

A Study on the International Policy of Cancer Drug Expenditures in Countries with
Universal Healthcare

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Abstract

Cancer is the leading cause of death in developed countries; it is also one of the most costly diseases to treat. In the past decade, the cost of new cancer therapies has risen exponentially. This, combined with the increasing cost of healthcare globally, represents a significant economic burden for many if not all national governments. This paper examines 5 different countries (Netherlands, Australia, the U.K., Canada and the U.S.) and their respective healthcare system. As well, this paper looks at what policies are in place to ensure equitable care while evaluating whether these new costly therapies are justifiably priced. Each country has a different mechanism and/or threshold for evaluating cost-effectiveness and therefore determining whether a drug will be publicly funded. Finally, this paper suggests three different solutions to make new cancer therapies more cost-effective: government price negotiations, tying drug approval to price negotiation, and pricing drugs based on their expected life outcomes.

April 24, 2014

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List of Abbreviations

CDR	Common Drug Review
CEA	Cost-Effectiveness Analysis
CML	Chronic Myelogenous Leukemia
CUA	Cost-Utility Analysis
DIN	Drug Identification Number
EMA	European Medicines Agency
ICER	Incremental Cost-Effectiveness Ratio
MEB	Medicines Evaluation Board
NCCP	National Cancer Control Programmes
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NME	New Molecular Entity
NOC	Notice of Compliance
PBAC	Pharmaceutical Benefits Advisor Committee
PBS	Pharmaceutical Benefits Scheme
pCODR	pan-Canadian Oncology Drug Review
PCPA	Pan-Canadian Pricing Alliance
PFS	Progression Free Survival
QALY	Quality-Adjusted Life Year
RIVM	National Institute for Public Health and the Environment
RSA	Risk-Sharing Agreement
SPAS	Special-Pricing Agreements

Thesis:

This paper examines how different countries deal with the high-cost of new oncology drug therapies. In particular, how countries with universal healthcare, such as Canada, Australia, the U.S., the U.K., and the Netherlands have developed strategic initiatives to deal with the financial burden of funding these new therapies.

1.1 Introduction

Cancer is the leading cause of death in Canada with an estimated 187,600 new cases diagnosed in 2013 (Canadian Cancer Society's Advisory Committee on Cancer Statistics May 2013). It is responsible for almost 30% of all mortalities amounting to 75,000 deaths (Appendix 1). While the disease has significant personal and social impacts, it also has a major economic impact on a personal, jurisdictional and national level (Canadian Cancer Society's Advisory Committee on Cancer Statistics May 2013). As one of the most costly diseases in Canada, spending on cancer care amounted to \$22.5 billion in costs for 2009, a change from \$17.2 billion in 2000 (Canadian Cancer Society's Advisory Committee on Cancer Statistics May 2013, Thomson, Greve Young 2011). Cancer is the second leading cause of death in developed countries, not just Canada; its costs are unavoidable and the economic burden is high.

The past decade has seen a huge shift in the way we treat disease. Now, new therapies are not a one-size-fits-all, but are referred to as targeted therapies. In May

2001, and perhaps one of the most powerful and provoking examples, Time Magazine featured a new drug called Gleevec on the cover. The headline read, “There is new ammunition the war against cancer. These are the bullets” (Buchdunger, Cioffi et al. 2000, Heinrich, Griffith et al. 2000, Pray 2008). Gleevec, used to treat a rare form of cancer called chronic myelogenous leukemia (CML), was one of the first targeted therapies in the war against cancer. The drug targeted an overactive receptor caused by a chromosomal translocation, referred to as the Philadelphia chromosome. Gleevec changed the way doctors treated CML, resulting in an increase of 5-year survival from 30% to 89%(Buchdunger, Cioffi et al. 2000, Heinrich, Griffith et al. 2000, Pray 2008). Gleevec was a miracle drug.

These miracle cures are costly, often accounting for 27% of the total costs (Uyl-de Groot, de Groot et al. 2010). And in light of the increasing cost of healthcare, dealing with these swelling costs at both the individual and the societal level, while retaining effective, equitable and accessible cancer care, poses a major challenge for most health care systems (IMS Institute for Health Informatics 2011). There is also a widely held belief that higher spending always results in better outcomes for patients with cancer (Porter 2009, Uyl-de Groot, deVries et al. 2014, Philipson, Eber et al. 2012). Yet, this is not necessarily the case (Davis, Schoen et al. 2010). There are correlations that indicate the higher cost-per-capita expenditure on healthcare result in outcomes such as increased life expectancy (Uyl-de Groot, deVries et al. 2014). For example, a study by Phillipson et al showed that the average survival from time of diagnosis was 11.1 years in the US, compared to 9.3 years in any European country (Phillipson, Eber et al. 2012, Porter 2009). This was attributed to

the fact that the US spends the more per capita on healthcare than any European country. However, there is conflicting evidence to suggest that is the case (Uyl-de Groot, deVries et al. 2014).

1.1.1 Factors Affecting Drug Cost

Expensive new drugs are entering the market at a rapid pace. In 2012, the FDA approved 12 new cancer drugs (Experts in Chronic Myeloid Leukemia 2013), 11 of which cost €73,000 per treatment per patient. But getting them funded with their new outrageous price tags is another matter. At the time of its introduction in Canada, Gleevec cost \$24.35 per pill, or approximately \$30,000 annually (Patented Medicine Review Board 2011). Yet now, over a decade later, the same treatment costs an estimated \$76,000 (Cowley 2013).

The price of new drugs has soared over the past several decades. The demand for these life-saving therapies is price-inelastic. Why are they so expensive? There are a lot of pre-conceived notions regarding the cost of drugs several of which may include greedy pharmaceutical companies and intellectual property issues. However, the science of drug discovery is extremely difficult and the costs of development are astronomical. This is the major reason drugs are so expensive (Jogalekar 2014). The complexity of biological systems is the reason that only 32 of 920 drugs tested (1990-2006) in the US made it through clinical trials (DiMasi, Grabowski 2007). The rate of failure is absurdly high. In fact, a higher percentage of oncology drugs, compared to all other therapeutics classes, failed after entering phase III testing (DiMasi, Grabowski 2007). The average cost of development is

anywhere from \$1 billion to \$2 billion dollars per drug (Pisano 2006), although this differs significantly depending on therapeutic class (Herper 2010, DiMasi, Grabowski 2007). While many critics believe the actual cost of bringing a drug to market is closer to \$90 million, which does not include and all the failed attempts that resulting in one successful drug candidate (Besser 2013). Innovation is expensive.

