original contributions

Understanding Molecular Testing Uptake Across Tumor Types in Eight Countries: Results From a Multinational Cross-Sectional Survey

Pinkie Chambers, MPharm[1,2]; Kenneth K.C. Man, PhD[1,3,4]; Vivian W.Y. Lui, PhD[5]; Sheila Mpima, MRES[6]; Paola Nasuti, MPharm[6]; Martin D. Forster, MBBS, PhD[7]; and Ian C.K. Wong, PhD[1,2,3]

QUESTION ASKED: Does variation in molecular testing exist among Asian and Western European countries across a number of tumor types (namely, breast, colorectal, gastric, non–small-cell lung cancer [NSCLC], and melanoma)?

SUMMARY ANSWER: Statistically significant differences in uptake of molecular testing were determined among countries for NSCLC, gastric, and colorectal cancers, with China having the lowest uptake of molecular testing overall. However, for breast cancers, for which *HER2* testing is more established and there is a high incidence in all countries, uptake was generally consistently high, showing promise for the future. Use of *HER2* testing for gastric cancers was lower in some European countries compared with Japan and South Korea, which can be attributable to the incidence of cancer in these countries. Likewise, in the case of melanoma, the rate of *BRAF* testing was greater in European countries.

POTENTIAL BIAS AND CONFOUNDING FACTORS: The cross-sectional survey design is a major limitation of our findings and the original questionnaire was not designed for our research purpose. For these reasons, we could only report at a high level the differences between countries and not in-depth findings on possible other reasons for variations. We tried to limited bias in our analyses; however, biases involved in questionnaire delivery and completion were beyond our control.

REAL-LIFE IMPLICATIONS: Variations in molecular testing may be attributed to differences in incidence of certain cancers or genetic mutations present in different populations of patients: a high incidence may prompt investment in better treatments for that cancer. This approach may seem logical for a country; however, the approach disadvantages the individual patient with a "rare" cancer for that country. We have demonstrated with the example of breast cancer that consistency between countries is attainable. There is an urgent need to improve access for patients to both molecular testing and targeted treatments in countries where incidence of a tumor type is not high. Our findings can guide future policy to enable equitable access internationally.

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HEALTH POLICY

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Understanding Molecular Testing Uptake Across Tumor Types in Eight Countries: Results From a Multinational Cross-Sectional Survey

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abstract

PURPOSE The growth in understanding of molecular biology and genomics has augmented the development of targeted cancer treatments; however, challenges exist in access to molecular testing, an essential precursor to treatment decision-making. We used data from a cross-sectional survey to evaluate the differences in uptake of molecular testing,

METHODS Using the aggregated results of a questionnaire developed and distributed to clinicians by IQVIA, including treatment details and investigations undertaken for patients, we compared proportions of patients receiving molecular testing and targeted treatment by cancer type for the United Kingdom, France, Italy, Germany, Spain, South Korea, Japan, and China. We used multivariable logistic regression methods to understand the effect of country on the odds of receiving a molecular test.

RESULTS There was a total of 61,491 cases. Across countries and cancer types, uptake rates for molecular testing ranged between 2% and 98%, with the greatest differences seen in gastric cancers (range, 23% to 70%), and significant variations were observed for both European and Asian countries. China consistently demonstrated a significantly reduced uptake for all molecular tests assessed; however; uptake of drug treatment in gastric cancers after testing positive for the human epidermal growth factor receptor 2 gene was higher than in some European countries (China, 85%; European range, 8% to 66%). The uptake of epidermal growth factor receptor gene testing was greater in some Asian countries relative to the United Kingdom, where incidence of lung cancer is higher (Japan: odds ratio, 3.1 [95% CI, 2.6 to 3.8]; South Korea: odds ratio, 2.7 [95% CI, 2 to 3.4]).

CONCLUSION We have highlighted inequity in access to molecular testing and subsequent treatments across countries, which warrants improvements.

