Cancer drugs in 16 European countries, Australia, and New Zealand: a cross-country price comparison study

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Summary

Background **Cancer drugs challenge health-care systems because of their high prices. No cross-country price comparison of cancer drugs for a large number of countries has been published. We aimed to survey the prices of cancer drugs in high-income countries (Europe, Australia, and New Zealand).**

Methods **Based on comparability in terms of the economic situation and of the pharmaceutical system, we surveyed official list prices per unit at ex-factory price level of 31 originator cancer drugs in 16 European countries, Australia, and New Zealand as of June, 2013. Drug price data for the European countries were provided by the Pharma Price Information (PPI) service; Australian and New Zealand drug price data were retrieved from the respective pharmaceutical schedules.**

Findings **In Austria, Denmark, Finland, Germany, Italy, Norway, Sweden, and the UK, price information was available for all or all but one drug surveyed whereas the availability of price data was restricted for some drugs in other countries, especially in New Zealand and Portugal. The difference of a drug price between the highest priced country and the lowest priced country varied between 28% and 388%. A few drugs had lower outliers, especially Greek and UK prices, and upper outliers (particularly prices in Switzerland, Germany, and Sweden). Overall, Greek prices ranked at a low level, whereas Sweden, Switzerland, and Germany showed price data in similarly high ranges.**

Interpretation **Our results showed variations in ex-factory prices of originator cancer drugs in the 18 surveyed countries. However, the surveyed prices do not include discounts negotiated by funding organisations because these discounts are confidential. Because pricing authorities can also only use these official undiscounted prices when they set prices through the common policy of external price referencing, they risk overpaying. Our findings provide an evidence base for policy makers to decide whether further policy measures related to drug prices are needed.**

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Introduction

Cancer is a major cause of morbidity and mortality worldwide, especially in high-income countries.[1–3] Access to cancer treatment, including drugs, remains a major public health challenge even across rich European countries.[4] Spending on cancer constitutes about 5% of health-care cost in Organisation for Economic Co-operation and Development (OECD) countries, and this number is growing.[2] This increase is attributable to increasing incidence and prolonged survival, but also to high costs of new drugs and technologies.[1,5] In Australia, public pharmaceutical expenditure on cancer drugs rose from Aus$65 million in 1999–2000 to $466 million in 2011–12 with an average increase of 19% per year.[6] For the then 27 European Union (EU) member states, the health-care cost related to cancer was estimated to be €51·0 billion in 2009, with pharmaceutical expenditure accounting for 27% (€13·5 billion).[7] Concerns about high prices of cancer drugs have been raised in several high-income countries.

Drug prices vary between countries. According to studies in European countries published in the past decade, Sweden, Germany, Switzerland, and Denmark tended to be high-priced countries related to originator drugs, whereas originator drug prices in Greece, Portugal, Spain, and, recently the UK, ranked at the lower end.[8–12] The Australian medicine price level was below the average of other high-income countries,[13–15] whereas no pattern of drug prices in New Zealand compared with European countries has been identified.[16]

Cancer drugs are usually expensive.[17] Although prices of cancer drugs were included in the panels of some price studies or were analysed for individual countries or a few countries, no cross-country price comparison of this group of drugs for a larger number of countries has been published. In this context, we aimed to survey the prices of cancer drugs in European countries, Australia, and New Zealand and to explore differences between the countries.

Method

Country selection

Criteria for the inclusion of countries in the study were their comparability in terms of the economic situation and of the pharmaceutical system. Based on these criteria, we selected 18 high-income countries: Austria, Australia, Belgium, Denmark, Germany, Greece, Finland, France, Italy, Ireland, the Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, and the UK. All included countries regulate prices and reimbursement of high-cost medicines such as cancer drugs.[18]

Research in context

Evidence before this study

Cancer drugs challenge health-care systems because of their high prices. We searched PubMed and GoogleScholar between Feb 16, 2015, and March 12, 2015, to identify cross-country medicine price surveys published in English or German. Search terms included: "medicine(s)" OR "pharma$" OR drug(s) AND "price(s)" AND "Europe$", the name of European countries, "Australia" OR "New Zealand". We also hand-searched the references of these reports. We found no published reports of price comparison for cancer drugs in several European countries, Australia, and New Zealand.

Added value of the study

Despite continuing discussion about high prices of cancer drugs, a comprehensive evidence base is missing. Price data were only published for a few products or a few countries either with a focus on the USA or on Europe. To our knowledge, this is the first study to assess prices of originator cancer drugs in high-income countries. Our findings provide price information about a range of, mainly new, drugs with oncology indications in several high-income countries in Europe and Asia-Pacific.

