



Proposal to integrate information on treatment burden into clinical practice guidelines

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3 **Proposal to integrate information on treatment burden into clinical practice guidelines**
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3 *Clinical practice guidelines should explicitly state the treatment burden that patients face*
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5 *when enacting a guideline recommendation.*
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8 9 **Introduction**

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11 There is increasing recognition that implementation of medical treatment regimens, whether
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13 pharmacological or non-pharmacological, demands a lot of time and effort. This can result in
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15 substantial treatment burden to patients with chronic conditions. While treatment burden in
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17 particular affects patients with multi-morbidity, a single chronic condition, such as cystic
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19 fibrosis or insulin-dependent diabetes mellitus, can also result in a significant treatment
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21 workload for patients.
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27 Guideline recommendations are traditionally made from a perspective that places the highest
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29 value on achieving a certain clinical outcome (such as reducing shortness of breath or
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31 increasing survival). More recent guidelines may include value and preferences statements,
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33 and address acceptability and feasibility of the recommended action. Here, we propose that
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35 information on treatment burden, especially the estimated time and effort that patients need to
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37 spend to enact a guideline recommendation, should be included in guideline
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39 recommendations. This would support patients in making informed decisions about
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41 treatments in line with their values and capacity.
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46 **The construct of burden of treatment**

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48 The burden of disease is a well-known epidemiological concept. However; the burden of
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50 treatment is a less known and fairly recently coined term. The cumulative treatment workload
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52 for patients with chronic conditions when enacting all disease-specific guideline
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54 recommendations can be overwhelming.¹ In order to cope with the demands of complex self-
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3 care, patients rely on a range of personal, social and health care resources.² When patients
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5 have a severe disease or multiple chronic conditions, disease treatment can occupy a big part
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7 of their day and limit the amount of time they can spend on other activities such as work,
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9 studying, leisure, childcare, and being with friends and family. A study found that in order to
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11 comply with all disease-specific guidelines, patients with three chronic conditions (any
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13 combination of three conditions out of: chronic obstructive pulmonary disease (COPD),
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15 coronary heart disease, diabetes, osteoarthritis, hypertension and depression) would take a
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17 minimum of 6 to 13 medications per day, visit a health caregiver 1.2 to 5.9 times per month
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19 and spend a mean (standard deviation, SD) of 49.6 (27.3) to 71.0 (34.5) hours/month in
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21 health-related activities.¹ In patients with all six chronic conditions, the workload rose to 18
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23 medications per day, 6.6 health care visits per month and 80.7 (35.8) hours/month in health-
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25 related activities.¹
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31 A single chronic condition can also be associated with considerable treatment burden. A
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33 study of 204 adults with cystic fibrosis found that the median number of daily therapies
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35 reported was 7 (interquartile range 5-9) and the mean reported time spent on treatment
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37 activities was 108 minutes per day (SD 58 min).³
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42 The work that patients do to manage their health often remains invisible to health
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44 professionals, who only see the results of patients' work (e.g. attended exercise program,
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46 achieved weight loss, glucose measurement log), but not the work itself.⁴ This will often lead
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48 to underappreciation of patients' treatment-related work. Components of the work that
49
50 patients must do to care for their health include: learning about their conditions and care,
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52 filling prescriptions, taking medications, attending medical appointments, monitoring their
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54 health status (e.g. regular measuring of lung function using a peak flow meter in patients with
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3 asthma, glucose monitoring in patients with diabetes), making lifestyle/ behavioural changes
4 (exercise, diet, smoking cessation) and managing medical equipment/ devices (e.g. regularly
5 cleaning a nebulizer for application of inhaled treatments in asthma/ COPD).⁵
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10 11 **Consequences of the burden of treatment: Patient self-guided prioritization of** 12 **treatments** 13

