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Research Needs on Physical Activity and Chronic Obstructive Pulmonary Disease: Bridging the Gap between Knowledge and Behaviour

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ABSTRACT

Maintaining a sufficient amount of physical activity in patients with chronic obstructive pulmonary disease is critical for their prognosis and quality of life. Yet no intervention has been identified that can modify the physical activity behaviour of these patients. The present narrative review discusses, by means of examples, some research habits and paradigms that need to be adapted in order to bridge the gap between knowing that physical activity is good and changing the physical activity behaviour.

First, because effective behavioural interventions are not possible if the causes of the behaviours are unknown, the research base about determinants of physical activity in chronic obstructive pulmonary disease should boost and widen its scope from individual (biological and psychological) to societal, environmental, and policy determinants. Second, research questions should be framed in a direct, actionable manner in order to provide results that are useful for designing interventions and easy to communicate to health professionals, patients, and policy makers. Third, since most existing research on physical activity and chronic obstructive pulmonary disease suffers from serious methodological flaws, a higher concern about epidemiological and statistical methods is essential to provide valid (and consequently, useful) results. Finally, the single-, multi-, or interdisciplinary nature of research needs to be acknowledged and analyzed on a project basis in order to use the best integrative solution that provides top quality, helpful data.

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To conclude, this review proposes an integrated research model for the promotion of physical activity in chronic obstructive pulmonary disease patients. It underlines the need for not only (more) experimental research, but also valid information from research on determinants, levels, and effects of physical activity in chronic obstructive pulmonary disease. Additional efforts are required in all areas to define applicable research questions, improve methodology, and finding the precise level of discipline integration. New approaches, like causal inference methods embedded in a multilevel framework, offer complementary guidance. **(BRN Rev. 2015;1:92-104)**

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INTRODUCTION

Physical inactivity is a major contributor to mortality and disability worldwide, and the benefits of being physically active go beyond the absence of disease, contributing to a better quality of life, improved sleep, reduced stress, sense of purpose and value, and social connectedness[1]. However, one third of the world's population is physically inactive[2]. Consequently, the design and evaluation of strategies to promote physical activity for whole populations and at-risk groups have increased during the past decades, leading to acceptable increases in physical activity among people of various ages and from different social groups, countries, and communities[3].

In subjects with chronic obstructive pulmonary disease (COPD), a higher amount of regular physical activity has been consistently related to a reduced risk of exacerbations and mortality[4]. In fact, physical activity has been shown to be the most important independent predictor of all-cause mortality in this population[5]. In addition, research has repeatedly shown that COPD patients spend less time in physical activity and practice activity at a lower intensity than their healthy, age-matched counterparts[6]. The reduction in physical activity is already present early in the disease[7,8]. For these reasons, increasing physical activity levels of COPD patients is a priority reflected by its recommendation in the most internationally renowned COPD guidelines[9,10].

The existing interventions on physical activity[3], designed for the general population or other subgroups, cannot be applied to subjects with the pathophysiological characteristics of COPD[10]. Hence, research specifically focused on designing and evaluating physical activity interventions for COPD patients is required. However, and despite a recent exponential increase of research in this field, no intervention has yet been identified that could modify the physical activity behaviour in COPD patients[4].

The present narrative review proposes that the identification of such interventions will not be achieved only with more research on physical activity interventions. The following four

sections discuss, by means of examples, some research habits and paradigms that need to be changed and adapted to bridge the gap between knowing that physical activity is good for COPD and changing the physical activity behaviour of patients. The last section presents novel approaches that can complement traditional research in order to build interventions that effectively result in a change in behaviour.

THE ROLE OF RESEARCH ON DETERMINANTS OF PHYSICAL ACTIVITY

Effective behavioural interventions are not possible if the causes of the behaviours are unknown[11]. It could be speculated that interventions to change physical activity behaviour in COPD patients have not been effective so far because of problems in the understanding of the determinants of such behaviour. Firstly, the number of studies on determinants of physical activity in COPD is still limited and fewer than the number of studies about interventions to modify physical activity in COPD, as identified by a recent systematic review of the literature published in 2013[4]. In the last couple of years, the number of studies about interventions has exponentially increased, while the amount of research about determinants has remained fairly stable.