The typical drug development process involves a finding target protein and *in vitro* testing followed by extensive research in animal models (*in vivo*). Following this, drugs must be approved to move forward into clinical testing. The clinical testing phases range from phase I-IV. Phase I involves testing the drug on a small cohort to assess a drug's safety profile, maximum tolerated dosage and side effects. Phase II trials begin to look at whether a drug is effective and further evaluate its safety in a larger group of patients. Phase III trials are the most crucial and involve testing large groups of patients to evaluate the drug's effectiveness, compare it to the effectiveness of the current standard of care, and monitor the occurrence of side effects in greater detail. The last phase, phase IV, is largely to monitor a drug's characteristics in different populations (demographics) and effects of long-term use. Additional costs imposed by regulatory bodies, such as the FDA, to increase the timeliness of drug approval have also contributed to higher costs.

While drug development is a long and daunting process, there is some evidence that these costs may be over exaggerated to justify the price tag. Estimates have suggested the actual cost may be closer to 4% to 25% of the estimate (Light, Warburton 2011, Kantarjian, Fojo et al. 2013).

1.1.2 Buyers as Price Makers: The Zaltrap Example

Traditionally, large pharmaceutical companies have deeper pockets and more bargaining power when it comes to selling and negotiating with governments. Drug prices remain constant. That is, the supplier does not offer reduced prices in order to maintain a consistent global price. Traditionally, the consumers are the price takers. However, there is one exception to that rule when it comes to the drug Zaltrap.

Zaltrap is a drug manufactured by Sanofi Oncology for metastatic colorectal cancer. Zaltrap was introduced to the US market in 2012 at a price of \$11,000 per month. However, after Zaltrap failed to be more effective than the cheaper gold standard of care, Avastin, a major cancer center in the US, Sloan Kettering Memorial, rejected it. In an unprecedented move, Sanofi decided to slash the price by 50% (Goldberg 2012). Sanofi cited that 'market resistance' was the real reason for the reduction in price.

In general, pharmaceutical companies have different ways of making a drug more cost-effective. The reality is that drug pricing is full of confidential agreements, typically referred to as risk-sharing agreements (RSAs) or other price-reduction tactics collectively referred to as special-pricing agreements (SPAS) (Cheema, Gavura et al. 2012). These could include price-volume agreements, price or volume caps, outcome based payments or rebates. Offering rebates is extremely common in Canada. After a jurisdiction agrees to purchase and reimburse a drug, they can submit a claim to the manufacturer and get a cash rebate (for example, for 25% of the drug cost) at year-end. In a study of 13 different countries (including the ones

discussed in this paper), 9 had taken part in some sort of RSAs for at least one cancer drug (Cheema, Gavura et al. 2012). Netherland was the one country mentioned in this paper that had not taken part in one of these agreements (Cheema, Gavura et al. 2012).

1.2 The Basis for Drug Approval: Cost-Effectiveness Analysis (CEA)

Most countries have a special committee that conducts a review process in order to decide whether a drug should be publicly reimbursed. Canada has pCODR for oncology drugs and the Common Drug Review (CDR) for all others. The CEA is an economic analysis that relates health gains attributed to a drug to the net cost associated with that particular drug's use (or indication) (Cheema, Gavura et al. 2012, United Kingdom, Office of Fair Trading 2007, Clement, Harris et al. 2009).

The analysis is performed by pCODR. As mentioned, it not only takes into account the price of purchasing a drug, but also its safety and effectiveness. The type of CEA that is typically performed is called a cost-utility analysis (CUA). The CUA measures effectiveness in units called Quality-Adjusted Life Years (QALYs). The CUA evaluates the costs in relation to how a new drug performs to improve the quality of life and the number of years lived when compared with other treatment options, most commonly, the current gold standard of care. The QALY is the number of additional years of life expected due to treatment multiplied by the quality of life of the additional years.

The review committees in each country typically set an acceptable range for cost per QALY. For example, in the UK, it is £20,000-£30,000 per QALY; in the U.S. it is \$50,000 per QALY. In Canada there is no threshold value per se, but rather a range of incremental cost per quality-adjusted life-year values (\$20,000-\$100,000), and is then considered in the context of a decision maker's priorities (PCPA) and the interventions' place in therapy.

1.2.1 Incremental Cost Effectiveness Ratio (ICER)

An incremental cost-effectiveness ratio is also performed to compare the efficacy of the new drug to an existing gold standard of care. It compares the cost and health outcomes of two therapies that compete for the same resources. The ICER ratio is the difference in cost of the two drugs divided by the difference in their effectiveness, which will give you an incremental cost per QALY. Sometimes drugs are ranked using the ICER ranking method to determine the most efficient way of allocating funds in a static budget. This method ranks drugs from the least additional cost for the most additional benefit (Pan-Canadian Oncology Drug Review and the Canadian Partnership Against Cancer 2013).

1.2.2 Criticisms of Pharmacoeconomic Analyses

Cost-effectiveness analysis is a widely accepted method for evaluating innovative new therapies around the world. The UK uses CEA expressed as cost per quality adjusted life year gained, while in the Netherlands, the Dutch Health Insurance Board (CVZ) uses CEA criterion in their advice to the minister on adding new technologies to their standard benefit package.

But one of the major underlying assumptions for this analysis is that drug cost and a drug's effect remain constant over time (van de Wetering, Woertman et al. 2012). However, a study by Wetering et al. showed that is not the case, even in the short run, and the costs may deviate significantly from the original CEA outcome (van de Wetering, Woertman et al. 2012). Additionally, a study by Yong et al analyzed 15 different pharmacoeconomic drug submissions (Yong, Beca et al. 2013). They found that many of the analyses had significant problems that distorted the results and were unable to determine the cost-effectiveness of a drug suggesting that there may be better and more critical ways to evaluate new therapeutics (Yong, Beca et al. 2013).

2.0 Different Jurisdictional Approaches

2.1 Canada: A Historical Perspective on Drug Funding

Following a drug's approval by Health Canada, it is issued a notice of compliance (NOC). This means the drug can legally be marketed and sold anywhere in the country. However, for patients to gain access to a drug, it must be listed on a provincial formulary, and each province has its own.

