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Why We Don't Need "Unmet Needs"! On the Concepts of Unmet Need and Severity in Health-Care Priority Setting

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Abstract

In health care priority setting different criteria are used to reflect the relevant values that should guide decision-making. During recent years there has been a development of value frameworks implying the use of multiple criteria, a development that has not been accompanied by a structured conceptual and normative analysis of how different criteria relate to each other and to underlying normative considerations. Examples of such criteria are *unmet need* and *severity*. In this article these crucial criteria are conceptually clarified and analyzed in relation to each other. We argue that disease-severity and condition-severity should be distinguished and we find the latter concept better reflects underlying normative values. We further argue that unmet need does not fulfil an independent and relevant role in relation to condition-severity except for in some limited situations when having to distinguish between conditions of equal severity (and where other features also equals each other).

Keywords Priority setting · Rationing · Severity · Unmet need

Introduction

Given the increased discrepancy between available and required resources to meet demographic challenges, medico-technical development and raised expectations, the challenges of priority setting in health-care has been more pressing during the last years. Democratic expectations for decisions in publicly financed health-care

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systems are that they are transparent, legitimate, and that decision-makers are held accountable for decisions. This requires that priority setting decisions are open, systematic and well-founded [11, 35]. Moreover, priority-setting decisions are basically value-decisions, implying the need to balance different and often conflicting moral values and ethical principles of what characterizes an ethically optimal (just, fair etc.) distribution of resources. This has brought to the fore a number of different suggestions and models for how to make priority-setting decisions, both in terms of *formal processes* for how to make priority decisions (e.g. the accountability for reasonableness (A4R) framework [11]) but also suggestions for *substantive* principles to follow [48], or crucial aspects to take into account (and different combinations of these approaches) [20]. However, listing different aspects (whether processual or substantive or both) to consider, raises issues about their logical and normative relationships and rationales—something that hitherto seems to have been largely unexplored. Two such aspects, playing an increasingly important role during the last few years, being part of legislation on both compassionate use of drugs and on orphan drugs, are *severity* and *unmet need*. For example, in the European Union legislation on compassionate use, having an unmet need[1] and a serious condition are requirements to get access to drugs through compassionate use [3, 7]. In a review of orphan drug legislation globally, unmet need and severity are essential components to acquire orphan drug designation, market authorization and exclusivity etc. [18]. However, the relationship between severity of disease (or condition) and unmet need in these, as well as in other, contexts, appears unclear and may muddle the priority setting process—e.g. if there is considerable conceptual overlap (as will be argued in this article) there will be "double counting" in relation to other fields where only severity is taken into account (cf. also the use of these concepts in other contexts [15, 19, 21, 31, 38]). Moreover, it may make practical prioritization more confusing and challenging.

The aim of this article is to explore the conceptual and normative relationships between severity of disease (or condition) and unmet need. It will be argued that there is a considerable conceptual and normative overlap between these concepts and that there are reasons to limit the use of the criteria unmet need, given that *severity of condition* turns out to be a central feature of priority setting. It could be argued, that different priority setting aspects will have different roles in different priority setting context. The focus of this article is priority setting of existing treatments within the health-care sector. An adjacent area of priority setting is research priorities, i.e. to prioritize funding of research within different health-care areas. We will return to this area in the section on innovation at the end of the article.

[1] A partly conceptually overlapping concept to unmet need is lack of alternative treatment or therapy, which, for example, is the parallel to unmet need in FDAs guidelines on compassionate use (what they call expanded access) [50]. In this context they will be treated as on par, even if there obviously are situations when they do not have the same extension, e.g. when there is not treatment whatsoever to consider for a specific need. That is an unmet need, but it would be strange to say that there is a lack of *alternatives*, since there is no treatment to have an alternative to.

Methodology

The analysis in this article draws both on methods for conceptual analysis found in philosophy [5, 6, 37] as well as on the methodology of reflective equilibrium, commonly used in normative analysis [9, 16]. In conceptual analysis, existing definitions of concepts are analysed to see whether they seem to fit with the purpose (normative and others) they are supposed to be used for and if not, amendments or stipulative definitions might be suggested. This is an important part of the wider normative analysis, where different suggestions for moral values and aspects are tested against other values and norms held within the field at hand. This is done in order to see if they can be held consistently at the same time. If not, different suggestions for how values and norms can be altered to arrive at consistency are explored. Here we should normally be more reluctant to change well-established values and norms before changing those that are less established and well-founded.

Disease-Severity and Condition-Severity

Let us start with a preliminary conceptual point about severity, which is central to the following analysis. In the literature we seem to find two general ways in which severity is applied in priority setting situations, here labelled *disease-severity* and *condition-severity* [36, 44]. *Disease-severity* refers to the severity of the underlying disease regardless of existing treatment. If we are considering a new treatment option for patients with Type II Diabetes, it is the severity of Type II Diabetes (untreated) that is the basis for the assessment. With this approach, severity will be assessed as high, since untreated Type II Diabetes is a disease with high impact on quality of life (QoL) and with risk of premature death. *Condition-severity*, on the other hand, refers to the actual impact of the disease on the patient taking relevant treatment options into account. When considering a new treatment for Type II Diabetes we will then look at the actual condition patients with Type II Diabetes are in and how it impacts on their lives. If they generally have access to effective treatment already and the new treatment is an alternative or an add-on to such treatment, the severity of their condition will be rather moderate (unless the new treatment is targeting a special risk group where previous treatment is less effective). Whether we understand severity in terms of disease- or condition severity, is central to how severity will affect priority setting as will be shown in the following analysis.