Secondly, the evidence from research about determinants of physical activity in patients with COPD is unclear. Although physical activity has been consistently related to lung hyperinflation, gas exchange, exercise capacity, dyspnoea, systemic inflammation, previous exacerbations, quality of life, and self-efficacy, there are methodological limitations that challenge the interpretation of these factors as determinants of physical activity (Fig. 1)[4]. Most studies have used cross-sectional designs, which identify correlates of physical activity but limit the interpretation in terms of causality; only longitudinal or experimental studies could identify factors that have causal associations with physical activity and so describe them as determinants. Another difficulty is that most studies did not adjust observed associations for potential confounders, so the true causal relationship could exist between these confounders and physical activity, instead of the factors under study. Apart from the factors mentioned above, the role of certain clinical features typical of COPD, such as forced spirometric parameters, low body mass index, or comorbidities, as well as the role of sociodemographic, lifestyle, and environmental factors as potential determinants of physical activity in COPD patients, is inconsistent across studies (Fig. 1)[4]. This may be due to a real lack of causal effect or to the before-mentioned methodological limitations that are generally present in this research area.

A third problem in the study of the determinants of physical activity in COPD patients is that it has been limited to individual factors, mostly in the biological arena. The traditional discourse states that abnormalities in pulmonary function and gas exchange (leading to higher ventilatory requirements during exercise) combined with skeletal muscle dysfunction contribute to the perception of increased exertional dyspnoea and leg fatigue, which lead patients to reduce their daily activities and result in an inactive lifestyle. However, this model is incomplete in comparison with the commonly accepted ecological model that guides most research about determinants of physical