As a result of the individual provincial formularies, the long-standing issue of unequal access to cancer care across Canada has been deemed as a 'postal code lottery' or geographic lottery. For smaller provinces, this is particularly true, as each province has its own healthcare budget, with larger provinces often having more room in their budgets for expensive drug treatments. Larger provinces were also approached first by drug manufacturers, so they often received access to new drugs first. The way new drugs are funded in Canada has changed significantly in the past 3-4 years as result of the Pan-Canadian Pricing Alliance.

2.1.1 The Pan-Canadian Pricing Alliance

The pan-Canadian pricing alliance (PCPA) was established in 2010 in an effort to combat the high cost of new drugs in Canada. It was founded under the Council of the Federation's Healthcare Working Innovation Group. The PCPA banded the buying power of multiple provinces combined and sought to make pricing more consistent, increase the access to drug treatments options, and improve the consistency of coverage criteria access across Canada. All of the

provinces, with the exception of Quebec and Nunavut, are participating in the PCPA. Appendix 1 illustrates how the PCPA fits into the drug approval process in Canada.

After the CDR or PCODR releases its final recommendation on a drug, the PCPA then discusses whether to proceed forward with negotiations for a particular drug. One province steps up to take the lead in negotiating with the drug manufacturer. If an acceptable agreement can be reached between participating provinces and the manufacturer, a Letter of Intent will be signed by both negotiating parties. The Letter of Intent will then be shared with all participating provinces. It is then up to each province to make the final decision on funding the drug through the PCPA agreement, or to enter into an agreement alone with the manufacturer.

Pricing negotiations with drug manufacturers only take into account therapies that are new to the market and have yet to be funded, while the costs of previously purchased/negotiated drugs remains high. Yet, there is a silver lining. Occasionally, pre-existing drugs gets marketed and approval for a new indication and need to go through the process of getting that drug funded for the new indication in each provincial formulary. The PCPA has the opportunity to renegotiate the price of the drug with the manufacturer if they choose to fund the drug for the new indication.

2.1.2 Drug Pricing Prior to the PCPA

Prior to the PCPA's existence, the process was very similar, however, each province did the negotiations with the manufacturer individually. Each province had their own criteria for listing a drug and as a result, there was (and still is) variability

in a drug's listing status, a drug's cost, coverage criteria and product listing agreement. Larger provinces tended to receive better pricing agreements as a result of the volume of expected sales.

2.1.3 The Rise of Privatized Care in Canada

As a consequence of the irregular access to cancer drugs in Canada, the past decade has seen a significant rise in the number of for-profit medical clinics. These specialty clinics have arisen to meet the demand of patients who are willing to cover the cost of an expensive cancer drug that their province may have been unable to fund, and allowing the patient access to the treatment (Flood, Hardcastle 2007). These clinics are expensive as they have significant overhead costs and require a specially trained staff. Additionally, they are not as abundant as patients would like and this has led to patients requesting the ability to purchase these drugs and have them administered in their local hospital or private clinic (CanWest MediaWorks Publications Inc 2007). If cancer drugs were more funded adequately and equitably funded across the country, there wouldn't be a need for private clinics.

2.2 Australia

Australia's healthcare is a complicated mix of commonwealth and government state funded initiatives as well as private insurance (Australian Institute of Health and Welfare 2012). While it sounds complex, the Australian healthcare system reportedly delivers above-average health outcomes (Faden,

Chalkidou et al. 2009). In 2009, it was reported that the Australian government spent \$5 billion dollars on cancer care (Australian Institute of Health and Welfare 2012, Karikios, Schofield et al. 2014). A significant portion of that is spent on cancer drugs. A study by Kariokis et al found that the expenditure on cancer drugs in Australia rose from \$64.8 million in 1999-2000 to over \$560 million in 2011-2012 (Australian Institute of Health and Welfare 2012, Karikios, Schofield et al. 2014). The study also found that the median cost to the Pharmaceutical Benefits Scheme (PBS) for a year of a new cancer drug treatment was \$60,000 (Australian Institute of Health and Welfare 2012, Karikios, Schofield et al. 2014).

The body responsible for making drug recommendations on the public reimbursement of new drugs is the Pharmaceutical Benefit Advisory Committee (PBAC). Similar to many regulatory bodies, the PBAC partly makes recommendations based on the cost-effectiveness of a drug following approval by the Therapeutic Goods Administration (Chustecka 2013). However, as a result of their two-tiered system with public and private insurance, there is a lot of variability in patient care and access to cancer drugs. Now, any drug estimated to cost more than \$20 million dollars per year must undergo further approval by the Minister of Health who then signs off on the final decision. If a drug is not on the reimbursement list, it is unavailable to patients unless they can afford to cover the full costs, as private insurance does not cover the costs of chemotherapy (Chustecka 2013). Like every country, fiscal considerations come first and fore front. However, occasionally negotiations between the drug manufacturer and Government are unsuccessful and represent a significant hindrance in the access to new cancer

medicines. The process for approval has been criticized for its lack of transparency. In particular, the PBAC does not have clear guidelines for approving drugs by not specifying a threshold for cost-effectiveness (Medicines Australia Oncology Industry Taskforce 2013). Notably, Australia has the highest age-standardized incidence of cancer in the world (Dutch National Cancer Control Programme 2010). Just like many countries, the population seeks faster access to life-enhancing breakthrough drugs. One particular drug, Yervoy (ipillimumab), has been shown to extend patients with metastatic melanoma survival by up to 10 years. The drug was only recently added to the list of subsidized medications in June 2013, almost a full year after being approved in Canada and Germany, leading to a lot of frustration and criticisms of the Australian health care system (Chustecka 2013).

2.3 Netherlands

As of 2006, all residents of the Netherlands are mandated to purchase statutory health insurance (SHI) from private insurers. The policies are regulated under the Dutch law. Of the OECD countries, the Netherlands has the highest percentage of its healthcare funded by private insurance, at 77% (OECD 2013).

According to the Dutch government, the Netherlands spends less on healthcare and has been shown to have better healthcare outcomes (Davis, Schoen et al. 2010). However, with respect to cancer, the National Institute for Public Health and the Environment (RIVM) announced that in the past six years (2006-2012), the money spent on cancer care as a percentage of the healthcare spending has almost doubled,

going from % 4.6 to % 8.7 (DutchNews.nl 2013) and has been the leading cause of death in Netherlands for the past 4 years (The European Commission: Eurostat 2013).