Implications of all the available evidence

Our results can be used to inform policy makers in the 18 surveyed countries how the price of cancer drugs in their country compares with those in other countries; some of these countries are probably reference countries in price setting (ie, external price referencing). This information provides an evidence base for policy makers to decide whether further policy measures related to drug prices are needed. Our study supports those policy makers and researchers that call for higher price transparency. Information about drug price information is scarce and not transparent by confidential discounts and similar arrangements (eg, managed-entry agreements). As policy makers cannot consider such agreements because they are confidential, they risk overpaying when setting prices through external price referencing.

Medicine selection

The survey contained a sample of 31 cancer drugs, most of which had been centrally approved by the European Medicines Agency. The selection of drugs was guided by practical data availability considerations because the Austrian Public Health Institute provided, for research purposes, a drug price data sample out of their Pharma Price Information (PPI) service. The sample had more than 100 drugs of different indications. We selected those drugs that had been authorised for oncology indications by European Medicines Agency. From this dataset of prices for cancer drugs in European countries, we chose the drugs for which a comparable presentation was available on the market in at least ten of the 16 European countries. We also excluded drugs that had been withdrawn from the market. Table 1 provides an overview of the selected drugs with regards to their indications, their possible designation as an orphan medicinal product in Europe and Australia, and their date of marketing authorisation in Europe. We only compared prices for the originator drugs (two molecules, gemcitabine and zoledronic acid, had generic versions on the market in a few countries) because pricing policies for originator drugs differ substantially from generic policies.

See Online for appendix

Data sources

The price data of the 16 European countries were provided by the PPI service of the Austrian Public Health Institute. For Australia, the June, 2013, dispensed prices were extracted from the February, 2013, efficient funding of chemotherapy S100 arrangements supplement (still valid in June, 2013) for injectable products and from the June, 2013, schedule of pharmaceutical benefits for oral products, denosumab, everolimus, interferon alfa 2b, and zoledronic acid. New Zealand price data were sourced from the pharmaceutical management agency (PHARMAC) August, 2013, pharmaceutical schedule (the appendix p 4 shows references and further specifications). The price data of all 18 countries are the official prices as published by the pricing authorities without consideration of, usually confidential, discounts and rebates.

Statistical analysis

For each drug, we determined one presentation (defined as a medicine in a specific pharmaceutical form, strength, and pack size) that was to be included in the price analysis. A prerequisite for the inclusion into the price comparison was that the selected presentations were available in the same pharmaceutical form and the same strength in the surveyed countries. Ideally, the presentations also had the same pack size, but we also included drugs of the same pharmaceutical form and same strength but with a different pack size (nearest pack size). The choice of the presentation for the price analysis was done based on the European dataset that contained all presentations (ie, all pharmaceutical forms, strengths and pack sizes) of the selected drugs on the market.

As unit of measurement, we selected the ex-factory price (manufacturer price) per unit (ie, per tablet, per vial). This is a common approach in price comparisons and allows for comparing drugs of different pack sizes. Table 1 shows what presentations in terms of pharmaceutical form, strength, and pack size we selected for the comparison, and whether we included different pack sizes in some countries because of the missing data of the selected presentation. Table 1 also displays the unit used to define the unit price. Price data for Australia,