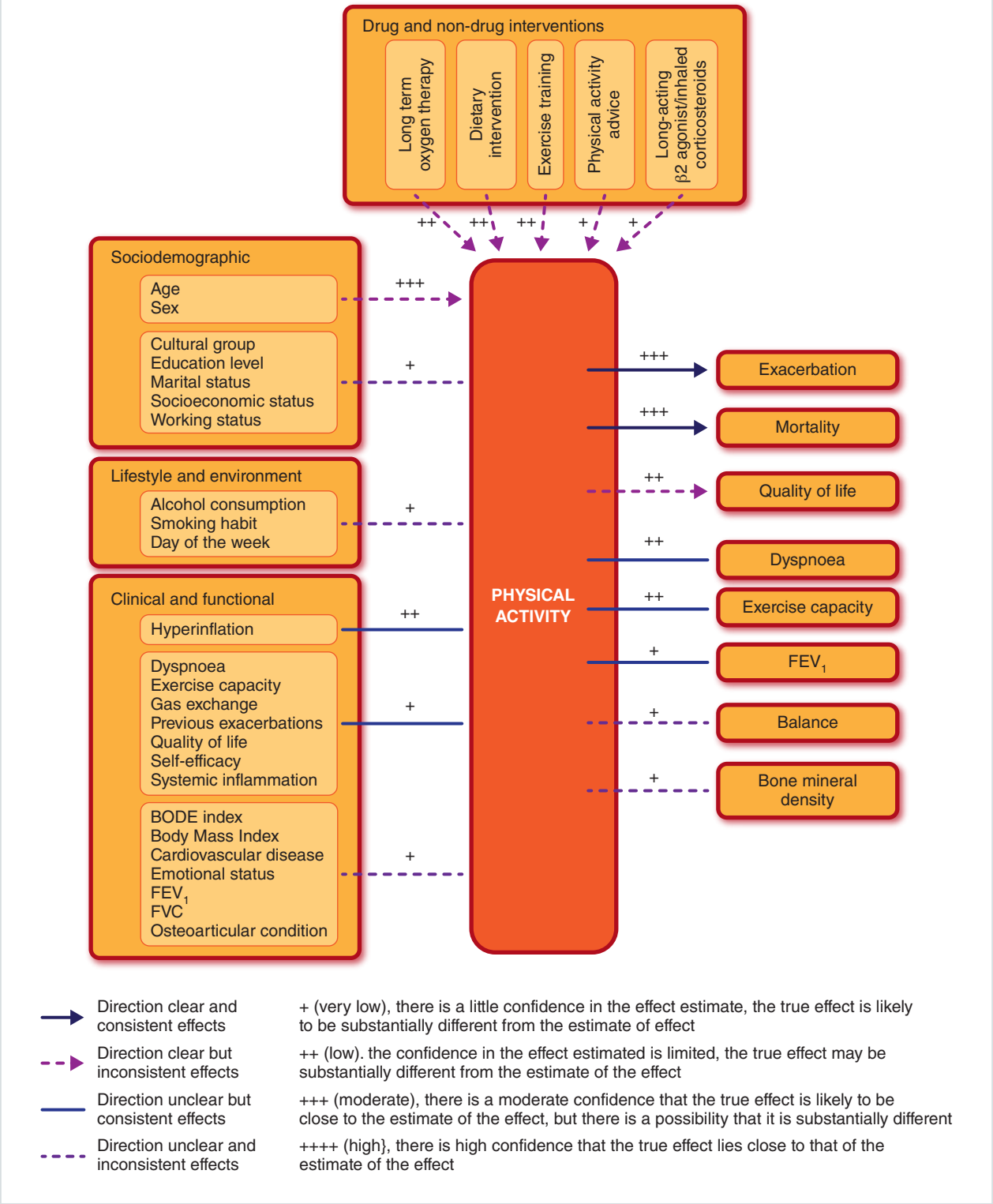

Figure 1. Conceptual model of physical activity in patients with COPD *(reproduced with permission from Gimeno-Santos et al.[14])*. FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity.

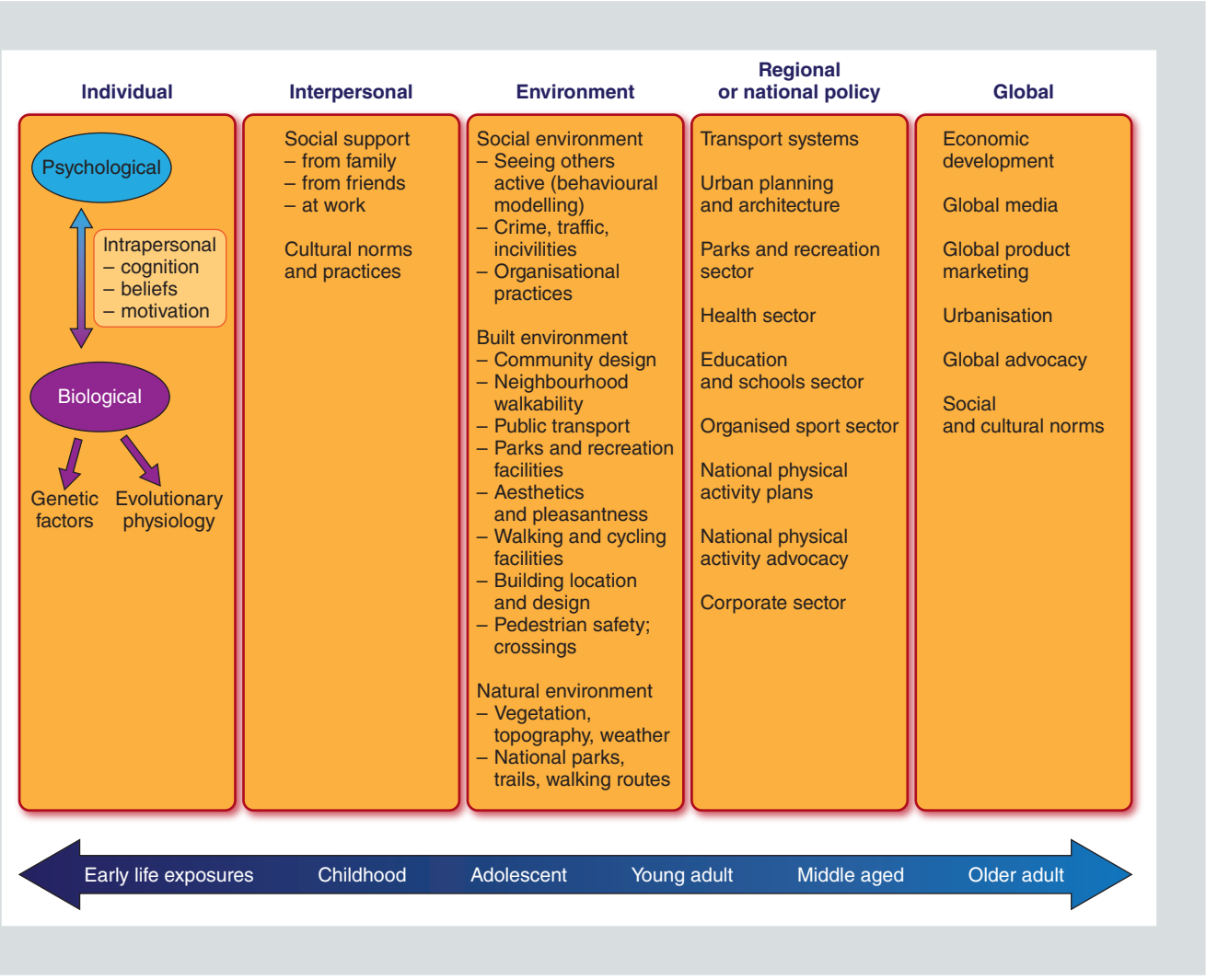

Figure 2. Ecological model of the determinants of physical activity *(reproduced with permission from Bauman et al.[11]).*

