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Preference-Based Assessments

Evaluating Canadians' Values for Drug Coverage Decision Making

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ABSTRACT

Background: Decision makers are facing growing challenges in prioritizing drugs for reimbursement because of soaring drug costs and increasing pressures on financial resources. In addition to cost and effectiveness, payers are using other values to dictate which drugs are prioritized for funding, yet there are limited data on the Canadian public's priorities. **Objectives:** To measure the relative societal importance of values considered most relevant in informing drug reimbursement decisions in a representative sample of Canadians. **Methods:** An online survey of 2539 Canadians aged 19 years and older was performed in which 13 values used in drug funding prioritization were ranked and then weighted using an analytic hierarchy process. **Results:** Canadians value safe and efficacious drugs that have certainty of evidence. The values ranked in the top 5 by most of our subjects were *potential effect on quality of life* (65.4%), *severity of the disease* (62.6%), *ability of drug to work* (61.1%), *safety* (60.5%), and *potential to extend life* (49.4%). Values related to patient or disease characteristics such as *rarity*, *socioeconomic status*, and *health and lifestyle choices* held the lowest rankings and weights. **Conclusions:** Canadians value, above all, treatment-related factors (eg, efficacy and safety) and disease-related factors (eg, severity and equity). Decision makers are currently using additional justifications to prioritize drugs for reimbursement, such as rarity and unmet need, which were not found to be highly valued by Canadians. Decision makers should integrate the public's values into a Canadian reimbursement framework for prioritization of drugs competing for limited funds.

Keywords: coverage, decision making, drugs for rare diseases, health technology assessment, orphan drugs, policy, reimbursement, values

Introduction

Given continually increasing drug prices, growing pressures to fund new technologies, and the fact that Canadian provincial governments are spending in excess of 40% of their budgets on healthcare, public and private payers in Canada must be more diligent with their spending and consider the opportunity cost of funding a new treatment.[1] Because expenses on pharmaceuticals have become one of the highest healthcare expenditures,[1,2] limited resources combined with the many new drugs and technologies competing for these resources make judicious spending imperative. For at least 3 decades, reimbursement decisions have been supported by economic evaluations. Some health technology assessment agencies, such as the United Kingdom's National Institute for Health and Care Excellence, use explicit willingness-to-pay thresholds when deciding whether a new drug is cost-effective—in this case, between £20 000 and £30 000 per quality-adjusted life-year added, with special allowances for end-of-life treatments and rare diseases.[3] In Canada, no official willingness-to-pay threshold is used, although an informal threshold of Can$50 000 per quality-adjusted life-year is often considered.[4] Nevertheless, with increasing costs, many new drugs and technologies do not meet these thresholds for cost-effectiveness.[5]

Conflicts of interest: None of the authors have any competing interests to declare.

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For example, drugs used to treat rare diseases are often extremely expensive (>Can$500 000 per year per patient), have limited clinical data available resulting in uncertain estimates of their effectiveness, and often do not meet the traditional criteria of cost-effectiveness because of high cost and/or limited effectiveness, leading to recommendations by the Common Drug Review (the pan-Canadian health technology assessment body for noncancer drugs) to not cover these drugs as insured benefits, or to list with the condition of a substantial reduction in price.[4,6–9] For conditions without other treatment options (which is the case for many rare diseases), this conflicts with the principle of equity that underlies most healthcare systems and creates an ethical and moral dilemma when it is not possible for most patients to pay out of pocket even if they would want to, and payers have little leverage to negotiate cost-effective prices.[10] In addition, drugs for more common diseases are also demanding prices higher than ever before. For example, drug therapy for hepatitis C, which affects 1 in 100 Canadians, and chronic diseases such as asthma and hypercholesterolemia have treatments priced at tens of thousands of dollars per patient each year.[11–13]

Despite recommendations to not fund on the basis of traditional funding criteria, provincial health ministries and private payers in Canada often fund very expensive medications (eg, aldurazyme, eculizumab, and imiglucerase).[7–9] One consideration used by the Canadian Agency for Drugs and Technology in Health to make positive recommendations despite uncertain economic or clinical benefit is "significant unmet need," and specifically references the rarity of the condition.[14] It is unknown whether the society values unmet need in the same way decision makers do, or whether given the significant opportunity costs, unmet need should be prioritized over certainty of evidence. Specifically, expenditures on orphan drugs in the United States have risen from $15 billion in 2007 to $25.6 billion in 2013, accounting for 4.8% and 7.6% of total drug expenditures, respectively, to treat a very small number of patients.[15]

