PRÓ-REITORIA DE PESQUISA E PÓS-GRADUAÇÃO
MESTRADO EM CIÊNCIAS DA SAÚDE

ALESSANDRO PIERUCCI

USO DE M-HEALTH ASSOCIADO A PROGRAMA DE REABILITAÇÃO CARDIOVASCULAR SOBRE CAPACIDADE FUNCIONAL, ADERÊNCIA E FATORES DE RISCO CARDIOVASCULARES: REVISÃO SISTEMÁTICA E METANÁLISE

Presidente Prudente - SP
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Dissertação apresentada Pró-Reitoria de Pesquisa e Pós-Graduação, Universidade do Oeste Paulista, como parte dos requisitos para obtenção do título de mestre em Ciências da Saúde. - Área de concentração: Ciências da Saúde.

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DEDICATÓRIA

A minha família por toda dedicação e paciência, contribuindo diretamente para que eu pudesse trilhar um caminho mais fácil e prazeroso durante esses dois anos.

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"Escolha uma ideia. Faça dessa *ideia* ***a sua vida. Pense nela, sonhe com ela, viva pensando nela. Deixe cérebro, músculos, nervos, todas as partes do seu corpo serem preenchidas com essa ideia. Esse é o caminho para o sucesso."*** (Swami Vivekananda)

RESUMO

Uso de M-Health associado a programa de reabilitação cardiovascular sobre capacidade funcional, aderência e fatores de risco cardiovasculares: revisão sistemática e metanálise.

Introdução: Aplicativos de smatphones para saúde (M-Health) parecem superar barreiras ao acesso a Programas de Reabilitação Cardiovascular (PRCV), favorecido pelo seu alto grau de aceitabilidade e podendo influenciar positivamente na frequência do exercício físico. Objetivo: Analisar evidências sobre os benefícios da associação entre o uso de M-Health e PRCV nos desfechos primários e secundários (qualidade de vida, aderência e manejo de fatores de risco cardiovasculares). Desenho: Revisão Sistemática e Metanálise. Métodos: Foram utilizadas as bases de dados: PubMed, EMBASE e SPORTDiscus com texto completo (EBSCOhost) a partir do registro mais antigo até o dia 20 de abril de 2018. Entre os critérios de inclusão estão cardiopatas maiores de 18 anos submetidos ao M-Health associado ao PRCV. Resultados: 8 ensaios clinicos randomizados (ECR) foram elegíveis. O risco de viés foi considerado moderado e as intervenções com M-Health consistiram em mensagem de texto, e-mails e por aplicativos. Nos desfechos primários seis desses estudos avaliaram VO2pico, TC6min e IPAQ em curto e intermediário prazo. Nos desfechos secundários, seis estudos abordaram a aderência as intervenções, questionários de feedback e qualidade de vida. Para análise quantitativa houveram estimativa de efeito favorável a associação do M-Health e PRCV para as variáveis aptidão cardiorrespiratória, frequência cardíaca, colesterol total, LDL e triglicerídes. Conclusão: Há alta qualidade de evidência e força de recomendação favorável associação da intervenção do M-Health ao PRCV na melhora da aptidão cardiorrespiratória a curto prazo, e colesterol total e triglicérides para o período intermediário, já para frequência cardíaca e LDL a evidência é com fraca força de recomendação.

Palavras-chave: Ensaio Clínico Randomizado, Exercício por aplicativo de celular; aplicativo de saúde; condicionamento físico; VO2max; VO2pico; cuidado usual; reabilitação supervisionada; aderência ao tratamento; reabilitação de cardiopatas.

ABSTRACT

Use of m-health associated with the cardiovascular rehabilitation program on functional capacity, adherence and cardiovascular risk factors: systematic review and metanalysis

Introduction: Smartphone applications for health (M-Health) seem to overcome barriers to access to Cardiovascular Rehabilitation Programs (CRP), favored by their high degree of acceptability and can positively influence the frequency of physical exercise in weight loss. Objective: Analyze the influence of the association between M-Health and CRP in cardiorespiratory fitness, adherence to CRP and in management of cardiovascular risk factors, when compared to cardiac patients inserted in isolated CRP (without association with M-Health). Design: Systematic Review and Meta-Analysis Methods: The following databases were used: Medline via Ovid, EMBASE, Central, PEDro and SPORTDiscus via EBSCOhost from the oldest record until December 20, 2019. Among the inclusion criteria are cardiac patients older than 18 years submitted to M- Health associated with CRP. Results: 14 randomized controlled trials (RCTs) were eligible. The risk of bias was considered moderate and the interventions with M-Health consisted of text messages, e-mails, and applications. In the primary endpoint, thirteen of these studies assessed VO2 peak, 6MWT and IPAQ; in secondary outcomes, eight studies addressed cardiovascular risk management and nine assessed adherences to interventions and feedback questionnaires. For quantitative analysis, there were estimates of effects favorable to the association of M-Health for the variables: cardiorespiratory fitness, resting heart rate, diastolic blood pressure and triglycerides. Conclusion: There is high quality of evidence and strength of recommendation favorable to the intervention of M-Health in improving cardiorespiratory fitness and triglycerides. This favorable effect extends to the behavior of heart rate and diastolic blood pressure, despite lower levels of quality of evidence.

Keywords: randomized controlled trials, Exercise, app health, cardiac rehabilitation, physical fitness, cardiorespiratory fitness e VO_2peak

LISTA DE TABELAS

Table 1 -	Risck of bias in selected studies……	34
Tabel 2 -	Characteristics of the studies included in the review…….	35
Table 3 -	Assessment of the quality of evidence of primary and secondary outcomes……..	40

LISTA DE FIGURAS

Figure 1 - Organization chart of the articles selection process…… 41

Figure 2 - Forest plot of comparison: 1 M-Health vs CRP – Cardiorespiratory, primary outcome, VO2peak, TC6min and Self Reported measure of Physical Activity……. 42

Figure 3 - Forest plot of comparison: 2 M-Health vs CRP - Second Outcomoes, outcome: 2.7 Diastolic Blood Pressure……. 44

Figure 4 - Forest plot of comparison: 2 M-Health vs CRP – Second Outcomes, outcome: 2.11 Triglicerydes…….. 45

Figure 5 - Forest plot of comparison: M-Healt vs CRP – Cardiorespiratory Function – Physical Tests ubgrups (Supervised and no-supervised CRP)....……. 50

SUMÁRIO

ARTIGO CIENTÍFICO 12
Introduction 14
Methods 16
Results 20
Discussion 25
Conclusion 29
References 30
ANEXO - REGISTRO PROSPERO 47
APÊNDICE - SEARCH STRATEGY 48

ARTIGO CIENTÍFICO

USO DE M-HEALTH ASSOCIADO A PROGRAMA DE REABILITAÇÃO CARDIOVASCULAR SOBRE CAPACIDADE FUNCIONAL, ADERÊNCIA E FATORES DE RISCO CARDIOVASCULARES: REVISÃO SISTEMÁTICA E METANÁLISE

USE OF M-HEALTH ASSOCIATED WITH THE CARDIOVASCULAR REHABILITATION PROGRAM ON FUNCTIONAL CAPACITY, ADHERENCE AND CARDIOVASCULAR RISK FACTORS: SYSTEMATIC REVIEW AND METANALYSIS

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ABSTRACT

Introduction: Smartphone applications for health (M-Health) seem to overcome barriers to access to Cardiovascular Rehabilitation Programs (CRP), favored by their high degree of acceptability and can positively influence the frequency of physical exercise in weight loss.

Objective: Analyze the influence of the association between M-Health and CRP in cardiorespiratory fitness, adherence to CRP and in management of cardiovascular risk factors, when compared to cardiac patients inserted in isolated CRP (without association with M-Health).

Design: Systematic Review and Meta-Analysis

Methods: The following databases were used: Medline via Ovid, EMBASE, Central, PEDro and SPORTDiscus via EBSCOhost from the oldest record until December 20, 2019. Among the inclusion criteria are cardiac patients older than 18 years submitted to M- Health associated with CRP.

Results: 14 randomized controlled trials (RCTs) were eligible. The risk of bias was considered moderate and the interventions with M-Health consisted of text messages, e-mails, and applications. In the primary endpoint, thirteen of these studies assessed VO2 peak, 6MWT and IPAQ; in secondary outcomes, eight studies addressed cardiovascular risk management and nine assessed adherences to interventions and feedback questionnaires. For quantitative analysis, there were estimates of effects favorable to the association of M-Health for the variables: cardiorespiratory fitness, resting heart rate, diastolic blood pressure and triglycerides.

Conclusion: There is high quality of evidence and strength of recommendation favorable to the intervention of M-Health in improving cardiorespiratory fitness and triglycerides. This favorable effect extends to the behavior of heart rate and diastolic blood pressure, despite lower levels of quality of evidence.