activity (Fig. 2)[11]. The ecological model explains physical activity as a result of the effects of individual (psychological and biological), social, environmental, policy, and global factors and their inter-relations, both in the general population and in subjects with chronic diseases.

In summary, understanding why COPD patients are physically active or inactive is needed for evidence-based planning of interventions. The research base about determinants needs to boost, improve causal inference, and adopt an ecologically broader vision.

THE NEED FOR APPLICABILITY OF RESEARCH QUESTIONS

Initial steps in designing health interventions are (i) obtaining knowledge of the target population, (ii) defining in detail the primary goal, and (iii) pre-testing the intervention[12]. This section will argue, by means of examples, that these steps cannot be satisfied in the process of designing interventions to promote physical activity in COPD because research questions usually provide non-applicable answers.

The first step (i.e., obtaining knowledge of the target population) should be guided by facts about the prevalence of the behaviour that is putting COPD patients at risk. However, research has not typically informed whether these patients practice sufficient physical activity or not, because research questions (e.g., what are the physical activity levels of COPD patients) have not been framed according to expected answers (e.g., COPD patients do, or do not, adhere to physical activity recommendations). Adults are considered sufficiently active when they accumulate 30 consecutive minutes of at least moderate intensity physical activity on ≥ 5 days every week[13]; for the elderly and subjects with chronic diseases, the recommendations allow accumulating these 30 minutes in bouts of at least 10 minutes[14]. Instead of answering whether these criteria are met, results from most existing studies quantify the time spent along the day in non-consecutive minutes of moderate activity, the proportion of daily time spent in locomotion activities, or the ratio of the total daily energy expenditure to the whole-night sleeping energy expenditure. Only a recent paper[15] specifically addressed the adherence of COPD patients to the physical activity guidelines for older adults. Results showed that about 25% of the COPD patients satisfied the recommendation of engaging in ≥ 30 consecutive minutes of moderate physical activity five or more days per week, and the proportion increased to almost 60% when the duration of ≥ 30 min per day was achieved through the accumulation of bouts of ≥ 10 minutes duration. This analytical approach, matched with recommendations, directly informs medical and policy actions and should be pursued as it has been successfully used to develop recommendations for the primary prevention, treatment, and control of other chronic conditions, like arterial hypertension or obesity[16,17].

The second step requires a clear definition of the goal of the intervention that one hopes will bring a change in behaviour. As examples, interventions to change physical activity may aim for patients to start a new activity, change their working habits, or engage in certain community events. The research in COPD is very consistent, stating that physical activity reduces exacerbations and mortality risks. However, the common way of expressing results (e.g., COPD patients in the highest quintile of units of movement have 50% lower risk of all-cause mortality than those in the lowest quintile) does not allow defining precise goals for interventions that would result in health benefits. This situation is partly attributable to the fact that physical activity in COPD is still a young research area, but it brings as a consequence that interventions so far have been designed and tested in the absence of knowledge on the variables (and levels) they were supposed to change. If research on the effects of physical activity in COPD is to contribute to the design of interventions, some decisions should be considered at an early phase of the study plan. First, the selection of physical activity variables could prioritize those that can be easily interpreted and/or match the physical activity recommendations (e.g., number of daily steps or consecutive minutes in moderate-to-vigorous physical activity). Second, categories of physical activity could go with clinically relevant or guideline-oriented cut-offs, so the observed effects could help in quantifying the potential effects of hypothetical interventions. Third, and because it is highly unlikely to force an increase in physical activity up to the highest quintile

(whatever it is) for patients in the lowest quintile, a study of the effects of different physical activity levels should be complemented by a study of the effects of changing the physical activity levels. The later is still scarce in COPD patients, but some results from longitudinal observational studies support that the physical activity behaviour may change over time (for good or bad) and that this change has health effects; a decline in physical activity levels was associated with an increased mortality risk in a Danish population-based cohort[18], while an increase in physical activity was related to a lower rate of exacerbations requiring hospitalization in a Spanish clinic-based cohort[19].

