**Appendices**

**Appendix A: PRISMA flow diagram for literature search.**



**Appendix B:** **List of experts contacted for interview**

|  |  |  |
| --- | --- | --- |
|  | **Country**  | **Type** |
| 1 | England | Former public payer |
| 2 | England | Former public payer |
| 3 | England | Former public payer |
| 4 | England | Former public payer |
| 5 | England | Former public payer |
| 6 | England | Therapeutic Area Expert |
| 7 | England | Health economics and HTA expert |
| 8 | England | Therapeutic Area Expert |
| 9 | Canada | Health economics and HTA expert |
| 10 | Canada | Former public payer |
| 11 | Canada | Former public payer |
| 12 | Canada | Health economics and HTA expert |
| 13 | Canada | Former public payer |
| 14 | Canada | Therapeutic Area Expert |
| 15 | Canada | Therapeutic Area Expert |
| 16 | New Zealand | Former public payer |
| 17 | New Zealand | Former public payer |
| 18 | Australia | Health economics and HTA expert |
| 19 | Australia | Therapeutic Area Expert |
| 20 | Australia | Health economics and HTA experts |

**Appendix C: Expert interview guide**

**Research plan**

This discussion guide is designed for interviews with payers, policymakers and patient groups in Australia, Canada, England, Ireland, New Zealand

Interviews will be scheduled for up to one hour and will be led by a member of the project team. The outcomes of this interview will be reported only in an anonymous form.

**Introduction for participants**

The purpose of this interview is to support an analysis of the challenges in conducting value assessment for broad molecular profiling and broad panel gene testing.

The discussion, which will last around 60 minutes, is structured around four broad topics:

1. **The benefits of broad molecular profiling and broad panel gene testing**
2. **Current process for value assessment and funding of diagnostics in your country and the associated challenges**
3. **Your perceptions of future policy changes and impact in your country**

This analysis is part of a project that Charles River Associates have been commissioned to complete on behalf of a pharmaceutical company. Your input into this project will be used to inform the eventual outcomes of the analysis, but we will not report your comments directly or in any attributable form.

This document is intended only as a guide to the discussion and we may structure the discussion differently, leave questions out or go into more detail in some areas, depending on your response. The flow of the discussion may change throughout the course of the research as the project team reviews outcomes of the interviews and reflects on the insights gained.

Before we begin, we would like your permission to record the discussion for analysis purposes; this data will be used only by CRA for note-taking and will not be shared with any third parties.

**Section 1: Understanding the benefits of broad molecular profiling and broad panel gene testing**

1. To begin with, could you give a quick overview of your role and your experience related to diagnostics?
	1. Have you been involved in the assessment or funding process for diagnostics in the past?
2. What do you understand to be the main differences in benefits across more targeted diagnostics tests, compared to broad molecular profiling? What are the key differences between:
	1. Diagnostics associated with a particular product (companion diagnostics)?
	2. Diagnostics associated with a class of products (complementary diagnostics)?
	3. Diagnostic tests associated with a set of genes (small panel testing through NGS)?
	4. Broader molecular profiling through broad panel gene testing?
3. How would you characterise the clinical impact of broad molecular profiling on patient:

Probe:

* More treatment options for patients?
* Faster diagnosis and getting patients on the best treatment more quickly?
* Help prescriber guide decision-making? Shifting treatment away from trial-and-error prescribing?
* Direct patients to better-suited therapies and reduce adverse events?
1. How would you characterise the impact of broad molecular profiling on care delivery and healthcare system?
	1. Is there any clinical utility to be gained from the value of ‘knowing,’ to help support patient’s decisions and lead to spill-over effects?
2. How would you characterise the broader societal impact of broad molecular profiling?
	1. To what extent do you think it is valuable (as a payer) that broad panel gene testing can facilitate clinical trial enrolment and supports future research and development?
3. To what extent do you feel that these benefits are accounted for from a payer perspective?

**Section 2: Current process for funding of diagnostics and conducting value assessment**

In your experience, is access to broad molecular testing and broad panel gene testing a challenge in your market?

* 1. What is the reason for this access challenge? (e.g. lack of awareness, lack of funding, lack of regulatory approval)

How are other diagnostics services funded?

