The median follow-up time was 68 days after discharge (range = 34 to 365 days).

There were 2 studies that used range of motion [38,49], 4 studies [16,39,43,47] that used ambulation, and 13 studies [6,14,15,39,41–43,45–47,50–52] that used multicomponent interventions. The average duration of intervention sessions was 30 minutes. Specifically, the median duration of the intervention sessions was 25 minutes for range of motion (range = 20 to 30 min), 37.5 minutes for ambulation (range = 30 to 60 min); and 30 minutes for multicomponent (range = 20 to 60 min). The average frequency was 10 sessions per week for range of motion and ambulation, and 8 sessions for multicomponent interventions. Estimated intervention doses were 100 [49]; 150 [38], and 200 [43] METs-min/day for range of motion; 50 [44,48], 150 [40], and 200 [16] METs-min/day for ambulation; and 50 [14], 100 [40,41,50–52], 150 [6,15,43,45,47], and 250 [42,46] METs-min/day for multicomponent interventions. Network geometry combining all these treatments is depicted in Figure 2.

Several tools were used to assess functional capacity in the included studies: the 6-Minute Walking Test (6-MWT) [51]; Activities of Daily Living [15]; the Barthel Index [6,41,42,45,49]; days to first out of bed [16]; the Morton Mobility Index [39]; Gait speed [50]; the Katz Index [38,44]; the Life-Space Assessment (LSA) questionnaire [40]; the Short Physical Performance Battery (SPPB) [14,46–48]; the Sit-to-Stand test [51]; and the Timed-Up-and-Go (TUG) test [43].

Functional capacity

Dose-response associations

We detected an inverted U-shaped dose-response relationship between increasing energy expenditure (i.e., dose) and functional capacity (Figure 3). The optimal dose was estimated at 159 METs-min/day (SMD = 0.41, 95% CrI 0.08 to 0.72). The minimal dose associated with significant changes in functional capacity was predicted at 99 METs-min/day (SMD = 0.26, 95% CrI 0.01 to 0.53). The maximal tolerated dose was observed at 184 METs-min/day (SMD = 0.37, 95% CrI 0.01 to 0.72). Prediction intervals suggested that physical activity interventions could have a lower effect than that observed in the included trials (Supplementary Figure 8).

Intervention-specific dose-response relationships are shown in Figure 4. The optimal response for ambulation was estimated at 143 METs-min/day (SMD = 0.76, 95% CrI 0.35 to 1.16). Optimal dose for multicomponent interventions was 174 METs-min/day (SMD = 0.61, 95% CrI 0.46 to 0.77). For ambulation, the minimal effective dose was estimated at 74 METs-min/day (SMD = 0.25, 95% CrI 0.01 to 0.50); and the maximal tolerated dose was estimated at 187 METs-min/day (SMD = 0.21, 95% CrI 0.01 to 0.41). For multicomponent intervention, the minimal effective dose and the maximal tolerated dose were observed at 89 and 241 METs-min/day (SMD = 0.15, 95% CrI 0.01 to 0.29; SMD = 0.15, 95% CrI 0.01 to 0.29), respectively. We did not detect a significant relationship between range of motion interventions and functional capacity. A league table showing all between-treatment effects comparisons is supplied in the Supplementary File 6. Our ranking analysis showed that a dose of 150 METs-min/day for ambulation had the highest probability of retrieving the greatest response on functional capacity (Supplementary File 6). Power analysis showed that ambulation (150

METs-min/day) and multicomponent (100 and 150 METs-min/day) treatments yielded the highest power values, although only ambulation presented an evidential power over 80%.

The dose-response model including only low risk-of-bias studies mirrored the pattern of association of our base case model (Supplementary Figure 15). The results were also robust to different modelling strategies (i.e., natural spline assuming fixed-treatment effects, and quadratic functions; Supplementary File 7), though these were a poorer fit to the data.

Time-course effectiveness

The effectiveness of physical activity interventions increased from admission to discharge (SMD = 0.11, 95% CrI 0.10 to 0.12; median time = 7 days), and from this time point to approximately two weeks after discharge, achieving the greatest predicted effect at around 19 days after discharge (SMD = 0.23, 95% CrI 0.20 to 0.25). From that time point, there was some indication that the effect may slightly decrease (Figure 5).

Adverse events

We observed a decrease in the rate of adverse events in the active intervention groups when compared with usual care (Figure 6). At discharge, the RoM was 0.96 (95% CrI 0.95 to 0.97). Corresponding outcomes were 0.94 at 1 week post discharge (95% CrI 0.93 to 0.95), 0.93 at 2 weeks (95% CrI 0.92 to 0.95); and 0.92 at 4 weeks post discharge (95% CrI 0.91 to 0.93).