Keywords: *randomized controlled trials*, *Exercise*, *app health*, *cardiac rehabilitation*, *physical fitness*, *cardiorespiratory fitness* e *VO_2peak*

Introduction

Cardiovascular rehabilitation program is considered highly effective for the treatment of evidence-based cardiovascular disease, especially when focused on lifestyle modification after a cardiovascular event.[1,2]

However, acceptance and adherence to training are often impaired due to the barriers encountered by patients, since the attendances are performed in specialized centers, thus, resorting to difficulties in locomotion, lack of time, professional commitments, among others. In this way, it is necessary to introduce new intervention strategies to encourage adherence to a healthy lifestyle.[3,4]

In this scenario, interventions with smartphones have been considered an effective tool to help the patient in the management of some chronic diseases.[5] Mobile applications have the advantage of breaking the limitation of mobility and can be applied in several areas in the health field, such as remote monitoring, support for diagnosis as well as support for decision-making.[6]

Successful interventions use personalized content, that is, an intervention adapted to the characteristics of the individual, generally based on an individual's responses to a questionnaire and as a result are generally perceived with more interest and more personal relevance and more discussed than non-personalized educational material.[7] In addition, with the help of health-related smartphone apps, patients with chronic conditions felt safer knowing that their illnesses were closely monitored and participated in their own health management more effectively.[5]

The use of new technologies, such as software and mobile phone or applications or SMS, specifically in Cardiovascular Rehabilitation Programs (CRP) has been studied in improving the frequency of cardiac patients exercising remotely, at home, (m-Health), featuring a supervised or semi-supervised intervention. General

or personalized guidance as to the course of the disease, identification of signs and symptoms, correct use of medications, and nutritional guidelines are also complementary objectives of this form of intervention. The results of primary studies seem to indicate positive effects of the association of all these actions, which reflect on the clinical improvement of this group of patients, associated with lower costs when compared to the conventional program. [3-8]

Confirming the importance and applicability of this topic, in 2015 a systematic review was conducted with meta-analysis[8] in order to investigate the influence of internet-based interventions on mortality and lifestyle changes in the secondary prevention of cardiovascular risk factors. Nevertheless, the evidence found was of low quality and the size of the effect uncertain due to the few studies and methodological weaknesses found, thus suggesting the development of more primary studies on this type of intervention.

For this reason, due to the increased use of technologies in care and manipulation in patients participating in the CRP, it is important to analyze, through a systematic review of the literature, the influence the use of these technologies to the CRP, on the patient's functional capacity, adherence, and the perception of the M-Health group participant to the frequency of exercise and management for the control of cardiovascular risk factors.

Therefore, this study aims to analyze evidence through a systematic review and meta-analysis, on the influence of the association between M-Health and CRP in cardiorespiratory fitness, adherence to CRP and in management of cardiovascular risk factors, when compared to cardiac patients inserted in isolated CRP (without association with M-Health).

Methods

This systematic review was recorded by the international database of systematic reviews in health and social assistance PROSPERO (registration number CRD42019137017) and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyzes. (PRISM)[9]. The prospective registration of systematic review protocols increases the reliability and transparency in conducting the studies.[10]

Search strategies and inclusion criteria

The studies were selected through the databases: Medline via Ovid, EMBASE, Central, PEDro and SPORTDiscus via EBSCO, from the oldest record until december 2019. The terms and keywords used to improve the searches were selected with *randomized controlled trials*, *Exercise*, *app health*, *cardiac rehabilitation*, *physical fitness*, *cardiorespiratory fitness*, VO_2max e VO_2peak (Appendix).

Randomized controlled trials (RCT) which used interventions associating cardiovascular rehabilitation programs with new Technologies were selected, such as software and mobile phone or applications or sms to improve the frequency of cardiac patients exercising remotely, at home, (m-Health), featuring a supervised or semi-supervised intervention of the CRP (Cardiovascular Rehabilitation Program), and so comparing their cardiorespiratory fitness to cardic patients involved in standard cardiovascular rehabilitation program[3].

There was no restriction on the language of the studies, characteristics of the participants and duration of the intervention. To be eligible, studies should include the following criteria: i) RCT comparing the use of m-health associated with the

cardiovascular rehabilitation program with the use of the cardiovascular rehabilitation program only; ii) Pre and post intervention assessment of at least one of the studied outcomes (primary and secondary); iii) Patients enrolled in a cardiovascular rehabilitation program.

Primary and secondary outcomes

As a primary endpoint, functional capacity was adopted, using $VO_{2\ peak}$ (ml/kg/min) measured by means of a maximal exercise test and indirect evaluations, e.g., 6-minute walk test (6MWT) or Self Reported measure of Physical Activity by by specific questionnaires. The values of mean and standard deviation in meters extracted by the 6MWT were converted to ml/kg.min, using the formula previously described by Robert et al.[11]

The secondary outcomes of the present study were adherence and the perception of the M-Health group participant, to increase the frequency of exercise and management for the control of cardiovascular risk factors such as body mass index (BMI), resting heart rate (HRR) behavior, sistolyc (SBP) and diastolic (DBP) blood pressure control, lipid profile (Total Cholesterol, LDL, HDL, Triglycerides).

Selection of studies

The study selection process was carried out by two independent reviewers (AP and NSA). After excluding duplicates, titles and abstracts were excluded according to the eligibility criteria. After exclusion by title and abstract, the full texts of the selected studies were examined. Necessary case, was consulted a third reviewer (ACCGT). The reference lists of the included studies were analyzed to obtain potentially eligible studies that were not found by the search strategy.

Data extraction

Data on primary and secondary outcomes were extracted including initial and final values of means, standard deviations and sample size, by two independent reviewers (AP and NSA) and disagreements between authors regarding data extractions were resolved by consensus.

The data extraction process was carried out using a standardized form, which included details such as characteristics of the participants, the cardiovascular rehabilitation program, inclusion of M-Health in the cardiovascular rehabilitation program, cardiorespiratory fitness analysis procedures, as well as compliance and change in behavior of cardiovascular risk factors, sample size, course of treatment, baseline data and treatment methods for both groups.

Bias Risk Assessment

The individual assessment of the risk of bias in the included studies was carried out using the PEDro Scale.[12] This scale aims to help users of the PEDro database to assess the methodological quality of clinical trials. This process was completed in two phases, initially, the note on this scale was searched on the PEDro database website, and only for studies that had not been evaluated and listed in this database, they were subsequently evaluated, manually using those same criteria by two independent reviewers (AP and NSA) and in the possibility of divergences, the consensus method (ACCGT) was again adopted.

A score greater than or equal to 7 was considered "high quality", a score of 5 or 6 was considered "moderate quality" and less than or equal to 4 of "poor quality" [12]. The methodological quality classification was not an inclusion criterion.

Assessment of the quality of evidence

The quality of the evidence was assessed using the *Grading of Recommendations Assessment, Development and Evaluation* (GRADE)[13, 14]. GRADE makes it possible to assess the quality of the evidence and the results found through the meta-analysis reported in a systematic review. Fact that allows judgments to be made about the strength of the evidence, in addition to being an effective method to link the quality of the evidence and the clinical recommendations.

Briefly, the GRADE classification was initially regarded as “high” but downgraded by one level for each of the following domains we considered: (1) Risk of bias (downgraded when more than 25% of participants from studies with “low methodological quality” [PEDro score <5]); (2) inconsistency of results (I^2 statistic, downgraded when more than the presence of heterogeneity, downgrading 1 level [I^2> 50% to 75%], downgrading 2 levels, [I^2> 75%] 15-21; (3) Indirectness (downgraded when there was the presence of any of these criteria: i) patients different from the population of interest, ii) differences in the intervention under analysis; iii) substitute outcomes, other than those predefined as relevant; and iv) results from analyzes that did not directly compare the interventions (head-to-head), but through network meta-analysis (network meta-analysis); (4) and imprecision (<400 participants in total for each result). Assessment of publication bias, using the funell plot was not performed, as the number of studies selected for each outcome was not more than 10.[13]

To characterize the quality of the evidence, the following factors were considered: high quality - it is unlikely that further research will alter our confidence in the estimate of the effect; moderate quality - research is likely to have a major impact on our confidence in the effect estimate and may change the estimate; low quality - new research is likely to have a major impact on our confidence in the effect estimate

and likely to change the estimate; and very low quality - we are not sure about the estimate[13, 14]

Data analysis

All meta-analyzes were conducted using the Review Manager - RevMan software (version 5.3, Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014). Pooled estimates were calculated using a random effect model. The I^2 statistic was used to assess the proportion of variation between studies attributed to heterogeneity and can be classified as homogeneous when $I^2 = 0\%$, low heterogeneity 1% to 50%, moderate heterogeneity 50% to 75% and high heterogeneity when $I^2 > 75\ \%$.[15-21]

The data were grouped in meta-analyzes and described as differences between the means (mean difference - MD) and standardized mean differences (standardized mean difference - SMD) with 95% confidence intervals (CI). The effect size was interpreted as 0.2 representing a small effect size, 0.5 as moderate and 0.8 as a large effect size. [20]

Results

The search in the aforementioned databases identified 5028 studies, Besides, 2 more studies[7, 22] were found manually by reading the bibliographies and added. From these, 1388 were identified as duplicates and only 52 were selected for reading the abstract. Then, 21 were excluded after reading the abstracts, and finally, when reading the full text, 17 were excluded for the following reasons: No RCT (n = 7), other forms of technology, not M-Health (n = 5), publications of study protocols (n = 1) and studies that are not related to the inclusion requirements (n = 4). Thus, the

eligible studies[3, 6, 7, 22-32] were published between the years 2010 and 2019. Figure 1 shows the schematic process of selecting studies based on a PRISMA flowchart.[9]

*****Figure 1*****

The fourteen eligible studies[3, 6, 7, 22-32] comprised a total of 2917 participants, aged over 40 years, and respecting the inclusion criteria of this review, all study participants have heart disease and belonged to a CRP. It should be noted that among the selected studies there are different approaches to M-Health, thus all the characteristics of the selected studies can be seen in table 1.