* 1. Other diagnostics tools such magnetic resonance imaging (MRI) and how the cost of these are allocated and share if they are used in diagnosis
	2. The cost of specialists (e.g. pathologists and geneticists)
1. What are the current funding mechanisms in place for broad molecular profiling compared to companion diagnostics?

When considering the impact of broad molecular profiling on care delivery, how are decisions made in your country regarding which patients would receive this diagnostic intervention?

Who should pay for broad panel genomics testing, and how do HTA bodies take into this into account in value assessment over time?

How can specific patients be targeted to use broad molecular proofing who are most likely to benefit from its application?

What are the current differences in the value assessment process between different types of diagnostics?

* 1. Diagnostics associated with a particular product (companion diagnostics)?
	2. Diagnostics associated with a class of products (complementary diagnostics)?
	3. Diagnostic tests associated with a set of genes (small panel testing through NGS)?
	4. Broader molecular profiling and broad panel gene testing?

To what extent is broad panel gene testing integrated with the assessment of associated therapies or assessed individually

* 1. If there is a co-dependent HTA system in the valuation of a drug and diagnostic test? What happens when the diagnostic is not linked to a specific drug?
	2. Do you see the approach of “one test, one patient, one drug” as sustainable going forward?
	3. How do you address the emergence of tumour-agnostic label, i.e. moving away from a one test per one drug situation?

What are the evidence requirements for assessing broad molecular profiling?

* 1. Does this need to include the full testing cost in evaluations.

What do you see as the main challenges in assessing the value broad molecular profiling? How do you expect that these challenges will be dealt with?

* 1. Does the use of cost-effectiveness analysis represent a challenge?
	2. How do you deal with follow on drugs that use the same biomarker, and which will not have the test included in the cost/benefit analysis?

Are there any learnings from the value assessment and funding mechanisms for other high cost diagnostic techniques that could support future access?

* + 1. Probe on current assessment and funding mechanisms for MRI machines

**Section 3: Your perceptions of future policy changes and impact in your country**

How do you see the genomics landscape evolving in your country?

1. Is there a need for a strategy of focusing on the use of companion diagnostics, narrow panels to broad testing?

Thinking broadly about your country and the adoption of novel diagnostics, would you say that your country is a *leader* in diagnostics adoption, *about the same* as most other markets, or *lagging behind* other countries?

What are the most significant barriers to accessing broad molecular profiling in your country?

***Leave respondent answer unaided and then probe on those specific points:***

* Ability to pay for / affordability - Price? lack of funding?
* Infrastructure – availability of technologies and testing systems
* Lack of adoption (i.e. majority of physicians do not consider it relevant / needed),
* Challenging interpretation of the results (i.e. high amount of information, lack of comprehensive database for “variants of uncertain significance”),
* Reliability (absence of standard operating procedures, end-to-end sample tracking)
* Absence of clear guidelines (i.e. which test to use and at what stage of the disease?)
* Capacity (i.e. limited number of diagnostic centres)
* Others?

What, for you, are critical success factors or the most important drivers of uptake of broad molecular profiling and broad panel gene testing in your country in the future?

***Leave respondent answer unaided and then probe on those specific points:***

* Infrastructure (e.g. availability of testing platforms, quality of available tests, shared services across hospitals, public / private laboratories, data platforms)?
* Policy and guidelines (such as national plans to promote NGS)?
* Funding (reimbursement) for diagnostic tests?
* Greater stakeholder awareness of the importance of broad panel gene testing?
* Better regulatory pathways and approval?

Are there specific changes to policy impacting broad molecular profiling that are underway or under consideration in your country?

* 1. In terms of priority/guidelines?
	2. In terms of assessment/evaluation?
	3. In terms of funding/access?
	4. What is stopping deciding on this strategy?

Before we finish the interview, is there anything else that you would like to raise in relation to anything that we have discussed today?