The distribution of different types of adverse events was similar across the different interventions, with falls being the main adverse event reported across studies and interventions (Supplementary Figure 13). An inverted U-shape dose-outcome trend was observed, in which doses of physical activity between 100 and 150 METs-min/day presented the lowest number of adverse events (Supplementary Figure 14A). Sensitivity analyses using alternative smoothing techniques supported this trend (Supplementary Figure 14).

Risk of bias

Domain-level and overall-level risk-of-bias judgements by reviewers' consensus are provided in Supplementary File 10. At overall-level, 7 studies were classified as low risk-of-bias [15,39,40,44,45,50,51], 2 studies as unclear risk-of-bias [14,52], and 10 studies as high risk-of-bias [6,16,38,41–43,46–49].

Certainty of evidence

Summary of Findings (SoFs) tables are presented in Supplementary File 11. The evidence presented in this meta-analysis for functional capacity outcomes was classified as low-moderate. Six treatment estimates were deemed of low certainty of evidence due to imprecision (i.e., 95% CrIs cross zero or are wide, suggesting uncertainty in the estimate) and risk of biased estimates. These include ambulation at 50 and 200 METs-min/day; and multicomponent at 50, 100, 150, and 250 METs-min/day.

Discussion

Main findings

The current study has several key findings with important clinical implications. First, our investigation confirms the benefits of physical activity interventions to reduce the functional

declines and adverse events associated with acute hospitalisation in older adults. Second, this dose-response meta-analysis highlights a novel, non-linear relationship between physical activity dose and functional capacity. The minimal effective dose was estimated at ~100 METs-min/day (~40 min/day of light effort or 25 min/day of moderate effort activities), and the optimal response at 159 METs-min/day (~70 min/day of light effort or ~40 min/day of moderate effort activities). Doses beyond ~190 METs-min/day (more than ~90 min/day of light effort or ~60 min/day of moderate effort activities) did not show clear benefits. Third, we detected different dose-response patterns for each of the different types of physical activity interventions available in the literature. Fourth, our study highlights the superior effects of ambulation over other active intervention modalities. Lastly, physical activity interventions were effective to reduce the adverse events of older adults with acute hospitalisation. Taken together, these findings provide an evidence-based opportunity to inform physical activity-based interventions and change in care practice aimed to reduce the burden associated with acute hospitalisation in older adults, a growing public health problem [52].

Strengths and limitations of this review

There are several key strengths to our study. First, this study comprised a relatively large sample size of acute-hospitalised older adults, which provided adequate statistical power for the study aims. Second, we applied current state-of-the-art meta-analytical techniques [19] for pooling data from different studies to investigate the dose-response between physical activity dose and functional capacity. This novel method allowed us to determine the most efficient (optimal) dose of physical activity to improve functional capacity and reduce adverse events in the population under study. Third, through direct, indirect and network estimates, we were able to compare the relative efficacy of different active interventions. The latter led to the identification of ambulation as the most effective in-hospital intervention to improve the functional capacity of older adults. Fourth, we showed that the effect estimates of the optimal doses associated to ambulation and multicomponent (i.e., the most effective interventions) suggested acceptable statistical power to detect significant "true" effects. Lastly, our data enabled first-time modelling of the effects of physical activity on adverse events, a key factor in decision-making processes to support physical activity interventions in hospital settings.

This study also has some limitations. First, there was a paucity of available data related to follow-up time points after discharge and we could not model reliable time-course outcomes estimates for specific physical activity interventions. Second, studies considered here included only participants who had the minimum capacity to move on their own and hence generalisation to other populations is not possible. Third, the currently available aggregated data did not allow the modelling of covariate-specific dose-response patterns or ascertainment of the dose at individual level. Finally, half of the studies in this review were classified with a high risk of bias. However, sensitivity analysis removing these studies showed similar dose-response association patterns.

Comparison with existing evidence

To date, only two systematic reviews have addressed the effectiveness of physical activity interventions to improve functional capacity outcomes in hospitalised older adults [5,54]. Although not directly comparable, the review by Scheerman et al. [54] could not confirm the

benefits of physical interventions, including exercise, to improve physical performance in older adults admitted to hospital. In contrast, more recent work by Valenzuela et al. [5] concluded that inpatient supervised physical activity is effective to improve functional capacity in older adults and showed comparable effect sizes (SMD of 0.57) to those reported in the current meta-analysis. Descriptively, the same review by Valenzuela et al. [5] stated that in-hospital physical activity interventions are safe. Our review empirically demonstrated the superior effects of physical activity over usual care to reduce the probability of adverse events at different follow-up time points. Although not formally tested, previous work [5] also suggests the existence of different responses to different physical activity interventions, an observation factually confirmed in our meta-analysis. Former research has also indicated the superior effects of multicomponent interventions [5,6,15,48]. Nevertheless, we provide for the first time meta-analytic evidence highlighting the value of ambulation, over and above other physical activity interventions. This suggests that change in hospital care practices that simply allow and promote patients walking while in care might have very important benefits. This finding supports grass root clinician-led movements to promote ambulation in hospitals such as #endPJparalysis [55]. It is plausible that multicomponent intervention sessions result in compensatory behaviour with an overall (counterintuitive) increase of sedentary behaviour that might displace time previously dedicated to ambulation [56]. This in term may limit the expected gains from engaging in such interventions. Future studies may want to test this hypothesis and if true, plan more holistic (24-hour) interventions. In addition, we did not observe any benefits associated with range of motion-based exercise programmes, which was also suggested by Valenzuela et al. [5] in their review. Nevertheless, our work, and that of others suggest the need to incorporate feasible physical activity programmes into the daily care routine of older adults admitted to hospital.

