



November 13, 2020

Nakela L. Cook, MD, MPH
Executive Director
Patient-Centered Outcomes Research Institute (PCORI)
1828 L Street, NW, Suite 900
Washington, DC 20036

RE: PROPOSED Consideration of the Full Range of Outcomes Data: PCORI's Principles

Dear Dr. Cook:

Haystack Project appreciates the opportunity to comment on PCORI's proposed set of principles for its consideration of the full range of outcomes data (Proposed Principles).

Haystack Project is a 501(c)(3) non-profit organization enabling rare and ultra-rare disease patient advocacy organizations to coordinate and focus efforts that highlight and address systemic reimbursement obstacles to patient access. Our core mission is to evolve health care payment and delivery systems with an eye toward spurring innovation and quality in care toward effective, accessible treatment options for Americans living with or caring for someone with a rare or ultra-rare condition. The Rare Cancer Policy Council (RCPC) is one of our initiatives, and is the only rare cancer council developed to focus on and respond to reimbursement, access and value issues across the rare cancer community.

Haystack generally supports the proposed principles within the context of PCORI's overarching goal of prioritizing the patient voice through patient-centered outcomes research. We appreciate PCORI's reiteration of its key mission as well as the statutory limitations on its funded research:

The authorizing law further directs PCORI to "ensure that the research findings... do not include practice guidelines, coverage recommendations, payment, or policy recommendations." PCORI has implemented this mandate in its funding announcements and guidelines by stating that applications for funding that seek to conduct a formal cost-effectiveness analysis or whose findings will result in coverage recommendations, payment or policy recommendations, or clinical practice guidelines will be nonresponsive. This will remain the practice of PCORI moving forward. (citations omitted)

Our comments:

- Provide a brief contextual background on the unique challenges for rare and ultra-rare diseases and rare cancers that PCORI should consider as it seeks to improve "the science and methods of comparative clinical effectiveness research by developing and periodically updating" methodological standards for research; and

Haystack Project is a 501(c)3 with a core mission to evolve health care payment and delivery systems to make access to innovative quality treatments more accessible to the patients they were meant to reach.

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- Outline our recommendations on PCORI's proposed principles.

Background

While countless lives have been improved or saved by new therapies enabled by Congress' incentives for orphan drugs to address rare disorders, millions of Americans affected by a rare disease are still waiting and hoping for treatment or a cure. Innovation in how we understand and address disease mechanisms are currently advancing at a previously unthinkable pace. Targeted gene therapy and regenerative medicine, and immunologic approaches to rare, serious, and life-threatening conditions give renewed hope to patients and their caregivers. Novel treatments have, however, been accompanied by increased concerns that the treatments we need will not be accessible due to increasing concerns that their high cost might unduly burden overall health care spending.

Comparative effectiveness assessments, particularly those that incorporate cost considerations, can have an unintended consequence of triggering reimbursement mechanisms and hurdles that not only constrict access to the subject innovation, but can tip the scales for or against pursuing specific drug candidates to address rare and ultra-rare diseases.

As affected patient populations dwindle below 20,000 or even into and below the hundreds, the balance of existing incentives against clinical trial and reimbursement risks is far too fragile. We believe that PCORI's focus on patient-preferred outcomes, as well as costs and burdens from a patient-centered perspective, can provide an important counter-balance to the growing tendency to evaluate "cost-effectiveness" of new orphan drugs at or before FDA approval.

Principle #1: PCORI-funded research may consider the full range of outcomes important to patients and caregivers, including burdens and economic impacts.

Haystack appreciates PCORI's inclusion of potential burdens and economic impacts that may affect patients and their caregivers, including:

- Time in hospital
- Time home from work or usual activities
- Cost/time for transport
- Childcare costs when seeking care
- Out-of-pocket costs (copays and deductible as well as items not-covered such as drugs or care providers)
- Hours spent caregiving
- Foregone wages

We urge PCORI to clarify to all stakeholders that the listed burdens and impacts present examples of the types of economic and cost information, rather than a full listing. For specific disease states, potential impacts may have different affects or vary in their relative importance, so we appreciate clarification that PCORI will afford patient and caregiver advocates the



opportunity to communicate a holistic view on burdens and economic impacts, including disease-specific, unforeseen impact not included in PCORI's list.

Haystack also encourages PCORI to add additional examples of burdens and economic impacts as it finalizes its principles, including:

- **Lost wages for patients.** While PCORI's proposed list includes caregiver lost wages, patients can face significant financial burdens if their disease state makes it difficult to retain employment;
- **Non-familial, paid caregivers.** For patients without sufficient caregiver support, or requiring respite care, health care needs can make it necessary to pay for caregiver support.
- **Non-economic costs on caregivers.** Caregiver burden can extend beyond the economic impact of lost wages to include physical or mental health impacts. Alzheimer's disease caregivers, for example, face significant non-economic burdens that have been captured and quantified in research studies.