[CLOSE AND THANK RESPONDENT]

**Appendix D: Full reference list**

1. Ali, S. M., Hensing, T., Schrock, A. B., Allen, J., Sanford, E., Gowen, K., ... & Elvin, J. A. (2016). Comprehensive genomic profiling identifies a subset of crizotinib-responsive ALK-rearranged non-small cell lung cancer not detected by fluorescence in situ hybridization. The oncologist, 21(6), 762.
2. Anhorn, R., Roberts, G., Skovhus, M., & Khorshid, M. (2017). Impact of Comprehensive Genomic Profiling of Patients With First Line Non-Small Cell Lung Cancer In The UK. Value in Health, 20(9), A575.
3. Boccia, S., Mc Kee, M., Adany, R., Boffetta, P., Burton, H., Cambon-Thomsen, A., ... & Khoury, M. J. (2014). Beyond public health genomics: proposals from an international working group. The European Journal of Public Health, 24(6), 877-879.
4. Broad, Hybrid Capture-Based Next-Generation Sequencing Identifies Actionable Genomic Alterations in Lung Adenocarcinomas Otherwise Negative for Such Alterations by Other Genomic Testing Approaches. Clin Cancer Res. 2015 Aug 15;21(16):3631-9.
5. Burns, B. L., Bilkey, G. A., Coles, E. P., Bowman, F. L., Beilby, J. P., Pachter, N. S., … Nowak, K. J. (2019). Healthcare System Priorities for Successful Integration of Genomics: An Australian Focus. Frontiers in public health, 7, 41. doi:10.3389/fpubh.2019.00041
6. Burstein, M. D., Tsimelzon, A., Poage, G. M., Covington, K. R., Contreras, A., Fuqua, S. A., ... & Brown, P. H. (2015). Comprehensive genomic analysis identifies novel subtypes and targets of triple-negative breast cancer. Clinical Cancer Research, 21(7), 1688-1698.
7. CADTH (2019). Guidelines for the Economic Evaluation of Health Technologies: Canada, 4th Edition. Appendix - Specific Guidance for treatments with companion diagnostics. Ottawa.
8. CADTH Conference, 25 April 2017. “Assessing the value of diagnostic innovation: A growing role for HTA?” Available at: https://www.cadth.ca/sites/default/files/symp-2017/presentations/april25-2017/Concurrent-Session-E1-Assessing-the-Value-of-Diagnostic-Innovation-A-Growing-Role-for-Health-Technology-Assessment.pdf
9. Chalmers, Z. R., Connelly, C. F., Fabrizio, D., Gay, L., Ali, S. M., Ennis, R., ... & Huang, F. (2017). Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden. Genome medicine, 9(1), 34.
10. Chawla, A., Janku, F., Wheler, J. J., Miller, V. A., Ryan, J., Anhorn, R., ... & Signorovitch, J. (2018). Estimated cost of anticancer therapy directed by comprehensive genomic profiling in a single-center study. JCO Precision Oncology, 2, 1-11.
11. Clarke, G. M., Conti, S., Wolters, A. T., & Steventon, A. (2019). Evaluating the impact of healthcare interventions using routine data. bmj, 365, l2239.
12. Clinical applicability and cost of a 46-gene panel for genomic analysis of solid tumours: Retrospective validation and prospective audit in the UK National Health Service. PLoS Med. 2017 Feb 14;14(2):e1002230. doi: 10.1371/journal.pmed.1002230. eCollection 2017 Feb
13. Concepts of 'personalization' in personalized medicine: implications for economic evaluation. Pharmacoeconomics. 2015 Jan;33(1):49-59. doi: 10.1007/s40273-014-0211-5.
14. Drilon, A., Wang, L., Arcila, M. E., Balasubramanian, S., Greenbowe, J. R., Ross, J. S., ... & Ladanyi, M. (2015). Broad, hybrid capture–based next-generation sequencing identifies actionable genomic alterations in lung adenocarcinomas otherwise negative for such alterations by other genomic testing approaches. Clinical cancer research, 21(16), 3631-3639.
15. Dugger, S. A., Platt, A., & Goldstein, D. B. (2018). Drug development in the era of precision medicine. Nature Reviews Drug Discovery, 17(3), 183.