The Netherlands is one of many countries in the EU that has recently undertaken a National Cancer Control Programme (NCCP) to address the cancer burden. The Dutch NCCP is an initiative that is neutral in terms of budget and that would realize reallocation on the basis of priorities. The programme covers all aspects of cancer control, ensures coherent priorities and measurable objectives (Dutch National Cancer Control Programme 2010). The goal of the program was not to raise more funds for cancer care, but rather, to more efficiently allocate them.

What is most interesting about the Dutch health care system is that it is entirely based on private insurers (van de Ven, Schut 2008). As a result, the provision of cancer care is the responsibility of each hospital (Dutch National Cancer Control Programme 2010). This means that cancer care actually varies from hospital to hospital, despite the introduction of minimum standards (DutchNews.nl 2014). However, in contrast to many other countries with private insurers, the private providers are highly regulated and the insurance plans are standardized. People are welcome to change companies as they please, allowing for some competition in the market. To prevent loss of profitability from chronically ill patients, they have a risk equalization system where insurance companies are compensated for providing service to those patients who need it most (van de Ven, Schut 2008). It is a sophisticated ex-ante risk adjustment system that compensates companies for actuarially health expenditure differentials that result from various socio-

demographic factors (Halbersma, Mikkers et al.). It also helps to equalize the playing field for insurance companies by allowing them to engage in price competition for premium coverage (Schut, Van de Ven 2005, Halbersma, Mikkers et al.).

In a scenario where a patient becomes ill and requires expensive therapies, they are able to purchase more insurance to help them cover the costs. In reality, to be able to afford a risk equalization system, the health care system is funded through two streams: the health insurance act and a scheme for long-term care services under a regime of price and supply regulation (Exceptional Medical Expenses Act).

2.3.1 Expensive Therapies and Drug Pricing

In Netherlands there are legal and regulatory mechanisms in place to control drug pricing (Dutch Ministry of Health 2011), but this is largely aimed at wholesalers and retailers. In 2005, they introduced competition into the Netherlands hospital market (Halbersma, Mikkers et al.). The problem with this is that it only negotiates the cost of health services and not the drugs themselves but has shown to reduce the cost of healthcare. Additionally, Netherlands is only country of 13 surveyed that was shown not to have engaged in special pricing agreements (SPAS) with drug manufacturers (Cheema, Gavura et al. 2012).

Approximately 20% of the costs of expensive drugs are covered in hospital budgets while the other 80% is covered by the Dutch Health Authority (Uyl-de Groot, de Groot et al. 2010). The Medicines Evaluation Board (MEB) is responsible

for marketing authorization of medicines based on criteria such as efficacy, safety and quality, in addition to pharmacovigilance, and providing scientific advice (Schurer). New treatments are approved either via the MEB or via the European Medicines Evaluation Agency (EMA). The Dutch Health Authority makes the final decision of whether or not expensive drugs will be considered for extra hospital income after receiving an analysis of the therapeutic value and the budgetary impact of the new drug (Uyl-de Groot, de Groot et al. 2010). This requires the submission of health economic data comparable with the UK, Canada and Australia.

Most medicines are reimbursed through health insurance and while necessary medicines for particular conditions are publicly provided free of cost (Table 1).

Table 1. Adapted from (Stolk, Rutten).

Condition	Covered
Tuberculosis	Yes
HIV/AIDS	Yes
Sexually transmitted diseases	Yes
Enhanced vaccination program for children	Yes

If the medicines are not reimbursed or only partially reimbursed, then the patient is responsible for the rest of the fees. Patients can potentially pay up to 80% of the cost of an expensive drug but may be able to purchase additional insurance to cover the costs (Stolk, Rutten). Under certain conditions, however, new expensive

therapies for life-threatening illnesses may be available under centrally subsidized provisions (Stolk, Rutten). The Dutch health care system classifies expensive treatments or “dure geneesmiddelen”, as therapeutics that exceed a cost of €500/prescription. Not surprisingly, oncology drugs comprise almost half of the cost of these expensive treatments yet oncology patients pay no out-of-pocket costs for these drugs (Schurer). In the Netherlands cost effectiveness thresholds are higher than for countries such as the UK (20–80,000E/QALY gained) and based on disease severity and medical need, meaning high cost drugs are more often approved there than other EU countries (Aggarwal, Ginsburg et al.).

Similar to Australia, the Netherlands do not have a formalized threshold value to indicate cost-effectiveness (Boersma, Broere et al. 2010). But unlike the Australian system, the Dutch health care system has one of the highest satisfaction rates in the world (van de Ven, Schut 2008). They consume relatively less pharmaceuticals than other countries, but manage to have one of the highest per capita expenditures on healthcare and cancer care (OECD 2013, Aggarwal, Ginsburg et al.).

2.4 The United Kingdom

The U.K.’s National Health Service (NHS) was established in 1948 and is funded by the government through a taxation system, similar to Canada. It is universal and free for all residents of the U.K. with the exception of some co-pay services. Budgets are reviewed every three years by the government and approved

by Parliament. There is also a very small segment of the market that is privatized (Faden, Chalkidou et al. 2009, Tapay, Colombo 2004). Notably, a study by Reinhardt, Hussey and Andersen found that the prices of expensive drugs in this privatized segment were cheaper than the listing prices in the U.S. market (Reinhardt, Hussey et al. 2004).

One of the strengths of the U.K.'s system is that it's got one of the least restrictive pharmaceutical pricing and reimbursement in the world (Faden, Chalkidou et al. 2009). Following a drug's regulatory approval, it is available for a set price that is determined by the manufacturer. Eventually, almost all drugs become available through the NHS. When an expensive therapy comes along that has the potential to incur significant costs to the NHS, a central decision must take place in order to decide whether to make the drug available to all NHS patients. The National Institute for Health and Clinical Excellence (NICE), established in 1999 to determine which drugs offer significant clinical benefit and cost effectiveness, plays a major role in the decision process (Pearson, Rawlins 2005, Faden, Chalkidou et al. 2009). NICE considers a drug cost-effective if it costs under £20,000 per QALY, and drugs over £30,000 per quality-adjusted life year (QALY) are generally considered not to be a worthwhile investment for the NHS (McCabe, Claxton et al. 2008). Drugs that fall in between require some other justification for acceptance. Although in past years, the system has come under criticism for having a low threshold range per QALYs, while others disagree (Garau, Shah et al. 2011).