*****Tablet 1*****

The methodological quality of the included studies, analyzed by the PEDro scale[12] presented an average of 6,93±1,27 points. Five studies[3, 6, 7, 29, 31] were considered to be of "moderate quality" and the other nine studies[22-28, 30, 32] were of "high quality", as shown in table 2.

*****Tablet 2*****

For quantitative analysis, between the extracted data, for the primary and secondary outcomes, it was possible to summarize the VO_2peak variables (ml/kg/min)[3, 23 25, 26, 31, 32], the maximum distance covered in the 6MWT minutes (meters)[6, 22, 29, 30], which were converted to ml/kg/min.[11] On the other hand, studies that presented a Self Reported measure of Physical Activity (METS/min/week)[7,24] were not converted and thus analyzed in forest plot separately. Both analyzes are represented in figure 2.

In the secondary endpoint, it was possible to summarize the behavior of the variables that involve the management of cardiovascular risk factors, such as Body

Mass Index, Waist Circumference, Hip Circumference, Waist-to-Hip-Ratio, Heart Rate Rest, Systolic Blood Pressure, Diastolic Blood Pressure, and Profile Lipid as can be seen in Figures 3, 4 and 5 respectively.

During the data extraction process, four authors[6, 7, 22, 25] were contacted for clarification and request for data, two studies[7, 25] sent the spreadsheet to extract the mean and standard deviation values. Another study[22] sent mean values and standard deviations for the variable VO2 for both groups in the post-intervention moment. Finally, the study[6], which presented its final results in graph format, had its data estimated to compose the meta-analysis. Data from SBP, DBP, and Self Reported measure of Physical Activity by IPAQ, referring to the study[25], are unpublished data that were inserted in the analyzes, due to the author's prior authorization.

Regarding the research protocols that were initially considered for reading the full text to contact the authors and obtain the values of its variables, only Dorje et al.[22] forwarded the full text, which was published after the date of the first database search.

Primary outcomes

Thirteen studies were found that address the cardiorespiratory capacity of patients inserted in supervised[7, 22-27, 30, 32] or semi-supervised[3, 6, 29, 31], who underwent M-Health intervention compared to unused control group interactivity through the cell phone.

Figure 2 shows the forest plot of functional capacity values measured by physical and self-reported tests. In both graphs, the estimate of the effects does not include zero, thus showing differences in favor of M-Health with a high effect size for

the variable VO2 (0.81 [0.26, 1.37]), but for the results obtained by the questionnaires, the effect was research (0.33 [0.04,0.63]).

*****Figure 2*****

Secondary outcomes

In the quantitative analysis of the management of cardiovascular risk factors, the studies included Varnfield et al[6], Dorje et al[22], Frederix et al[23], Chow et al[24,] Maddison et al[25, 26], Dale et al[28] e Peng et al[29], however, not all variables were common among the studies cited.

The estimate of the effect for 72.7% of the variables analyzed touched the line of the non-effect, BMI: 0.42 [-0.88, 1.72], WC: -0.32 [-6.03, 5.40], HC: -0.55 [-8.78, 7.68], Waist -To-Hip-Ratio 0.01 [-0.09, 0.12] SBP: 4.54 [-3.44, 12.52], Total Cholesterol: 0.00 [-0.22, 0.23], HDL: -0.02 [-0.05, 0.01] and LDL: -0.03 [-0.16, 0.10].

However, there is a reduction in these values and high estimates of the favorable effect after the associated M-Heath intervention for the variables HRR and DBP, (-2.95 [-4.82, -1.09]), (-1.67 [-3.28, -0.06]), respectively and for Triglicerydes (-0.16 [-0.27, -0.04]) there is a low effect size, significant to M-Health, involving a sample of more than a thousand participants in each analysis, as can be seen in figures 3, 4 and 5.

*****Figure 3*****

*****Figure 4*****

*****Figure 5*****

Among the selected studies, variables that were not included in this review were evaluated, as they are not related to the inclusion criteria, such as quality of life[3, 6, 22, 23, 25-32], costs of implementing M-Health[25-27], mortality[26, 31], adverse events[25, 30, 32], and the number of hospitalizations[26, 31]. However, in general, studies converge in their results, showing improvement in the variables of the M-Health group compared to the control group, except for mortality and the number of hospitalizations.

Positive results regarding adherence and factors related to satisfaction concerning aerobic training associated with M-Health were investigated in nine studies[6, 7, 22-25, 28, 30, 32]. The evaluations addressed by these studies were conducted through questionnaires prepared by their authors, or by accessing and viewing educational messages or videos. It should be noted that among the M-health interventions, forms, and the period of evaluations proposed by the primary studies for these comparisons, a pattern was not found that would allow a more objective comparison by this review, so the results of each study are described in following paragraphs.

In the study by Chow et al[24], 87% of the participants answered the feedback questionnaire on the applied intervention, and among these questions stand out those reported regarding the patients' perception of usefulness (91%) and easy compression (97%) messages sent. Besides, 81% of the participants adhered to healthy diets and food, and 73% improved their level of physical activity measured through a questionnaire (IPAQ) and justified these changes due to the fact that they felt more motivated about changes in habits and quality of life.

The findings on feedback from the intervention proposed in the study by Frederix et al[23] report that 97% of the participants in the intervention group that the

messages were easy to read, and the program easy to use, 95% were very satisfied or satisfied, and 89% reported that they would continue to use even after the study is finished.

In another article, Frederix et al[27] (2018) presented the 2-year follow-up of the study published in 2015, conserving approximately 91% of participants, in which the improvement in the quality of life showed lower costs for M-Health participants compared to control. For the last study[22] that evaluated the perception of the participants in the intervention group, they observed that 100% of their participants stated an improvement in their quality of life.

Added to this, the adherence rate assessed by the studies[6,25,28,30,32] was higher and significant when compared to the control group, except Antypas et al[7], who assessed adherence after discharge from the M-health intervention, and report that their values were higher, but not significant.

Moreover, the visualization rates of messages and educational videos also showed higher and expressive results for the intervention group M-health[25,28], with rates between 57% to 100%. Also, the study by Dale et al[28] assessed medication adherence, and the M-health group behaved significantly higher when compared to control (mean difference: 0.58, 95% CI 0.19-0.97; P = .004).

Discussion

For quantitative analysis, the association of M-Health with CRP is effective when compared to conventional CRP in increasing cardiorespiratory fitness. Besides, for the secondary outcome, for the HRR, DBP and Triglicerydes variables, they showed significant behavior favorable to the association of M-health and CRP use.

The qualitative analysis of the selected articles shows a coherent and positive trend in the influence of the use of M-Health to the CRP, as can be seen by the adherence and acceptability in increasing the practice of physical activity and healthier eating habits, when compared to the intervention groups conventional CRP.

As for the quality of the evidence evaluated and presented in Table 3, the cardiorespiratory fitness variables measured by physical tests are classified as high quality, favorable, and strongly recommended for the association of interventions. However, when assessing self-reported cardiorespiratory fitness, the evidence is classified as low quality, due to the inconsistency and indirectness criteria and favorable with a strong recommendation. Factors such as heterogeneity above 50%, low sample size, extensive confidence interval, and the subjectivity of the evaluation through questionnaires were criteria that reduced the quality of this evidence.[12,13]

All the quantitative variables of secondary outcomes show favorable behavior and are strongly recommended for the intervention. Only the variable Triglicerydes showed high quality, unlike the HRR and DBP variables on which moderate and low qualities are observed respectively, since the inconsistency criteria, justified in table 3.

Cardiorespiratory fitness can be assessed using different instruments, such as the maximum ergospirometric test (direct VO2 measurement), or indirectly by maximum exercise tests, and 6-minute walking, or by using a device such as an accelerometer or even subjectively reported through physical activity level questionnaires. Due to intolerance to the efforts of patients with cardiorespiratory disorders, oxygen consumption indirectly assessed by the 6-minute walk test does not differ statistically when compared to the maximum direct consumption obtained by VO_2peak[33, 34].