16. Eric Falkner et al. (2020) Being Precise About Precision Medicine: What Should Value Frameworks - Incorporate to Address Precision Medicine? A Report of the Personalized Precision Medicine Special Interest Group VALUE HEALTH. 2020; 23(5):529–539
17. Eric Falkner et al. Being Precise About Precision Medicine: What Should Value Frameworks Incorporate to Address Precision Medicine? A Report of the Personalized Precision Medicine Special Interest Group VALUE HEALTH. 2020; 23(5):529–539
18. Faulkner, E., Holtorf, A. P., Walton, S., Liu, C. Y., Lin, H., Biltaj, E., ... & Siebert, U. (2020). Being precise about precision medicine: what should value frameworks incorporate to address precision medicine? A report of the Personalized Precision Medicine Special Interest Group. Value in Health.
19. Garrison, L., Mestre-Ferrandiz, J., & Zamora, B. (2016). The value of knowing and knowing the value: improving the health technology assessment of complementary diagnostics. White paper. London: Office of Health Economics, EPEMED.
20. Gavan, S. P., Lu, C. Y., & Payne, K. (2019). Assessing the Joint Value of Genomic-Based Diagnostic Tests and Gene Therapies. Journal of personalized medicine, 9(2), 28. doi:10.3390/jpm9020028
21. George, J., Lim, J. S., Jang, S. J., Cun, Y., Ozretić, L., Kong, G., ... & Thomas, R. K. (2015). Comprehensive genomic profiles of small cell lung cancer. Nature, 524(7563), 47-53.
22. Ginsburg, G. S., & Phillips, K. A. (2018). Precision Medicine: From Science To Value. Health affairs (Project Hope), 37(5), 694–701. doi:10.1377/hlthaff.2017.1624
23. Gong, J., Pan, K., Fakih, M., Pal, S., & Salgia, R. (2018). Value-based genomics. Oncotarget, 9(21), 15792.
24. Hainsworth, J. D., Meric-Bernstam, F., Swanton, C., Hurwitz, H., Spigel, D. R., Sweeney, C., ... & Beattie, M. (2018). Targeted therapy for advanced solid tumors on the basis of molecular profiles: results from MyPathway, an open-label, phase IIa multiple basket study. Journal of Clinical Oncology, 36(6), 536-544.
25. Haslem, D. S., Chakravarty, I., Fulde, G., Gilbert, H., Tudor, B. P., Lin, K., ... & Nadauld, L. D. (2018). Precision oncology in advanced cancer patients improves overall survival with lower weekly healthcare costs. Oncotarget, 9(15), 12316.
26. Hatz, M. H., Schremser, K. and Rogowski, W. H. (2014). Is individualized medicine more cost-effective? A systematic review. Pharmacoeconomics, 32(5): 443-455.
27. Hollebecque, A., Silverman, I., Owens, S., Féliz, L., Lihou, C., Zhen, H., ... & Melisi, D. (2019). Comprehensive genomic profiling and clinical outcomes in patients (pts) with fibroblast growth factor receptor rearrangement-positive (FGFR2+) cholangiocarcinoma (CCA) treated with pemigatinib in the fight-202 trial. Annals of Oncology, 30, v276.
28. Hyman, D. M., Taylor, B. S., & Baselga, J. (2017). Implementing genome-driven oncology. Cell, 168(4), 584-599.
29. Impact of a Biomarker-Based Strategy on Oncology Drug Development: A Meta-analysis of Clinical Trials Leading to FDA Approval. J Natl Cancer Inst. 2015 Sep 15;107(11). pii: djv253. doi: 10.1093/jnci/djv253. Print 2015 Nov.
30. Implementing Genome-Driven Oncology. Cell. 2017 Feb 9;168(4):584-599. doi: 10.1016/j.cell.2016.12.015.
31. Jakka, S., & Rossbach, M. (2013). An economic perspective on personalized medicine. The HUGO journal, 7(1), 1-6.
32. Johnston, K. M., Sheffield, B. S., Yip, S., Lakzadeh, P., Qian, C., & Nam, J. (2020). Costs of in-house genomic profiling and implications for economic evaluation: A case example of non-small cell lung cancer (NSCLC). Journal of medical economics, (just-accepted), 1-1.
33. Kang, H., Pettinga, D., Schubert, A. D., Ladenson, P. W., Ball, D. W., Chung, J. H., ... & Ali, S. M. (2019). Genomic profiling of parathyroid carcinoma reveals genomic alterations suggesting benefit from therapy. The oncologist, 24(6), 791.