Finally, the third step, pre-testing the intervention, requires that it is acceptable and understood by the target population[11]. However, interventions have been designed, so far, with little attention to what physical activity means to COPD patients. Research on the determinants, levels, effects, and interventions has been using Caspersen's definition of physical activity (i.e., "any bodily movement produced by skeletal muscles resulting in energy expenditure")[20]. This definition has value in that it reflects a crucial aspect of physical activity in terms of maintenance of health, but it does not necessarily capture what COPD patients mean when their most frequent complaint is "not being able to complete the activities they like to do"[21]. Recently, as part of the Innovative Medicine Initiative's PROactive project, a series of consecutive qualitative studies identified that patients' experience of physical activity is reported using diverse themes such as "amount of" (what activities they do), "symptoms during" (how do they feel when doing these activities), or "need for adaptations" (how they perform these activities)[22]. Subsequent PROactive quantitative studies supported that the concept of physical activity in COPD patients is not one-dimensional, but has two domains: amount of and difficulty with physical activity (Fig. 3)[23]. Because the improvement in physical activity can be seen as a patient-centred therapy, behavioural interventions should focus on physical activity as experienced by patients; therefore, they should target the levels of both "amount of" and "difficulty with" physical activity. Interestingly, future intervention studies should note that the assessment of both domains requires a combination of questionnaires and activity monitors (Fig. 3). Whether the new generation of wearable devices will help to measure activity –or even change behaviour– in a manner more understandable to patients is to be explored.

Overall, research on interventions to promote physical activity can be fed by the research on levels (amount and difficulty) and/or effects of physical activity if the research questions better match the research answers required to design and evaluate interventions. The emphasis on applicable research questions will also help to communicate research results to health professionals, patients, and policy makers. Behavioural research has a crucial role in this process.

APPROPRIATE METHODOLOGY – A RESEARCH MUST

The section on determinants of physical activity in COPD patients has already highlighted a number of methodological limitations that preclude valid interpretations of results. Unfortunately, research on interventions to modify

