INTRODUCTION

- Companion diagnostics – critical building blocks in personalized medicine - straitly subgroups of patients by likelihood of response to or safety of a specific pharmaceutical therapy.¹
- Considering the clinical utility of a drug and a companion diagnostic in a subpopulation of interest, drug reimbursement would imply diagnostic reimbursement.²
- However, even in cases of co-developed combinations drug reimbursed was not accompanied by a diagnostic reimbursement.³
- Currently, the most pressing challenges in the reimbursement system included obtaining affirmative coverage, appropriate coding, and value-based payment for novel diagnostics.⁴
- A number of companion diagnostic tools are commercially available for breast cancer. Here, we review and analyze the insurance coverage policies for companion diagnostics in breast cancer.

OBJECTIVE

- To review the insurance coverage policies for genomic tests in breast cancer, the evidence basis for these decisions, and the extent of coverage.

METHODS

- The US Food and Drug Administration (FDA) website⁵ was searched to identify the list of cleared or approved companion diagnostic devices in US.
- An online search was performed (August 2014) to identify the coverage policies for genomic tests by the leading private insurers in US.²
- Ten private insurers were selected: Kaiser, Coventry Corporation, UnitedHealthcare, Independence Blue Cross, Aetna, Highmark, Humana, WellPoint/Anthem, HCSC, and Cigna Health.
- ‘Gene,¹‘DNA,’ ‘Mutation,’ ‘Genomic,’ and ‘Breast Cancer’ were used as search terms for genomic policies.
- Each coverage policy was reviewed to identify the specific test, evidences considered (if provided) and the policy decision.
- We also reviewed whether the test was cleared or approved by FDA.
- Data were analyzed descriptively.

RESULTS

- A total of 14 products has been cleared or approved by US FDA as companion diagnostic tools; these include 10 different HER2 tests, ProSigna®, Mammaprint®, GeneSearch®, and Dako TOP2A.
- Among all policies identified, overall 7 unique tests were discussed for diagnosis, prognosis and risk assessment of breast cancer (Table 1). Of these, only 3 were cleared or approved by FDA, while 4 others were identified from the policies.²
- Majority of these diagnostic tests (6/7) were indicated for measuring the recurrence risk of breast cancer.
- Of the 7 tests discussed, Oncotype DX® and Mammaprint® were the only two tests that are reimbursed by various private insurers.

Table 1: Summary of coverage policies for disease-related genomic tests by insurers

<table>
<thead>
<tr>
<th>Test</th>
<th>FDA approval</th>
<th>Clinical guidelines</th>
<th>Reimbursement</th>
<th>Key clinical studies</th>
<th>Clinic sensitivity</th>
<th>Decision made by insurer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncotype DX</td>
<td>BC recurrence risk</td>
<td>No</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>Mammaprint</td>
<td>BC recurrence risk</td>
<td>Yes</td>
<td>C</td>
<td>C</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>Mammastrat</td>
<td>BC recurrence risk</td>
<td>No</td>
<td>C</td>
<td>C</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Prosigna</td>
<td>BC recurrence risk</td>
<td>Yes</td>
<td>NF</td>
<td>NF</td>
<td>NF</td>
<td>C</td>
</tr>
<tr>
<td>Signature</td>
<td>Gene recurrence risk</td>
<td>Yes</td>
<td>NF</td>
<td>NF</td>
<td>NF</td>
<td>C</td>
</tr>
<tr>
<td>THEROS</td>
<td>BC recurrence risk</td>
<td>No</td>
<td>NF</td>
<td>C</td>
<td>NF</td>
<td>NF</td>
</tr>
<tr>
<td>Rotterdam</td>
<td>76-Gene</td>
<td>BC recurrence risk</td>
<td>No</td>
<td>NF</td>
<td>NF</td>
<td>NF</td>
</tr>
</tbody>
</table>

DISCUSSION

- The coverage for disease-related genomic testing is low, mainly due to the lack of adequate clinical evidence.
- A variation in coverage was evident among insurers, as some of the insurers are willing to reimburse despite limited clinical evidence.
- Acceptance by oncologists seems to be important for insurers. For example, Oncotype DX® is not approved by FDA, but is favored for reimbursement by all insurers as it was adopted widely by the oncologists based on its clinical utility.
- Challenges in the current reimbursement system³
  - No policy assessed cost-effectiveness
  - Lack of transparency
  - Variability across payers
  - Traditional coding system limits sponsors from value-based reimbursement
- Possible solutions: To secure a sufficient and predictable reimbursement for companion diagnostics, the payers need to:
  - Assess high-level clinical and economic evidence
  - Develop innovative pricing and access strategies to mitigate reimbursement deficiencies
  - Develop efficient coding system

CONCLUSION

- The insurers should use an imperative approach to develop coverage policies for novel diagnostics considering clinical utility, economic value, and other health care system factors.
- Additional studies on variability among coverage policies for cutting-edge technologies such as personalized medicine is warranted.
- Since recent FDA guidance recommended contemporaneous⁶ approval of companion diagnostics and its corresponding therapeutic product, sponsors are likely to intensely innovation in this domain

REFERENCES