	ATC	Cancer-related indications*	Year of marketing authorisation†	Orphan medicinal product‡ (EU/AUS)	Presentation included in the analysis§		Country coverage		Unit price is price of
					Selected presentation	Variation in countries	Number of countries	Missing data	
Abiraterone acetate	L02BX03	Prostatic neoplasms	2011	No / No	120 tablets 250 mg	..	15	AU, EL, NZ	One tablet
Bendamustine hydrochloride	L01AA09	Leukaemia	2010	No / No	Five vials containing 2·5 mg/mL powder for concentrate for solution for infusion	CH, FR: one vial	13	AU, EL, IE, NZ, PT	One vial
Bevacizumab	L01XC07	Breast neoplasms, carcinoma, non-small-cell lung carcinoma, renal cell colorectal neoplasms, ovarian neoplasms	2005	No / Yes	One vial containing 25 mg/mL concentrate for solution for infusion 25 mg/mL	..	17	NZ	One vial
Bortezomib	L01XX32	Multiple myeloma	2004	No / Yes	One vial containing 3·5 mg powder for solution for injection	..	18	..	One vial
Cabazitaxel	L01CD	Prostatic neoplasms	2011	No / No	One vial containing 60 mg concentrate and solvent for solution for infusion	..	12	CH, EL, FR, IE, NZ, PT	One vial
Cetuximab	L01XC06	Colorectal neoplasms, head and neck neoplasms	2004	No / No	One vial containing 5 mg/mL solution for infusion	..	14	EL, IE, NZ, PT	One vial
Clofarabine	L01BB06	Lymphoblastic leukaemia	2006	Yes / Yes	One vial containing 1 mg/mL concentrate for solution for infusion	ES, IT, UK: four vials	12	AU, CH, IE, NL, NZ, PT	One vial
Denosumab	M05BX04	Treatment of bone loss in men receiving treatment for prostate cancer	2010	No / Yes	One pre-filled syringe containing 60 mg solution for injection	..	15	FR, PT, NZ	One syringe
Eribulin mesylate	L01XX41	Breast neoplasms	2011	No / Yes	One vial containing 0·44 mg/mL solution for injection	..	11	AU, BE, EL, ES, IE, NZ, PT	One vial
Erlotinib	L01XE03	Non-small-cell lung cancer, pancreatic neoplasms	2005	No / Yes	30 film-coated tablets 150 mg	..	18	..	One film-coated tablet
Everolimus	L01XE10	Breast neoplasms, pancreatic neuroendocrine tumours, renal cell carcinoma	2009	Yes / Yes	30 tablets 10 mg	..	16	NZ, PT	One tablet
Gefitinib	L01XE02	Non-small-cell lung cancer	2009	No / No	30 film-coated tablets 250 mg	..	18	..	One film-coated tablet
Gemcitabine	L01BC05	Bladder cancer, breast cancer, pancreatic cancer, non-small-cell lung cancer, ovarian cancer	No EMA marketing authorisation	No / No	1 vial containing 1 g powder for solution for infusion	BE, EL, PT: originator not on market, generic gemcitabine on the market	15	BE, EL, PT	One vial
Imatinib	L01XE01	Myeloid leukaemia, lymphoblastic leukaemia, myelodysplastic/ myeloproliferative diseases, eosinophilic leukaemia, gastrointestinal stromal tumours, and dermatofibrosarcoma protuberans	2001	Yes / Yes	60 film-coated tablets 100 mg	BE, FI, IT: 120 film-coated tablets; AT: 180 film-coated tablets	18	..	One film-coated tablet
Interferon alfa 2b	L03AB05	Hairy-cell leukaemia, chronic myeloid leukaemia, multiple myeloma, follicular lymphoma, carcinoid tumour, and malignant melanoma	2000	No / No	One multi-dose pen containing 3 million IU/0·5 mL solution for injection	..	16	ES, NL	One pen

(Table 1 continues on next page)

	ATC	Cancer-related indications*	Year of marketing authorisation†	Orphan medicinal product‡ (EU/AUS)	Presentation included in the analysis§		Country coverage		Unit price is price of
					Selected presentation	Variation in countries	Number of countries	Missing data	
(Continued from previous page)									
Lapatinib ditosylate	L01XE07	Breast cancer	2008	No / No	70 film-coated tablets 250 mg	ES, PT, NL: 140 film-coated tablets	17	BE	One film-coated tablet
Lenalidomide	L04AX04	Multiple myeloma	2007	Yes / Yes	21 capsules 10 mg	..	16	NZ, PT	One cap
Nelarabine	L01BB07	Precursor T-cell lymphoblastic leukaemia	2007	Yes / No	Six vials containing 5 mg/mL solution for infusion	..	15	AU, NZ, PT	One vial
Nilotinib	L01XE08	Chronic myeloid leukaemia	2007	Yes / Yes	112 capsules 150 mg	..	16	NZ, PT	One cap
Ofatumumab	L01XC10	Chronic lymphocytic leukaemia	2010	Yes / No	Three vials containing 100 mg concentrate for solution for infusion	IE: ten vials	10	AU, BE, CH, ES, FR, NZ, PT, UK	One vial
Paclitaxel albumin	L01CD01	Breast cancer	2008	No / No	One vial containing 5 mg/mL powder for suspension for infusion	..	12	BE, CH, FR, IE, NZ, PT	One vial
Panitumumab	L01XC08	Colorectal neoplasms	2007	No / No	One vial containing 20 mg/mL concentrate for solution for infusion	..	15	AU, NZ, PT	One vial
Pazopanib	L01XE11	Renal-cell carcinoma, soft-tissue sarcoma	2010	No / Yes	30 film-coated tablets 200 mg	BE, DK, FI, NO, SE: 90 film-coated tablets	16	FR, PT	One film-coated tablet
Pemetrexed	L01BA04	Lung cancer	2004	No / No	One vial containing 100 mg powder for concentrate for solution for infusion	..	17	NZ	One vial
Plerixafor injection	L03AX16	Haemopoietic stem-cell transplantation in patients with lymphoma or multiple myeloma	2009	Yes / Yes	One vial containing 20 mg/mL solution for injection	..	12	AU, CH, IE, NL, NZ, PT	One vial
Sorafenib	L01XE05	Hepatocellular carcinoma, renal cell carcinoma, differentiated thyroid carcinoma	2006	Yes / Yes	112 film-coated tablets 200 mg	AU: 120 film-coated tablets	16	NZ, PT	One film-coated tablet
Sunitinib malate	L01XE04	Gastrointestinal stromal tumour, metastatic renal cell carcinoma, pancreatic neuro-endocrine tumours	2006	No / Yes	28 capsules 50 mg	AT, BE, DE, EL, ES, IT, NO, SE: 30 capsules	17	PT	One cap
Temsirolimus	L01XE09	Renal-cell carcinoma, mantle-cell lymphoma	2007	Yes / Yes	One vial containing 30 mg concentrate and diluent for solution for infusion	..	15	AU, IE, NZ	One vial
Trastuzumab	L01XC03	Breast cancer, stomach cancer	2000	No / Yes	One vial containing 150 mg powder for concentrate for solution for infusion	..	18	..	One vial
Vemurafenib	L01XE15	Melanoma	2012	No / Yes	56 film-coated tablets 250 mg	..	13	AU, EL, ES, NZ, PT	One film-coated tablet
Zoledronic acid	M05BA08	Prevention of bone complications in adults with advanced cancer	2001	No / Yes	One vial containing 4 mg/5 mL concentrate for solution for infusion	..	14	AT, IT, NL, NO	One vial