Following our methodology, we then need to establish the normative rationale of severity in priority setting. The use of severity as a criterion for priority setting is well-established in several health-care contexts [49]. In some countries, it is even part of a legal framework for priority setting, e.g. in Sweden and Norway [43]. The normative rationale for taking severity into account is related to ideas that health-care should be *needs-based*. Recent developments in the conceptualization of need suggest definitions along the following lines:

> Person X having a health-care need means that X can be benefited by a health-care intervention Y to move X from the current level of the health-care value Z to a higher level of Z [22–24].

Ignoring for now exactly how we should demarcate health-care interventions, we are focusing on the Z-dimension. Z denotes the value or values health-care is supposed to promote, e.g. health, health-related QoL, life-length etc. Let us in the following assume that Z is health in the health-care system we are considering.

The concept of *health-care need* is used in normative principles of need with the implication that the larger the need, the greater the claim on health-care resources (ceteris paribus). These normative principles in turn are related to general theories of distributive justice like egalitarianism [25, 45], sufficientarianism [8, 17, 29], and prioritarianism [30, 42]. The exact understanding of how health-care need should impact priority setting depend on which theory, or combinations of more general normative considerations, that lay at the foundation of the principle of need. However, regardless of this, any needs-based priority setting scheme will have to consider the gap between the patient's current level of health and the potential level of health the patient can achieve. Another name for this gap is *severity*. Hence, we would claim that severity has a strong standing as a central criterion supported by different well-established normative background theories within health-care priority setting. In the literature, we find different ways in which severity is assessed in terms of which factors to take into account. Just to give a few examples. *Absolute shortfall* equals severity to the health loss (for example in terms of quality adjusted life-years (QALY)) in relation to some ideal or expected health gain in life [46]. *Proportional shortfall* equals severity to the proportional health loss in relation to potential health gain left in life. *Loss of health during the life course* does not only take into account the loss of prospective health, but also the health loss of a person at the time of diagnosis [4, 36, 46]. We also find more multidimensional frameworks for assessing severity, like the Severity Framework used in the Swedish context which is based on ICF (international classification of functioning, disabilities and health) in combination with life-length effects [44]. To be sure, some of the severity approaches above might be more commonly associated with a specific conceptual understanding, e.g. absolute shortfall seems generally applied in terms of disease-severity, but there is nothing inherent in the concept hindering this from being used in terms of condition-severity. For example, in the recent Norwegian legislation on priority setting, using a version of absolute shortfall, condition-severity is assessed [43]. Based on this, we hypothesize that all of the different frameworks for how to assess severity, can be combined with both disease- and condition-severity.

Unmet Need

With this backdrop, let us move on to a preliminary conceptual clarification of unmet need. The European parliament has proposed the following definition of unmet medical need (or unmet need for short) [7]:

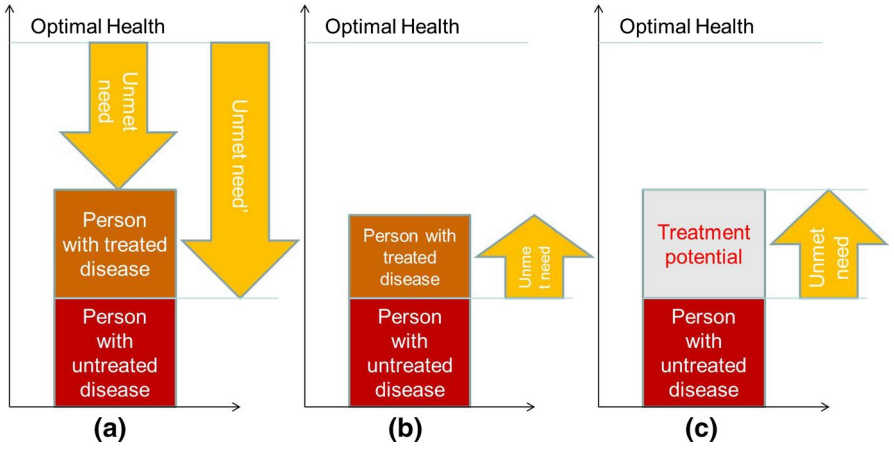

Fig. 1 The dynamic of unmet need

> 'unmet medical needs' means a condition for which there exists no satisfactory method of diagnosis, prevention or treatment…

A first glance at the concept could indicate that "*unmet* need" implies that there exists no treatment whatsoever to meet the need in question. Following the definition, this is not necessarily the case. There can be treatment, which is deemed inadequate for some reason. When talking about inadequate treatment we need to define what is meant with "inadequate." As observed by for example McCabe in the discussion on orphan drugs (where we often find the concept of unmet need), even patients suffering from rare diseases will generally have access to comfort or palliative care that might to some extent handle the patients' symptoms [32]. In a universal coverage system, all patients, whatever condition they are suffering from should at least have access to comfort or palliative care for their conditions.

