Different uses of the word "benefit" and their definitions:

- Benefit-risk: The process of assessing whether the potential benefits of a drug outweigh the potential risks.
- Benefit-effort: The process of determining the effort required to achieve the desired benefits.
- Benefit-cost: The process of comparing the benefits of a drug to the costs associated with its use.

These uses of the word "benefit" are important in different stages of drug development, from early research to post-market evaluation. It is crucial to consider all potential benefits and risks when making decisions about drug development.

**OPPORTUNITIES TO INTEGRATE PATIENTS’ VOTES**

- **Discovery Stage**
  - Incorporate patient reported outcome measures early
  - Focus on slowing/stopping disease progression
  - Invest in developing early diagnostic and prognostic measures

- **Development Stage**
  - Develop convenient formulations considering patient adherence
  - Include endpoints that matter most
  - Improve accessibility of clinical trials
  - Provide quick and rapid feedback on clinical trials

**Results**

<table>
<thead>
<tr>
<th>GAPS</th>
<th>Discovery Stage</th>
<th>Development Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical trial restrictions</td>
<td>No gold standard for diagnosis</td>
<td>Standard of care only mild/mild symptoms</td>
</tr>
<tr>
<td>Diagnosis is done after symptom manifestation</td>
<td>Age dependent effect</td>
<td>Lack of comprehensive clinical scenario</td>
</tr>
</tbody>
</table>

**Discussion**

Even though drug development in rare diseases is rapidly growing, there is still an unmet need in many aspects of treatment options. The FDA’s initiative to organize PFDD meetings is the first step in the right direction to incorporate patients’ voices in the drug development process. This is a way to find out and develop outcome measures that really matter to the patients and have the most effect on their quality of life. The comparison of PFDD meeting reports and available literature of the reviewed disease states found the gaps indicated in our results section. The FDA has conducted over 25 meetings so far. This initiative could lead to significant changes in benefit-risk assessments and drug development. This is a great opportunity for companies to invest in the process of collecting and implementing patients’ needs into their early phases of drug development. The timeline represents the current drug development process, and important milestones that can benefit from incorporating patients’ perspectives.

**Limitations**

Although 3 PFDD meetings were analyzed, the FDA has conducted over 25 meetings to gather patient perspective on various disease states. Due to the demographic of each meeting being limited to patients and/or family members or caregivers affected by the disease in question, participation has may be observed. The PFDD meetings were used as the sole marker of patient voice in our analysis, and other methods could be used to determine patient perspective. We also extrapolated the findings of patients to potential clinical trials endpoints of disease states other than those already reviewed.

**Conclusion**

With the redetermination of PDUFA, the FDA will be considering patient voice in the benefit-risk assessment process and drug development. Currently, gaps exist between research and patient needs due to clinical trial endpoints considering symptoms and function, however we need to consider activities of daily living and quality of life related endpoints. PFDD meetings aim to fill this gap between current research and patient needs, however they are a platform for patients and caregivers to express their viewpoints on the disease directly to the FDA. Barriers exist in the adoption of patient centered value measures due to the perception lack of scientifically validated methods to quantify patient preferences. However, this study highlights the incorporation of both qualitative and quantitative patient reported outcome endpoints in the early stages of clinical trials, the trajectory of drug development can be impacted.