34. Kathryn A. Philips (2020) Methods for Moving the Evaluation of Precision Medicine Into Practice and Policy. VALUE HEALTH. 2020; 23(5):527–528
35. Keltie, K., Bousfield, D. R., Cole, H., & Sims, A. J. (2016). Medical Technologies Evaluation Programme: A review of NICE progression decisions, 2010–2013. Health Policy and Technology, 5(3), 243-250.
36. Kohler, J. N., Turbitt, E., & Biesecker, B. B. (2017). Personal utility in genomic testing: a systematic literature review. European Journal of Human Genetics, 25(6), 662.
37. Lakdawalla, D.N., Doshi, J.A., Garrison Jr, L.P., Phelps, C.E., Basu, A. and Danzon, P.M., 2018. Defining elements of value in health care—a health economics approach: an ISPOR Special Task Force report [3]. Value in Health, 21(2), pp.131-139.
38. Le, D. T., Durham, J. N., Smith, K. N., Wang, H., Bartlett, B. R., Aulakh, L. K., ... & Wong, F. (2017). Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. Science, 357(6349), 409-413.
39. Marshall, D. A., Gonzalez, J. M., MacDonald, K. V., & Johnson, F. R. (2017). Estimating Preferences for Complex Health Technologies: Lessons Learned and Implications for Personalized Medicine. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research, 20(1), 32–39. doi:10.1016/j.jval.2016.08.737
40. McKenzie, A. J., H. Dilks, H., Jones, S. F., & Burris III, H. (2019). Should next-generation sequencing tests be performed on all cancer patients?. Expert review of molecular diagnostics, 19(2), 89-93.
41. Medicines Australia (2018). Proposal for the regulation of IVD diagnostics. Available at: https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2018/12/20181214-TGA-consultation-Proposal-for-the-regulation-of-IVD-CDx-MA-submisssion.pdf
42. Merlin, T., Farah, C., Schubert, C., Mitchell, A., Hiller, J. E., & Ryan, P. (2013). Assessing personalized medicines in Australia: a national framework for reviewing co-dependent technologies. Medical Decision Making, 33(3), 333-342.
43. Morash M et. All The Role of Next-Generation Sequencing in Precision Medicine: A Review of Outcomes in Oncology. J Pers Med. 2018 Sep; 8(3): 30
44. Mosele, F., Remon, J., Mateo, J., Westphalen, C. B., Barlesi, F., Lolkema, M. P., Normanno, N., Scarpa, A., Robson, M., Meric-Bernstam, F., Wagle, N., Stenzinger, A., Bonastre, J., Bayle, A., Michiels, S., Bièche, I., Rouleau, E., Jezdic, S., Douillard, J. Y., Reis-Filho, J. S., … André, F. (2020). Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group. Annals of oncology : official journal of the European Society for Medical Oncology, 31(11), 1491–1505. https://doi.org/10.1016/j.annonc.2020.07.014
45. MSAC (2021). Guidelines for preparing assessments for the Medical Services Advisory Committee, Version 1.0 May 2021. D. o. Health.
46. National Institute for health and care excellence (2020) - Final appraisal document Entrectinib for treating NTRK fusion-positive solid tumours - June 2020 – accessible at https://www.nice.org.uk/guidance/gid-ta10414/documents/final-appraisal-determination-document
47. National Institute for health and care excellence (2020) - Final appraisal document - Larotrectinib for treating NTRK fusion-positive solid tumours- April 2020 – accessible at: https://www.nice.org.uk/guidance/ta630/documents/final-appraisal-determination-document
48. Nesline MK et al. Oncotarget 2019; 10: 4616–4629
49. Next-Generation Sequencing in Oncology: Genetic Diagnosis, Risk Prediction and Cancer Classification. Int J Mol Sci. 2017 Feb; 18(2): 308.
50. NICE (2014). Developing NICE guidelines: the manual. N. I. f. H. C. Excellence.
51. OECD (2017), Tackling Wasteful Spending on Health, OECD Publishing, Paris. oe.cd/tackling-wasteful-spending-on-health
