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Industry-Payor Agreements for Pharmaceuticals
Backgrounder for Roundtable

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Institute of Health Economics

The Institute of Health Economics (IHE) is a non-profit Alberta-based research organization committed to producing, gathering, and disseminating evidence-based findings from health economics, health policy analyses, health technology assessment and comparative effectiveness research to support health policy and practice.

The IHE is governed by a Board of Directors led by Dr. Lorne Tyrrell and CEO, Dr. Egon Jonsson. Board members include five who represent the Government of Alberta and public agencies/authorities, eight who represent the Universities of Alberta and Calgary, including the faculties of pharmacy and medicine, and five members from the innovative pharmaceutical industry. Established in 1995, it is a unique collaborative arrangement among government, academia, and industry.

The IHE has a staff of 25 that includes health economists, health technology assessors, research associates and policy analysts, information specialists, and project and administrative personnel. The Institute is a member of the International Network of Agencies for Health Technology Assessment (INAHTA) and the World Health Organization's Health Evidence Network (WHO HEN) and operates is the secretariat for Health Technology Assessment International (HTAi) www.htai.org .

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Founded in 1990, the Institute on Governance (IOG) is an independent, Canada-based, not-for-profit public interest institution with its head office in Ottawa and an office in Toronto. Their mission is *'advancing better governance in the public interest,'* which they accomplish by exploring, developing and promoting the principles, standards and practices which underlie good governance in the public sphere, both in Canada and abroad.

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Industry-Payor Agreements for Pharmaceuticals: Outcomes and risk in reimbursement

Abstract: This paper provides a typology of "innovative" industry-payor agreements, and focuses on examples of health outcomes-based approaches that are in place around the world and within Canada to explain the diversity of approaches currently being used. In addition, the paper provides information on the main barriers and facilitators that are identified in moving forward with "innovative" agreements.

Introduction

The Institute of Health Economics (IHE) has been performing a project investigating "innovative" Industry/Payor Agreements in the pharmaceutical world.[1] In support of this work we have been assisted by the Institute of Governance in conducting stakeholder interviews and summarizing current literature. This report provides an overview of such agreement approaches, providing a typology of approaches and some of the main barriers and facilitators that exist to implementing "innovative" agreements more widely. This paper feeds into the roundtable being held by the IHE on April 3rd, 2011 in conjunction with the annual meeting of the Canadian Agency for Drugs and Technologies in Health. The roundtable will help to identifying building blocks for success, knowledge gaps and areas for research and policy tool development. This initial report will be built upon, from points raised in discussions and presentations from experts and stakeholders, to form a final report that will hopefully support policy development in this area. Through the interviews and survey information some general messages emerged:

- There is need for early dialogue between industry and payors to create a shared understanding of the new therapeutic and a shared vision of how to bring it to the patients that need it;
- There is a definite need to develop good approaches for ongoing evidence development for therapeutics in the real world;
- There is a need for better understanding of when and where particular categories of formal "innovative" product agreements can add value to the health system(s) in Canada and reduce uncertainty for payors and industry.

Formal product specific agreements are not necessarily appropriate for all new therapeutics. It is clear that such arrangements make sense for certain products and to address certain issues of uncertainty and require some very specific skills and capacity in developing and monitoring. They can be expensive in terms of time and effort so need to be tailored to particular circumstances. They do however provide a potential vehicle to allow quicker and better access for patients to valuable medicines while providing measures to address payor concerns about outcomes, cost and appropriate use.

Purchasing pharmaceuticals is an expensive business. In the OECD countries, pharmaceutical spending accounts for 17% of total health spending on average (OECD 2010). In Canada, we

[1] This IHE project is supported by internal funding from the Institute of Health Economics and through project funding received from Astra Zeneca. Funding was dedicated by Astra Zeneca (global) to support different jurisdictions in conducting policy research and knowledge transfer activities regarding reimbursement approaches.

fall almost exactly on this average, with 17.5% spend in 2005 (CIHI 2006). Finding ways to provide value for money in this spending will have significant impacts on health care budgets.

One way to improve value is to create closer collaboration between industry and government payors, something that the EU's High Level Pharmaceutical Forum has formally endorsed (EU 2008). They have promoted the principle of active collaboration between member states and stakeholders, including industry, to provide: improved evidence generation; partnerships for patient education and involvement; ongoing engagement to match health system and innovation priorities; and development of pricing structures that appropriately recognize value.

As noted in a recent OECD Report on *Value for Money in Health Spending*:

> *"Product-specific agreements could well prove to be a useful new instrument in promoting patient access to innovative treatments while linking public funding to therapeutic value. However, as yet, there is insufficient evidence to be confident in their utility. As these agreements are developing quickly in OECD countries, their results in terms of benefits and costs need to be assessed. The assessment should focus on their design (are all agreements workable?) as well as their final outcomes."* (OECD 2010, 172)

This quote serves to highlight two key factors around "innovative" agreements. First, that they are likely to become more prominent. Second, that they are currently poorly understood, particularly in terms of concrete outcomes. While the first of these points speaks to the need for this IHE and IOG work, the second point guides our thinking on what the work should entail. As such, the following issues paper in support of the IHE roundtable discusses the breadth of "innovative" agreements around the world, and then focuses in on what the challenges are in developing these approaches in the Canadian context.