ATC=anatomic, therapeutic, chemical code according to the WHO classification. O=originator. AT=Austria. AU=Australia. BE=Belgium. CH=Switzerland. DE=Germany. DK=Denmark. EL=Greece. ES=Spain. FI=Finland. FR=France. IE=Ireland. IT=Italy. NL=Netherlands. NO=Norway. NZ=New Zealand. PT=Portugal. SE=Sweden. *Approved indications according to the European Medicines Agency (EMA). †Year of the marketing authorisation granted by the EMA; all drugs of the sample except bendamustine hydrochloride (decentralised marketing authorisation) and gemcitabine are drugs approved through the centralised procedure of the EMA. ‡Information about whether the drugs have an orphan medicinal product designation in Europe (granted by the EMA, valid for the whole European Union) and in Australia; no orphan medicinal product designation exists in New Zealand. §The selected presentation defines a drug of a specific pharmaceutical form, strength, and pack size that was chosen for the analysis. Variations in the pack size were accepted if the drug was not available in the pack size of the selected presentation (see the column "variation in countries"). Prices were analysed per unit (eg, for one tablet in case of abiraterone acetate or for one vial in the case of bendamustine hydrochloride and bevacizumab).

Table 1: **Background information about drugs included in the analysis and their selected presentations, and unit prices**