52. Pennell, N. A., Mutebi, A., Zhou, Z. Y., Ricculli, M. L., Tang, W., Wang, H., ... & Wu, K. Y. (2019). Economic impact of next-generation sequencing versus single-gene testing to detect genomic alterations in metastatic non–small-cell lung cancer using a decision analytic model. JCO Precision Oncology, 3, 1.
53. Personalized Medicine Coalition (2018). Personalized Medicine and Value Assessment Frameworks: Context, Considerations, and Next Steps. PMC website http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM\_and\_VAFs.pdf accessed January 2021
54. PHARMAC (2015). Guidelines for Funding Applications to PHARRMAC. P. M. Agency.
55. Plumpton, C. O., Pirmohamed, M., & Hughes, D. A. (2019). Cost‐Effectiveness of Panel Tests for Multiple Pharmacogenes Associated With Adverse Drug Reactions: An Evaluation Framework. Clinical Pharmacology & Therapeutics, 105(6), 1429-1438.
56. Phillips, K. A., Sakowski, J. A., Trosman, J., Douglas, M. P., Liang, S. Y., & Neumann, P. (2014). The economic value of personalized medicine tests: what we know and what we need to know. Genetics in medicine, 16(3), 251-257.
57. Phillips, K. A., Deverka, P. A., Marshall, D. A., Wordsworth, S., Regier, D. A., Christensen, K. D., & Buchanan, J. (2018). Methodological issues in assessing the economic value of next-generation sequencing tests: many challenges and not enough solutions. Value in Health, 21(9), 1033-1042.
58. Precision oncology in advanced cancer patients improves overall survival with lower weekly healthcare costs. Oncotarget. 2018 Feb 2;9(15):12316-12322. doi: 10.18632/oncotarget.24384. eCollection 2018 Feb 23.
59. Precision oncology in advanced cancer patients improves overall survival with lower weekly healthcare costs. Haslem DS et al. [Oncotarget.](https://www.ncbi.nlm.nih.gov/pubmed/29552312) 2018 Feb 2;9(15):12316-12322
60. Rare cancers: Challenges & issues. Indian J Med Res. 2017 Jan; 145(1): 17–27.
61. RAS and BRAF in metastatic colorectal cancer management. J Gastrointest Oncol. 2016 Oct;7(5):687-704.
62. Regier, D. A., Weymann, D., Buchanan, J., Marshall, D. A., & Wordsworth, S. (2018). Valuation of health and nonhealth outcomes from next-generation sequencing: approaches, challenges, and solutions. Value in Health, 21(9), 1043-1047.
63. Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices repeals Directive 98/79/EC and Commission Decision 2010/227/EU on in vitro diagnostic medical devices
64. Reitsma, M., Fox, J., Borre, P. V., Cavanaugh, M., Chudnovsky, Y., Erlich, R. L., ... & Anhorn, R. (2019). Effect of a Collaboration Between a Health Plan, Oncology Practice, and Comprehensive Genomic Profiling Company from the Payer Perspective. Journal of managed care & specialty pharmacy, 25(5), 601-611.
65. Routine molecular profiling of patients with advanced non-small-cell lung cancer: results of a 1-year nationwide programme of the French Cooperative Thoracic Intergroup (IFCT). Lancet. 2016 Apr 2;387(10026):1415-1426. doi: 10.1016/S0140-6736(16)00004-0. Epub 2016 Jan 15.
66. Samstein, R. M., Lee, C. H., Shoushtari, A. N., Hellmann, M. D., Shen, R., Janjigian, Y. Y., ... & Kaley, T. J. (2019). Tumor mutational load predicts survival after immunotherapy across multiple cancer types. Nature genetics, 51(2), 202-206.
67. Sarcoma: concordance between initial diagnosis and centralized expert review in a population-based study within three European regions. Ann Oncol. 2012 Sep; 23(9): 2442–2449.
68. Schrock, A. B., Frampton, G. M., Herndon, D., Greenbowe, J. R., Wang, K., Lipson, D., ... & Wollner, M. (2016). Comprehensive genomic profiling identifies frequent drug-sensitive EGFR exon 19 deletions in NSCLC not identified by prior molecular testing. Clinical Cancer Research, 22(13), 3281-3285.