Rather, unmet needs in this context seem to imply that there exists no treatment that is 'good enough' in affecting the trajectory and/or symptoms of the disease or condition. Even with existing treatment, patients with the condition will die prematurely, have a progressing deterioration of their QoL (broadly understood), or not have their symptoms properly managed. Since there is a gradual scale of how treatment affects a disease, unmet need implies that existing treatment have a rather modest effect on the condition. As the concept is generally used, it seems strange to claim that we still have an unmet need if we have not managed to fully cure a condition, especially when existing treatments have a considerable impact on the condition only leaving minor complications. Following this, "unmet need" does seem to be a label associated with conditions or diseases on the higher end of the severity spectrum, as is also indicated in the above referenced policy uses. Lacking an effective cure for seasonal cold does not seem to warrant labelling the cold an unmet need on the above definition (or on the uses of unmet need in priority setting contexts).

Still, even accepting this, there are different potential understandings of what a patient has an unmet need in relation to, i.e., what is the reference for unmet need.

Is it related to optimal health (see Fig. 1a)? If so, patients with treated and untreated diseases might both have unmet needs (and so also the patient with seasonal cold) even if of different magnitude. Is it related to comparable patients with treated disease (see Fig. 1b)? In that case we have the problem of identifying or demarcate which is the comparator group. Moreover, we face problems with the definition of"unmet needs" above, in terms of what counts as"satisfactory… treatment." Or, is a need unmet in relation to the treatment potential of a specific disease? In this case we have the problem of identifying what the treatment potential is for the disease (see Fig. 1c). Is it the treatment potential in relation to existing treatment or rather in what ideally would be effective treatment of the disease—something which is relevant if unmet need should also play a role in prioritizing research funding? In this dynamic, we find it reasonable to understand a need as unmet in relation to an optimal level of health (Fig. 1a). This implies that unmet need is more important to take into account, the greater the unmet need is, which emphasises even more its covariation with severity. Hence, even a seasonal cold is an unmet need but of such a small magnitude that it should not have major impact on priority setting. This also implies that unmet need is a matter of degrees and not a dichotomous concept.

Following this co-variation between severity and unmet need—are they still both warranted concepts to catch important aspect in a priority setting situation? Before delving into the more exact conceptual relationship between severity (on some understanding) and unmet need, let us say something about the normative rationale for taking unmet need into account.

One reason for applying the concept of unmet need could be to avoid abandoning the patient. However, since we have conceptualized unmet need in a way that implies that patients with highly unmet needs will (should) have access to comfort care or palliative care—abandonment cannot be the main reason. Rather, than to avoid abandonment, the reason that unmet need should be met is that the patient is suffering, or in bad health, or is at the risk of dying etc.—i.e., that the patient is in a less than optimal situation from the perspective and values of healthcare, e.g. health. Expressed in terms of the needs-definition above—the person has a level of health that can be improved in relation to some optimal level of health—which is then a (prima facie) reason for us to act and try to meet the unmet need. Another, but (to some extent) related, rationale is that the fact that a person has an unmet need is unfair in relation to other persons who have their needs met, and unfair situations should be avoided (at least all things being equal and to the extent we can). Given this, we seem to have similar reasons for tending to an unmet need as we have for tending to severity.

Conceptual and Normative Relationships Between Disease-Severity, Condition-Severity, and Unmet Need

These preliminaries make us ready to focus on the central aim of the article, the conceptual and normative relationships between disease-severity, condition-severity, and unmet need. We will do so by exploring how different uses of disease-severity,

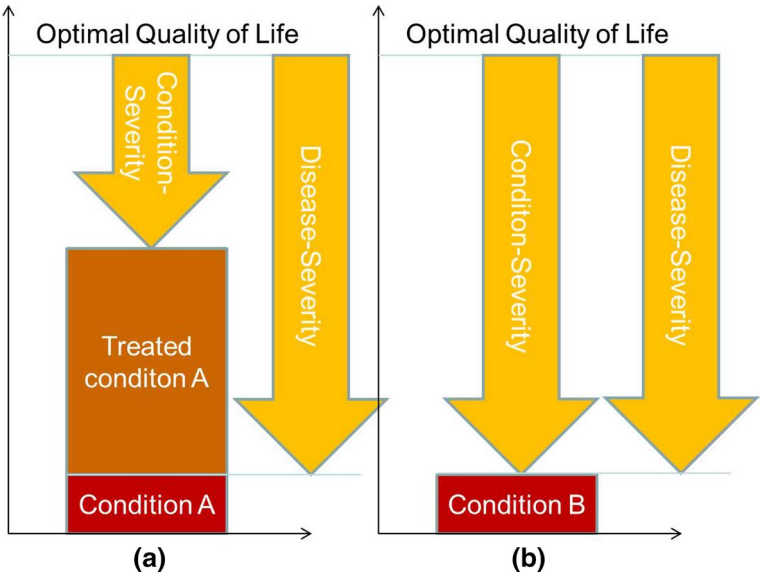

Fig. 2 Illustration of Example 1

condition-severity, and unmet need explains our intuitions in relation to different cases.