A study by Richards indicated that since the establishment of NICE in 1999, approximately 30% of their decisions have pertained to new cancer drugs (Richards

2006). If the NICE fails to approve a drug, a patient in need can appeal the decision. While the NHS may not fund the drug, individual PCTs can still choose to fund the drug for the patient. Of the patient appeals made, approximately 65%-90% were approved. This clearly illustrates the variability in drug access in the U.K., similar to the Canadian system prior to the PCPA.

2.5 The United States

In a country without universal healthcare, how do people afford the price tag on these new therapies? In 2011, the US spent an estimated \$2.7 trillion on healthcare, an estimated 18% of their GDP (Kantarjian, Fojo et al. 2013). According to a 2012 IMS report on the global use of medicines, and a separate OECD study, the US has the highest per capita expenditure on healthcare in the world (Appendix 4) (IMS Institute for Health Informatics 2011). Total Medicare expenditures were estimated at over \$500 billion in 2011 (Himmelstein, Woolhandler 2012). A study by Cheema et al indicated that the US has some of the broadest access to publicly funded cancer drugs (Cheema, Gavura et al. 2012).

In contrast to many countries with universal healthcare, the U.S. has many payers who use different standards and different processes to determine if a new expensive cancer drug should be purchased and reimbursed (Faden, Chalkidou et al. 2009). As a result, it is difficult to assess the access to cancer care and financing of new and expensive therapies. Similar to Canada's individual provincial formularies, there are an excessive amount of formularies in the US, each affected by purchasing

power, state laws, funding programs, and other factors (Faden, Chalkidou et al. 2009). As such, the federal government and some states address needs/deficiencies directly. For example, the Breast and Cervical Cancer Prevention and Treatment Act was created in 2000. It is a Medicaid waiver that allows uninsured women who would otherwise not be eligible for breast or cervical cancer treatment through Medicaid.

A component of the Medicare, Part B, covers drugs that are administered in a clinical setting. It is required to cover and cancer drug that has received a 'medically accepted indication', which would include drugs and uses, approved by the FDA and other sources (Bach 2009, Faden, Chalkidou et al. 2009). While approximately 99% of the population have Part B coverage and are therefore insured for these pricey cancer therapies, they do not have full financial coverage. This can result in some extremely high out-of-pocket costs for both drugs administered in a clinical setting and prescriptions.

Interestingly, one of the major contributing factors to the high drug prices in the US is the law. It is illegal for any government body (such as Medicare) to negotiate lower drug prices, although other bodies, such as Veteran Affairs, are allowed and do negotiate lower prices (25-50% cheaper on average than Medicare) (Kantarjian, Fojo et al. 2013). In 2003 a Medicare drug benefit was extended and additional provisions were added to the law, prohibiting government from bargaining for prices on drugs (Kantarjian, Fojo et al. 2013). Economist Dean Baker estimated 6 years ago that without this provision, the government could have saved

an estimated 50-80 billion per year on drug prices (Kantarjian, Fojo et al. 2013, Lee, Chertow et al. 2009). In Obama's proposed budget for 2014, he requested for Congress to require large drug companies to sell their medications to Medicare at the best price they offer private insurance companies (Potter 2013).

2.5.1 The Affordable Care Act

How does Obama's Affordable Care Act affect this? Obamacare certainly has its critics, particularly when it comes to its effects on people with life-threatening illnesses, but there is literature supporting its negative and positive attributes, with respect to cancer patients.

The arguments against Obamacare with respect to cancer patients are plentiful. First, people are concerned that the Affordable Care Act makes some of the nation's elite cancer clinics off-limits for those insured (Associated Press 2014). This also means that existing cancer patients may no longer have access to the same network of doctors they were seeing previously.

On the other hand, the American Cancer Society argues that the Affordable Care Act will actually benefit those touched by cancer by largely increasing access to cancer treatment. First, the act covers those who did not previously have insurance to receive coverage as a part of each state's high-risk pools; as well, health plans are now banned from setting annual dollar limits on treatment, ensuring patients will no longer have to put off treatments until the new year (The American Cancer Society 2013).

3.1 Discussion

After reviewing the strategies of several countries, the majority with universal healthcare, it begs the question- how can you reduce healthcare spending and still maintain the same efficacy and patient safety (or standard of care)? A summary of health care expenditure can be seen in Appendices 5 & 6. No one country has a completely equitable health care system, but the Netherlands undoubtedly comes the closest with their standardized, mandatory, insurance policies. The question remains as to whether there is an optimal mix of public and private health insurance.

While the sky-high cost of new drugs may have logical roots, there is no reason why drugs like Gleevec still cost \$100,000 a year (Cowley 2013). Often times, these costs are a result of large pharma trying to mitigate the loss in revenues that occur when the patents on their drugs expire and a generic version is introduced. With respect to Gleevec, the earliest of these patents expires in January 2015, as per the FDA Orange Book. The costs of drugs like Gleevec remain astronomically high, despite having earned substantial profits and paid off the cost of its development years ago. For example, in the US alone, the 2013 sales of Gleevec were \$4.69 billion, the same as 2012 and 2011 (as per Novartis' product sales reports). Assuming a conservative cost of development of \$2 billion, Gleevec has more than recouped its costs.

It is clear that there is no one solution to the drug-pricing dilemma. The literature extensively describes the ubiquitous nature of these struggles facing governments in affording new expensive therapies for patients. The rising cost of new innovative therapeutics contributes to the fact that healthcare expenditure in virtually every developed country is on the rise (IMS Institute for Health Informatics 2011). Based on the market landscape and existing data on the previously described countries, there are three proposed solutions. First, allowing the government to have more control over negotiating drug price, second, tying regulatory approval in each country to drug price, and lastly, tying the drug price to expected patient outcomes. All three options will require government intervention to mandate these changes; that being said, they are not necessarily mutually exclusive either.

3.1.1 Government Negotiations

In the US, a simple change such as giving Medicare the ability to negotiate the cost of drugs would save the government billions of dollars each year. Canada has already taken a step in the right direction by forming the PCPA, allowing them to negotiate with drug manufacturers on behalf of all participating provinces. While the PCPA sounds good in theory, the system has many critics in terms of its execution (Dempster, Blanchard et al. 2013).