According to the aforementioned information, it is understood that the summary of the differences between the means of the VO2 results and the distance covered in the 6MWT becomes adequate, accurate and of high confidence, thus being considered its conversion, as can be observed, in figure 2.

Previous studies [35, 36, 37], affirm that the cardiopathic patient's physical fitness gain seems to be more pronounced between 8 to 12 weeks after the beginning of the regular practice of aerobic and/or resistance physical activity, for those inserted in conventional[38]. This fact can be justified by the association of cardiorespiratory disorders and dysfunctions of the peripheral skeletal muscle apparatus[38], resulting from the history of sedentary lifestyle, intensified by the aging process[39, 49].

Based on the results of the summarization represented by figure 2, the preference for the association of M-Health and CRP for the increase in functional capacity is verified, as it is believed that the conditioning gains were higher since interactivity through the cell phone-enabled better acceptability, adherence and motivation to initiate changes in behavior and lifestyle habits such as regular physical activity [7, 24, 25].

Another aspect that reflects improved physical fitness is the reduction in heart rate values[41, 42]. The behavior of this variable can be observed in figure 4, which corroborates the results found for VO2 and 6MWT favorable for the associated intervention of M-Health and CRP, because low heart rate values have been referred to as an increasing factor in tone vagal, which promotes electrical stability of the heart as well as reduction of peripheral vascular resistance, reducing BPD values, while increased sympathetic activity would increase the vulnerability of the heart and the risk of cardiovascular events, such as hypertensive conditions[43].

As for the positive results in the improvement of triglycerides, a direct relationship with the approaches mentioned by the authors of the primary studies[6, 22, 24] selected for summarization can be seen, since among the interaction approaches they emphasized nutritional guidelines and feedback from the study participant's diet to the researcher, in which a food diary was built, for example, employing the photographic record[22].

These results were not observed by the Cochrane review by Devi et al.[8], in which he assessed secondary prevention factors for cardiovascular diseases associated with the use of the internet and cardiovascular rehabilitation programs. It is noteworthy that in this study when compared with the review published by Cochrane 5 years ago, more studies and a more specific comparison involving only interactivity through the cell phone as well as the comparison on cardiorespiratory fitness were added.

For these reasons, the limitation of this study is related to the presence of inconsistency for some secondary outcomes. This fact can be justified as it is a current topic, many studies are still under development which may update these results and reflect changes in the quality of the level and evidence, the strength of recommendation, and the inclusion of the analysis of publication bias (*funnel plot*).

Although adverse effects and hospitalizations were performed in some selected studies[25, 26, 30, 32], this information was not planned as an outcome in the registration protocol and was also not reported by all included studies. Thus, due to the importance of this information for the safety of the M-Health intervention, this is a weakness of the present review. It is necessary to understand why they happen and to have more adverse events reported in the M-Health group that are perceived in the studies[26, 30] However, in the other two studies[25, 32], the similarities between

adverse events/mortality are reported[32] and there was only one adverse event in the study of Maddison et al[25].

As for the strengths of this review, there is a great favorable effect of high quality and strength of recommendation for the implementation of M-health when compared to the CRP aimed at improving cardiorespiratory fitness. This classification allows us to guarantee that new research is unlikely to alter the confidence in the estimate of the effect found by the present review. Among the selected studies, few presented a comparison of the intervention costs[25-27], which were lower for the M-health group evaluated in different follow-ups. Also, the diversity of M-health approach presented by the selected studies, allows each CRP to implement this type of associated intervention in a supervised and semi-supervised manner, according to its budget.

Conclusion

From the evidence summarized in this review, among the selected studies, high quality of evidence was found, strong recommendation strength and the favorable association between M-Health intervention and CRP in improving cardiorespiratory fitness and levels of triglycerides. This favorable effect extends to the behavior of heart rate and diastolic blood pressure, despite lower levels of quality of evidence. Adherence to the practice of remote physical activity was shown to be significantly higher in primary studies, however, this review did not summarize these effects.

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Table 1 – Risck of bias in selected studies

Scale PEDro / selected studies	Pfaeffli et al 2015	Peng et al 2018	Frederix et al 2017	Hwang et al 2017	Maddison et al 2018	Piotrowicz et al 2010	Piotrowicz et al 2019	Duscha et al 2018	Chow et al 2015	Frederix et al 2015	Varnfield et al 2014	Maddison et al 2015	Seto et al 2012	Dorje et al 2019	Antypas et al 2014
Random distribution	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Hidden distribution	1	1	0	1	1	0	1	0	1	0	1	1	1	1	0
Comparisons to the starting point	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Blinding of subjects	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blinding therapists	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blinding of evaluators	0	1	1	1	1	0	1	0	1	1	0	1	0	1	1
Ratings> 85%	1	0	1	1	1	1	1	0	1	1	0	1	1	1	0
Treatment intention analysis	1	0	1	1	1	0	1	1	1	1	1	1	1	1	0
Intergroup comparisons	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Precision and variability measures	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Total Score	7/10	6/10	8/10	8/10	8/10	5/10	8/10	5/10	8/10	7/10	6/10	8/10	7/10	8/10	5/10

Tabel 2- Characteristics of the studies included in the review

Studies	Sample characteristics	Intervention	Outcome Primary/Secondary
Antypas (2014) Norway	**Total sample:** 1st month (n=24); 3rd month (n=19) **Intervention group:** 1st month follow-up: n=10 3rd month follow-up: n=7 **Control group:** 1st month follow-up: n=14 3rd month follow-up: n=12 **Diagnosis:** cardiovascular disease **Medicines:** Not reported by the authors	**M-Health and Supervised CRP:** Personalized content based on health behavior models through website and text message **CRP**: supervised **Intervention time:** one month and three months	**Primary:** Self-reported General Physical Activity (IPAQ) **Secondary:** Self-efficacy, social support, anxiety and depression (HADS)
Chow (2015) Sydney, Australia	**Total sample:** 710 (582 men; 128 women) **Intervention group:** 352 **Control group:** 358 **Diagnosis:** Coronary artery disease diagnosed by cineangiography and/or history of acute myocardial infarction. **Medicines:** Aspirin, beta-blockers, statin, Angiotensin-converting enzyme inhibitor.	**M-Health and Supervised CRP:** Weekly text message via smartphone **CRP**: supervised **Intervention time:** 24 weeks	**Primary:** low-density lipoprotein cholesterol (LDL-C) **Secondary:** SBP, BMI, physical activity level (IPAQ) and smoking
Dale (2015) Auckland, New Zealand	**Total sample:** 123 **Intervention group:** 61 **Control group:** 62 **Diagnosis:** Myocardial infarction,	**M-Health and Supervised CRP:** Automated text messaging and support website **CRP**: supervised **Intervention time:** 24 weeks	**Primary:** Adherence to healthy lifestyle behaviors, measured using a self-reported composite health score (≥3) at 3 and 6 months. **Secondary:** included clinical outcomes, medication adherence score, self-efficacy,

	Unstable angina and Angina. **Medicines:** Not reported by the authors.		perception of illness and anxiety and / or depression at 6 months.
Dorje (2019) Multicentric Shanghai, China Perth, Australia	**Total sample:** 312 **Intervention group:** 156 **Control group:** 156 **Diagnosis:** coronary artery disease **Medicines:** Aspirin, clopidogrel, beta-blocker, statin, angiotensin-converting enzyme inhibitor	**M-Health and Supervised CRP:** Application for patients with coronary heart disease **CRP**: Unsupervised **Intervention time:** 8 and 24 weeks	**Primary:** 6MWT short and long term. **Secondary:** self-reported quality of life questionnaires GAD-9, PHQ-9, SF-12.
Duscha (2018) California EUA	**Total sample:** 25 **Intervention group:** 16 **Control group:** 9 **Diagnosis:** Ischemic origin with low or preserved ejection fraction, acute myocardial infarction, valvulopathy, stable angina **Medicines**: Aspirin, calcium channel beta blocker, statin, beta blockers, angiotensin converting enzyme inhibitor, anticoagulant and diuretic.	**M-Health and Semii-supervised CRP:** Sending text messages through the app, calls, conference calls and supervised exercises **CRP**: supervised **Intervention time:** 12 weeks	**Primary:** Long-term VO_2 **Secondary:** medical adherence and frequency of angina
Frederix (2015) Multicentric Belgium	**Total sample:** 139 **Intervention group:** 69 **Control group:** 70 **Diagnosis:** Heart failure with lowered or preserved ejection fraction and acute myocardial infarction	**M-Health and Supervised CRP:** Tele-rehabilitation system via email and SMS for cardiac patients and participants in the traditional CRP with supervised exercises **CRP**: supervised **Intervention time:**6 weeks and follow-up in 6 month	**Primary:** VO_2 short and long term. **Secondary:** daily physical activity recorded by triaxial accelerometer.