Let us start with an example where we, due to resource constraints, will have to choose between two different interventions, which are relevantly similar in all respects, and that benefit two different conditions (A and B):

> Example 1: Condition A has a very high disease-severity untreated. There is previous treatment for A but not for B and since all patients with A are treated, they now have a high (but not very high) condition-severity of their condition. Condition B has a very high disease-severity and a very high condition-severity, since there is no previous treatment with adequate effect.

A strong intuition in this situation is that patients with condition B should have the intervention that will improve their condition. This can be explained in two different ways. Using disease-severity, it could be argued that A and B have the same severity, but since B is an unmet need—that tips the balance in favour of B. Using condition-severity, it could be argued that since B has a very high severity but A only high severity—that difference in severity tips the balance—and the aspect of B being an unmet need is redundant. So do we have reasons to prefer one approach before another? Following Occam's razor, it might be argued that if one aspect can fully capture what two other aspects capture in a situation, we have reason to reduce the number of aspects considered (Fig. 2).

So does condition-severity fully capture the combination of disease-severity and unmet need? And can it even be argued that disease-severity and unmet need clouds the assessment of situations in which condition-severity would give a more straightforward answer. Consider the following situation, involving conditions A and C:

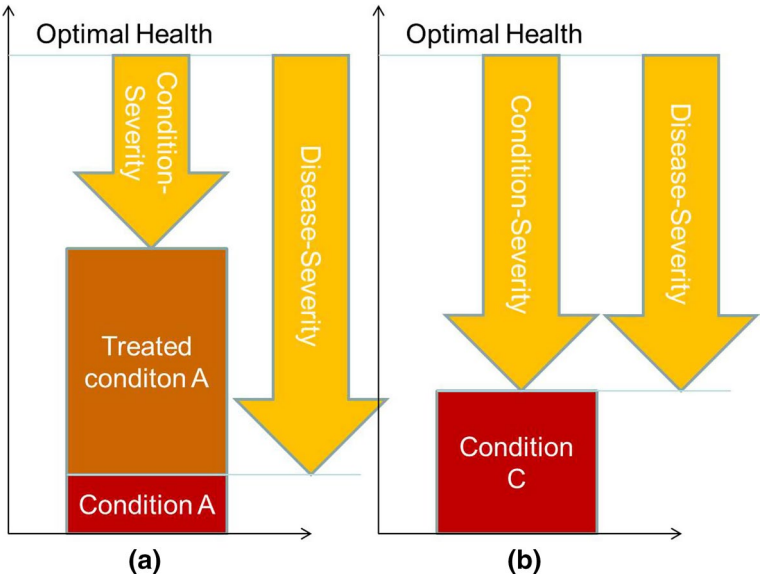

Fig. 3 Illustration of Example 2

> Example 2: Condition A has a very high disease-severity untreated. There is previous treatment for A but not for C and since all patients with A are treated, they now have a moderate condition-severity of their condition. Condition C has a high disease-severity and a high condition-severity, since there is no previous treatment with adequate effect. Condition C is hence also the unmet need in distinction to condition A.

In this situation, we have a strong intuition that patients with condition C should be treated. Using condition-severity it could be argued that this is simply since C has a higher severity than A. Using disease-severity we have the following situation: A has a higher severity than C, but C is on the other hand an unmet need. So, in order to explain our intuition, we need a way to balance the aspect of disease-severity against unmet need. Obviously, this gives us a less straightforward explanation or answer to the dilemma, and does not as easily explain our intuition (Fig. 3).

On first inspection, we therefore have some reasons to adopt condition-severity instead of the combination of disease-severity and unmet need. When using condition-severity, unmet need seems redundant in the above examples. Can we find examples where unmet need still will fill a role to explain our intuitions? Consider Example 3 with conditions C and E.

> Example 3: Condition C has a high disease-severity and a high condition-severity and there is no previous treatment with adequate effect. Hence condition C is also an unmet need. Condition E has a very high disease-severity but a high condition-severity since there is one previous treatment with reasonable effect.