	AT	AU	BE	CH	DE	DK	EL	ES	FI	FR	IE	IT	NL	NO	NZ	PT	SE	UK
Abiraterone acetate	27·50	NA	27·50	26·78	36·67*	28·17	28·33	NA	25·24	27·50	29·07	28·95	27·50	25·02	NA	27·50	29·07	25·08
Bendamustine hydrochloride	301·20	NA	274·91	293·42	274·91	277·94	273·81	NA	305·82	273·81	NA	259·35	295·17	281·96	NA	NA	393·07*	283·28
Bevacizumab	1338·0	1213·8	1214·3	1505·4*	1326·4	1168·6	992·00	1272·9	1359·9	1088·8	1319·5	1224·5	1209·7	1095·7	NA	1236·1	1336·1	1085·1
Bortezomib	1166·0	1209·5	1064·4	1365·1*	1357·3	1001·6	855·63	1120·1	1188·7	1043·9	1141·6	1173·2	1144·0	945·66	1134·4	1143·0	1215·8	894·91
Cabazitaxel	4890·0	4476·3	3834·0	NA	4395·0	4237·5	NA	4100·0	4254·3	NA	NA	3971·0	4203·7	4409·0	NA	NA	4978·5*	3796·2
Cetuximab	199·00	240·63*	177·00	233·08	229·92	218·78	NA	192·30	211·35	189·00	NA	179·60	197·83	184·80	NA	NA	233·49	182·93
Clofarabine	1675·0	NA	1675·0	NA	1675·0	1477·6	1347·1	1666·6	1594·6	1356·8	NA	1591·2	NA	1532·0	NA	NA	2032·2*	1362·1
Denosumab	179·55	179·94	188·10	225·28	238·00	206·81	176·76	185·00	173·80	NA	220·97	199·50	214·35	187·80	NA	NA	242·01*	187·96
Eribulin mesylate	400·00	NA	NA	367·64	400·00	368·62	NA	NA	391·57	320·00	NA	360·99	374·00	377·16	NA	NA	410·85*	370·78
Erlotinib	68·97	74·41	73·32	86·57*	76·97	67·41	53·57	68·18	60·84	67·45	69·95	65·42	69·03	62·62	78·93	70·00	73·59	63·84
Everolimus	120·00	87·15	117·28	151·91*	126·86	103·24	97·98	110·03	107·45	126·20	114·50	115·52	106·03	102·45	NA	NA	139·44	116·21
Gefitinib	78·24	87·15	73·32	91·74	92·50*	66·14	60·77	68·18	64·10	69·20	70·20	73·01	79·31	65·43	33·97	74·43	76·32	74·22
Gemcitabine	175·28	42·91	NA	107·00	120·00	188·87	NA	43·70	159·83	102·91	75·35	147·48	124·60	166·45	209·33*	NA	106·36	167·17
Imatinib	21·22	21·86	19·37	24·39*	23·92	17·97	15·45	19·74	17·97	17·47	19·62	16·73	19·68	17·07	23·98	17·98	21·64	16·87
Interferon alfa 2b	270·63	175·18	147·49	298·94	338·51*	194·19	104·65	NA	164·81	187·20	197·57	166·40	NA	222·63	187·75	161·65	269·36	128·10
Lapatinib ditosylate	17·64	16·34	NA	20·39*	17·64	15·08	12·76	14·49	15·15	16·58	16·27	16·62	15·95	14·63	16·26	15·24	18·59	11·80
Lenalidomide	260·72	189·63	245·29	278·87*	266·00	239·75	195·59	250·78	199·04	165·16	243·62	240·06	240·01	207·93	NA	NA	240·05	184·88
Nelarabine	331·00	NA	331·00	395·40*	331·00	318·04	254·20	275·13	312·09	324·24	318·89	367·33	326·32	340·41	NA	NA	340·83	228·02
Nilotinib	23·34	27·23*	23·34	26·81	26·85	21·56	20·15	24·16	19·95	24·25	23·75	26·36	26·42	20·77	NA	NA	23·63	25·50
Ofatumumab	206·00	NA	NA	NA	252·08*	207·61	188·61	NA	204·93	NA	224·95	228·95	215·99	207·87	NA	NA	247·74	NA
Paclitaxel albumin	320·00	283·31	NA	NA	320·00	300·90	223·67	240·00	361·77	NA	NA	221·11	309·49	282·25	NA	NA	396·35*	252·67
Panitumumab	1700·0	NA	1448·3	1762·4	1953·6*	1669·9	1343·9	1520·0	1740·3	1720·0	1700·0	1534·3	1738·6	1453·5	NA	NA	1924·1	1558·3
Pazopanib	27·76	26·62	26·37	25·31	30·82*	20·93	18·78	26·13	25·58	NA	26·40	27·33	25·19	21·85	26·67	NA	28·08	19·19
Pemetrexed	1588·0	1100·8	1253·4	1499·8	2020·0*	1318·7	870·17	1200·0	1419·4	1140·0	1140·6	1372·7	1300·0	1083·2	NA	977·29	1505·3	939·07
Plerixafor injection	5650·0	NA	5800·6	NA	5650·0	5692·5	4918·5	5482·3	5950·0	5650·0	NA	6215·0	NA	6163·5	NA	NA	7703·5*	5015·1
Sorafenib	35·70	37·11*	31·95	33·84	35·09	28·28	25·88	30·44	28·60	28·83	32·35	28·70	31·29	32·61	NA	NA	31·65	31·24
Sunitinib malate	175·33	170·14	173·54	218·81*	194·63	156·98	127·20	168·41	155·84	175·24	170·30	176·00	163·12	145·54	198·28	NA	188·60	115·14
Temsirolimus	875·00	NA	874·04	853·83	897·00	811·74	698·40	875·00	886·93	792·00	NA	889·86	829·90	854·20	NA	799·99	974·50*	636·22
Trastuzumab	690·00	726·98	623·89	788·18	676·59	570·45	458·06	596·52	650·82	536·87	669·76	608·38	579·57	523·23	809·26*	784·24	695·02	478·22
Vemurafenib	38·41	NA	37·09	40·59	41·25*	36·23	NA	NA	38·11	37·09	37·09	37·07	35·36	36·50	NA	NA	39·38	32·20
Zoledronic acid	NA	294·12	214·51	138·47	282·75	253·89	128·34	256·37	207·79	215·68	273·61	NA	NA	NA	329·70*	258·00	305·89	204·45