If drug-pricing schemas are ever going to change, it will require actions that could, in effect, significantly impact the sales of expensive drugs. Take the case of Zaltrap as an example. One major cancer center in the US decided against funding Zaltrap, largely due to cost. This in turn resulted in the drug manufacturer slashing

the cost by approximately half. The economic reality is that the U.S. is the largest pharmaceutical market in the world by value (IMS Institute for Health Informatics 2011). The primary customers in the US are not patients or doctors. The customers are the government (through Medicare and Medicaid) and private insurance companies. And since the insurer or government is picking up the check, companies can and do set prices that few individuals could pay. In the jargon of economics, the demand for therapeutic drugs is “price inelastic”: increasing the price doesn’t reduce how much the drugs are used. Prices are set and raised according to what the market will bear, and the parties who actually pay the drug companies will meet whatever price is charged for an effective drug to which there is no alternative. Governments could be encouraged to set maximum allowable prices, similar to how some governments regulate the cost of generic drugs. This approach would effectively help bring down the cost of expensive new therapies, while allowing drug companies to recoup their costs over time.

3.1.2 Regulatory Approval and Expected Life Outcomes

Prior to a new drug being sold in a new market, it must receive approval from the governing regulatory body, such as the EMEA, FDA or Health Canada. After this, the drug can be legally purchased in that market. The decision by the regulatory body does take into account cost-effectiveness. That part of the process occurs afterwards when either pCODR or the CDR reviews it. There is little or no correlation between a drug’s efficacy and its price, but maybe there should be (Hillner, Smith 2009). In a free market, one would expect the price to eventually

settle and reflect the true benefit, but that doesn't happen. Of the 12 drugs approved by the FDA for cancer treatment in 2012, only 3 prolonged survival (2 of the drugs by only 2 months), and $\frac{3}{4}$ of them cost over \$10,000 per month (Kantarjian, Fojo et al. 2013).

Drug approval should be directly tied to more parameters than just safety and efficacy. It should also assess cost, and the cost associated with QALYs. For example, a drug that confers 6 months of progression/disease free survival (PFS) should cost more than a drug that increased life expectancy by 1 month. In this way, drugs could be categorized based on various levels of efficacy and costs assigned accordingly. It would also act as an incentive for pharmaceutical companies to develop therapies that prolong PFS and a better quality of life as opposed to pushing therapies with minimal efficacy through the process.

4.1 Conclusion

There is a lot of literature citing the astronomical cost of drug development (Baras, Baras et al. 2012, Morgan, Grootendorst et al. 2011, DiMasi, Grabowski 2007), which may be inflated for the sake of Big Pharma (Kantarjian, Fojo et al. 2013). However, the pharmaceutical industry remains highly profitable, at least in North America, despite concerns that it is an industry headed for crisis (Sams-Dodd 2013).

The situation facing governments and access to cancer care is multi-faceted. They must ensure equal access without prejudice across jurisdictions in a way that does not come with a negative social impact due to cost constraints. Multi-tiered health care insurance also complicates things, as those with a better socioeconomic status are more often able to afford better care. Additionally, political forces sometimes prohibit governments from fully leveraging their ability to negotiate with drug manufacturers.

This paper suggests two key strategies for addressing the high cost of cancer therapies. The first, giving governments the ability to negotiate drug costs on a large scale, as well as tying drug approval to acceptable costs by setting maximum allowable pricing schemes. Secondly, re-structuring drug costs based on hierarchical pre-determined ladder of health benefits to the patients. The implementation of a particular solution addressing the cost issue is the hardest area to address. Regardless, it seems that patients and governments are willing to pay more for greater societal and personal benefits.

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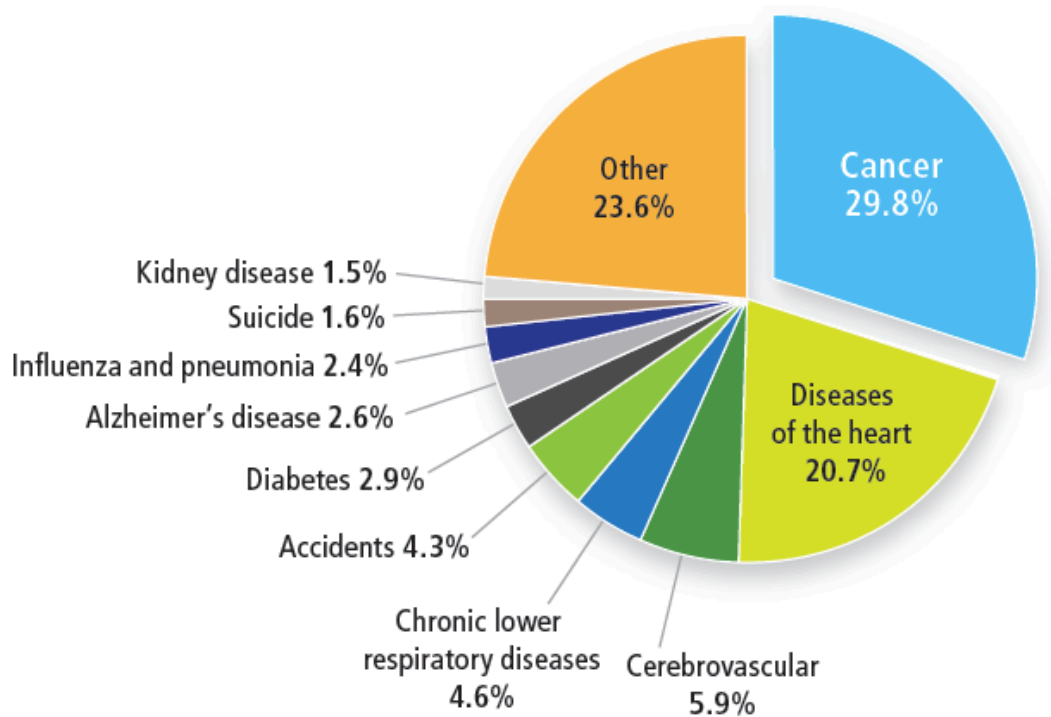
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APPENDICES

Appendix 1. Proportion of deaths due to cancer and other causes, Canada, 2009.