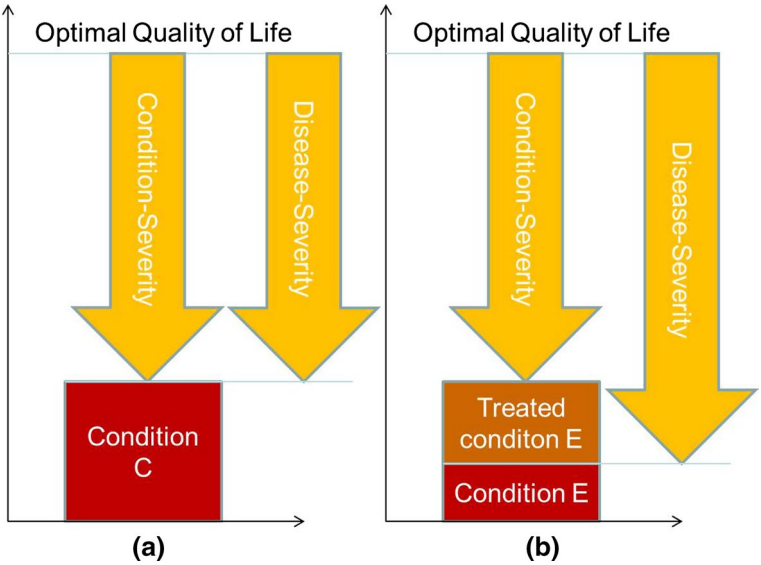

Fig. 4 Illustration of Example 3

In this situation, we do not have any clear intuitions about which patients should be prioritized to have an intervention. Do we get any guidance from our different aspects? Using disease-severity would imply that patients with condition E should have the intervention since they have the higher original severity. However, in relation to Example 2 we argued that if a condition with disease-severity is treated to have a lower condition-severity than competing conditions, we should not take disease-severity into account. If so, it seems the only reason why we should do so in this situation is because that would work as a tie-breaker, when condition-severity is that same. Could we provide any reason for why we should use disease-severity as a tie-breaker? Especially, since another tie-breaker in Example 3 could be unmet need? Interestingly enough, in this situation, disease-severity and unmet need, would favour different conditions if used as tie-breakers (Fig. 4).

A conclusion from this section is that condition-severity explains a number of intuitions on severity better than references to disease-severity and unmet need, but fails to give guidance in situations of similar condition-severity. In the next section we will therefore explore whether disease-severity and/or unmet need can fill the role of tie-breakers in such situations.

Tie-Breakers in Situations of Equal Condition-Severity

In this section we will explore different suggestions for whether disease-severity and/or unmet need, are reasonable to use as tie-breakers in situations of equal condition-severity. We will do so by exploring Example 3 further.

A Historical Perspective

One idea could be that we should not only consider the current situation for the patient groups involved in Example 3, but should take a historic perspective, when trying to find distinguishing aspects to use as trumps or tie-breakers. First, it could be argued that even if the two patient groups currently have equal condition-severity, historically, patients with condition E have suffered more or have had a worse life. Until the first effective treatment arrived for condition E, patient suffering from E had a worse life than patient suffering from condition C. At first glance this looks like a consequentialist rationale, but it is difficult to support this in terms of the total amount of suffering in each group, since the extra suffering in condition E untreated could well be outnumbered by having a larger group of patients suffering from condition C.

A more fruitful idea could be an idea of fairness, claiming that all patients over time should have a similar distribution of benefits and burdens. Life-time egalitarianism would argue this when it comes to individuals [10, 26]. This would then require that the patients now suffering from condition E have experienced a time when treatment for E did not exist and hence over their life-span—in comparison with patients with C—they have had a worse life that now needs compensation until the two groups' lives end up having a similar balance of benefits and burdens. Disease-severity would then work as a tie-breaker until patients in both groups reach an equal distribution over life. However, with a new generation of patients, where no patient has experienced a time without treatment—disease-severity would no longer have this function. In such cases, we will have to expand the life-time egalitarianism to cover also intergenerational justice, i.e. egalitarianism over different patient generations.

Most of the discussion on intergenerational justice relates to what present generations owe to future generations or how present generations should think about present distributions in relation to future distributions of benefits and burdens [12, 34, 41]. In this case, we are however dealing with whether distributions in relation to past generations should impact on the distribution of present generations. We also find discussions about this within the academic field on intergenerational justice, focusing on two different aspects: whether we have reasons to compensate for past wrongdoings and whether we can have remaining duties to dead people [34]. As to wrongdoings, before treatment for condition E existed, there was no wrongdoing involved in patients with E not receiving treatment (since there was no treatment to receive)—hence they have no claim on compensation for the period before treatment existed (even if it was a time of unequal suffering). Furthermore, in cases where compensation of past wrongdoings are discussed, it is normally assumed that present generations are still suffering the consequences of wrongdoings to past peers or ancestors. In this case, patients with condition E have already been "compensated" for their past suffering in having received treatment. When it comes to duties, before treatment existed we had duties towards attention, care, and palliation of patients suffering from E. We may also have had a duty to try to develop and test treatments for condition E (see the discussion on innovation below), but not to provide treatments that did not (yet) exist. Moreover, even if we accepted such an (strange) idea,

it is difficult to see how these duties can be fulfilled by providing another treatment to present patients suffering from condition E.

