BACKGROUND
Patient reported outcomes (PROs) are an accepted and often actively solicited source of evidence used by health authorities and payers in evaluating and approving pharmaceutical interventions in addition to demonstration of the efficacy and safety of the intervention. There is, however, limited information on how payers value PRO data in reimbursement decisions. The clinical evidence section of value dossiers often includes PRO data while health related quality of life (HRQoL) data is often incorporated into cost effectiveness analyses of economic models. A multitude of endpoints and variation in how payers in different countries assess evidence makes it difficult to understand the value of PRO data in reimbursement decisions.

An assessment was undertaken to gauge the current and future impact of PRO data on health care decision making in centralized markets, specifically in the oncology therapeutic area.

OBJECTIVE
To determine the impact of PRO data from clinical trial programs on market access decision making in oncology and other disease areas in centralized markets.

METHODS
Public MEDLINE, Embase, ISPOR databases, and regulatory and health technology assessment (HTA) websites for the EMA, the UK, France, and Germany were searched to identify PRO data included in regulatory and HTA submissions of oncology products. Comparator trial data and real world clinical experience were also reviewed. A total of 77 surveys (Australia and South Korea) by payers from the RTI Health Solutions Global Payer Advisory Panel.

The profiles of the payers and payer advisors interviewed are listed in Table 1. All ten respondents were professors of health economics.

Table 1: Payer Profiles

<table>
<thead>
<tr>
<th>Country</th>
<th>Advisor Payer Profile</th>
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<tbody>
<tr>
<td>Australia</td>
<td>Advisor to Medical Services Advisory Committee (MEAC) and</td>
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<td></td>
<td>Regulatory Authority Committee (MAC)</td>
</tr>
<tr>
<td>France</td>
<td>Advisor to Haut Autorité de Santé (HAS)</td>
</tr>
<tr>
<td>Germany</td>
<td>Member of the arbitration board for drug process in the statutory health insurance (i.e. sickness funds)</td>
</tr>
<tr>
<td>Korea</td>
<td>Advisor to Health Insurance Review and Assessment (HIRA)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Advisor to Zorginstituut Nederland (ZINL, formerly CVZ)</td>
</tr>
<tr>
<td>Poland</td>
<td>Advisor to Agency for Technological Medycyna (ATMM)</td>
</tr>
<tr>
<td>Sweden</td>
<td>Advisor to Therapeutics – svenkonsumentforeningen (TSF)</td>
</tr>
<tr>
<td>Taiwan</td>
<td>HTA advisor</td>
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<tr>
<td>Turkey</td>
<td>Advisor to public and private insurance providers</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Advisor to the National Institute for Health and Care Excellence (NICE)</td>
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RESULTS
When asked “what the role of PRO data in market access decision making is,” respondents indicated:

- It's important when assessing therapy
- It is a plus for the review process
- It is accepted for reimbursement
- It is a PRO measure or a clinical input

"PRO measures have a minor role in overall HTA (Health Technology Assessment) and market decision process. It is an additional information that we would like to see for incremental benefit. The most important dimensions are the severity of the condition (for oncology, it is not a problem), efficacy, safety and then other dimensions such as cost needs, mode of administration, mode of action and then the most important thing is in the future we expect that the HTAs will gain more importance." - France

"PROs are included in the reimbursement decision. In HE [Health Evaluation] (cost per QALY), there is willingness to accept new diseases, hence need QOL data for this. In some cases, companies have also used PRO data for other endpoints such as efficacy. Somewhere, the HTA will be based on the clinical data. Limited evidence of PROs in oncology outcomes." - Germany

"Continue to use for new drugs as a new tool to assess disease-specific measures to confirm and support evidence and direction of measures of utility, but they are subsidiary." - United Kingdom

"The key role of PROs is getting to the key bit of QALYs which is quality of life in terms of measurements of utility. They add also to new symptoms of disease specific measures to confirm and support evidence and direction of measures of quality of life, but they are subsidiary." - Sweden

When asked to rate the level of importance given to PRO data for market access of new oncology treatments:

- on a scale of 1 to 7 where 1 means ‘not important’ and 7 means ‘extremely important’, the average rating was 4.5 (Figure 1)

Figure 1: Rating of the level of importance given to PRO data

Payer's advice for pharmaceutical manufacturers with respect to communicating PRO evidence to decision makers:

- "Payers should only be used to support and to translate what we have from the patients' (clinical) benefits of the treatment. If you don't have an effective drug, forget PROs." - France
- "If the PRO analysis is made in a different culture, you cannot translate the results to another culture easily…if you are talking about caregiver burden, it’s quite different in different cultures." - Turkey

CONCLUSIONS
When asked to describe the specific characteristics that a PRO endpoint for treatment in oncology should have, respondents listed the following:

- Validated, objective, reliable measures that encompass a broad range of effects and symptoms and are relevant to all patients receiving treatment
- Statistical significance and clinical relevance; should produce QALY weights and translate to utilities

Respondents indicated that PRO data is more useful in the evaluation of chronic or palliative therapy options and that overall the importance of PRO data will increase in the future:

- Overall, the respondents indicated that PRO data had measured well in clinical trials of oncology therapies.
- PRO data should optimally be collected in Phase 3 and post-marketing trial data with emphasis on comparator trial data and real world clinical experience.
- PRO data are very important, especially in the advanced metastatic stage of chronic diseases.
- There were minimal differences in the usefulness of PRO measures by cancer indication.
- Assessment of symptoms and health-related QoL were consistently ranked as the PRO measures with greatest value (Figure 2).
- PRO data has the greatest impact at the local level where positive data could impact uptake, reimbursement, and market share.

Figure 2: Rating of the Value of PRO data by Type

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Respondents indicated that PRO data is more useful in the evaluation of chronic or palliative therapy options and that overall the importance of PRO data will increase in the future:

- "PRO is new for Taiwan. There is not a strong requirement yet, but in the future, it is a PRO measure or a clinical input." - Taiwan
- "It is a plus for the review process…" - Poland
- "[PROs] have a minor role in overall HTA (Health Technology Assessment) and market decision process. It is an additional information that we would like to see for incremental benefit. The most important dimensions are the severity of the condition (for oncology, it is not a problem), efficacy, safety and then other dimensions such as cost needs, mode of administration, mode of action and then the most important thing is in the future we expect that the HTAs will gain more importance." - France

"Payers are not used to PRO data and they need to be educated." - Netherlands

"Adoption by the US and Europe is key...if information is available from FDA or EMA then we trust it more..." - Australia

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