Moreover, we encourage PCORI to assess treatment options in a manner that sufficiently captures *potential* long-term benefits of treatments addressing rare and ultra-rare disorders, most of which are genetic and chronic. Studies of rare disease treatments directed toward patients with high short-term mortality and no remaining treatment options cannot ethically randomize patients to palliative care or off-label treatments once potential efficacy is established. These promising, and potentially life-saving innovations rarely have a robust set of data supporting long-term durability of response. We urge PCORI to ensure that its analyses, including consideration of costs and burdens, does not disadvantage breakthrough treatments - existing and yet-to-be-developed - that cannot demonstrate long-term benefits unless a sufficient number of patients can access the therapy upon FDA approval.

Principle #2: PCORI-funded research may consider the full range of outcomes relevant to other stakeholders, when these outcomes have a near-term or longer-term impact on patients.

Haystack appreciates that PCORI seeks to capture the "full range of outcomes to other stakeholders, when these outcomes have a near-term or longer-term impact on patients." We are, however, concerned that there are insufficient details on how PCORI might implement its proposal to incorporate "stakeholders such as payers, employers, health systems, and other decision-makers responsible for designing health plans, formulary decisions, or health system improvements make decisions that have near-term and long-term impacts on patients."

Payer perspectives on costs, for example, can lead to conclusions that approach "willingness to pay" thresholds and reduce benefits and costs to monetary terms that are diametrically opposed to patient-centered perspective on value. The concept that payer coverage of a costly treatment for rare diseases would result in reduced access to care for other patients rests on a vertical



equity paradigm that Haystack views as antithetical to the US health care system. We urge PCORI to ensure that its methodologies reflect our common understanding that the US health system is driven by the concept that an insured individual is covered for medically necessary treatments whether their disease is common and its treatment costs are low, or their disease is rare with one, costly, available treatment. Commercial and public entities are capable of mitigating and responding to risk over time with price changes (for manufacturers) and marginal premium increases, formulary strategies, and other tools (for payers). Patients unable to access potentially life-saving treatments, or parents and caregivers struggling to ensure that their child receives the only therapy with potential to halt disease progression, bear the true consequences of a risk allocation mechanism that puts payer costs at parity with patient burden.

Haystack does, however, expect that there may be unique circumstances where use of a treatment may have a societal or patient cost burden. One recent example of this is in the stockpiling of hydroxychloroquine during the early months of the COVID-19 pandemic. Patients managing conditions such as lupus were informed by their health insurers that the product would no longer be available to them since available supplies were diverted to potential use in COVID-19 patients. We believe that in this instance, PCORI's analysis of relative burdens and economic costs across patient populations and stakeholders may have highlighted important public policy considerations without crossing the line into cost-effectiveness conclusions.

Principle #3: The collection of data on burdens and economic impacts of treatment options must be appropriate and relevant to the clinical aims of the study.

Haystack supports PCORI's proposal to preclude funding for studies for which cost and economic impacts are the primary outcome, and to require that funding applicants engage relevant stakeholders in formulating research questions and study design, including identification of outcomes to be measured. We encourage PCORI to independently reach out to patient and caregiver advocacy organizations, particularly when data on burdens and economic impacts are studied, to ascertain the adequacy of stakeholder engagement, and condition funding on applicant demonstration of a continuing engagement strategy throughout the research study.

Principle #4: Beyond the collection of burden and economic impact data, PCORI may support the conduct of certain types of economic analyses as part of a funded research study, to enhance the relevance and value of this information to health care decision-makers.

Haystack appreciates that PCORI remains committed to the reauthorizing legislation's prohibitions against PCORI conducting cost-effectiveness analyses and/or developing cost-per-quality-adjusted-lifeyear thresholds. We urge PCORI to limit its funded research in rare and ultra-rare diseases to studies that enhance the patient-centered information available to health care decisionmakers.



Haystack Project participants include patients with serious rare and ultra-rare disorders, their caregivers, as well as those who have experienced the life-changing loss of a loved one to a disease for which no treatment exists. We remain concerned that economic analyses intended to **inform** health care decision-makers can all-too-frequently be operationalized and implemented to **drive treatment and reimbursement decisions**. The potential that PCORI's work toward patient-centered outcomes analyses could have unintended consequences is particularly concerning for individuals with rare and ultra-rare diseases and their families. A recent study examining the relationship between disease rarity and treatment cost found, not surprisingly, that the cost of orphan drugs in European markets is inversely proportional to disease prevalence, and another study predicted that price thresholds could slow drug innovation by 23-32 percent with as much as a 60 percent reduction in Research and Development (R&D) on early stage projects.

Finally, we urge PCORI to place patient and caregiver engagement at the center of its funded research, with a goal of achieving a better understanding of the outcomes that are relevant and meaningful to patients. Patient and caregiver stakeholders should be brought into the process early and given sufficient time and opportunities for engagement to devise proactive and meaningful input, including, where relevant, patient-directed, disease-specific survey instruments.

Conclusion

Haystack appreciates that PCORI's proposed principles seek to provide patients and other stakeholders with a more robust base of information on treatments and services, including clinical and economic impacts. We look forward to working with PCORI as it finalizes and implements the principles and begins the next steps of developing methodologies to measure non-clinical outcomes and incorporate these considerations into funded research.

If you have questions or need further information, please do not hesitate to contact me at Jim.Caro@haystackproject.org.

Sincerely,

Jim Caro
Chief Executive Officer