If, instead, we explore unmet need as a tie-breaker, we could reason in a similar way. Does the fact that patients suffering from condition C have remained untreated for generations now give rise to a claim on treatment in Example 3? Life-time egalitarianism does not seem applicable here, since in comparison with patients with condition E they have had an equal or better distribution of benefits and burdens in their lives (only taking account their respective conditions and assuming equal lives on all other accounts). That past generations have not received treatment is not a wrongdoing that needs compensation, since no treatment existed to be distributed to these patient generations and once again it is difficult to see that this would have created a duty towards these past generations that can now be compensated by taking unmet need into account as a tie-breaker.

In conclusion, we do not find it convincing that the experiences of past patient generations would generally give rise to any claims by present generations in the priority setting situation. However, maybe disease-severity could be given some role in a situation where patients with condition E have lived without treatment previously in their lives accepting life-time egalitarianism. Still, that would imply a limited role and we then have a more practical problem of assessing *how* disease-severity should impact on current compensation.

Taking Turns

Another argument here would be that it is patients' with condition C turn to have treatment, if nothing else distinguishes the patient groups. This would then support unmet need, and not disease-severity as a tie-breaker. In some areas when we do not have any strong substantial reason for making a difference between people, but there are still limited resources that we need to share, we apply a formal fairness approach in terms of *taking turns*. We all know this from being kids and trying to distribute the only swing among us, or when arguing about who should sit in the front seat of the car. Could we argue that unmet need in Example 3 will function as an indicator of who should take turns? After having treated the patients of condition E with a treatment, it is now time for patients with condition C to get treatment (having been waiting for their turn).

The idea of taking turns is used to handle benefits on the same level for all included and by taking turns all should have their fair or rather same share of this limited benefit. This does not really reflect our Example 3.

Now, even if we cannot apply the traditional taking turns practice, maybe we could use this idea in an adapted way. More formally, such an idea could be expressed in the following manner:

> If two persons (or groups) have the same legitimate claim on an undividable, limited and equivalent benefit, the person (group) receiving the latest benefit should allow the other person (group) to take turns.

Compare this idea with the following ideas:

> If two persons (or groups) have the same legitimate claim on an undividable, limited and equivalent benefit, the persons (groups) should: flip a coin/draw straws/take part in a lottery with equal chances etc.

Is there a moral difference between these different ideas, or more specifically, between the idea about taking turns and the ideas about letting chance decide? The taking turns idea implies that the one taking turns, has a greater claim than the one having to take a step back—at least once the taking turns practice have been set in motion. In a normal taking turns practice, the one taking the first turn, has no greater claim than anyone else of taking the first turn. But once she has taken the first turn, someone else of those competing over the limited benefit, will have a more legitimate claim to take the next turn than her, and so on… until all have had their first turn. Then it starts all over again, with everyone being down to no legitimate claims again. When applying a strictly chance based approach, we do not claim that anyone, at any time, have a greater legitimate claim than anyone else. Basically, this would mean that if we were only to settle a single case of distributing a limited and undividable benefit—no one would have a more legitimate claim than anyone else—and in that sense they would be on par with each other. However, in such a case, it would seem that the purely chance based approach would actually have some moral advantages. Additionally, there are practical advantages, as no turn-taking logistics is necessary. Moreover, unless one finds good ways to give people the first turn by flipping a coin or drawing a straw, i.e. leaving it up to chance, it is often the bold, the dominating, the powerful, the quick ones etc. who gets the first turn. That is, the first turn may favour some types of persons in a systematic way, which is generally unfair.

Returning to our example above, if claiming that persons with condition C should take turns as an interpretation of unmet needs, we do seem to imply that they have a legitimate claim on the treatment. So it is not the first turn, rather it is their turn since persons with condition E already have had their turn. When E have gotten their last treatment, they do not any longer have a legitimate claim trumping C's claim on the new treatment. At that point, both claims are equally legitimate—and we are not helped by the idea of taking turns to solve the situation. We are then facing the first, and for all we know, only turn, and this would be better solved by chance.

Even accepting this, could there be special situations, where the taking turns practice could actually give some guidance? Consider the following version of Example 3, Example 3':

> Example 3': Patients with conditions C and E are in the same situation as in Example 3. Hence, they have the exact same severity of condition. There are a number of treatments (n = 10 for each condition) developed that would give each of the conditions C and E added benefits up to no severity (i.e. optimal health). Due to the budget situation of the health-care system it is projected that during the next 20 years only one treatment can be added to the benefits package each year (due to subsequent efficiency measures within the system).

In this situation, applying a chance approach could turn out in the following way. During the first 10 years, condition E gets all the added treatments up to optimal

health, and then condition C gets their 10 treatments successively during the next 10 years. In such a situation, taking turns would seem like a more fair approach. In the second year, if persons with condition E have received an added treatment the first year, there would be condition-severity reasons to add another treatment to persons with condition C. In the third year, they would be on par again as to condition-severity reasons, and the taking turns approach would seem like a fair solution. Either by taking turns every year (or by taking turns every other year, allowing condition-severity reasons to decide the matter in the year between). At this point, we have left the idea about unmet needs far behind. Our conclusion is that the idea about unmet needs and taking turns then does have much in common—and in such special cases we would be better advised to introduce the idea of taking turns.