Payers make healthcare coverage decisions while considering the value for money that a new drug or technology provides, and thus the relevance of the cost-effectiveness evaluation.[16] Given that new healthcare interventions that would not be considered cost-effective at conventional thresholds are being covered, this suggests that payers believe that the "value" of these treatments to society is greater than can be quantified by their cost-effectiveness. Thus, a number of "value frameworks" have been proposed to reflect the broader societal values that should potentially be considered when making a reimbursement decision, including a proposal by Sculpher et al to explicitly incorporate the opportunity cost of a decision into the value framework.[17–20]

The values incorporated into the value frameworks differ, which begs the question of what constitutes the value of a new drug therapy beyond cost-effectiveness. The DrugAbacus framework for the US Food and Drug Administration specifically includes rarity of the disease as 1 of the 7 values, and allows for up to a 3-times value premium for drugs for rare diseases; nevertheless, the selection of the values incorporated into the framework, and the magnitude of each value multiplier, is not clear.[21] Similarly, in Canada, the Patented Medicines Pricing Review Board is considering using market size (prevalence) as a multiplier in how high a drug can be priced.[22]

In support of the value framework concept, the decisions to fund many expensive drugs for rare diseases would suggest that payers are assuming these drugs do provide value, from the societal perspective; there is, however, little empiric evidence of this or of what society values in terms of drug reimbursement decision making. Recently, Paulden et al[23] undertook a scoping review of the literature to identify the specific values that could be explicitly considered in making coverage decisions for drugs for rare diseases and then proposed a framework to incorporate patients, physicians, and societal preferences for each of the values into the decision. Although the list of values is extensive as derived from the literature, the preference weights remain unknown.

Thus, there is growing consensus that decision makers' criteria of "value" must be expanded beyond cost-effectiveness and efficiency. Because decision makers in a democratic system are expected to reflect the public's (ie, taxpayers') priorities, informing value-laden decisions with an evidence-based understanding of societal values increases the democratic legitimacy of such decisions, and certainly the funding of expensive drugs for rare disease can be deemed to be a highly value-laden and preference-sensitive decision. Therefore, the objective of this study was to determine the relative value of 13 factors that could be considered most relevant in informing a drug reimbursement decision in a representative sample of Canadians. The overarching aim of the study was to help inform Canadian reimbursement decision makers about what Canadians value, and lay the groundwork for the development of a broader, Canada-specific value framework to support drug reimbursement decision making. In addition, understanding Canadian values provides the opportunity to also make important comparisons across countries.

Methods

Setting

Canada has a population of about 35 million people and a decentralized federal system of government composed of 10 provinces and 3 territories. Responsibility for the governance of healthcare lies primarily with the provincial and territorial governments, although the federal government sets minimum standards for universal coverage, provides a share of funding, and manages direct coverage for specific populations. Publicly funded care accounts for approximately 70% of total spending on healthcare, with access to hospital care and physician visits provided on a universal basis and coverage for prescription drugs and long-term care provided on a targeted basis to varying degrees depending on the province or territory.[24]

Study Development and Design

We measured Canadians' values for drug reimbursement decisions using a nationally representative survey of Canadian adults. We conceptualize values as general orientations that are "stable and enduring, and as such may predispose people to take certain positions on social and political issues."[25] Because healthcare access and rationing in general are extremely salient political and personal issues for most Canadians, we should expect them to have a stable set of values in this area (see Table 1), even if their experience with specific healthcare policy challenges is limited. The survey included both an analytic hierarchy process (AHP)[26–28] task, which is presented in this article, and a set of more context-specific questions related to funding scenarios for rare diseases, which have been reported on elsewhere.[29]

After an introductory section, the survey began with the AHP task. Respondents were asked to rank the relative importance that the 13 factors should have in healthcare prioritization decision making followed by pairwise comparisons to determine the relative weight of the factors (Table 1). The factors presented reflect a list of values that were derived from a systematic review on criteria used by reimbursement decision makers, and supplemented by a review of the existing literature on the societal value of funding the treatment of rare or expensive diseases (eg, studies by Gershon,[30] Gallego et al,[31] National Institute for Health and Clinical Excellence,[32] Guindo et al,[33] Lim et al,[34] and Linley and Hughes[35]). The final list of values was reviewed by an expert

Table 1 – Values relevant to drug reimbursement.