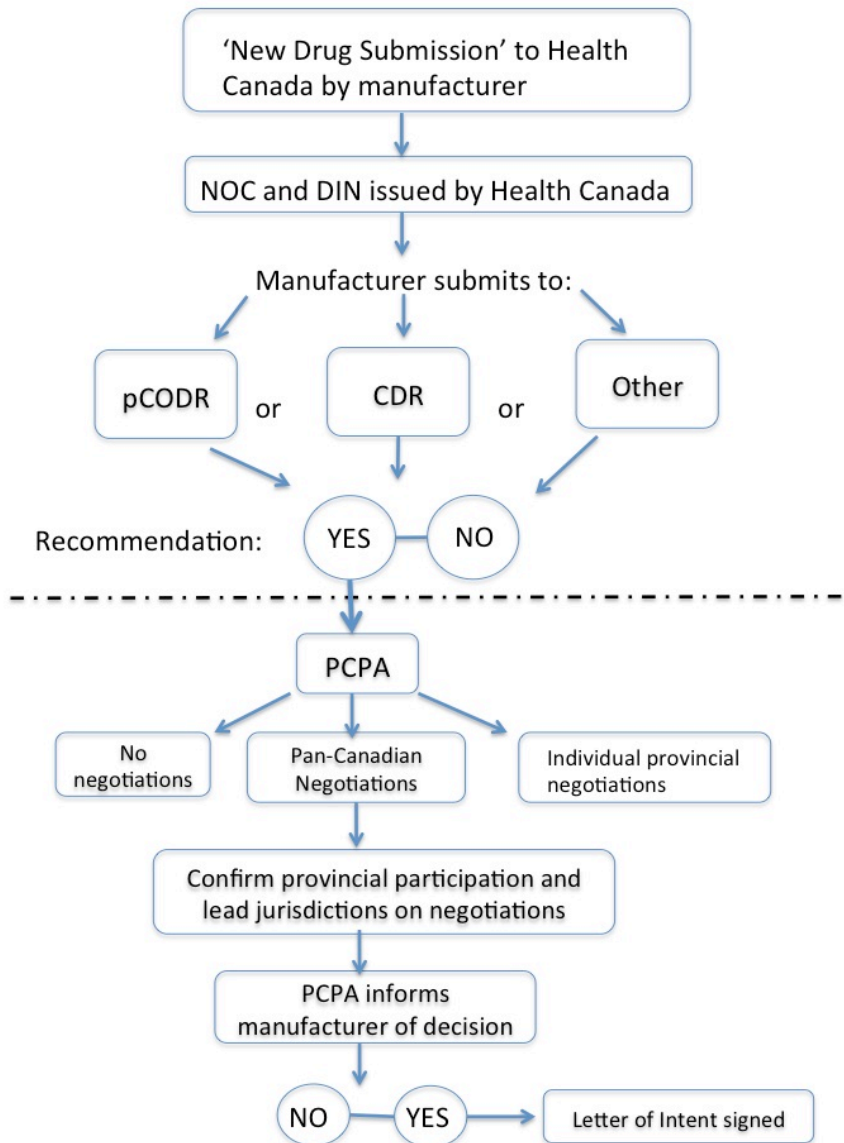


Note: The total of all deaths in 2009 in Canada was 238,418

Adapted from: Statistics Canada. Leading Causes of Death in Canada, 2009, CANSIM Table 102-0561

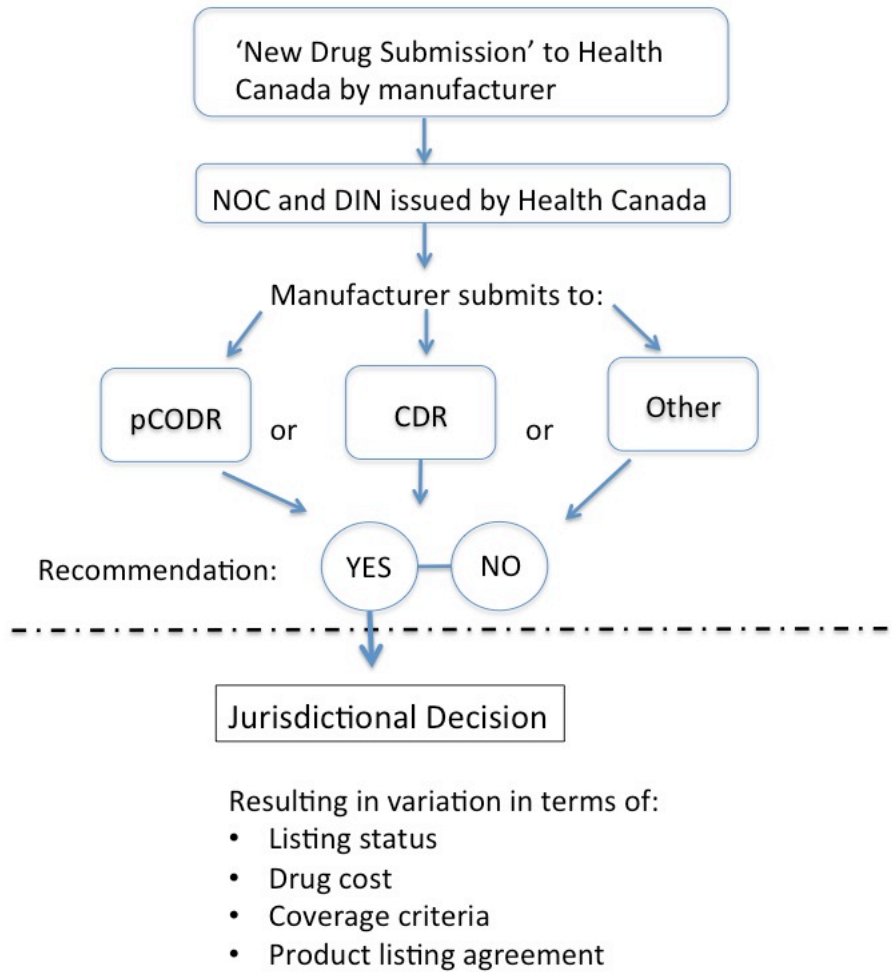
Taken from (Canadian Cancer Society's Advisory Committee on Cancer Statistics May 2013).

Appendix 2. An illustration of how the PCPA fits into the drug purchasing process in Canada.