Hope of Treatment

A third idea could be related to the fact that patients find hope in having access to treatment. If we return to Example 3 above, could a relevant difference between condition C and E be that for the originally very highly severe but treated condition E, previous innovations have raised expectations and hope for yet another step to further ease or even cure the condition which now might be fulfilled? For condition C, the patients have also had expectations and hope for a cure, which might now finally be fulfilled. However, due to no earlier innovations within the field of condition C, patients have more often become disappointed and robbed of hope. Finally, both groups have available treatment that could satisfy their hopes. Should we prioritize patients with condition C since they have long hoped for a cure, and have experienced many disappointments, rather than patients with condition E, whose hopes more often have been realized in terms of successful innovations? Or vice versa?

We have previously discarded the historic perspective, but for a limited application, and it is difficult to see that historically disappointed hopes would fare any different. That is, unmet needs might not be a good proxy of disappointed hopes—we might easily imagine that patients suffering from more severe conditions during the course of research development have suffered a number of disappointments before reaching their current level of hopes and expectations. Hence, indicating a relationship between hope and disease-severity. Maybe, we could even claim that the worse a condition is, the stronger the hope for cure and thereby also the greater the disappointment with frustrated hopes. Hence, it is difficult to see which tie-breaker is supported by this line of argument. Moreover, hopes depend on a wide variety of factors, and hype is one of them. It appears problematic to include assessment of hope and hype in priority setting. The same argument can be used on other emotional or attitude-related conceptions of disease, such as status or prestige of diseases [1].

In conclusion, in this section we have not found any strong support for using disease-severity and/or unmet need as tie-breakers in situations of equal condition-severity. Although, we find some support for using disease-severity in rare situations if we accept life-time egalitarianism, and we find some support for using a taking-turns approach in another type of rare situations, we do not find any support for the use of unmet need as tie-breaker.

Stimulating Innovation, Rare Conditions etc

Let us investigate another line of argument supporting unmet need as a criterion for priority setting. It could be argued that we should stimulate innovation within the area of previously untreated conditions and that reference to unmet need could be a way to express this? However, first, it is not uncommon to have both unmet need and innovation potential on the list of factors to consider when deciding what to prioritize in a situation of scarcity (see [2]). Hence, if stimulating innovation is a reason behind taking unmet needs into account, we need to decide which one to maintain to avoid double counting (if indeed any one of them).

Second, it seems we have reason to stimulate innovation within areas where there have previously been no available treatments (or at least no innovative treatments) [33]. Relating it once again to severity, if having to choose between stimulating innovation in relation to very severe conditions or in relation to mild conditions, it is obvious we have stronger reasons to do so in relation to very severe conditions. Simply, since it is more important to have treatment affecting a very severe than a mild condition, averting risk of death, minimizing suffering etc. A similar line of argument could be given in relation to stimulating the innovation of treatment as the argument in relation to offering existing treatment above. That is, it is strongly related to condition-severity.

Let us try to analyse this, starting from another end and ask ourselves in relation to which kind of conditions we usually emphasise that there are unmet needs (and where there hence is a need for stimulating innovation). One area where we often find reference to unmet needs is in relation to rare conditions [28, 32]. Due to factors like public pressure, market size, public health impact etc. pharmaceutical companies and academic scientist have had strong reasons to focus on developing treatments for common conditions (to a large extent regardless of severity). Historically, this has left rare conditions largely untreated. However, as common conditions now, to a great extent, have access to effective treatments and given special incentives for developing treatment for rare conditions, we see a constant development of new (and expensive) treatments for rare conditions [13, 14, 27, 51]. Should we use these developed treatments (despite cost) since they will meet unmet needs and will the fact that these needs are unmet give extra reason on top of severity to accept higher cost-effectiveness thresholds?

It is possible to provide a formal equal-treatment reason for why we should accept higher cost-effectiveness thresholds for orphan drugs or other treatments of rare conditions [47]. This formal equal-treatment reason could be related both to having access to treatment (i.e. opportunity) and to actually achieving a higher level of health (i.e. outcomes). Unmet need obviously signals that there is no previous effective treatment before the one we are considering and this could therefore also signal that we have reason to accept higher thresholds. Something we do not have if it is a need that has been met. But do we really need the concept of unmet need to signal that? Look at the following example:

> Example 4: Condition F is rare, highly disease-severe and a condition for which an effective treatment with low cost-effectiveness has been developed.

> The cost-effectiveness is still below the higher threshold for rare diseases and the patients therefore get access to this treatment. Since the treatment is effective, patients suffering from F now have a moderate condition-severity.

In Example 4 it seems we can argue for patients suffering from condition F receiving treatment by referring to criteria like severity, effectiveness, and rarity to balance the low cost-effectiveness. And we do not have to add the criterion of unmet needs (see [47]). But if we do not use the concept of unmet need, does that not mean that we also should accept other treatment for similar conditions despite the fact that there is already effective treatment? Consider Example 5:

> Example 5: Another treatment is developed for condition F. This is somewhat more effective than the first treatment and will bring the patients up to light condition-severity.