Value	Description	Example
Drug-related factors		
Potential effect on quality of life	Estimated impact on the quality of life and well-being of a patient, both mentally and physically	A drug that reduces pain and discomfort or allows more activity or stabilizes a disease
Potential to extend life	The effect on early death and the difference in life expectancy with the drug and without the drug	A drug that prevents death, increases the time to death, or cures a disease
Safety	How safe a drug is, or how well the safety of a drug is known	A drug may have serious side effects, which have to be balanced with the drug's benefits
Ability of the drug to work	How certain or sure we are that a drug will work; the presence of strong and complete studies and the quality and uncertainty of evidence	A drug may have many excellent scientific articles showing how well it works, or it may not have good studies making its benefits uncertain
Unmet need	A medical or therapeutic need for a drug, often because of a lack of any other drug or treatment alternative	A disease for which there is no other drug treatment available
Adherence	The ability of a person to comply with taking a medication	People may not take their medications properly because of personal reasons, or because a drug is more difficult to take, which can result in the drug not working
Disease-related factors		
Severity of disease	How severe or serious the disease is and its effect on quality and quantity of life	A severe stroke can result in coma, significant long-term disability, and decreased function
Rarity	A disease that is very rare in the Canadian population, often defined as affecting <1 in 2000 people	Gaucher disease affects 1 in 100 000 people, whereas a common condition, asthma, affects 1 in 7
Equity, fairness, and compassion	Enabling equal access to patients with lower public advocacy or minority populations	A drug for a disease that is not well known medically or that occurs in a small marginalized group of people
Patient-related factors		
Age	The age of the patients who are to receive the drug and also how long they are expected to live without the condition	A drug may be used to treat infants, children, middle-aged people, or seniors
Family commitments or dependents	The burden the individual with the disease may have in caring for dependents	Individuals may have children, parents, or others to support financially, emotionally, or as caretakers
Health and lifestyle choices	The health choices of the individual patient who is to receive a drug, or the population who is affected by a certain disease	Some people may choose to exercise regularly and not to smoke or expose themselves to harmful substances
Socioeconomic status	The measure of an individual's economic and social position relative to others, usually based on income level, education, and occupation	There are people in the society who do not work and have a low social position, and there are those who have a high job status and income

panel. Cost and related factors such as future savings were excluded from our list of values because we are interested in knowing the relative importance of values other than cost in decision making. A more detailed description of the process used to develop this list is provided in the Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.008.

Subjects were introduced to the task through a brief explanation of drug coverage decisions that provincial ministries of health must make. The 13 factors were presented in a randomized list, and subjects were then asked to rank the factors in order of the most important to the least important (using a "drag-and-drop" interface). Once the factors were ranked, subjects were then asked to complete a set of pairwise comparisons between the 6 factors they had ranked the highest, with respondents asked to indicate their level of preference for the higher ranked factor on a 1 ("equally preferred") to 5 ("extremely preferred") scale. Only the top 6 factors were used to keep respondent burden to an acceptable level, because 6 factors require 15 pairwise comparisons, whereas 13 factors would require 78 comparisons. Following guidelines for AHP analysis,[26,27] comparison scores were rescaled to a 1 to 9 scale, and the scores for each respondent were used to populate the top right half of a 6×6 matrix, with the diagonal elements coded as "1" and the bottom left half populated by the reciprocals of the comparison scores. The relative priority of the top 6 values ranked by each respondent was estimated by computing the normalized principal eigenvector of the comparison matrix, which yielded a set of weights between 0 and 1. These weights sum to 1 for each respondent and exist on a ratio scale, so we can use them not only to confirm the initial ranking provided by the subjects but also to calculate the extent to which they judge one factor to be more important than another. A consistency ratio (CR) was also calculated for each respondent to assess the logical consistency (and therefore the validity) of the pairwise comparisons made by that respondent. The CR is the ratio of the consistency index (calculated using the principal eigenvalue of the comparison matrix) and a consistency index for a randomly populated comparison matrix of the same dimension. CR values of 0.2 or lower are acceptable in applied settings.[26] Further details are provided in the Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.008.