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INTRODUCTION

The increasing incidence of cancer has been alleviated, in part, by an exciting upturn in drug development for the disease,[1] particularly treatments for which clinical responses can be reliably predicted on the basis of the presence or absence of molecular changes or genetic mutations. The use of these targeted agents involves the detection of molecular or genetic variations in patients, rather than simply identifying the presence of tumor; using this information to inform treatment decisions is referred to as "precision medicine" (PM).[2]

PM in cancer has been established for over two decades, beginning with the licensing of trastuzumab for *HER2*-positive breast cancers[3] (in 1998) followed by imatinib (in 2001) for Philadelphia-positive chronic myeloid leukemia.[4] Other cancers benefitting from developments are non–small-cell lung, gastric, melanoma, and ovarian cancers, and GI stromal tumors. For colorectal cancers, *RAS* gene mutations predict nonresponse to targeted drug therapy[5] and, through appropriate patient selection, can lessen the burden of treatment costs and unnecessary adverse events for patients.[6] Companion molecular testing for relevant cancers is fundamental to delivering PM and international consensus guidelines for indicated tests and subsequent prescribing are available for a number of indications.[7-11]

In reality, several challenges exist in multinational implementation,[12] leading to the delayed use of the

"right drugs" for some patients. Factors influencing adoption of PM can be multiple and are not simply restricted to cancer-drug access, including the cost, convenience, and availability of molecular testing[13-15] and, in the case of non–small-cell lung cancer (NSCLC), the limited tissue sample available at diagnosis.[16] Age and ethnicity also have been identified as determinants of PM.[17]

Disparities in uptake of molecular testing have been recognized regionally within and between countries[12]; however, with the growing number of molecular tests required in a variety of tumor groups, priority in policy may not be given where the tumor burden in the country is low, disadvantaging the patient. We sought to understand the variation in molecular testing across several tumor groups and different countries. The primary aim of our research was to evaluate the differences in rate of molecular testing across a number of countries and tumors. A data set made available by IQVIA (Durham, NC) and based on a cross-sectional survey undertaken by clinicians regarding their patients, enabled us to achieve this, guided by the following objectives: to understand the uptake of molecular testing in eight countries and the final use of the recommended targeted treatment after testing.

METHODS

Data Source

Data were used from an anonymized cross-sectional survey conducted by IQVIA from January 1 to December 31, 2017. The survey was originally designed to capture data on current treatments received by patients with cancer, line of therapy received, and prior treatments. The survey was not designed for this study; however, we, like others, were able to extract fields relevant for our study.[18,19]

Data Collection

The survey was translated and distributed to a large panel of cancer-treating physicians in China, France, Germany, Italy, Japan, Spain, South Korea, and the United Kingdom. IQVIA distributed a similar version of the survey in the United States, but these data were unavailable for research purposes at the time of request. Clinicians were invited to provide unidentifiable details for patients under their care in a sequential manner for a given quarter and for a maximum of 20 patients per clinician. Clinicians were representative across all specialties, involved in the treatment of each cancer type, and from differing treatment locations and facility types within the country. Each quarter, a maximum of three clinicians were recruited from the same hospital to avoid duplication of patient cases. A total of 6,033 clinicians reported on cases from the tumor groups in 61,628 patients. Data were reported in an anonymized format through a predefined, Web-based questionnaire and aggregated; all fields were mandatory to reduce bias. The survey included filters only relevant to specific cancer types and included additional demographic information about the patient, the funding routes, and any diagnostic tests conducted.

For fields relating to test results, clinicians were offered options to complete that included "test not performed," "results not available," and "not applicable," in addition to test-outcome result fields. For all cancers, stage was grouped in four categories: localized, locally advanced, advanced, and metastatic.

Eligibility criteria. Clinicians only reported patients if the patient was receiving systemic anticancer treatment under their care at the time of survey. Patients were aged 18 years or older and receiving treatment irrespective of funding route, stage of disease, and performance status. Patients were excluded if they had received systemic anticancer treatment but current treatment modality was radiotherapy or surgery.