Clinical implications and future research

This manuscript helps inform which dose and type of physical activity best improves functional capacity and reduces adverse events among acutely hospitalised older adults. Even low doses of ambulation (e.g., ~25 minutes/day of slow walking or daily life activities such as sit-to-stand) may elicit significant changes in functional capacity, which supports the previously stated general recommendation of staying active while in hospital [8]. However, higher doses of ambulation (e.g., ~45 minutes/day of slow walking) may result in optimal benefits. This strongly suggests that hospital care should be organised in such a way as to allow and promote older adult ambulation while in hospital. Similarly, short daily multicomponent intervention sessions may translate into functional capacity improvements (e.g., ~15 minutes/day of resistance bands and ~10 additional minutes/day of aerobic activities such as assisted-cycling with a device) albeit longer bouts may result in additional gains (e.g., ~25 minutes/day of resistance bands with ~20 minutes/day of aerobic activities). A key point to consider is the feasibility of in-hospital interventions. Multicomponent interventions require qualified personnel and multiple resources for its application, both of which are considered important barriers to the implementation of physical activity programmes in acutely hospitalised older adults [57]. In contrast, ambulatory activities may be easier and simpler to implement in hospital settings [58,59], hence such interventions may be a cost-effective solution to reduce the negative consequences of excessive bed-time in hospitalised older adults [60].

Nevertheless, the information provided in the current manuscript supports tailored physical activity advice adapted to individual preferences, needs, and availability of resources [61], which may facilitate the adoption of a patient-centred care approach [62].

Seniors are projected to comprise more than 60% of the total hospital inpatient population by 2030 [63]. Rooted on the existing evidence to date, this review has revealed the optimal type and dose of physical activity necessary to prevent functional decline and reduce adverse events in older adults admitted to hospital. These results may inform the design of new trials aimed to test the effectiveness of in-hospital physical activity interventions in older adults. Nevertheless, our findings warrant the collection of individual patient data to provide accurate subgroup-specific recommendations (e.g., for specific medical conditions or baseline functional capacity level) [64]. Adverse events should be more comprehensively reported in future trials [65].

Conclusions

This novel systematic review with dose-response meta-analysis revealed relevant ranges of (type-specific) physical activity doses to improve functional capacity and reduce the number of adverse events in acutely hospitalised older adults. If the most potent intervention is provided (i.e., ambulation), the beneficial effects of in-hospital supervised physical activity programmes can be maximised with as little as ~25 minutes/day of slow-paced walking, an achievable target for most hospitalised older adults. Together, this meta-analysis has yielded critical information to support the use of physical activity as a core part of the daily routine of acutely hospitalised older adults.

Competing interests

All authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work.

Author's contributions

DGG, BdPC, and JdPC conceptualised the study. DGG, JdPC, and BdPC drafted the manuscript; DGG and HP conducted the formal statistical analyses with critical input from BdPC; DGG, FAB, RMR, and JRM acquired the data; all authors revised the manuscript and provided critical input. DGG and BdPC have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. DGG and BdPC are the guarantors. The corresponding author (BdPC) attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Data availability statement

All data relevant to the study are included in the article or made available through a public repository (dgalgom; link: https://github.com/dgalgom/Optimal-dose-and-type-of-exercise-in-acutely-hospitalised-older-adults-data-analysis).

Transparency statement

The manuscript's guarantors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned have been explained.

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Figure legend

Figure 1. PRISMA flowchart of included studies.

Figure 2. Network geometry at treatment-level. *Note.* Treatment-level is considered the combination of a specific type of intervention and dose.

Figure 3. Dose-response relationship between physical activity dosage and functional capacity. *Note.* Point estimates and credible intervals from a "split" network meta-analysis in which each dose of physical activity is treated as an independent intervention.

Figure 4. Intervention-specific dose-response relationship between physical activity dose and functional capacity.

Figure 5. Time-course effectiveness. *Note.* The shaded zones represented the number of observations in the original dataset at each predicted time point.

Figure 6. Ratio of means (RoM) between intervention and usual care groups. *Note.* A RoM below 1 favours the intervention.