AT=Austria. AU=Australia. BE=Belgium. CH=Switzerland. DE=Germany. DK=Denmark. EL=Greece, ES=Spain. FI=Finland. FR=France. IE=Ireland. IT=Italy. NA=not available. NL=Netherlands. NO=Norway. NZ=New Zealand. PT=Portugal. SE=Sweden.
*Price in the highest priced country.

Table 2: **Ex-factory prices (€ per unit) of selected cancer originator drugs in the 18 surveyed countries, as of June, 2013**

New Zealand, and five of the European countries that did not have the Euro as their national currency were converted into Euro as of the average monthly exchange rate of May 2013, as indicated by European Central Bank.

Calculations were done in Microsoft Excel for Mac 2011 (version 14.4.9) and in R 3.1.2 GUI 1.65 Mavericks build (6833). All statistical analyses were descriptive.

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all of the data in the study and had the final responsibility for the decision to submit for publication.

Results

For five (bortezomib, erlotinib, gefitinib, imatinib, and trastuzumab; 16%) of the 31 products studied, price data were available in all 18 countries, for four products (bevacizumab, lapatinib, pemetrexed, sunitinib; 13%) data were available in 17 countries, for six products (everolimus, interferon alfa 2b, lenalidomide, nilotinib, pazopanib, sorafenib; 19%) data were available in 16 countries, and for five products (abiraterone acetate, denosumab, nelarabine, panitumuab, temsirolimus; 16%) data were available in 15 countries. The lowest data coverage was for erlibulin (11 countries) and ofatumumab (ten countries). Of the countries studied, New Zealand had the lowest data availability (missing data for 20 [65%] of the 31 drugs), followed by Portugal (19 [61%]) and Australia (ten [32%]). We noted rather low data availability in Ireland (missing data for eight drugs [26%]) and Greece (seven [23%]). Data were available for all 31 drugs surveyed in Denmark, Finland, Germany, and Sweden and for 30 drugs in Austria, Italy, Norway, and the UK. The paucity of data is attributable to the fact that drugs were not authorised at the time of the survey and to the coverage of some national databases that are limited to a segment of the market. The price database in New Zealand only contains funded drugs; thus data were not available for the prices of ten authorised but not (yet) funded drugs in New Zealand. In Portugal, price data of drugs used in hospitals have not been published from mid-2012 onwards.

Table 2 and appendix p 5 shows the unit ex-factory price data for the 18 countries. In our sample of 31 drugs, none had a unit price (ie, price per tablet, vial) lower than €10 in the 18 surveyed countries. Four drugs (13% of the sample) had a mean unit ex-factory price between €250 and €500, and two drugs (6%) had a mean unit price between €500 and €1000. Seven drugs (23%) had an average unit price higher than €1000, of which one (3%) was more expensive than €5000.

The difference between the prices of a drug in the highest priced country and in the lowest priced country was between 28% and 50% for ten drugs (32% of the drugs' sample), between 50% and 100% for 16 drugs (52%) and between 100% and 200% for three drugs (10%). The price of originator gemcitabine (average unit ex-factory price: €129) in the highest priced country was 388% higher than in the lowest priced country, for interferon alfa 2b the price difference amounted to 223%.

The figure provides a boxplot on indexed prices of the surveyed drugs (additional boxplots are shown in the appendix pp 1–2). Prices in Greece and UK were lower outliers for some drugs, whereas German, Swiss, and Swedish prices were upper outliers for some drugs: there were lower outliers for eribulin (France), lapatinib ditosylate (UK and Greece), nelarabine (UK, Greece, and Spain), sunitinib malate (UK and Greece), temsirolimus (UK), vemurafenib (UK) and upper outliers for abiraterone acetate (Germany), bendamustine hydrochloride (Sweden), everolimus (Switzerland), erlotinib (Switzerland), lapatinib (Switzerland), nelarabine (Italy and Switzerland), pemetrexed disodium (Germany), plerixafor (Sweden), and sunitinib malate (Switzerland).