Survey Respondents and Administration

Study participants had previously expressed interest in participating in research and were recruited from the 200 000 members of Ipsos Canada's online access panel, with the goal of recruiting a sample that was broadly representative of the Canadian adult population. The questionnaire was professionally translated into French and made available to French-speaking respondents in the province of Quebec. The survey, which was implemented on Lighthouse Studio (Sawtooth Software, Inc, Provo, UT) and hosted on a University of British Columbia server, was administered in English to respondents in all provinces other than Quebec in June 2013 and supplemented with French language data from Quebec in May 2014. British Columbia residents were oversampled, with a target quota of 556 respondents, and the Quebec sample had a target quota of 500 respondents. Only those respondents that completed the whole survey were included in the analysis. In addition, because of the complexity of the survey and the average time to complete, we included only those respondents who took a minimum of 5 minutes to complete the survey in the final analysis. The rationale behind this decision was that with a median completion time of about 15 minutes (interquartile range 9-23), respondents would be hard-pressed to complete the survey with adequate engagement and consideration in less than 5 minutes, and data from this group would be particularly likely to yield inconsistent value prioritization scores. Subgroup analyses that support this assumption are provided in Figure S2 in the Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.008.

Data Analysis

The frequency with which a value appeared in the first, last, and top-5 or bottom-5 ranked values was calculated for all respondents and values. The sample mean for the AHP weight score for each value was calculated to assess the overall prioritization of values within our sample. Because AHP weights were calculated for just the top 6 values for each respondent and some values were much more likely to appear in the top 6 than others, the weight for values outside a respondent's top 6 was assumed to be 0, which adjusted the averages of the weights for how frequently they were ranked in the top 6 and ensured that they reflect the overall prioritization of each value rather than the prioritization among those who ranked the value highly. To explore the impact of respondent consistency on value prioritization, mean weights were calculated separately for respondents with a CR greater than 0.2 and a CR of 0.2 or less. The association between respondent characteristics and AHP weights was estimated using a generalized linear model regression with a beta distribution assumed for the outcome and a logit link (see Table S3 in the Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.008). Analyses were performed using SAS software version 9.2 of the SAS system for Unix (SAS Institute, Cary, NC) and R statistical software version 3.5.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

The online questionnaire was completed by 2686 Canadians 19 years and older from across Canada, of whom 2539 (94.5%) completed the survey in 5 minutes or longer and were therefore included in the analysis. Although the panel is not a random sample of the Canadian adult population, our sample's demographic characteristics were broadly representative (Table 2). Overall, the sample had a similar level of education (26.6% university or higher vs 25.9%) and a similar mean age (41.9 vs 39.8 years) to that of the general Canadian population.[36,37]

Table 2 – Demographic characteristics (N = 2539).

Parameter	Value
Age (y), mean ± SD	41.9 ± 14.6
Sex, female, n (%)	1337 (52.7)
Have rare disease, n (%)	110 (4.3)
Family or friend with rare disease, n (%)	611 (24.1)
Health status, n (%)	
Poor	145 (5.7)
Fair	471 (18.6)
Good	947 (37.3)
Very good	708 (27.9)
Excellent	268 (10.6)
Income (Can$), n (%)	
>19 999	217 (8.6)
20 000-34 999	372 (14.7)
35 000-49 999	366 (14.4)
50 000-64 999	347 (13.7)
65 000-79 999	305 (12.0)
80 000-99 999	291 (11.5)
>100 000	398 (15.7)
Not answered	243 (9.6)
Education, n (%)	
Elementary	24 (0.95)
High school	900 (35.5)
Some postsecondary	536 (21.1)
Technical	373 (14.7)
Bachelor's degree	492 (19.4)
Master's or doctorate degree	183 (7.2)
Not answered	31 (1.2)
Province/territory, n (%)	
Nunavut	1 (0.04)
Alberta	212 (8.4)
British Columbia	518 (20.4)
Manitoba	96 (3.8)
Nova Scotia	86 (3.4)
Ontario	984 (38.8)
Quebec	468 (18.4)
New Brunswick	65 (2.6)
Newfoundland	38 (1.5)
Saskatchewan	59 (2.3)
Prince Edward Island	9 (0.35)
Yukon	2 (0.08)

Figure 1 shows the frequency with which respondents ranked each value first, last, in the top 5, and in the bottom 5. The values ranked in the top 5 by most of our subjects were *potential effect on quality of life* (65.4%), *severity of the disease* (62.6%), *ability of drug to work* (61.1%), *safety* (60.5%), and *potential to extend life* (49.4%). The values ranked in the bottom 5 by most of our subjects were *rarity* (65.7%), *adherence* (62.5%), *unmet need* (53.9%), *age* (46%), and *lifestyle* (41.7%). Safety was the most frequently top-ranked value (18.0% of subjects), whereas rarity held the lowest ranking, being ranked first by 0.10%.

