Impact of licensing and reimbursement discrepancies on patient access to cancer treatments across Europe and Canada

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Background

- A large number of new cancer medicines have been developed in recent years, with the potential to prolong life while also maintaining or improving quality of life.
- Regulatory agencies (e.g., the European Medicines Agency [EMA]) assess the benefit/risk of new therapies based on evidence from clinical trials to license effective cancer treatments. Initiatives exist to expedite approval for some medicines that address unmet medical need in the treatment of serious or life-threatening conditions, or offer a major therapeutic advantage over the standard of care.
- In today's economically constrained environment, payers have responded to the potential for significant budgetary challenges by conducting cost-effectiveness (value-for-money) assessments, which are performed by national and regional pricing and reimbursement (P&R) and health technology assessment (HTA) agencies.[2] These assessments may restrict access to new medicines to subpopulations of clinically eligible patients or indeed the full licensed population.
- This introduces the potential for discrepancies between clinically eligible patients (under the license) and the population that is eligible for treatment through public reimbursement.
- Previous studies have assessed the impact of discrepancies on a single cancer type in a single country[3,4] or to indicators of market access,[5] but this is the first known study to evaluate the impact of these discrepancies in the broader context of 12 countries and 6 cancer types and to enable comparison.

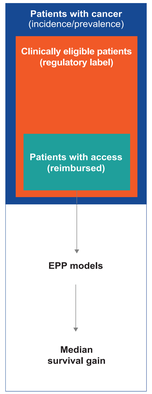
Objective

- To investigate whether there are discrepancies between regulatory licensing (EMA and Health Canada [HC]) and national reimbursement decisions for cancer treatments in 11 European countries and Canada.
- To quantify the effect of these discrepancies in terms of the number of clinically eligible patients without access under the license, and the projected impact on years of life lost (YLL).

Methods

- New oncology therapies (for 6 common cancers: breast, kidney, lung, melanoma, multiple myeloma, and prostate) granted a licence by the EMA and HC between January 2006 and June 2016 were identified (Figure 1).

Figure 1: Methodology for the assessment of the impact of reimbursement restrictions



1. Identify regulatory approvals	• 40 oncology medicines approved by the EMA in 2006–2016 • 63 approved indication combinations for 6 cancer types • The identified EMA approvals were matched with corresponding HC approved indications
2. Identify associated reimbursement assessments	HTA or P&R decisions were identified from national sources (2006–February 2017) Restrictions on reimbursed populations were classified as: • **No restriction:** available to all patients within the regulatory license • **Partial restriction:** available to subpopulation(s) of patients within the regulatory license • **Complete restriction:** not available to any patient within the regulatory license
3. Quantify impact of population restrictions	HTA data (e.g., NICE costing templates [UK] or TC/HAS reports [France]): • number of patients in licensed population • number patients with access (reimbursed population) **Number of patients affected by restrictions** is the difference between the licensed and reimbursed populations
4. Estimate YLL from restrictions	Median survival gain with treatment estimated per patient (from pivotal trial data) and applied to the restricted population (i.e., the potential survival foregone as a result of reimbursement decisions) **YLL** = median survival gain from therapy × number of patients affected

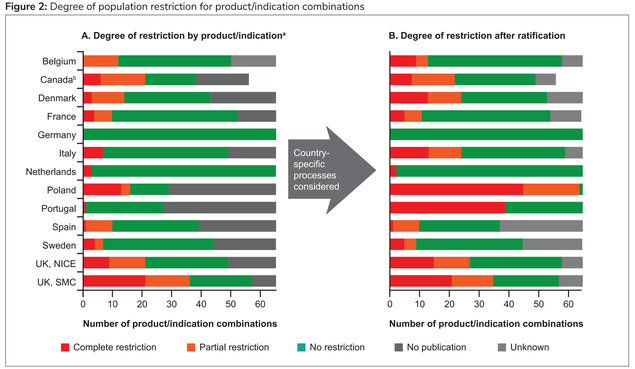
EMA, European Medicines Agency; EPP, eligible patient population; HAS, Haute Autorité de Santé (High Authority for Health); HC, Health Canada; HTA, health technology assessment; NICE, National Institute for Health and Care Excellence; P&R, pricing and reimbursement; TC, Transparency Commission; YLL, years of life lost

- The analyses presented here are based on published national HTA/P&R documents. Where relevant documents could not be identified (e.g., for Portugal), other publicly available information and communication with experts or HTA/P&R agencies were used to ratify the reimbursement status. Products or indications not listed on the Portuguese INFARMED website were considered to be completely restricted.
- The population clinically eligible for treatment and the reimbursed population were established, with each assessment considered independently.

Results

- A total of 65 reimbursement assessments were identified across the countries: 10 for breast cancer, 7 for kidney cancer, 20 for lung cancer, 13 for melanoma, 9 for multiple myeloma, and 6 for prostate cancer.
- The original data analysis estimated that 26% of all published assessments resulted in either a complete (12%) or partial (14%) restriction of the clinically eligible population. The extent of restrictions differed by country, ranging from 0% in Germany and 4% in Portugal to higher proportions in Poland and Scotland (Figure 2A).