Medicine prices varied across the surveyed countries: Greece, Portugal, Spain, and UK had prices at the lower end, whereas prices in Switzerland, Germany, Denmark, and Sweden were at the upper end. All Greek prices ranked in the first quartile, and their prices were the

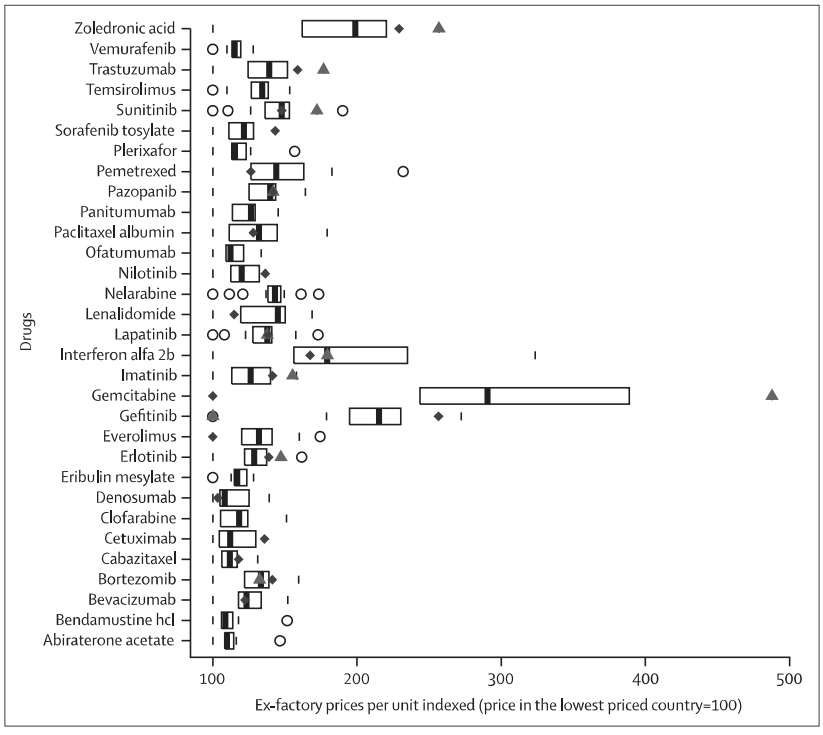

Figure: **Boxplot of drug prices (ex-factory price per unit) indexed (price in the lowest priced country=100), as of June 2013, in 16 European countries, Australia, and New Zealand**
The box displays the interquartile range (IQR); the bottom and top of the box are the 25th and 75th percentiles (the 1st and 3rd quartiles, respectively), and the band near the middle of the box is the median. The dashed lines describe the bottom and top whiskers. The small circles indicate extreme datapoints (commonly referred to as outliers). The blue diamond shows the datapoint for Australia, and the red triangle for New Zealand. The appendix shows boxplots without gemcitabine and without gemcitabine and interferon alfa 2b (for better readability).

lowest for 14 (58%) of the 24 drugs for which Greek price data were available (appendix p 3, pp 6–7). The price of cancer drugs in the UK was also low. Prices in Sweden were in the fourth quartile for 26 (84%) of the 31 cancer drugs, and the prices in Switzerland and Germany also frequently ranked in the fourth quartile (for 19 [73%] of 26 drugs in Switzerland and 22 [71%] of 31 in Germany; appendix p 3). Prices in Switzerland were the highest for nine of the 26 drugs with available data (35%), as were prices in Germany and Sweden for eight of the 31 medicines (26%) in both cases (appendix p 3, pp 6–7).

Discussion

Our results suggest that prices for cancer drugs vary across Europe, Australia, and New Zealand. Prices in Sweden, Switzerland, and Germany ranked high, and prices in Mediterranean countries such as Portugal, Spain, and especially Greece and the UK were at the lower end. These findings are in line with previous price studies of originator drugs in European countries.[8–11] The prices of cancer drugs in Australia and New Zealand were similar to prices in European countries, with no substantial outliers. The results of our study confirm findings of a previous comparison of originator drugs in European countries and New Zealand.[16] In previous comparative studies including Australian data, Australian prices (presented as a price index) were low.[13–15]

Within our sample, the price of originator gemcitabine had the highest range between the highest priced country (New Zealand) and the lowest priced country (Australia), and for zoledronic acid originator the price difference was also rather large between the highest priced country (New Zealand) and the lowest priced country (Greece). The existence of generics on the market might have affected originator prices in some countries. In some countries, originator prices might have decreased because of generic competition, whereas in other countries originator prices remained at a high level.