One respondent had missing data for the pairwise comparisons, so AHP weights and CRs were calculated for 2538 respondents. Of these respondents, 1697 (66.9%) had a CR of 0.20 or less. Mean AHP weights for subjects with a low or high CR (CR $\leq$ 0.20 and CR > 0.20) are shown in Figure 2. The final results of the AHP weights for consistent subjects (CR $\leq$ 0.2) are shown in Figure 3. Because the weights are relative and scaled to sum to 1, this means that those factors with the lowest scores, that is, rarity and adherence (weight of 0.02), were 5 to 7 times less important than values such as safety (0.147), ability to work (0.140), quality of

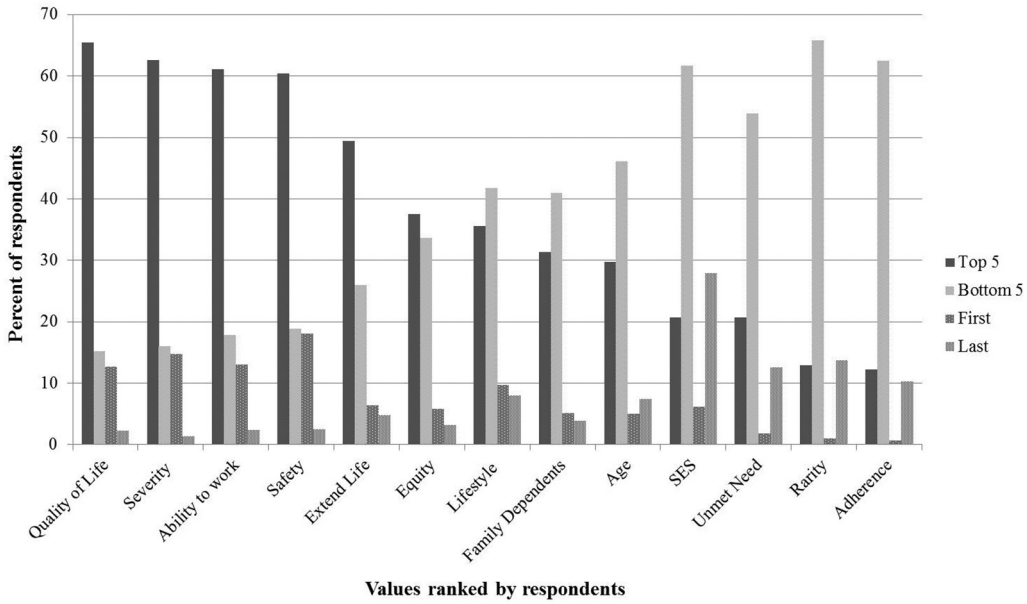

Fig. 1 – Value ranking: proportion of respondents ranking each value first, last, in the top 5, and in the bottom 5. SES indicates socioeconomic status.

life (0.137), severity (0.127), and potential to extend life (0.100). Visual inspection of Figure 3 indicates a break between these top 5 values and the other 8, suggesting that respondents more consistently prioritize this group of 5 values.

Respondent characteristics were generally not associated with AHP weights (see Table S3 in the Supplemental Materials), although age and province of residence appeared to have a consistent association with respondent preferences. Household income, health status, personal experience with rare diseases, and community type were not associated with any of the 13 values. Sex and education level were associated with the potential effect on quality of life (relative proportion ratios of 0.85 and 1.18). Quebec residents put less emphasis on safety (0.62) and more emphasis on the severity of the disease (1.55) and adherence (1.25) than did respondents in the rest of Canada. Finally, older respondents weighted the ability of the drug to work (1.013), potential effect on quality of life (1.016), and severity of disease (1.008) higher than younger respondents and health and lifestyle choices (0.995) and safety (0.994) lower.