Ethical considerations. The survey was classified as market research; recruited clinicians confirmed internal regulatory approvals were gained before submission of information. Clinicians were financially reimbursed for time taken to submit data.

Missing data. Due to the design of the Web-based questionnaire, it was not possible for fields to be incomplete, limiting missing data. Upon evaluation, we noted that "not applicable" was answered in one country (Italy) and one cancer (colorectal cancer). We decided that multiple imputation methods were not appropriate and decided to discard case data for these patients (n = 137).

Data Extraction

One author (S.M.) extracted the following data fields: country, disease stage, age, sex, Eastern Cooperative Oncology Group performance status, smoking status (NSCLC only), line of treatment, first- and second-line treatments, and molecular testing performed and corresponding results. Molecular tests performed included the *KRAS* and *NRAS* gene test for colorectal cancers; epidermal growth factor receptor (*EGFR*) gene test, anaplastic lymphoma tyrosine kinase (*ALK*) gene test, and programmed death ligand 1(PD-L1) immunohistochemical staining test for NSCLC; human epidermal growth factor receptor 2 (*HER2*) testing for breast and gastric cancers; and *BRAF* gene test for malignant melanoma.

Statistical Analysis

We used the outcome of "test not performed" as an indicator that the corresponding molecular test had not been performed. We grouped "results not available" within the test-performed category. Tests categorized as "not applicable" were regarded as missing. We described these results across all countries using percentages, with averages calculated using means.

Where there were sufficient event data available, with event defined as "tested" grouped with "awaiting results," logistic regression models were used to identify the factors contributing to "tested" versus "not tested." In addition to

country, other covariates were added to the final model, because the covariates were available and believed to be confounders. Variables were funding, age, performance status, stage, smoking status (NSCLC), sex, and line of treatment, and were all treated as categorical variables. All data manipulation (grouping data) and analyses were conducted using SAS, version 9.4 (SAS Institute, Cary, NC) by two authors (P.C. and K.K.C.M.).

For each cancer type that tested positive according to a molecular test, we investigated the prescribing of targeted treatment at first and second line only, using consensus guidelines as a guide to whether treatment was indicated. Colorectal cancer was excluded from these analyses because mutations in *RAS* would indicate a negative response to treatment. We included *BRAF*-mutant melanoma despite numbers being small in some countries and excluded patients who received immunotherapy from our analysis. For NSCLC, where three tests were evaluable, we chose the cases positive for *EGFR* mutation only for patients in the advanced and metastatic categories. We also restricted our cases to advanced and metastatic stages for gastric cancers. In the case of breast cancer, we excluded patients who received anthracycline or were only receiving hormonal treatment, but we included all stages of disease except localized.

RESULTS

Table 1 lists the different molecular tests, rates of not testing, and incidence of cancer and cancer-related deaths (raw values and age-standardized rates per 100,000 population) obtained from the World Health Organization.[20]. As expected, the numbers of patients included in the survey were reflective of incidence in various tumor groups within their respective countries, with the majority of patients falling into the breast, lung, and colorectal groups. Total cases were breast, 19,875; gastric, 5,411; NSCLC, 17,886; colorectal, 14,793; and melanoma, 3,526. A total of 739 patients (1.2%) were awaiting results and were grouped as "tested."

The percentage of patients receiving a molecular test was greater in countries where a particular cancer has a higher incidence and this was seen particularly for gastric cancer and melanoma.

There were fewer melanoma patients reported in the Asian countries, a finding concordant with that of another report[21] and this contributed to the relatively lower numbers of patients contributing to our data. Death data in Table 1 shows a higher proportion of deaths occurring in the Asian population of patients with melanoma compared with European countries. In addition, incidence of melanoma is smaller in the Spanish population than in other European countries; despite a high rate of *BRAF* testing, the rate of death among patients with the disease in Spain is similar to that in France, Germany, Italy, and United Kingdom.