Figure 2: Degree of population restriction for product/indication combinations

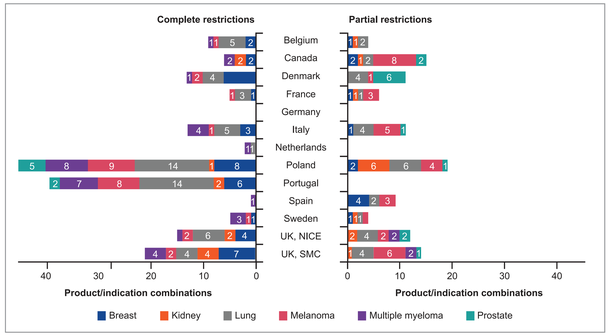


[a] Based on published assessments only; [b] Nine indications approved in Europe were not licensed in Canada

- When incorporating country-specific information on the missing assessments, the proportion of submissions with restrictions rose to 34% (21% complete and 13% partial-restrictions; Figure 2B), indicating that assessing only published national HTA/P&R reports does not establish the total impact of reimbursement decisions.
- The extent of restrictions differs across countries (Figure 2B).
  - There were no complete restrictions in Germany; however, complete restrictions were applied more extensively in Poland (69% of assessments), Portugal (60%), and Scotland (32%).
  - Partial restrictions were most commonly applied in Poland (29% assessments), Canada (27%), and Scotland (22%).
- In some countries, there was a considerable discrepancy between the estimates from published decisions and the actual P&R status of indications.
- Although the nature of restrictions can be identified, the rationale is not always clear and different reimbursed populations for the same combinations are observed across countries.

- There is not a clear pattern of restriction according to cancer type (Figure 3).
  - Complete restrictions were observed across all cancer types and ranged from 9% (prostate cancer) to 31% (breast cancer) of assessments.
  - Partial restrictions also differed by cancer type, ranging from 3% (multiple myeloma) to 20% (melanoma) of assessments.
- These findings indicates that decisions are not solely driven by clinical evidence.

Figure 3: Total number of product/indication combinations[a] with population restrictions (complete and partial)



[a] Based on 65 indications approved by EMA, and 56 indications approved by HC

Quantification of burden

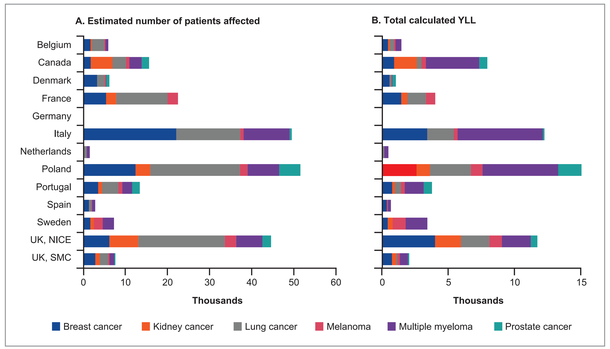
- When only published assessments are considered, the total number of patients potentially affected by restrictions was originally estimated to be over 100,000 across the scope countries, resulting in over 30,000 YLL.
- However, upon ratification of non-published HTA/P&R decisions, the estimated number of patients affected increased to more than 228,000 and over 60,000 YLL (Table 1).
- Differences in the level of impact between cancer types exist due to differences in epidemiology, and there is also the potential for overlap between assessments (i.e., different assessments may consider the same population, leading to double counting), which may result in the impact being overestimated.
- Differences in the level of impact between countries were also observed (Figure 4), but may again be due to differences in cancer epidemiology and population sizes.

Table 1: Estimated impact of reimbursement decisions by cancer type across 11 European countries and Canada

Cancer type	Total incidence across 12 countries[a]	Total estimated number of patients without access[b]	Total estimated YLL
Breast	331,505	62,548	15,417
Kidney	74,577	21,010	6,151
Lung	279,298	84,494	10,236
Melanoma	76,432	12,277	4,647
Multiple myeloma	31,805	36,057	22,950
Prostate	327,106	12,309	3,926
Total	**1,120,723**	**228,695**	**63,326**

[a] GLOBOCAN 2012 data; [b] Assumptions: 100% market uptake for every product/indication; each reimbursement assessment is independent, and assessments can be added together to estimate impact

Figure 4: Estimated number of patients[a] and total YLL[b] by country



[a] Assumptions: 100% market uptake for every product/indication; each reimbursement assessment is independent, and assessments can be added together to estimate impact; [b] These analyses do not account for differences in country population or cancer epidemiology differences between countries

- The extent of population restrictions does not appear to be related to national GDP per capita, with the exception of Poland (lowest GDP per capita and extensive restrictions).
- No relationship was observed between the extent of restrictions and the timing of HTA/P&R decisions; an exception was England (NICE), where a smaller proportion of combinations was restricted after the introduction of the Cancer Drugs Fund in 2011.

Discussion and conclusions

- Patient access to cancer products was restricted to varying degrees through national reimbursement assessments in Europe and Canada.
- Country-specific differences in P&R decision-making criteria play a pivotal role in determining the patient population eligible for reimbursement, as does the specificity of the licensed indication and strength of evidence base although those are more consistent across countries.
- The nature and extent of restrictions are not consistent across Europe and Canada, resulting in cases of inequitable access to new cancer medicines, which affects patients, families, caregivers, and clinicians.
- Variation across countries is anticipated in part due to different willingness-to-pay thresholds for oncology medicines.[6] Thresholds are influenced by health system characteristics such as health system structure, funding sources, and government prioritization of healthcare financing.
- **Our results are directly relevant to health policy initiatives in Europe that aim to improve access to medicines and diminish differences across member states.[7,8]**

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Footnotes

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