Using the criteria we used in Example 4, we can say that the concept of relatively higher threshold still holds, but since condition F now has moderate condition-severity (before the second treatment is administered) the cost-effectiveness threshold for this treatment is lower than for the first treatment. Hence, this new treatment must be more cost-effective than the first treatment. This new treatment is therefore not as easily accepted within the system. Since this will make a difference between treatments in examples 4 and 5, making it easier for treatment to be accepted in Example 4—it seems reference to unmet needs does not really make a difference either way.

At the outset of this article we acknowledged that unmet need might have a role in research funding priorities, i.e. at a stage before developed treatment is to be prioritized. Since we have found no support for that unmet need should fill a role in priority setting of existing therapies, given that condition-severity covers what is needed, should unmet need have a role in research funding priorities? Let us consider a final example:

> Example 6: A funding agency has to make priorities on where to channel research funding for the development of new medical treatments. The applications concern three different conditions. Conditions G and H both have high condition-severity; G since there is no previously existing treatment, and H as existing treatment that has brought it from very high to high condition-severity. A third application concerns condition I, which has moderate condition-severity, but with no access to previous treatment.

In this example, we argue that conditions G and H should be prioritised over condition I, implying that condition-severity, trumps unmet need. Unmet need could be used as a tie-breaker between conditions G and H, but as we have discussed above, it is difficult to find a reasonable rationale for this. Instead, there are probably a number of other factors that should be taken into account when trying to prioritise between G and H: has there been any previous funding of research on G, or is there simply a lack of research; has the fact that treatment has been developed for H lead to access to other funding sources or incentives (for example from the pharmaceutical industry) to continue development of treatments for H; is there a potential that given previous developments of research on H and previous failures when it comes

to G—resources are more effectively spent on H etc.? Once again, it is difficult to see that the concept of unmet need would fill an important role in prioritising research funding. In essence, we want to stimulate and have access to innovative therapies for conditions with high condition-severity, regardless of whether there is existing treatment or not and in situations when we have to choose between funding innovation of conditions with similar condition-severity, other factors are more relevant to take into account as tie-breakers.

A Practical Application

An important issue, following this theoretical analysis, is if this will have any practical application in concrete priority setting. Let us illustrate this by using two recent cases from a decision-making council in Sweden where condition-severity instead of disease-severity and unmet need is used. The cases concerns FreeStyle Libre, a glucose monitoring device for diabetes, in this case for diabetes type II; and Spinraza® (nusinersen) for spinal muscular atrophy (SMA), in this case SMA I and II. FreeStyle Libre will continuously monitor the glucose level in people with diabetes, a need for which there has not existed any solutions before—the alternative being to monitor manually and therefore intermittent. Using the concepts of disease-severity and unmet need it could be argued that FreeStyle Libre addresses a disease with very high disease-severity and is meeting an unmet need, which could indicate that it should be given a high priority. However, as indicated above, since most patients with diabetes type II in Sweden are well-managed, the condition-severity of their disease is rather moderate to small. Moreover, the need for continuous glucose monitoring for such patients, would seem to be a rather marginal need—more related to convenience than an actual medical need. Following this, it was decided that FreeStyle Libre for most patients with diabetes type II would have a low priority with exception for patients whose diabetes is not well-managed with recurring hypoglycaemic incidences (and therefore with a higher condition-severity) [40]. Using condition-severity instead of disease-severity and unmet need did seem to catch the important aspects to consider in this case. Comparing with Spinraza® for SMA I and II. Both SMA I and II are considered to have a very high disease-severity and being unmet needs (with no access to previous effective treatment) and would on this account be given a high priority. However, using condition-severity gives us the same result—both SMA I and II was considered to have very high condition-severity [39]. Hence, condition-severity can explain the decisions made in a better way than using disease-severity and unmet need showing the practical applicability of the above theoretical analysis. Moreover, sticking to one principle and one concept that is more clearly defined will, according to Occam's razor, make practical prioritization less complicated.

Summary and Conclusions

In this article, we have analysed the concepts of condition-severity, disease-severity, and unmet needs and their conceptual and normative relationships. We have found that condition-severity will better explain and cover central intuitions concerning prioritising between both existing treatments and between research and innovation projects, than disease-severity and unmet needs. Therefore, aspects of theoretical and practical simplicity (following Occam) give us positive reasons to generally avoid using the concepts of disease-severity and unmet need. In rare situations of equal condition-severity and where other aspects like effectiveness and cost-effectiveness cannot be discriminated between (situations likely to be of pure theoretical interest) we could resort to disease-severity as a tie-breaker if we accept life-time egalitarianism. However, we may generally be better advised to resort to lottery or a specific version of taking turns. For all practically interesting situations where the concepts of disease-severity and unmet needs now are used, they should be replaced by condition-severity for clarity and to better reflect the underlying normative rationale. This concerns both priority setting among existing therapies as well research funding priorities. Priority setting is complicated and complex. We do not need to add to this using redundant concepts.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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