There is a known high incidence of lung cancer in the Asian countries.[20] There was variation noted in *EGFR* testing for NSCLC in Asian countries, with 49% of Chinese patients within our sample not being tested for the mutation. Conversely, in Korea and Japan, the rate of testing was approximately 90%—higher than that of the European countries, where the rate was between 70% and 80%. Nonsmokers were 2.7 times more likely to receive a molecular test for the *EGFR* mutation than smokers (Data Supplement); *EGFR* mutation is more common in nonsmokers. In the sample of patients with advanced or metastatic disease with an *EGFR* mutation (Table 2), access to tyrosine kinase inhibitors was observed for > 90% of patients in all countries with the exceptions of China and South Korea, where targeted drug use occurred less frequently. Despite a high rate of testing, one-quarter of patients in South Korea were not prescribed a tyrosine kinase inhibitor.

The *ALK* testing rates were similar for most European countries (range, 64% to 72%) with the exception of Italy (52%). Korea and Japan had testing rates similar to those of the European countries; in China, however, only 26% of the population was *ALK* tested. South Korea was comparable to the United Kingdom for *ALK* testing; however, the proportion of patients tested for PD-L1 was significantly lower in South Korea (Table 3). Germany had a higher rate of PD-L1 testing compared with other European countries, with approximately 68% of patients being tested. In contrast, this particular test was seldom performed in China (< 5%), which may be a reflection of restrictions in access to the newer immunotherapy treatments.

In some cancers, proportions of patients receiving a test was relatively high. This was the case for *HER2* testing in breast cancer: in all countries, > 90% of patients had an *HER2* test across all disease stages. In addition, with the exception of China, the level of access to targeted treatments for breast cancer was comparable, demonstrating equitable availability across countries. In most countries, for patients with advanced or metastatic cancer, > 85% had access to trastuzumab or biosimilar, apart from China, where only 38% of patients received treatment. By contrast, in the case of gastric cancers, China had the highest rate of access to trastuzumab in *HER2*-positive patients (81%), whereas the United Kingdom and Germany were among those with lower rates (8% and 15%, respectively).

DISCUSSION

In this study, we aimed to understand the uptake of molecular testing and then drug access across several cancers in multiple countries where indicated, using data for 61,491 patients. Our results show there is noticeable variation that warrants improvement, particularly the possible lack of investment in molecular testing for cancers that are a low burden in a given country. Statistically significant differences were noted between countries for NSCLC and gastric and colorectal cancers, and China was found to

TABLE 1. Numbers of Patients Having Received and Not Received Appropriate Molecular Tests for Different Tumor Groups in Asian and European Countries