Discussion

Our study revealed clear Canadian values for guiding drug reimbursement decisions and demonstrated the relative importance of these values. These novel results can be applied broadly to

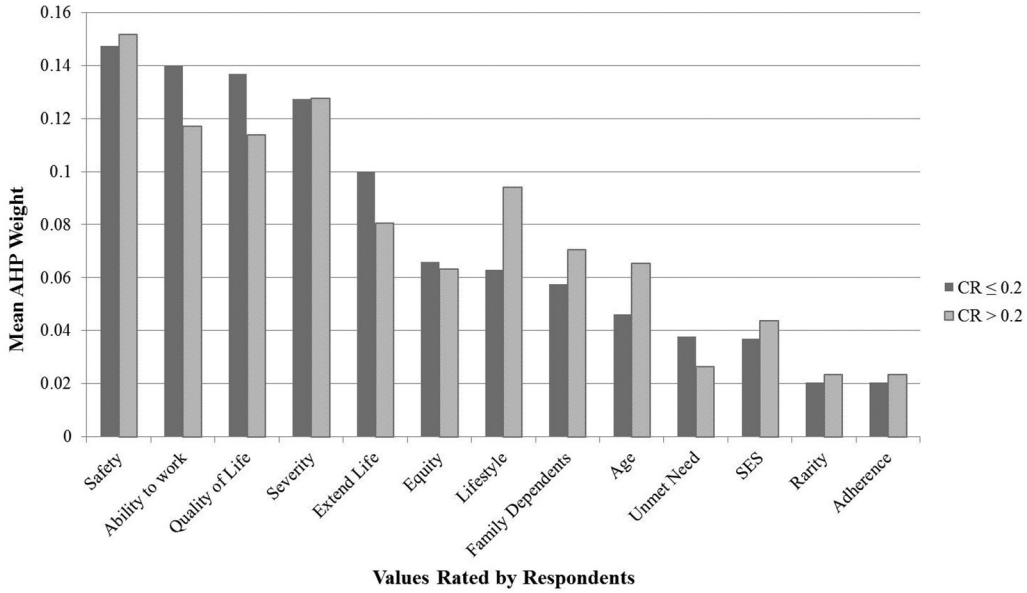

Fig. 2 – Value weightings by consistency score: AHP weights for each value for respondents with CR values >0.20 and <0.20. AHP indicates analytic hierarchy process; CR, consistency ratio; SES, socioeconomic status.

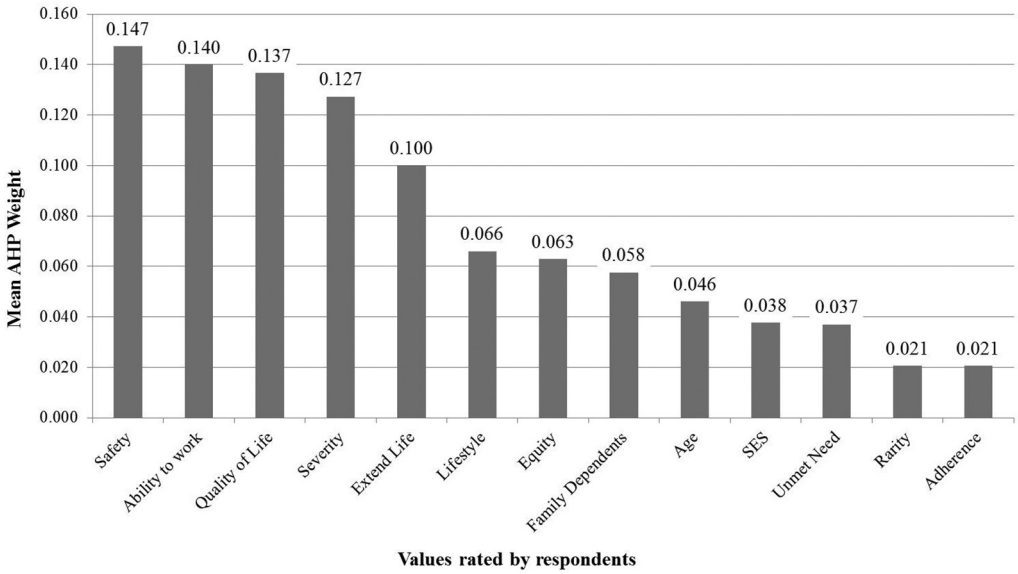

Fig. 3 – Final value weights: average AHP weights for respondents with CR values ≤0.20. AHP indicates analytic hierarchy process; CR, consistency ratio; SES, socioeconomic status.

pharmaceutical priority setting in Canada. We found that Canadians most highly value safety, the ability of the drug to work, improvement in quality and quantity of life, and the severity of the disease. These factors were 5 to 7 times more important than those values ranked the lowest (ie, rarity and adherence). These results support the traditional methods used in Canada to review common drugs, which stress the drug's effectiveness and the certainty of the evidence for effectiveness and safety.