	Medicines: Aspirin, beta-blockers and statins		
Frederix (2017) Multicentric Belgium	**Total sample:** 126 **Intervention group:** 62 **Control group:** 64 **Diagnosis:** Heart failure with lowered or preserved ejection fraction and acute myocardial infarction **Medicines:** Aspirin, beta-blockers and statins	**Intervention time:** follow-up in 2 years of the 2015 study	**Primary:** VO_2 peak **Secondary:** International physical activity and quality of life questionnaire (HRQoL)
Hwang (2017) multicentric Brisbane, Australia	**Total sample:** 49 **Intervention group:** 23 **Control group:** 26 **Diagnosis:** Heart failure with preserved ejection fraction, dilated idiopathic heart failure, acute myocardial infarction and ischemic cardiomyopathy **Medicines:** Beta-blocker, diuretic, aldosterone antagonist	**M-Health and Supervised CRP:** 60 min exercises twice a week and lifestyle monitoring using online video conferencing software **CRP**: supervised **Intervention time:** 12 weeks	**Primary:** 6MWT **Secondary**: Quality of life, patient satisfaction, participation rates in the program and adverse events
Maddison (2015) Auckland, New Zealand	**Total sample:** 171 **Intervention group:** 85 **Control group:** 86 **Diagnosis:** Coronary artery disease with angina **Medicines:** Not reported by the	**M-Health and Supervised CRP:** 3-5 text message by cell phone per week and once a week it was sent through the specialized website 3 videos messages. CRP was supervised **CRP**: supervised **Intervention time:** 24 weeks	**Primary:** VO_2 peak long-term **Secondary:** quality of life through questionnaires SF-36 and EQ-5D

	authors		
Maddison (2018) Tauranga, Auckland, New Zealand	**Total sample:** 140 **Intervention group:** 68 **Control group:** 72 **Diagnosis:** acute myocardial infarction and post-bypass coronary artery disease **Medicines:** Aspirin, beta blocker, statin, Angiotensin converting enzyme inhibitors, anticoagulant and calcium channel blocker	**M-Health and Supervised CRP**: Remotely monitored exercise-based cardiac telerehabilitation platform **CRP**: supervised **Intervention time:** 12 weeks and follow-up in 6 month	**Primary:** VO_2 peak **Secondary:** Accelerometry and HRQoL
Peng (2018) Hunan, Chengdu, China	**Total sample:** 98 **Intervention group:** 49 **Control group:** 49 **Diagnosis:** heart failure with preserved ejection fraction, dilated idiopathic heart failure and acute myocardial infarction **Medicines:** Not reported by the authors.	**M-Health and Supervised CRP:** 1-4 weeks (training 3x week / 20min) 5-8 weeks (training 5x week / 30min) and CRP unsupervised **CRP**: unsupervised **Intervention time:** 8 weeks more follow-up in 4 month	**Primary:** 6MWT **Secondary:** MLHFQ and Hospital Scale for Anxiety and Depression
Piotrowicz (2010) Warsaw, Poland	**Total sample:** 131 **Intervention group:** 75 **Control group:** 56 **Diagnosis:** Cardiac insufficiency, Implantable cardioverter defibrillator, Intraventricular arrhythmia, coronary artery disease, By pass	**M-Health and Semi-supervised CRP:** telerehabilitation used for exercises and questions about patient's condition, including fatigue, dyspnoea, blood pressure, weight and medications taken. 5 min warm-up and cool-down period and exercises lasting 30 to 40 min with intensity ranging from 40 to 70% of the reserve heart rate **CRP**: supervised	**Primary:** VO_2 peak and 6MWT **Secondary:** SF36, NYHA II and III

	Medicines: Aspirin, beta blocker, statin, angiotensin converting inhibitor, anticoagulant, diuretic, antagonist aldosterone and digoxin	**Intervention time:** 8 weeks	
Piotrowicz (2019) Multicentric Warsaw, Poland	**Total sample:** 781 **Intervention group:** 386 **Control group:** 395 **Diagnosis:** Heart failure with reduced ejection fraction, implantable cardioverter defibrillator, Acute myocardial infarction and By pass **Medicines**: Aspirin, beta blocker, statin, angiotensin converting inhibitor, anticoagulant, diuretic, clopidogrel and digoxin	**M-Health and Supervised CRP:** intervention encompassed telecare, telerehabilitation, and remote monitoring of implantable devices. **CRP**: supervised **Intervention time:** 9 weeks and followed up for 14 to 26 months after randomization.	**Primary:** VO_2 peak and 6MWT **Secondary:** SF36, NYHA I, II and III
Varnfield (2014) Queensland, Australia	**Total sample:** 94 **Intervention group:** 53 **Control group:** 41 **Diagnosis:** acute myocardial infarction **Medicines:** Not reported by the authors.	**M-Health and Semi-supervised CRP:** Use of an pplication for post myocardial infarction patients for telerehabilitation **CRP**: supervised **Intervention time:** 6 weeks and more follow-up in 6 months	**Primary:** 6MWT short and long term **Secondary:** Quality of life assessed through questionnaires EQ5D and HRQoL

Table 3 - Assessment of the quality of evidence of primary and secondary outcomes

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	M-Health	CRP	Absolute (95% CI)		
Cardiorrespiratory Function - Physical test											
10	RCT	not serious	not serious	not serious	not serious	none	962	926	MD **0.81 higher** (0.26 higher to 1.37 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Cardiorrespiratory Function - Self Reported mensure of Physical Activity											
3	RCT	not serious	serious [a]	serious [b]	not serious	none	455	482	SMD **0.54 higher** (0.07 higher to 1.01 higher)	⊕⊕◯◯ LOW	IMPORTANT
Heart Rate Rest											
4	RCT	not serious	serious [c]	not serious	not serious	none	563	556	MD **2.95 lower** (4.82 lower to 1.09 lower)	⊕⊕⊕◯ MODERATE	IMPORTANT
Systolic Blood Pressure											
7	RCT	not serious	very serious [d]	not serious	not serious	none	804	805	MD **4.54 higher** (3.44 lower to 12.52 higher)	⊕⊕◯◯ LOW	IMPORTANT
Triglicerydes											
4	RCT	not serious	not serious	not serious	not serious	none	574	576	MD **0.16 lower** (0.27 lower to 0.04 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT

Legend: RCT: Radomized Clinical Trial. CI: Confidence interval; MD: Mean difference; SMD: Standardised mean difference

Explanations: a. The summary presents a heterogeneity of 57%, presenting inconsistency of information and downgrading 1 level of evidence; b. Functional capacity assessed through; questionnaire, subjective assessment; c. The summary presents heterogeneity of 65%, presenting inconsistency of information and downgrading 1 level of evidence; d. The summary presents heterogeneity of 95%, presenting inconsistency of information and downgrading 2 levels of evidence.