Cancer Type	Molecular Test	Parameter	UK	France	Germany	Italy	Spain	Japan	South Korea	China	Total
Breast	*HER2*	Not tested	59 (3.6)	176 (6.5)	64 (2.7)	59 (2.2)	177 (7.7)	48 (4)	44 (6)	230 (8.8)	857 (5.1)
		Tested	2,263 (97.46)	3,154 (94.71)	3,250 (98.07)	4,328 (98.66)	2,591 (93.61)	830 (94.53)	606 (93.23)	1,996 (89.67)	19,018 (95.69)
		Total No. of patients	2,322	3,330	3,314	4,387	2,768	878	650	2,226	19,875
		Cancer incidence (ASR)	55,439 (93.6)	56162 (99.1)	71,888 (85.4)	57,039 (92.8)	32,825 (75.4)	66,101 (57.6)	23,476 (59.8)	36,7900 (36.1)	
		Cancer deaths (ASR)	11,849 (14.4)	13,353 (15.4)	19,376 (15.7)	12,501 (13.8)	6,421 (10.6)	15,452 (9.3)	2,730 (6)	97,972 (8.8)	
Gastric	*HER2*	Not tested	138 (39.4)	143 (41.9)	141 (26.1)	218 (29.8)	177 (41.3)	376 (38.7)	261 (33.8)	928 (72.8)	2,382 (44)
		Tested	212 (60.6)	197 (57.8)	400 (73.9)	513 (70.2)	251 (58.5)	594 (61.2)	512 (66.2)	345 (27.1)	3,024 (55.9)
		Total No. of patients	350	341	541	731	429	971	773	1,275	5,411
		Cancer incidence (ASR)	6,370 (3.9)	7,726 (4.9)	14,173 (6.7)	12,803 (7.2)	7,684 (6.6)	11,5546 (27.5)	37,266 (39.6)	456,124 (20.7)	
		Cancer deaths (ASR)	4,484 (2.5)	5,326 (3.1)	9,480 (3.9)	9,457 (4.7)	5,609 (4.3)	48,535 (9.5)	7,684 (7)	39,0182 (17.5)	
NSCLC[a]	*EGFR*	Not tested	434 (22.1)	544 (25.9)	578 (26)	1,161 (30.2)	378 (20.5)	190 (11.1)	83 (11.8)	1,714 (49.2)	5,082 (28.4)
		Tested	1,533 (77.9)	1,555 (74.1)	1,646 (74.0)	2,689 (69.8)	1,470 (79.5)	1,523 (88.9)	621 (88.2)	1,767 (50.8)	12,804 (71.6)
	ALK	Not tested	561 (28.5)	591 (28.2)	681 (30.6)	1,834 (47.6)	665 (36.0)	747 (43.6)	234 (33.2)	2,568 (73.8)	7,881 (44.1)
		Tested	1,406 (71.5)	1,508 (71.8)	1,543 (69.4)	2,016 (52.4)	1,183 (64.0)	966 (56.4)	470 (66.8)	913 (26.2)	10,005 (55.9)
	PD-L1	Not tested	891 (45.3)	1,381 (65.8)	716 (32.2)	3,014 (78.3)	1,141 (61.7)	1,106 (64.6)	454 (64.5)	3,398 (97.6)	12,101 (67.7)
		Tested	1,076 (54.7)	718 (34.2)	1,508 (67.8)	830 (21.6)	707 (38.3)	607 (35.4)	250 (35.5)	83 (2.4)	5,779 (32.3)
		Total No. of patients	1,967	2,099	2,224	3,850	1,848	1,713	704	3,481	17,886
		Cancer incidence (ASR)	52,320 (32.5)	47,133 (36.1)	66,749 (33.7)	39,989 (24.4)	27,351 (27)	118,971 (27.5)	28,879 (27.8)	774,323 (35.1)	
		Cancer deaths (ASR)	37,688 (22.2)	37,459 (26.3)	50,560 (23.8)	34,512 (19.2)	22,896 (21.2)	81,820 (16.2)	20,315 (18.1)	690,567 (30.9)	
Colorectal	*KRAS*	Not tested	858 (49.8)	453 (32.5)	651 (32.9)	1,690 (47)	861 (50.7)	430 (39)	222 (28)	1,862 (74.4)	7,027 (47.5)
		Tested	864 (50.2)	940 (67.5)	1,330 (67.1)	1,913 (53.1)	837 (49.3)	672 (61.0)	570 (72.0)	640 (25.6)	7,766 (52.5)
	NRAS	Not tested	934 (54.2)	518 (37.2)	775 (39.1)	1,773 (49.2)	963 (56.7)	637 (57.8)	283 (35.7)	2,044 (81.7)	7,927 (53.6)
		Tested	788 (45.8)	875 (62.8)	1,206 (60.9)	1,830 (50.8)	735 (43.3)	465 (42.2)	509 (64.3)	458 (18.3)	6,866 (46.4)
		Total No. of patients	1,722	1,393	1,981	3,603	1,698	1,102	792	2,502	14,793
		Cancer incidence (ASR)	47,892 (32.1)	47,025 (30.4)	58,047 (26.2)	49,327 (29.9)	37,172 (33.4)	148,151 (38.9)	43,363 (44.5)	521,490 (23.7)	
		Cancer deaths (ASR)	20,957 (11.1)	19,962 (10.2)	27,334 (10.1)	21,172 (10.2)	16,683 (12)	57,910 (12)	9,762 (8.7)	247,563 (10.9)	
Melanoma	*BRAF*	Not tested	31 (4)	21 (5.3)	52 (4.9)	55 (7)	38 (9)	30 (61)	5 (33.3)	7 (53.8)	239 (6.7)
		Tested	748 (96.0)	375 (94.7)	1,017 (95.1)	727 (93.0)	385 (91.0)	19 (38.8)	10 (66.7)	6 (46.2)	3,287 (93.2)
		Total No. of patients	779	396	1,069	782	423	49	15	13	3,526
		Cancer incidence (ASR)	17,852 (15)	14,616 (13.6)	31,432 (21.6)	12,299 (12.4)	5,319 (6.4)	1,818 (0.6)	657 (0.7)	7,379 (.036)	
		Cancer deaths (ASR)	2,764 (1.8)	2,249 (1.6)	3,641 (1.6)	2,314 (1.6)	1,171 (1.4)	651 (0.17)	350 (0.34)	3,766 (0.18)	