69. Schwarze, K., Buchanan, J., Taylor, J. C., & Wordsworth, S. (2018). Are whole-exome and whole-genome sequencing approaches cost-effective? A systematic review of the literature. Genetics in Medicine, 20(10), 1122-1130.
70. Signorovitch, J., Janku, F., Wheler, J. J., Miller, V. A., Ryan, J., Zhou, Z., & Chawla, A. (2017). Estimated cost of anticancer therapy directed by comprehensive genomic profiling (CGP) in a single-center study.
71. Signorovitch, J., Zhou, Z., Ryan, J., Anhorn, R., & Chawla, A. (2019). Budget impact analysis of comprehensive genomic profiling in patients with advanced non-small cell lung cancer. Journal of medical economics, 22(2), 140-150.
72. Table of Pharmacogenomic Biomarkers in Drug Labeling. Available at: https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling. (Accessed October 2019)
73. TGA. (2020). "IVD companion diagnostics: Guidance on regulatory requirements." Retrieved 28/10/2021, 2021, from https://www.tga.gov.au/publication/ivd-companion-diagnostics.
74. The Value of Knowing and Knowing the Value: Improving the Health Technology Assessment of Complementary Diagnostics. Available at: https://www.ohe.org/sites/default/files/WP\_EpemedOHE\_final.pdf
75. Trabucco, S. E., Gowen, K., Maund, S. L., Sanford, E., Fabrizio, D. A., Hall, M. J., ... & Hegde, P. S. (2019). A Novel Next-Generation Sequencing Approach to Detecting Microsatellite Instability and Pan-Tumor Characterization of 1000 Microsatellite Instability–High Cases in 67,000 Patient Samples. The Journal of Molecular Diagnostics, 21(6), 1053-1066.
76. Trosman, J. R., Weldon, C. B., Gradishar, W. J., Benson III, A. B., Cristofanilli, M., Kurian, A. W., ... & Phillips, K. A. (2018). From the past to the present: insurer coverage frameworks for next-generation tumor sequencing. Value in Health, 21(9), 1062-1068.
77. Tsao, A. S., Scagliotti, G. V., Bunn Jr, P. A., Carbone, D. P., Warren, G. W., Bai, C., ... & Adusumilli, P. S. (2016). Scientific advances in lung cancer 2015. Journal of Thoracic Oncology, 11(5), 613-638.
78. Tsimberidou, A. M., Elkin, S., Dumanois, R., & Pritchard, D. (2020). Clinical and Economic Value of Genetic Sequencing for Personalized Therapy in Non–small-cell Lung Cancer. Clinical Lung Cancer, 21(6), 477-481.
79. van der Velden, D. L., Hoes, L. R., van der Wijngaart, H., van Berge Henegouwen, J. M., van Werkhoven, E., Roepman, P., ... & Nederlof, P. M. (2019). The Drug Rediscovery protocol facilitates the expanded use of existing anticancer drugs. Nature, 574(7776), 127-131.
80. Wheler, J., Lee, J. J., & Kurzrock, R. (2014). Unique molecular landscapes in cancer: implications for individualized, curated drug combinations. Cancer research, 74(24), 7181-7184
81. World health report 2010. Chapter 4: More health for the money. Available at: https://www.who.int/whr/2010/10\_chap04\_en.pdf?ua=1. (Accessed October 2019)
82. Yarchoan, M., Hopkins, A., & Jaffee, E. M. (2017). Tumor mutational burden and response rate to PD-1 inhibition. The New England journal of medicine, 377(25), 2500.
83. Yip, S., Christofides, A., Banerji, S., Downes, M. R., Izevbaye, I., Lo, B., ... & Spatz, A. (2019). A Canadian guideline on the use of next-generation sequencing in oncology. Current Oncology, 26(2), e241.
84. Zamora, B, Mestre-Ferrandiz, J., Garrison, Lou (2016) The Value of Knowing and Knowing the Value: Improving the Health Technology Assessment of Complementary Diagnostics - Office of Health Economics Available at: https://www.ohe.org/sites/default/files/WP\_EpemedOHE\_final.pdf
85. Zhao, S., Zhang, Z., Zhan, J., Zhao, X., Chen, X., Xiao, L., ... & Zhang, L. (2021). Utility of comprehensive genomic profiling in directing treatment and improving patient outcomes in advanced non-small cell lung cancer. BMC medicine, 19(1), 1-10.