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15 When patients do not take prescribed medications or do not perform the prescribed daily
16 exercises, this may be interpreted as patients being irresponsible, neglectful, lacking
17 motivation and/ or insight into the importance of these treatments. Many patients who do not
18 adhere to prescribed treatments, however, say that they know that they should do differently
19 but that they intentionally do not adhere to treatments because they lack the information and
20 support to do so.⁶ Patients will also reject medical advice if the perceived benefit of following
21 the advice is considered insufficient in relation to the patient's investment of time, energy,
22 and cost to enact the treatment advice.⁷ These 'return-on-investment' assessments may be
23 done consciously or intuitively, particularly when patients are overburdened by their
24 treatment workload. In this case, they may resort to self-guided treatment prioritization
25 without discussing these choices with a health professional.
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41 The potential pitfall of this intuitive assessment and prioritization by patients is that
42 treatments that have an immediate and palpable effect are likely to be favoured by patients
43 (e.g. short acting beta agonists in patients with asthma used as 'rescue' medication),⁸
44 whereas preventive treatments or treatments that do not lead to rapid symptom relief, but may
45 be more effective in the long term (e.g. inhaled corticosteroids in asthma), are "dropped" by
46 patients.^{8,9} It is therefore important to give patients an opportunity to be guided through the
47 process of treatment prioritization by a health professional.
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5 Another reason why it is important that patients and clinicians go through the process of
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7 treatment prioritization together, based on the patients' values and preferences, is that
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9 patients' self-termination of treatments, interpreted as non-adherence, may result in restricted
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11 access to certain interventions in some health systems. Patients with severe asthma, for
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13 example, could be denied treatment with complex biological therapies (to avoid inappropriate
14
15 escalation of therapy), if they have not adhered to high dose inhaled and oral corticosteroids,
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17 which have well known and potentially serious adverse effects that some patients find
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19 difficult to tolerate¹⁰⁻¹².

20 21 22 23 24 **Strategies to reduce treatment burden**

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26 The need for strategies in situations where patients' capacity to implement all recommended
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28 treatments is overstretched, has been recognised, but there are currently no widely accepted
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30 solutions to address the problem. One approach that has been promoted is the concept of
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32 "minimally disruptive medicine".¹³ This approach is based on the concept of balance between
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34 a patient's capacity (to enact treatment recommendations) and workload (associated with
35
36 medical treatments), also referred to as the cumulative complexity model.¹⁴

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41 Rather than adding to patients' problems by increasing treatment burden through intensifying
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43 treatment, adding educational interventions etc., this approach aims to prioritize treatments
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45 from the patient perspective in order to achieve the goals that align with patients' values and
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47 preferences.
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51 52 **How do guidelines handle the burden of treatment?**

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3 Patients' work to enact specific treatment recommendations is usually ignored in older
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5 guidelines, which have typically emphasized the evidence for the effectiveness of an
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7 intervention (or lack thereof). Anecdotally, health professionals often seem to adopt this
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9 perspective by believing that patients should take prescribed treatments that have been shown
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11 to be 'effective' independently of how much resources (time, energy and money) patients
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13 need to invest and how likely they are to get the desired benefit (i.e. independently of whether
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15 the number needed to treat in order for one patient to benefit is 5 or 100).
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20 Modern guideline frameworks such as GRADE (Grading of Recommendations Assessment,
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22 Development, and Evaluation); which is the current gold standard and most adopted
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24 guideline approach, do attempt to capture the patient perspective. The Evidence to Decision
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26 (EtD) framework developed by the GRADE Working Group acknowledges the importance of
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28 patients' values and preferences.¹⁵ For example, the 2017 guidelines on prevention of COPD
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30 exacerbations published by the European Respiratory Society and the American Thoracic
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32 Society added a paragraph on "Values and preferences" to every treatment
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34 recommendation.¹⁶ An illustrative example: the conditional recommendation to use oral
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36 mucolytic agents to prevent future COPD exacerbations, is accompanied by the following
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38 "values and preferences" statement: "This recommendation places a high value on avoiding
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40 hospitalisations, and a lower value on the cost and burden of taking daily medication."
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46 The EtD also incorporates some parts of the construct of burden of treatment in the domains
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48 of acceptability and feasibility.¹⁵ Following the EtD, a strong recommendation for an
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50 intervention is contingent on this intervention being feasible to implement (by patients and
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52 clinicians) and acceptable (by patients and clinicians). Yet, the burden of treatment as a
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54 discrete construct is not a part of the EtD.
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Making treatment burden explicit in guidelines

If future guidelines are to help clinicians and patients to make treatment decisions taking into account patients' values and preferences, they should explicitly state the treatment burden associated with enacting different guideline recommendations. One important aspect of this burden is the time that patients on average spend on implementing a treatment recommendation. Besides the actual treatment time, this also includes 'hidden' time investments, e.g. when administering inhalation therapy twice daily via a spacer (holding chamber), the patient will spend additional time cleaning the spacer used to administer the inhalation therapy, obtaining prescriptions, and going to the pharmacy to fill prescriptions.