NOTE. Data are reported as No. (%) unless otherwise indicated. Table contains raw cancer incidence and death data for respective tumor types by country and the age-standardized rate per 100,000 population. Incidence and death data were obtained from the World Health Organization.[20]

Abbreviations: *ALK*, anaplastic lymphoma tyrosine kinase; ASR, age-standardized rate per 100,000 population; *EGFR*, epidermal growth factor receptor; *HER2*, human epidermal growth factor receptor 2; NSCLC, non–small-cell lung cancer; *PD-L1*, programmed death ligand 1 immunohistochemical staining test; UK, United Kingdom.

[a]Information for squamous and nonsquamous NSCLC could not be differentiated. See Data Supplement for additional breakdown on smokers, nonsmokers, and previous smokers tested versus those not tested by disease stage.

TABLE 2. Targeted Treatments Received After Molecular Test–Positive Results

Cancer Type/Test	Targeted Treatment	Data Category	UK	France	Germany	Italy	Spain	Japan	Korea	China	Total
Breast (*HER2* positive)	Trastuzumab	Total No. of patients	177	221	280	550	205	49	81	397	1,952
		Total received[a]	155	196	248	494	175	41	70	150	1,537
		%	87.6	88.7	88.6	89.8	85.4	83.7	86.4	37.8	78.7
Gastric (*HER2* positive)	Trastuzumab	Total No. of patients	36	29	69	73	39	62	60	42	410
		Total received[a]	3	19	11	33	10	21	22	34	153
		%	8.3	65.5	15.9	45.2	25.6	33.9	36.7	81.0	37.3
NSCLC (*EGFR* positive)	Any TKI treatment	Total No. of patients	501	410	349	941	519	792	220	705	4,437
		Total received[a]	476	376	313	896	495	754	167	398	3,875
		%	95.0	91.7	89.7	95.2	95.4	95.2	75.9	56.5	87.3
Melanoma (*BRAF* positive)	Any BRAF/MEK inhibitor	Total No. of patients	282	111	324	252	139	1	0	2	1,081
		Total received[a]	276	109	308	247	139	1	0	1	1,031
		%	97.9	98.2	95.1	98.0	100	100	N/A	50	97.3

NOTE. Patients included in analyses were those eligible for targeted treatment (eg, those with localized disease were excluded).

Abbreviations: *EGFR*, epidermal growth factor receptor gene test; *HER2*, human epidermal growth factor receptor 2; N/A, not applicable; NSCLC, non–small-cell lung cancer; TKI, tyrosine kinase inhibitor; UK, United Kingdom.