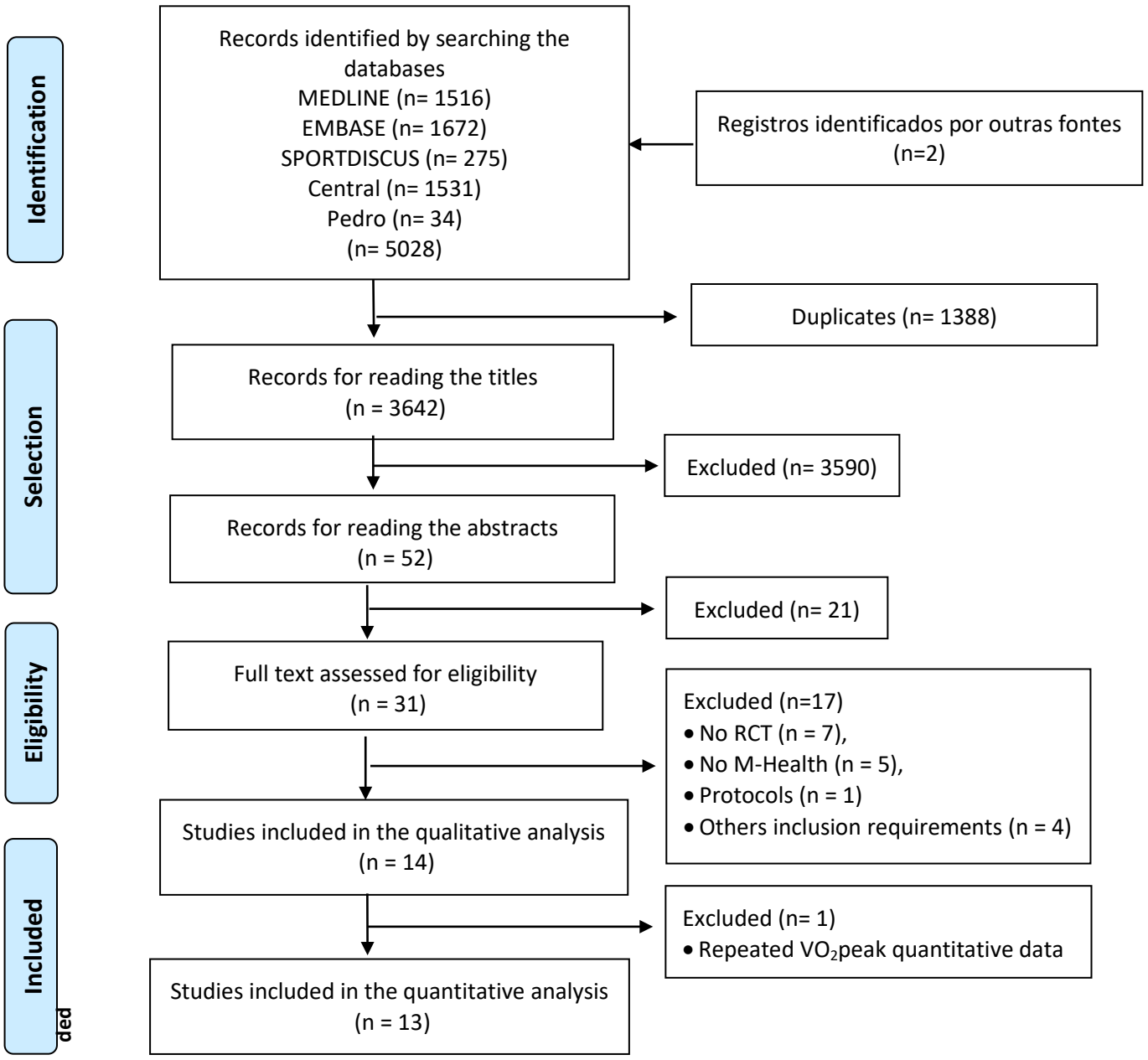
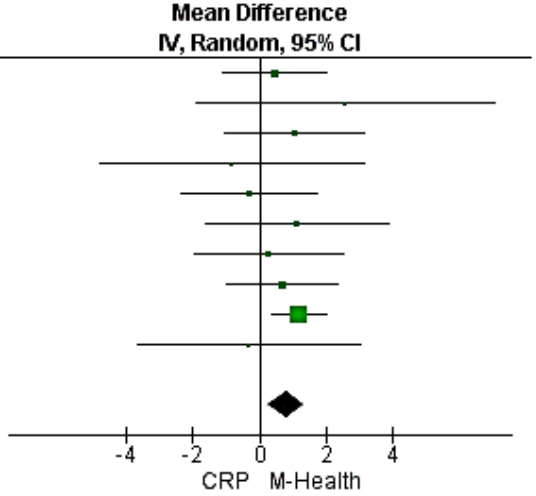


Figure 1 – Organization chart of the articles selection process

Study or Subgroup	M-Health Mean	M-Health SD	M-Health Total	CRP Mean	CRP SD	CRP Total	Weight	Mean Difference IV, Random, 95% CI
Dorje, 2019	17.4462	6.5005	134	16.9885	6.3326	131	12.9%	0.46 [-1.09, 2.00]
Duscha, 2018	21.7	5.6	16	19.1	5.5	9	1.5%	2.60 [-1.92, 7.12]
Frederix, 2015	23.91	6.74	62	22.86	5.37	64	6.7%	1.05 [-1.08, 3.18]
Hwang, 2017	13.55	6.995	23	14.378	7.317	26	1.9%	-0.83 [-4.84, 3.18]
Maddison, 2015	26.8	6.4	75	27.1	6.5	78	7.3%	-0.30 [-2.34, 1.74]
Maddison, 2018	30.52	9.63	68	29.39	6.75	72	4.0%	1.13 [-1.64, 3.90]
Peng, 2018	14.56775	5.17064	42	14.29474	5.23711	41	6.1%	0.27 [-1.97, 2.51]
Piotrowicz, 2010	19.7	5.2	75	19	4.6	56	10.8%	0.70 [-0.98, 2.38]
Piotrowicz, 2019	17.9	6.2	422	16.7	5.9	422	46.0%	1.20 [0.38, 2.02]
Varnfield, 2014	18.058	6.788	45	18.38	7.225	27	2.7%	-0.32 [-3.69, 3.05]
Total (95% CI)			**962**			**926**	**100.0%**	**0.81 [0.26, 1.37]**

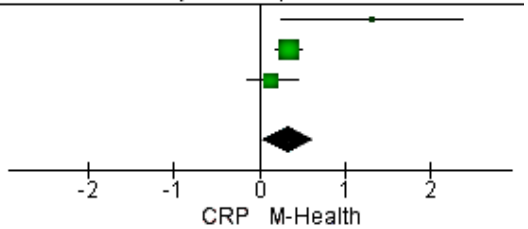
Heterogeneity: Tau² = 0.00; Chi² = 4.22, df = 9 (P = 0.90); I² = 0%
Test for overall effect: Z = 2.87 (P = 0.004)



Forest plot of comparison: 1 M-Health vs CRP - Cardiorespiratory Function - Physical Test, outcome: 1.1 Cardiorespiratory Function - Physical Test.

Study or Subgroup	M-Health Mean	M-Health SD	M-Health Total	CRP Mean	CRP SD	CRP Total	Weight	Std. Mean Difference IV, Random, 95% CI
Antypas, 2014	4,594.43	2,298.73	7	1,795.43	1,867.33	11	6.9%	1.31 [0.24, 2.37]
Chow, 2015	932	1,020.7207	341	587	1,010.2012	358	54.7%	0.34 [0.19, 0.49]
Maddison, 2015	5.634	4.465	85	4.978	4.43	86	38.4%	0.15 [-0.15, 0.45]
Total (95% CI)			**433**			**455**	**100.0%**	**0.33 [0.04, 0.63]**

Heterogeneity: Tau² = 0.04; Chi² = 4.65, df = 2 (P = 0.10); I² = 57%
Test for overall effect: Z = 2.20 (P = 0.03)

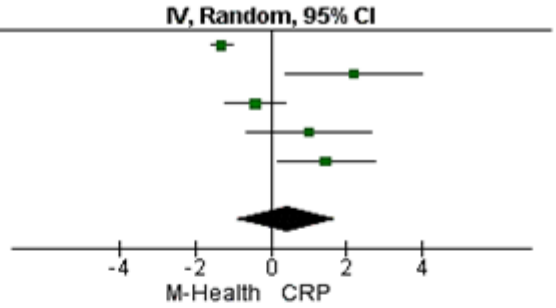


Forest plot of comparison: 1 M-Health vs CRP - Cardiorespiratory Function, outcome: 1.2 Cardiorespiratory Function - Self Reported measure of Physical Activity.

Figure 2 – Forest plot of comparison: 1 M-Health vs CRP - Cardiorespiratory Function, primary outcome, VO2peak, TC6min and Self Reported measure of Physical Activity.

Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Chow, 2015	29	1.9079	341	30.3	1.9242	358	24.1%	-1.30 [-1.58, -1.02]
Dale, 2015	30.3	5.4	57	28.1	4.4	59	16.6%	2.20 [0.40, 4.00]
Dorje, 2019	24.5	3.2	134	24.9	3.5	131	22.2%	-0.40 [-1.21, 0.41]
Frederix, 2015	28	5	69	27	5	70	17.4%	1.00 [-0.66, 2.66]
Maddison, 2018	29.03	4.32	68	27.58	3.34	72	19.7%	1.45 [0.17, 2.73]
Total (95% CI)			**669**			**690**	**100.0%**	**0.42 [-0.88, 1.72]**

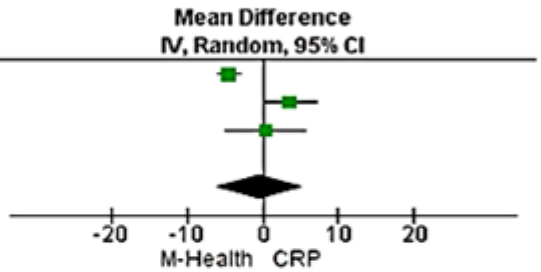
Heterogeneity: Tau² = 1.81; Chi² = 38.09, df = 4 (P < 0.00001); I² = 89%
Test for overall effect: Z = 0.64 (P = 0.52)



Forest plot of comparison: 2 M-Health vs CRP - Second Outcomes, outcome: 2.1 Body Mass Index.

	M-Health			CRP				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Chow, 2015	100.6	10.327	341	105	10.5831	358	37.5%	-4.40 [-5.95, -2.85]
Maddison, 2018	103.2	10.82	68	99.6	10.11	72	33.7%	3.60 [0.13, 7.07]
Varnfield, 2014	101.1	14.4	46	100.7	8.7	26	28.8%	0.40 [-4.94, 5.74]
Total (95% CI)			**455**			**456**	**100.0%**	**-0.32 [-6.03, 5.40]**

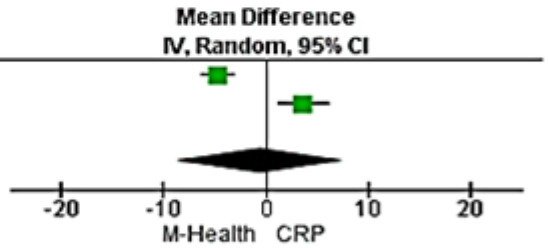
Heterogeneity: Tau² = 22.07; Chi² = 18.51, df = 2 (P < 0.0001); I² = 89%
Test for overall effect: Z = 0.11 (P = 0.91)



Forest plot of comparison: 2 M-Health vs CRP - Second Outcomes, outcome: 2.2 Waist Circumference.