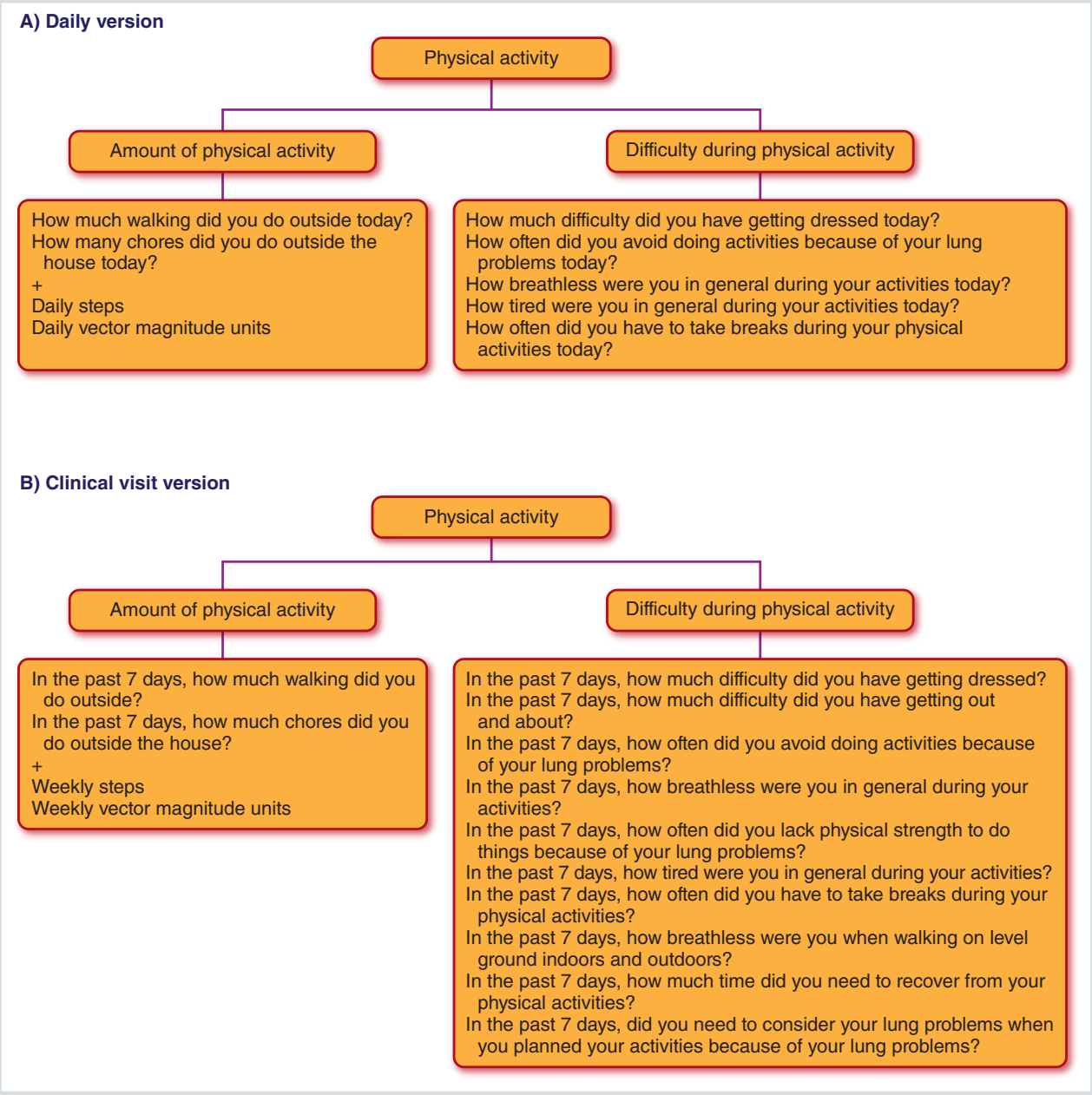

Figure 3. Conceptual framework of physical activity in COPD patients. Domains and items of a) the daily version of PROactive Physical Activity in COPD (D-PPAC) and b) the clinical visit version of PROactive Physical Activity in COPD (C-PPAC) instruments *(reproduced with permission from Gimeno-Santos et al.[23])*.

physical activity in COPD patients also suffers from serious methodological problems. The systematic review mentioned earlier[4] identified 33 studies, most of them clinical trials, testing the effectiveness of pharmacological treatment, long-term oxygen therapy, dietary interventions and, mostly, exercise training programs on the physical activity of COPD

patients (Fig. 1). The main findings of the review are that (i) none of the interventions shows consistent results across studies, and (ii) the quality of the evidence is poor-to-very poor due to methodological flaws. Although most studies were clinical trials, many of them did not include a control group or included a control group without randomized allocation. As a consequence, results cannot be attributed to the intervention. In the remaining studies, of observational design, the common lack of control for confounders prevents assigning effects to the interventions of interest. Finally, many studies included very small sample sizes, so random error cannot be discounted.

Without denying the need for prior pilot studies to test the effectiveness of interventions, it could be questioned whether some manuscripts are sent for publication as a result of competing interests (researchers' reputation, pressure to publish, pressure to get funding, financial conflict of interest, etc.)[24]. It has been proposed that scientific integrity is broader than just following research ethics rules and regulations[25]; it implies that researchers should be willing to take responsibility for their actions, including the appropriateness of methods chosen to answer their research questions. Consequently, the implicit public trust in the veracity of research, which is often publically funded, requires that measures are taken to safeguard scientific quality. Training, mentoring, and behaviour in research methodology should help research not constrained by competing interests, but devoted to its ultimate goal, the "desire to know the truth"[26], which in our specific case is how to effectively maintain or increase a sufficient physical activity level in COPD patients.

In view of existing research on interventions to increase physical activity in COPD patients, there is an obvious need for randomized controlled clinical trials to test the effectiveness of new and existing interventions. In addition, special care with epidemiological and statistical methods is vital to not generate confusion.

PURSUING THE PRECISE INTEGRATION OF DISCIPLINES

It is accepted that research about strategies to increase physical activity in COPD patients should involve multiple disciplines. As an example, the current Official American Thoracic Society/European Respiratory Society Statement on Pulmonary Rehabilitation included experts from different biomedical sciences (chest physicians, elderly care physicians, physiotherapists, occupational therapists, nurses, nutritional scientists, exercise physiologists, methodologists, psychologists/behavioural experts, and health economists) in an attempt to recognize the complexity of chronic respiratory diseases and health behavioural change[27]. More recently, since new interventions to increase physical activity in COPD patients have included pedometers[28-31], webs[32,33], or phone call services[34] as components that can facilitate health behaviour change[35], new disciplines such as applied sciences or technology will need to be incorporated. Finally, recent research on determinants of physical activity also points to a broader range of knowledge areas, from genetics or evolutionary biology to transport policy or work legislation, which need to be taken into account for the design, evaluation, and implementation of interventions to change physical activity behaviour[11]. In general, and because the ability to change a

behaviour appears to be a function of societal, psychosocial, and biological variables, the integration of biomedical and social scientists should be standard practice[36].