[a]Total No. of patients who received molecular testing.

have the lowest uptake of molecular testing. However, for breast cancer, for which testing is more established and there is a high incidence in all countries, uptake was generally consistently high, showing promise for the future. When investigating the prescribing of targeted drug treatments, in patients in whom molecular testing revealed a mutation, we found the largest variation in gastric cancers, with a generally poor uptake of the agent trastuzumab in all countries except China.

Variation may be attributed to differences in incidence of certain cancers or genetic mutations present in different populations of patients: a high incidence may prompt investment in better treatments for that cancer. Gastric cancers are more common among Asian populations, and Asian countries may prioritize treatment of this cancer, whereas melanoma has a much lower incidence. We were able to demonstrate this in our results. This approach may seem logical for a country; however, the approach disadvantages the individual patient who has a "rare" cancer for that country. Although differences in proportions of deaths for cancers considered rare in a particular country are seen, this cannot be directly assigned to molecular testing. Many other factors, such as stage at diagnosis, will influence deaths. Nonetheless, the data demonstrate improvements can be made for certain cancers.

The treatment of cancers has rapidly evolved over the past decade, with a growing understanding of the biomarkers that can accurately predict clinical responses to treatment. Using targeted treatments can significantly improve outcomes for patients and, in the longer term, could reduce the economic burden of cancer care.[22] The variation we have noted should act as a goad to improve global outcomes. European countries such as France and Germany have demonstrated a better rate of testing compared with Asian countries for some cancers, but for others, there is still progress to be made. Interestingly, testing rates in Asian countries such as Japan and South Korea were either comparable or superior to some European countries, including the United Kingdom. This was particularly evident in *HER2* testing for gastric cancers and for *EGFR* testing in NSCLC, where incidence of the disease is high in Asian countries. These findings are consistent with those of another study investigating intercountry variation, which reported Japan to be superior to many other countries in terms of uptake of molecular testing in NSCLC.[23] Conversely, China consistently had a lower-than-average uptake of molecular testing in all cancers, possibly attributable to their larger population and less funding. Yet, when indicated, the access to drug therapy for gastric cancer was actually better in China than in all other countries, although numbers were relatively small in this analysis.

Funding of cancer drug availability can influence access to targeted treatments and, in turn, molecular testing.[12] The data we extracted did specify how patients were funded, but within the options, there was a "funding unknown" option. In our multivariable analysis, this option showed significance across all molecular tests we investigated, meaning we could not draw conclusions in this area. Another indicator that funding was a determinant to PM uptake (both testing and drug treatment) was that we observed a high uptake of molecular testing in breast cancer. Here, targeted treatments feature on the World Health Organization list of essential medicines,[24] a list of medicines that should be accessible by all. The placement of additional targeted agents on this list may facilitate and increase future uptake in other cancers.

TABLE 3. Multivariable Logistic Regression Model Displaying Odds of Uptake of a Particular Molecular Test in Different Countries Compared with the United Kingdom