Adapted from:
http://www.councilofthefederation.ca/phocadownload/pcpa/scope_of_pcpa_process_2014.pdf

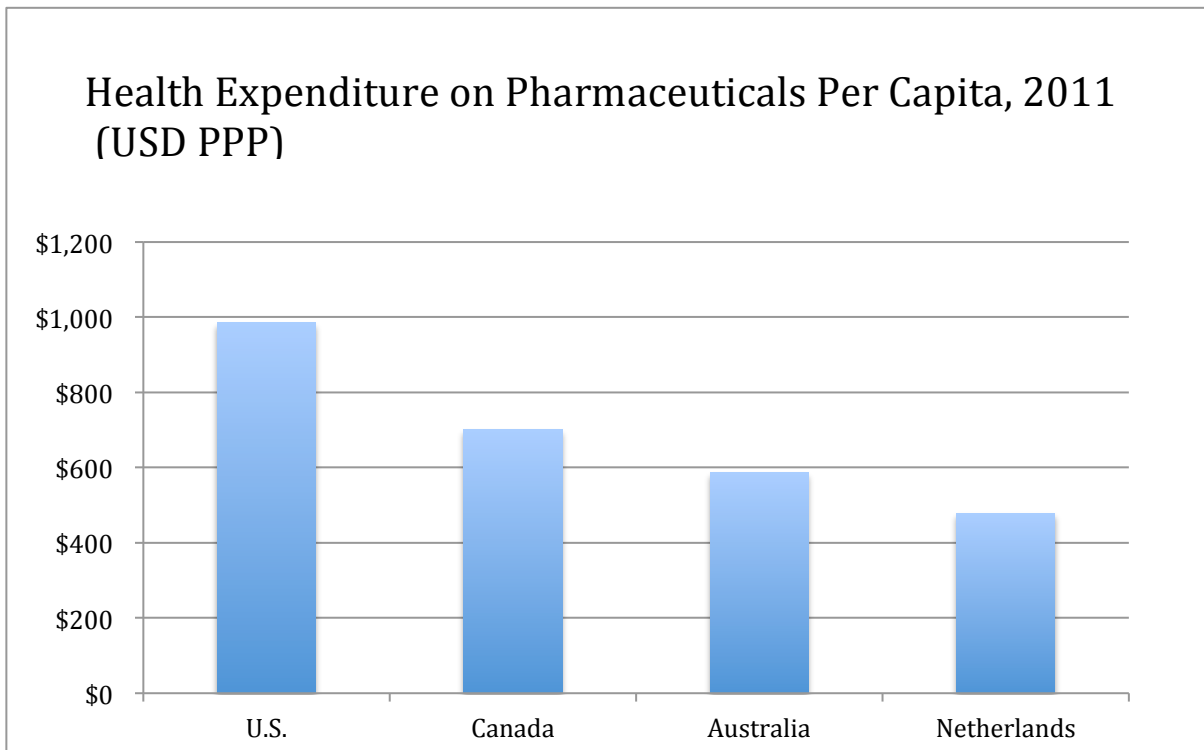
Appendix 3. Jurisdictional drug-approval process prior to the PCPA.



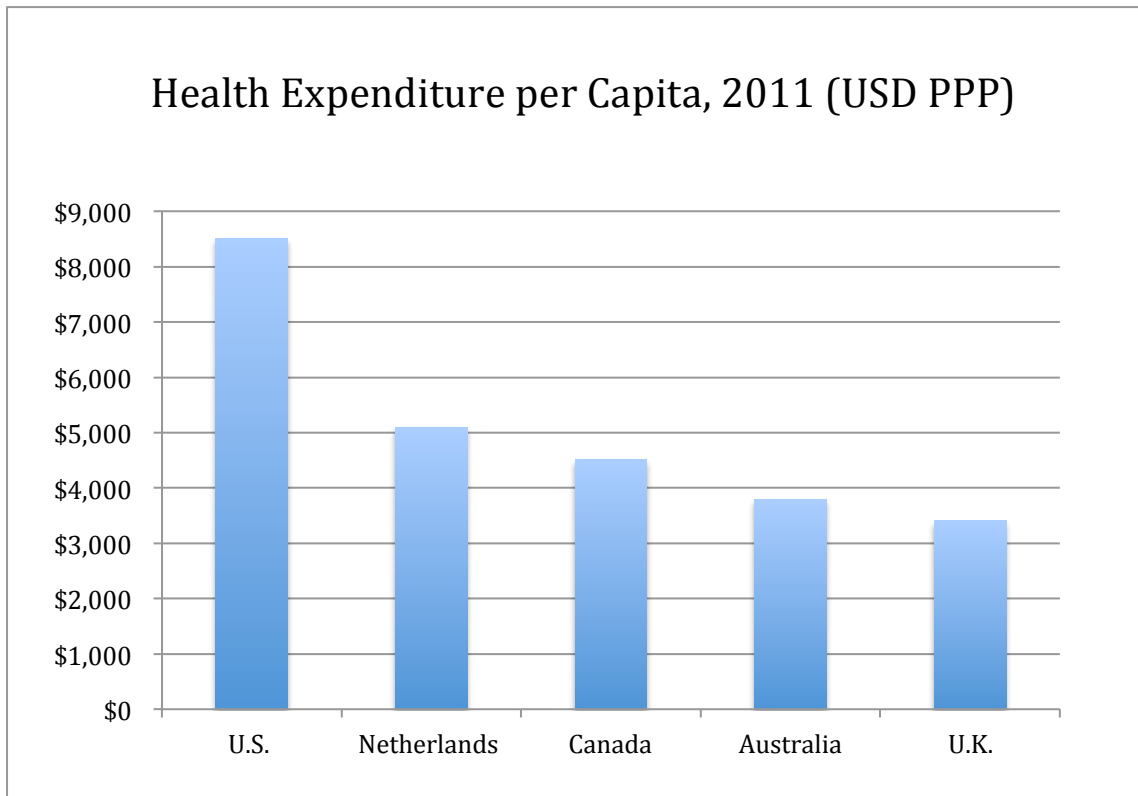
Adapted from:

http://www.councilofthefederation.ca/phocadownload/pcpa/pcpa-the_goliath_of_market_access_oct2013.pdf

Appendix 4. The per-capita expenditure on pharmaceuticals. Adapted from (OECD 2013).



Appendix 5. The health expenditure per capita. Adapted from (OECD 2013).



Appendix 6. The health expenditure as a share of GDP. Adapted from (OECD 2013).

The Health Expenditure as a Share of GDP (2011)