In view of the large effects on budgets of new cancer drugs, public payers have been considering managed-entry agreements (ie, arrangements between a manufacturer and payer or provider that enable access to [coverage or reimbursement of] a health technology, including a medicine, subject to specified conditions) as a possible funding and access policy.[19] Managed-entry agreements are increasingly used in Australia and several European countries, particularly Italy, UK, and the Netherlands,[20,21] whereas in New Zealand, access schemes are only starting to be introduced.[22] Although managed-entry agreements might contribute to ensuring patient access to new drugs, especially those with limited cost-effectiveness, they can lead to limited transparency because the content of these arrangements, including the agreed prices, is not usually made public.[19,20,23–25]

We did our study based on official, published list prices because we did not have data regarding agreed discounts in managed-entry and similar arrangements; this is confidential information. We know that discounts, rebates, and similar arrangements have a role,[26] and that managed-entry agreements have increasingly been concluded for cancer drugs.[21] The lack of transparency in discounting systems including managed-entry agreements has been addressed in the scientific literature,[24] and the paucity of data about the extent of such discounts has been confirmed—eg, for Australia[25] and Canada.[27]

The inaccessibility of confidential, discounted prices is a limitation of our study, and it is also a major shortcoming in pricing for public payers. Many European countries, and, to some extent Australia, apply the policy of external price referencing (ie, international price benchmarking)[28,29] that is the practice of using the prices of a drug in one or several countries to derive a benchmark or reference price for the purposes of setting or negotiating the price. Even if payers might be able to achieve lower prices in follow-up reimbursement negotiations, the initial price comparison is done based on list prices, and so payers risk overpaying. Additionally, the low list price level caused by the external price referencing method might lead to delays, and even non-availability, of drugs in the market. This might be because manufacturers are incentivised to launch these drugs in high-priced countries first and defer market entry in the lower priced countries so they will not be obliged to negatively affect the international reference price.[13,30]

In addition our analysis being based on officially published ex-factory prices rather than discounted prices, our study has further limitations. The initial selection of drugs was guided by data availability. The availability of price data in some countries, in particular New Zealand and Portugal, is low and restricts the reliability of our findings. European price data were not accompanied with the information about whether drugs were funded or not. In terms of the countries surveyed, the study lacks price data from the USA and Canada. Comparisons of ex-factory prices of originator drugs across major high-income countries, although not focused on cancer drugs and done before 2010, suggested a comparably high price level for the USA and, to a lesser extent, for Canada.[13–15] A 2010 report by Danzon and Taylor that aimed to assess the issue of prices, relative to value, for cancer drugs compared with other drugs in the USA drew from evidence of Canada because of the unavailability of US price data in the required format. These data suggested high prices of cancer drugs.[17]

In our study, we restricted the price survey for Europe to 16 countries. Nonetheless, the focus on these 16 European countries probably enhanced the methodological robustness of the comparison because these are countries

of similar economic situation (and also comparable with Australia and New Zealand), and possible data availability problems for some central and eastern European countries where new drugs might not have been marketed yet were avoided. Data are as of 2013 and are thus slightly outdated. Again, this is attributable to the fact that a set of European price data was provided to us that had been extracted from national databases as of June, 2013. The decision to use these data for an analysis of cancer drug prices was taken some time after the survey date, and because some of the national databases included in the PPI service do not allow for historic surveys, the inclusion of further countries with price data as of June, 2013, would not always have been possible. The study focused on the comparison of drug prices at comparable units. It does not provide information about (public) spending for these drugs because the expenditure is affected by volume. Additionally, data about the price per unit must be interpreted with caution because the unit price does not reflect the price of the treatment course. Finally, we did not factor in the economic situation in individual countries by weighting prices for gross domestic product or purchasing power parities. This decision was based on the over-riding economic similarities of the included countries, and also guided by the rationale that the list prices, and not GDP-adjusted ones, are the prices that provide the basis for negotiations of payers.

In conclusion, although data included in our analysis are the official undiscounted prices and not the possibly lower reimbursement prices that payers might be able to achieve, the list prices are of high relevance for policy makers because undiscounted list prices are applied in external price referencing which is a common pricing policy. Thus, public payers risk overpaying. The extent of benefits in terms of accessibility for patients and savings for payers that the disclosure of confidential discounts and similar arrangements could offer is yet to be explored.

Contributors

SV took the lead in the concept development (product selection, European country selection, and methodological issues), and AV and ZU-D-B reviewed the concept. SV reviewed Pharma Price Information to extract price data for European countries; AV surveyed dispensed medicine prices in Australia and calculated ex-factory prices, and ZU-D-B collected medicine price data from New Zealand. SV did the calculations to make price data comparable (exchange rate and unit price) and did the analyses. SV wrote the draft and revised versions of the manuscript, and AV and ZU-D-B were equally involved in reviewing and editing the article.

Declaration of interests

We declare no competing interests.

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