	KRAS **(colorectal)**		***HER2*** **(gastric)**		***EGFR*** **(NSCLC)**		***ALK*** **(NSCLC)**		***PD-L1*** **(NSCLC)**	
Country	**OR (95% CI)[a]**	***P*[b]**	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
United Kingdom (referent)	1	N/A	1	N/A	1	N/A	1	N/A	1	N/A
France	2.1 (1.7 to 2.8)	< .0001	0.6 (0.4 to 0.9)	0.01	0.6 (0.5 to 0.8)	< .0001	0.6 (0.5 to 0.7)	< .0001	0.4 (0.3 to 0.5)	< .0001
Germany	2.2 (1.9 to 2.5)	< .0001	2. (1.5 to 2.8)	< .0001	0.9 (0.8 to 1.1)	0.06	0.9 (0.8 to 1.0)	0.16	1.8 (1.6 to 2.)	< .0001
Italy	1.8 (1.4 to 2.2)	< .0001	1.3 (0.9 to 2.0)	0.16	0.5 (0.4 to 0.7)	< .0001	0.3 (0.2 to 0.3)	< .0001	0.2 (0.2 to 0.3)	< .0001
Spain	1.1 (.9 to 1.3)	0.18	1 (0.7 to 1.3)	0.96	1.2 (1 to 1.5)	0.08	0.7 (0.6 to 0.8)	< .0001	0.5 (0.5 to 0.6)	< .0001
Japan	0.9 (0.8 to 1.1)	0.36	1.4 (1 to 1.8)	0.01	2.8 (2.3 to 3.4)	< .0001	0.6 (0.5 to 0.7)	< .0001	0.5 (0.4 to 0.6)	< .0001
South Korea	2.7 (2.2 to 3.3)	< .0001	1.7(1.3 to 2.2)	< .0001	2.5 (1.9 to 3.3)	< .0001	0.9 (0.7 to 1.1)	0.15	0.5 (0.4 to 0.6)	< .0001
China	0.2 (0.2 to 0.2)	< .0001	0.2 (0.2 to 0.3)	< .0001	0.3 (0.2 to 0.3)	< .0001	0.1 (0.1 to 0.1)	< .0001	0.02 (0.02 to 0.03)	< .0001

Abbreviations: *ALK*, anaplastic lymphoma tyrosine kinase; *EGFR*, epidermal growth factor receptor; *HER2*, human epidermal growth factor receptor 2; OR, odds ratio; *PD-L1*, programmed death ligand 1.

[a]Odds ratios were adjusted for funding, age, Eastern Cooperative Oncology Group performance status, disease stage, sex, and line of treatment.

[b]P < .05 indicates a significant difference in molecular testing and is supported by narrow confidence intervals.

Limited resources are a cause of inequity[12] and clinicians may need to use their judgement when selecting patients for molecular testing. In our multivariable analysis (Data Supplement), we showed that smokers were less likely to receive an *EGFR* test; a higher rate of *EGFR* mutations among nonsmokers is understood,[25] explaining why this may be a significant factor that influences testing in this population. Incomprehensibly, female patients are more likely to receive an *EGFR* and *ALK* test but less likely to receive a PD-L1 test. Advanced age was associated with lower uptake of molecular testing, a finding similar to that of another study reporting inequity of cancer treatment access.[26] This type of clinician bias in favor of only testing those most likely to exhibit a mutation or those who are younger should be investigated further for this particular cancer.

The main strength of our work is the availability of data from a large number of patients from several countries, enabling us to understand the broad uptake of PM and intercountry variation. However, the cross-sectional survey design is a major limitation of our findings, as is that the original questionnaire was not designed for our research purpose. For these reasons, we could only report at a high level of differences between countries and not in-depth findings on possible other reasons for variations. Understanding in-depth variations such as genetic differences, socioeconomic status, and funding route can guide changes to practice. In our study, in-depth details on mutations could not be accurately reported, because there were patients for whom results of tests were unknown and details were unavailable about the types of tests undertaken and the platforms used. In our work, we tried to limited bias in our analyses; however, biases involved in questionnaire delivery and completion were out of our control. Ideally, this study would have been conducted using routinely collected data, but this method also has limitations and challenges.[27] We believe this study can be strengthened through amalgamation with other similar studies conducted in the United States, African countries, and Australasian and other Asian countries to provide a greater understanding.

In conclusion, precision medicine has the potential to transform clinical practice and improve patient outcomes. We have demonstrated with the example of breast cancer that consistency between countries is attainable. There is an urgent need to improve access for patients to both molecular testing and targeted treatments in countries where incidence of a particular tumor type is not high. Our findings can guide future policy to enable equitable access internationally.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Understanding Molecular Testing Uptake Across Tumor Types in Eight Countries: Results From a Multinational Cross-Sectional Survey

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