	M-Health			CRP				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Chow, 2015	101.7	11.2658	341	106.4	11.5452	358	50.6%	-4.70 [-6.39, -3.01]
Maddison, 2018	106	8.22	68	102.3	6.34	72	49.4%	3.70 [1.26, 6.14]
Total (95% CI)			**409**			**430**	**100.0%**	**-0.55 [-8.78, 7.68]**

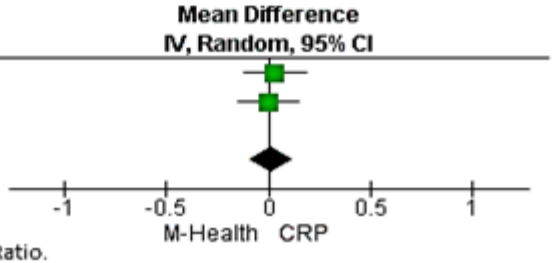
Heterogeneity: Tau² = 34.13; Chi² = 30.73, df = 1 (P < 0.00001); I² = 97%
Test for overall effect: Z = 0.13 (P = 0.90)



Forest plot of comparison: 2 M-Health vs CRP - Second Outcomes, outcome: 2.3 Hip Circumference.

	M-Health			CRP				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Dale, 2015	0.97	0.6	61	0.94	0.07	62	47.6%	0.03 [-0.12, 0.18]
Dorje, 2019	0.9	0.6	134	0.9	0.6	131	52.4%	0.00 [-0.14, 0.14]
Total (95% CI)			**195**			**193**	**100.0%**	**0.01 [-0.09, 0.12]**

Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 0.27 (P = 0.79)



Forest plot of comparison: 2 M-Health vs CRP - Second Outcomes, outcome: 2.4 Waist-to-Hip-Ratio.

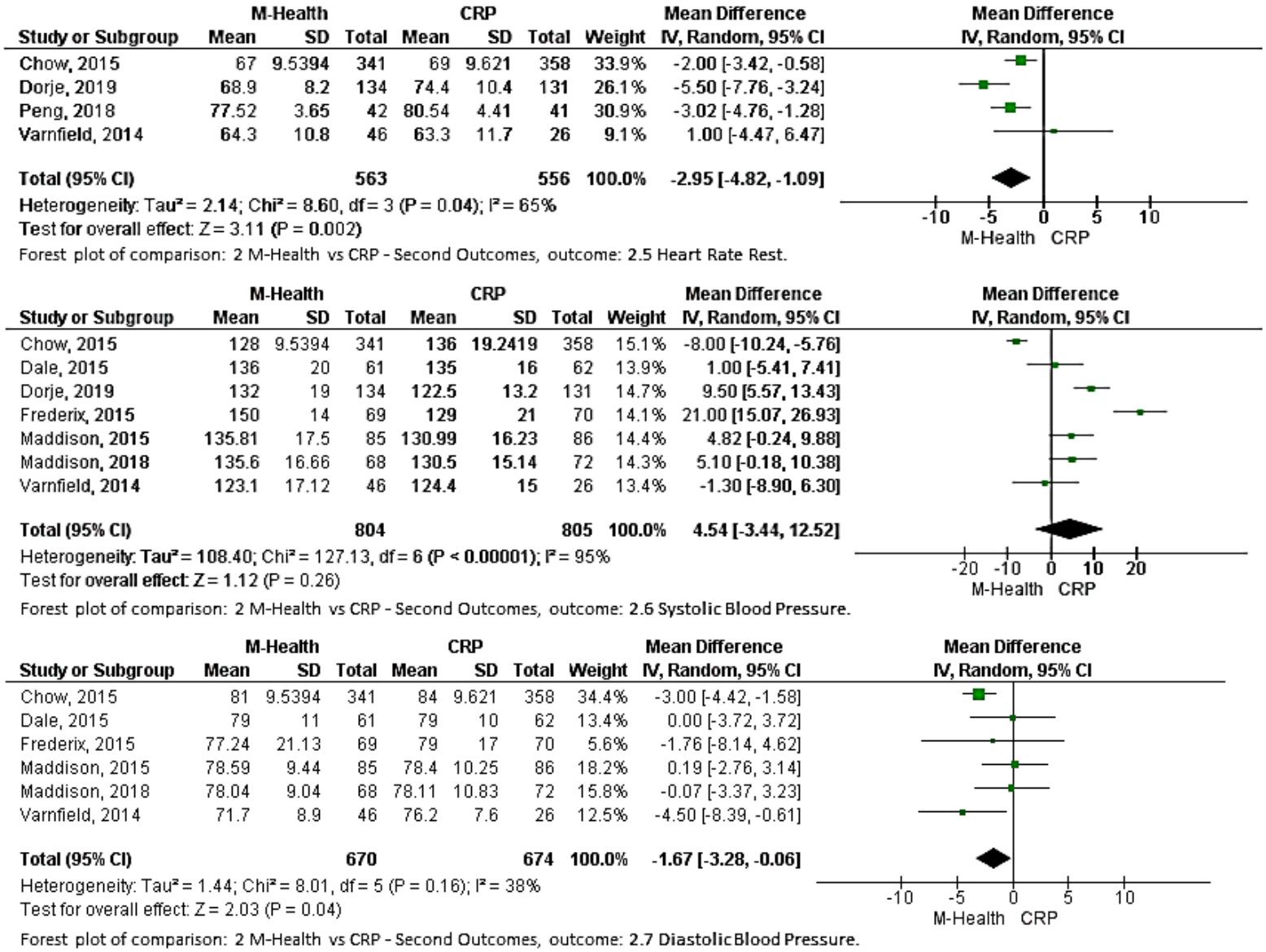


Figure 3 - Forest plot of comparison: 2 M-Health vs CRP - Second Outcomes, outcome: 2.7 Diastolic Blood Pressure