But the overwhelming evidence that changing the physical activity behaviour in COPD patients crosses boundaries of traditional disciplines is a trick insofar as it forces each researcher to (consciously or not) design and execute his/her research project as single-, multi-, or interdisciplinary. Moving away from terminological discussions and institutional interests, a solution is here proposed, structured in three steps. First, each specific research question needs to find its location as a simple part of a complex system. Secondly, the involvement of one or more disciplines needs to be decided, usually driven by the research question itself. In many cases (e.g. the assessment of exercise capacity in COPD patients) one single discipline will allow answering the research question at the highest level of quality. This type of project need not be disapproved, since it is only on solid disciplines that complex solutions can be built; "disciplines enable humans to address problems in an orderly way; disciplines discipline"[37]. Thirdly, when the nature of the problem requires multiple disciplines, the necessary level of integration has to be determined. In a slight integrative scenario (e.g. a supervised muscle-training program) each member contributes from a different professional perspective, sharing knowledge and comparing results, whilst maintaining a degree of coherence. For problems close to daily life (e.g., the design and validation of urban trails for the training of COPD patients[38]), higher levels of integration may be desirable, crossing methodological, epistemological, and ontological boundaries to jointly frame a problem, agree on a methodological approach, analyse data, and ultimately create new knowledge. Finally, in studies that seek transcendence (e.g., the multinational deployment of a telehealth wellness program for chronic patients[39]), it is necessary to engage with local and regional bodies.

Beyond the involvement of multiple disciplines, the design of interventions to change behaviour requires also non-academic participants, either in a consulting or in a participatory manner. As discussed above, involving patients and their caregivers in the design and implementation process will help both researchers and patients understand each other's perspectives, thus ensuring that the goals and priorities of both parts are met[40]. Ultimately, translating the results of scientific investigations into practical recommendations for healthcare professionals, work sites, community organizations, or health services agencies is critical. Working effectively with all these actors at all steps of research, the efforts devoted to designing effective health-promoting interventions will hopefully translate to evidence-based practices that improve public health[40].

On the whole, the study on how to modify the physical activity behaviour in COPD patients involves multiple disciplines. For each research question, admitting its position in the complex frame, identifying its requirements in terms of which disciplines to involve and how, and putting it into practice accordingly, appears a reasonable way to not get lost in complexity. Furthermore, understanding how each discipline fits with others and where its strengths and limits are will facilitate shared understandings of complex issues.

COMPLEMENTARY APPROACHES: CAUSAL INFERENCE METHODS AND THE EXAMPLE OF TOBACCO CONTROL

This review has shown the paucity and limitations of existing research on interventions to change physical activity in COPD patients. An additional shortcoming for the future is that even well-designed randomized controlled trials may be unethical, unfeasible, or too lengthy for timely decision making. In this case, causal inference methods can help by designing observational analyses in such a way that the results emulate those from hypothetical well-defined interventions. For example, observational data from a population-based cohort could be used to mimic the long-term effects of a hypothetical randomized physical activity experiment by comparing the observed outcomes of individuals who change versus those who do not change their physical activity during the study period. This approach is built into the counterfactual or potential outcomes framework generalized to time-varying exposures[41-44]. This strategy, still scarce in respiratory research[45], has been successfully used to estimate the population impact of lifestyle interventions on the risk of other chronic diseases like coronary heart disease[46,47].

The combination of the abovementioned potential outcomes framework with a multilevel framework, such as suggested in the "determinants" and "integration" sections, has been proven to be a useful approach to accommodate complex causal processes into interventions or policies[48].

A useful case study is the multicomponent strategy used in New York City to address the tobacco epidemic. Cigarette smoking and smoking-related diseases markedly fell after an aggressive strategy involving interventions at the individual, interpersonal, environmental, and regional policy levels[49-51]. The approach used was built on evidence from local surveys[52] and based on the framework that, apart from individual behaviour, the tobacco epidemic is driven by upstream factors (e.g., a powerful global industry), societal factors (e.g., peers and family habits, cultural acceptance of smoking), and genetic bases (e.g., susceptibility to nicotine addiction)[53].