Reimbursement decisions for rare disease treatments are complicated and often politically motivated, with factors outside of those surveyed such as media attention, political pressure, and other international funding experience often also playing a role. As a supplementary rationale for funding orphan drugs, decision-making bodies have cited the "rule of rescue," which is an obligation or ethical duty to help those in an immediate life-threatening position as well as "significant unmet need."[14,38] In addition, unmet need is a justification often used to fund high-priced drugs or those with low clinical evidence, even if the evidence for a drug's ability to meet the unmet need is poor. The public did not appear to value several factors related to these prioritization rationales, including unmet need and rarity, as strongly as decision makers. In particular, Canadians recognized that the ability of a drug to work (certainty of evidence) was a highly important factor that decision makers need to consider more prominently in their decisions. Orphan diseases can be severe, and treatments may improve length and quality of life. This, in conjunction with equity, suggests that Canadians value treatment- and disease-related factors beyond disease prevalence.

Our findings are similar to those of other studies that found that the public supported the allocation of funds to those who were most likely to benefit in terms of impact on quality and quantity of life and those who had a severe disease.[34,39,40] Our results somewhat differ from that of an Albertan citizens jury, which concluded that unmet need was highly valued, whereas the completeness of data on adverse events (safety and the ability of the drug to work) was less important.[40] Unmet need has been found by other studies to be highly valued; these studies, however, did not include as many factors for comparison as our study did, nor did they quantitatively determine its "relative importance," and so it may be that given the other alternatives that our study provided, it was not valued as highly, but still deemed important just less so than specific treatment and disease-related factors. This result is also rational in that unmet need, in the absence of a severe disease, would be anticipated to be a low priority for funding a therapy.

Ranking exercises have been found to have certain limitations in eliciting the public's views on complex issues.[41] Some studies have found a lack of internal consistency with ranking exercises, whereas others, including ours, have found the opposite.[42] The use of the online survey design also has limitations including respondents self-selecting into the Ipsos database and having online access. A further limitation to our survey design was that it did not allow for a detailed deliberation of the context of the factors used in decision making. As a result, subjects were unable to conceptually apply these factors to a decision problem.

Our study is representative of the Canadian population and ascertained the relative importance of key factors used in value-laden decision making. The AHP allowed us to measure the strength of a respondent's preferences and also served as a measure of validity.[26] This study represents an initial application of this methodology to this problem in a Canadian context, which we anticipate will help inform future studies that will be able to delve further into examining Canadian societal values for priority setting and decision making in the healthcare arena and support the development of a broader value-based decision-making framework.

Priority setting in healthcare is complex, and addressing equity concerns for the allocation of resources is a difficult task. There is significant pressure on Canadian jurisdictions from both orphan drug manufacturers and advocacy groups such as the Canadian Organization for Rare Disorders demanding special consideration and adaptive pathways to facilitate broader access and funding on the basis of a disease's rarity. Although market size may be a consideration for pharmaceutical pricing, it should not be the sole consideration for funding. On the basis of the results of our study, the considerations that should form the basis for prioritizing funding decisions would be treatment-related factors, including the effect of the treatment on both quality and length of life,

safety, the probability that the treatment will provide a benefit, and two disease-specific factors: severity of the disease and equity (or inequity) of treatment. Thus, decision makers need to ensure that any specialized strategy or the development of a separate funding pool for drugs for rare diseases considers the full spectrum of treatment and disease-related factors.

Conclusions

Our results provide drug plan administrators further insight into Canadian values related to reimbursement decision making. In the context of prioritizing drug therapies within limited healthcare budgets, and with the current pressure to evaluate rare treatments differently, decision makers may choose not to use the rarity of a disease as a consideration, particularly when there is poor evidence of efficacy to prioritize a drug therapy. Any considerations for adaptive pathways for specialized or high-cost drugs must incorporate societal values because of the substantial opportunity cost. Considering other currently proposed value frameworks to support reimbursement decision making,[16–20] next steps would include the integration of these results with other Canadian evidence into a Canadian decision-making value framework.

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Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2018.08.008.

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