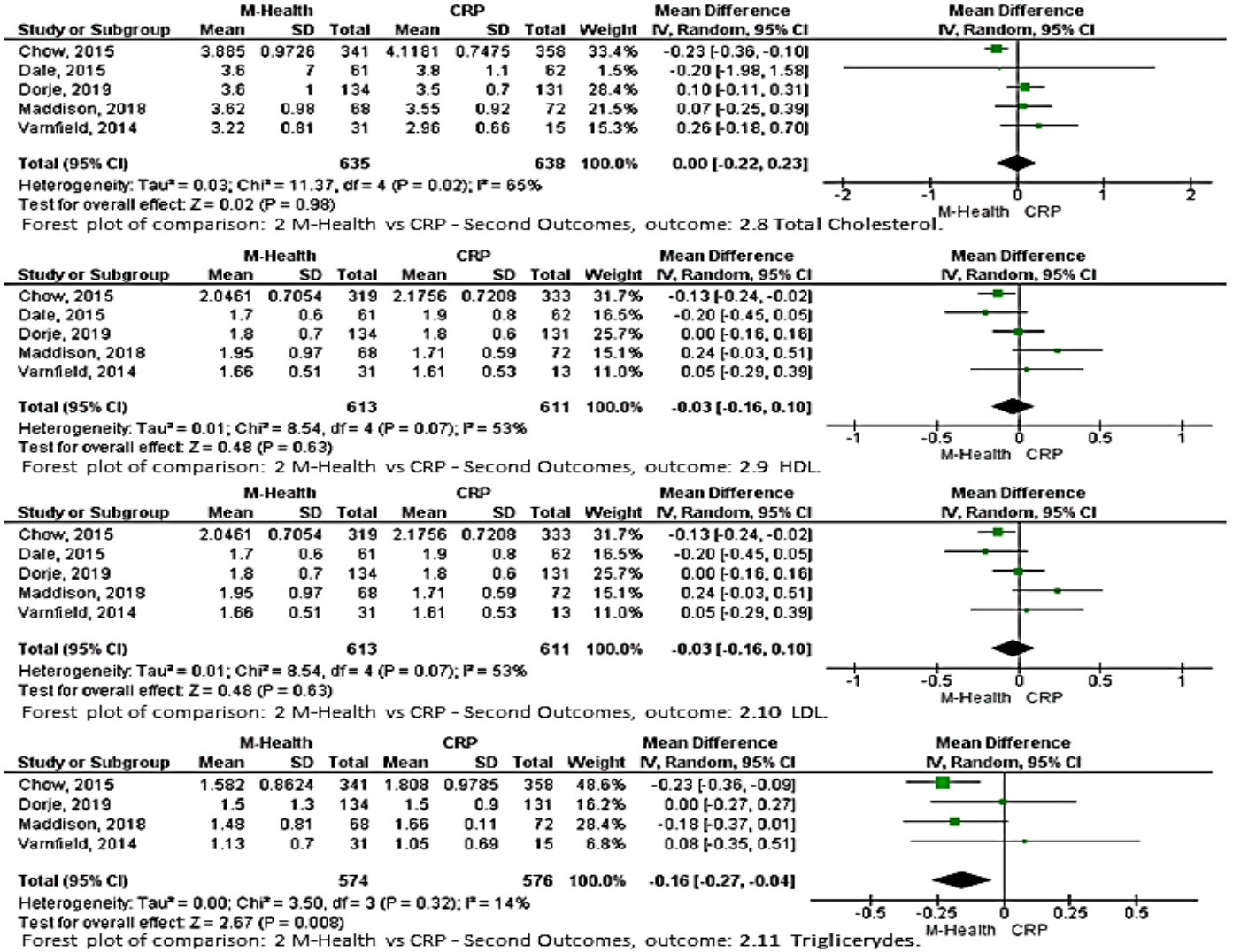


Figure 4 – Forest plot of comparison: 2 M-Health vs CRP – Second Outcomes, outcome: 2.11 Triglicerydes

Sensitivity Analysis

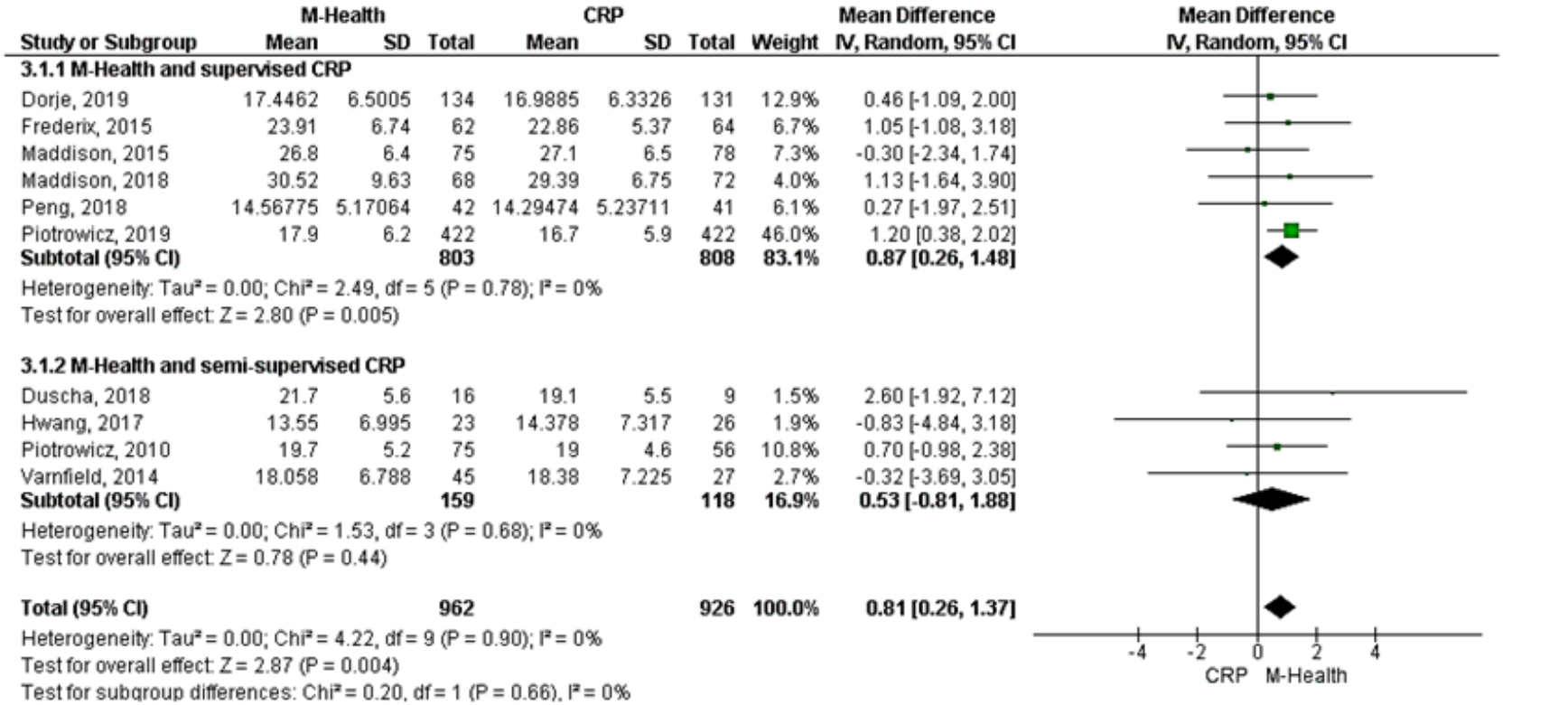


Figure 5– Forest plot of comparison: Forest plot of comparison: M-Health vs CRP - Cardiorespiratory Function - Physical Tests ubgrups (Supervised and sem-supervisied CRP)

ANEXO

Registro PROSPERO

NHS National Institute for Research

< Back

PROSPERO
International prospective register of systematic reviews

Dear Dr Toledo,

Thank you for submitting details of your systematic review "Use of M-health as a strategy to improve the cardiovascular performance of cardiac patients belonging to the cardiovascular rehabilitation program" to the PROSPERO register. We are pleased to confirm that the record will be published on our website within the next hour.

Your registration number is: CRD42019137017

You are free to update the record at any time, all submitted changes will be displayed as the latest version with previous versions available to public view. Please also give brief details of the key changes in the Revision notes facility and remember to update your record when your review is published. You can log in to PROSPERO and access your records at https://www.crd.york.ac.uk/PROSPERO.

Comments and feedback on your experience of registering with PROSPERO are welcome at crd-register@york.ac.uk

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Best wishes for the successful completion of your review.

Yours sincerely,

PROSPERO Administrator
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York YO10 5DD
t: +44 (0) 1904 321049
e: CRD-register@york.ac.uk
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PROSPERO is funded by the National Institute for Health Research and produced by CRD, which is an academic department of the University of York.

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APÊNDICE

Search Strategy

PubMed
Result: 1125

1. randomized clinical trial
2. controlled clinical trial
3. randomized
4. randomly
5. **or/1-4**
6. exercise therapy
7. exercise
8. rehabilitation
9. cardiac rehabilitation
10. rehabilitation program
11. physical therapy
12. physical training
13. **or/6-12**
14. cardiorespiratory
15. cardiorespiratory fitness
16. vo2peak
17. vo2max
18. physical fitness
19. exercise tolerance
20. aerobic capacity
21. exercise capacity
22. oxygen consumption
23. fitness
24. **or/14-23**
25. mobile health]
26. mobile application
27. mobile app
28. mobile device
29. mobile phone
30. smartphone
31. smartphone app
32. cell phone
33. mhealth
34. m-health
35. telehealth
36. technology

37. tablet
38. iPad
39. app
40. **or/25-39**
41. **5 and 13 and 24 and 40**

EMBASE
Result: 1024

42. randomized clinical trial
43. controlled clinical trial
44. randomized
45. randomly
46. **or/1-4**
47. exercise therapy
48. exercise
49. rehabilitation
50. cardiac rehabilitation
51. rehabilitation program
52. physical therapy
53. physical training
54. **or/6-12**
55. cardiorespiratory
56. cardiorespiratory fitness
57. vo2peak
58. vo2max
59. physical fitness
60. exercise tolerance
61. aerobic capacity
62. exercise capacity
63. oxygen consumption
64. fitness
65. **or/14-23**
66. mobile health]
67. mobile application
68. mobile app
69. mobile device
70. mobile phone
71. smartphone
72. smartphone app
73. cell phone

74. mhealth
75. m-health
76. telehealth
77. technology
78. tablet
79. iPad
80. app
81. **or/25-39**
82. **5 and 13 and 24 and 40**

SPORTDiscus with Full Text (EBSCOhost)
Result: 230

S1. randomized clinical trial OR controlled clinical trial OR randomized OR randomly
S2. exercise therapy OR exercise OR rehabilitation OR cardiac rehabilitation OR rehabilitation program OR physical therapy OR physical training
S3. cardiorespiratory OR cardiorespiratory fitness OR vo2peak OR vo2max OR physical fitness OR exercise tolerance OR aerobic capacity OR exercise capacity OR oxygen consumption OR fitness
S4. mobile health OR mobile application OR mobile app OR mobile device OR mobile phone OR smartphone OR smartphone app OR cell phone OR mhealth OR m-health OR telehealth OR technology
S5. tablet OR iPad OR app
S6. S4 OR S5
S7. S1 AND S2 AND S3 AND S6

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