CONCLUSIONS

Maintaining sufficient levels of physical activity in COPD patients is critical for their prognosis and quality of life. Research has the opportunity to help in this endeavour by designing and testing interventions targeted at these patients. However and uniquely, the design and testing of interventions will not help to maintain or increase physical activity; it needs to be fed with valid information from research on determinants, levels, and effects of (amount of and difficulty with) physical activity in COPD (Fig. 4). Specifically, the knowledge on determinants of physical activity should have a prominent role in future years, and it should widen its scope from individual (biological and psychological) to societal, environmental, and policy determinants. For research to be not only informative but also useful, research questions (on determinants, levels, or effects) should be framed in a direct, actionable manner. Moreover, and because existing data still suffer from methodological

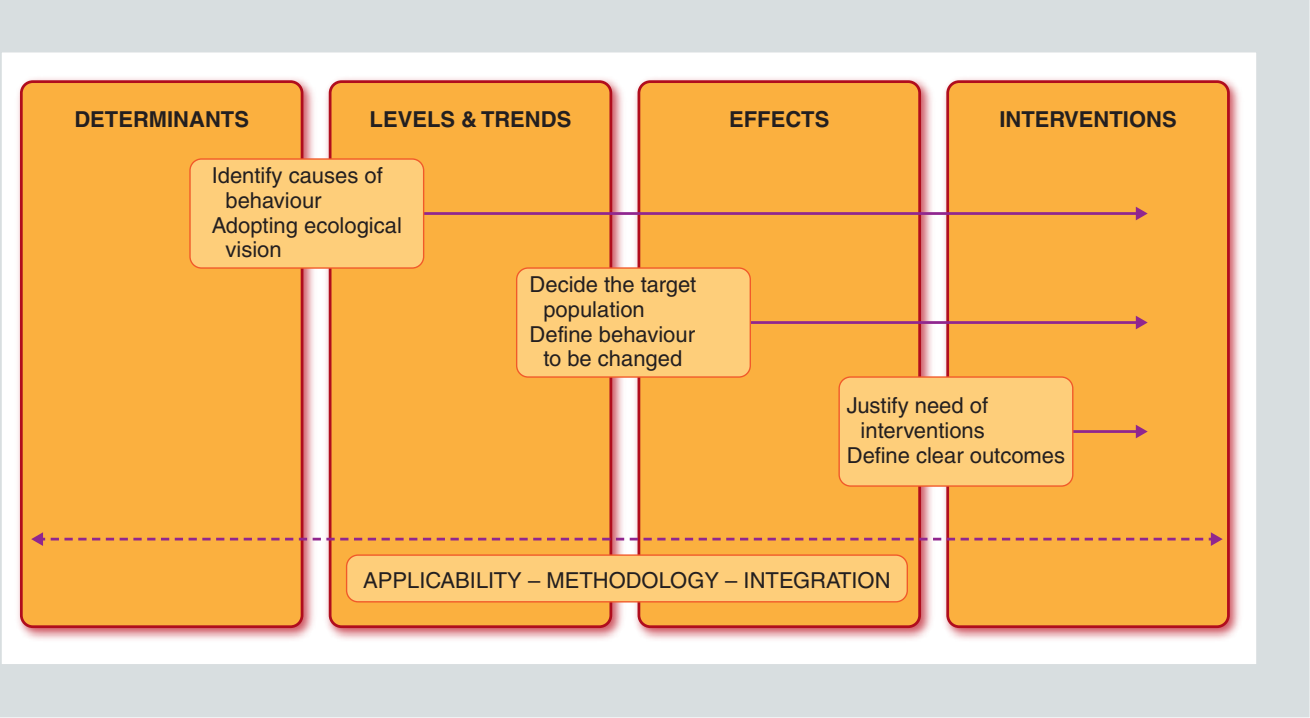

Figure 4. Integrated research model for the promotion of physical activity in chronic obstructive pulmonary disease patients.

defects that limit their validity and trustworthiness, a higher concern about epidemiological and statistical methods is essential. Finally, the multidisciplinary nature of our research topic needs to be acknowledged and analysed on a project basis in order to use the best integrative solution that provides top quality, helpful data. New approaches like causal inference methods embedded in a multilevel framework offer complementary guidance for the design, evaluation, and implementation of evidence-based interventions in physical activity for COPD patients.

CONFLICT OF INTEREST

Author declares no relevant conflict of interest.

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