Time spent by patients on health-related activities is of course only one aspect of treatment burden. Treatment work also includes aspects that cannot easily be quantified such as patients' emotional investment, and patients having to endure different levels of discomfort when enacting treatment recommendations (e.g. when experiencing breathlessness during exercise). Engaging in treatments, such as physiotherapy for airway clearance in cystic fibrosis, may leave patients lethargic, and patient may have limited capacity to engage in leisure activities for the remainder of the day. Patients then not only have to decide whether to engage in the treatment prescribed, and if so, for how long, but also the optimal time to do so, in order to reduce the residual effects of the treatment on other daily activities.

An illustrative example of how information on treatment burden could be included in guidelines is given in Box 1. Making treatment burden explicit in this way, would help patients to make informed decisions based on their time 'investment' and the 'return' that can

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3 be expected (quantification of the intervention's benefit, which can be obtained from
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5 evidence summaries).
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9 Clinical practice guidelines should also explicitly recommend that clinicians discuss values
10 and preferences with patients, especially for treatments associated with a high workload. This
11 would help clinicians to understand how patients prioritise different outcomes and treatment
12 burden and would help patients to understand what components of their treatment are the
13 'essentials' even on a bad day, so that they can prioritise treatments appropriately.
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22 Currently, the major barrier to including information on treatment burden in clinical practice
23 guidelines is the lack of reliable information, as these data are not usually collected in
24 randomized controlled trials. We suggest that future trials include information on the time
25 that patients spent on treatments, the timing of treatment (e.g. morning, evening, during
26 working hours) and the ease/ challenge of fitting the treatment into daily routine. 'Hidden'
27 time investments, e.g. time spent on filling prescriptions', will have to be gathered from real
28 life studies. Collecting information on other aspects of treatment burden, e.g. cost and
29 emotional investment should also be considered.
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42 **Conclusions**

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44 Patients with chronic conditions spend significant time and resources on enacting guideline
45 recommended treatments. However, information on treatment burden, in particular the time
46 required for treatment implementation, is not included in current clinical practice guidelines.
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48 Including information on treatment burden (together with quantification of the potential
49 benefit of an intervention), would help patients to make informed decisions about treatments
50 in line with their values and preferences. In order to be able to include this information in
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3 guidelines, information on time spent on treatments should be routinely collected in trials and
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5 in real-life studies.
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9 **Contributors and sources**

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11 CCD is a consultant respiratory physician at Liverpool Hospital, Australia, and currently a
12
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14
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46 publications including more than 50 guidelines. CCD and MHM conceived the initial idea.
47
48
49 CCD drafted the manuscript. All authors contributed to critical discussions of the ideas,
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51 revised the manuscript, and approved the final submission.
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Ethical approval

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Data sharing

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Box 1: Example of including treatment burden in guideline recommendations**The current approach:**

The 2017 guidelines on prevention of COPD exacerbations make a conditional recommendation for initiation of pulmonary rehabilitation within 3 weeks after hospital discharge.¹⁶ The current “values and preferences” sections states: “This recommendation places a high value on improving clinical outcomes and a lower value on the burden and cost of pulmonary rehabilitation.”

Proposed approach:

If the treatment burden was made explicit, the guideline could include a statement like this: “A typical effective pulmonary rehabilitation program lasts 8 to 12 weeks with 2 to 3 sessions per week, lasting one 1 hour each. Many pulmonary rehabilitation programs are fully or partially conducted in a hospital setting for outpatients, therefore travel time to exercise classes may be added to the treatment burden. While exercise is beneficial, more strenuous exercise is likely associated with (temporary) discomfort due to shortness of breath.”

Key messages box

- Treatment burden, the work that patients need to do for their own health care, is often substantial for patients with chronic conditions.
- Modern guideline frameworks, such as GRADE (Grading of Recommendations Assessment, Development, and Evaluation), attempt to capture the patient's perspective by acknowledging the importance of patient's values and preferences and consider the feasibility and acceptability of the intervention.
- The burden of treatment as a discrete construct is, however, not yet a part of the Evidence to Decision framework.
- Information on treatment burden associated with enacting recommendations in clinical practice guidelines would enable patients to make informed decisions about treatments.