The burning platform for understanding "innovative" approaches has been made clear by the international interest in this issue; with conferences and roundtables addressing the subject in many countries (with conferences in Germany, Singapore, the UK and the USA). For example, in February 2010, the Health Technology Assessment International (HTAi) Policy Forum, a venue for discussion between high-level global industry leaders, payors and assessment agencies, held a focused dialogue on managed market entry of new technologies.[2] The scope of discussion at the 2010 meeting addressed "*managed entry agreements"* and included strategies for adding value across the lifecycle of a technology, from early engagement with payors and regulators for evidence generation to optimizing technology performance in clinical settings.

What's in a name? Terms and nomenclature

So far we have referred to these agreements as "innovative". This is for two very good reasons. First, the concept of innovative is a relative term when considering a global market place for pharmaceuticals, and what is considered innovative in one jurisdiction may not be in another. Second, that "innovative" is really a cover-all term for a variety of different approaches to industry-payor agreements.

It is important before we move into assessing what exists internationally, that we provide some definitions of "innovative" agreements. In general, "innovative" agreements are those that move

[2] The Institute of Health Economics operates as the secretariat for HTAi and supports the HTAi Policy Forum and Board activities.

away from traditional pharmaceutical purchasing approaches of "pass or fail" admission to payor formularies. "Innovative" approaches therefore work on a drug-by-drug basis, where the individual qualities of the therapy relate to the formal payment agreement and payors and industry work together to what is a common goal of providing access to new medicines which provide value to patients.

Product listing agreements (PLAs) – This is the term most commonly used to describe "innovative" approaches (as broadly defined above). PLAs are formal agreements by product or defined group of products, between individual companies and payors to address uncertainty or risk around appropriate use, budget impact, or outcomes associated with the reimbursement and associated use of pharmaceutical products.

Managed entry – Another common term often referred to in discussions around "innovative" agreements, *managed entry* refers to the process of payors working with industry to manage the way that new therapeutics are brought into the market (Weetman 2008). By working together to manage the entry of the therapeutic, industry has a greater likelihood of succeeding in the market, while payors have greater knowledge of the therapeutic that is entering the market (HGS Consultancy, nd).

There are different names for these formal agreements focused on different objectives and parts of the product life cycle etc. (risk sharing agreements, price-volume agreements, product or outcome guarantees, coverage with evidence development (CED), access with evidence development (AED) (McCabe et al. 2010) and payment for outcomes or performance based reimbursement schemes (Carlson, Garrison et al. 2010). There are also innovative partnership arrangements being considered between payors and industry that support appropriate utilization, disease management initiatives or linking reimbursement with other local research investments. Approaches are either attempting to address some uncertainty or to achieve some specified outcome.

Different approaches

As identified above, within PLAs and managed entry, there are a number of different approaches that can be taken to relate the pricing of the therapeutic to its performance. Recent work has developed a typology of these approaches, splitting them into approaches that are health outcomes-based, and those that are non health outcomes-based (Carlson, Garrison. *et al* 2010).

Health outcomes-based schemes are those that relate the price of the drug/therapeutic to the health outcomes of individuals or populations that are using the therapy. As such, they relate the value of the drug to the health impact it can achieve. Within health outcomes-based approaches, there are a two main types of approach identified, each with a subset of approaches within them:

(1) Conditional coverage: schemes where coverage is granted conditional on the initiation of a program of data collection.

a. **Coverage with evidence development (CED):** binary coverage decision is conditioned upon the collection of additional population level evidence, from a pre specified scientific study, to support continued, expanded, or withdrawal of coverage.

CED has been suggested to have numerous benefits and risks for different stakeholders in the drug purchasing process. These are nicely summarized by Hutton et al (2007) and are presented in the table below.

Stakeholder	Benefits	Risks
Decision makers	• Allows patient demand to be met through managed entry of promising technologies with significant uncertainties. • Influence over evidence generation to ensure it meets decision-makers' needs.	• Potential for investing in technologies that prove not to be cost-effective. • Extra burden of monitoring and review in the light of further evidence (and possible costs of data collection if not fully borne by manufacturer). • Difficulty in withdrawing technologies that prove not to be cost-effective.
Healthcare providers	• Access to promising technologies earlier in their life cycle. • Increases treatment options available to patients.	• Risks involved in using technologies that are not fully evaluated or recommended by guidance. • May increase exposure to litigation.
Industry	• Adoption (initially limited, but with potential to expand) of technologies with equivocal evidence that otherwise might be rejected.	• Delays to market access for effective technologies. • Additional burden of data collection/analysis. • Restrictions on pricing decisions.
Patients	• Access to promising technologies that may otherwise not be available	• Access to technologies that may prove to be ineffective or for which dis-benefits may outweigh benefits.

i. **Only <u>in</u> research:** coverage (CED) conditional on individual participation in research (i.e. only patients participating in the scientific study are covered).

ii. **Only <u>with</u> research:** coverage (CED) conditional on a scheme to conduct a study that informs the use of the medical product in the full patient population.

b. **Conditional treatment continuation (CTC):** continuation of coverage for individual patients is conditioned upon meeting short-term treatment goals (e.g. tumor response or lower cholesterol).

(2) Performance-linked reimbursement (PLR): schemes where the reimbursement level for covered products is tied to the measure of clinical outcomes in the "real world".

a. **Outcomes guarantees:** schemes where the manufacturer provides rebates, refunds, or price adjustments if their product fails to meet the agreed upon outcome targets.

b. **Pattern or process of care:** schemes where the reimbursement level is tied to the impact on clinical decision making or practice patterns (e.g. whether or not patients adhere to the treatment course suggested by a risk predicting genomic test).

Non health outcomes-based schemes

1) **Market share** – also called "penetration pricing" – the use of low pricing at the entry point into the market in order to increase market share in the drug category. This becomes problematic for companies if pricing is benchmarked internationally.

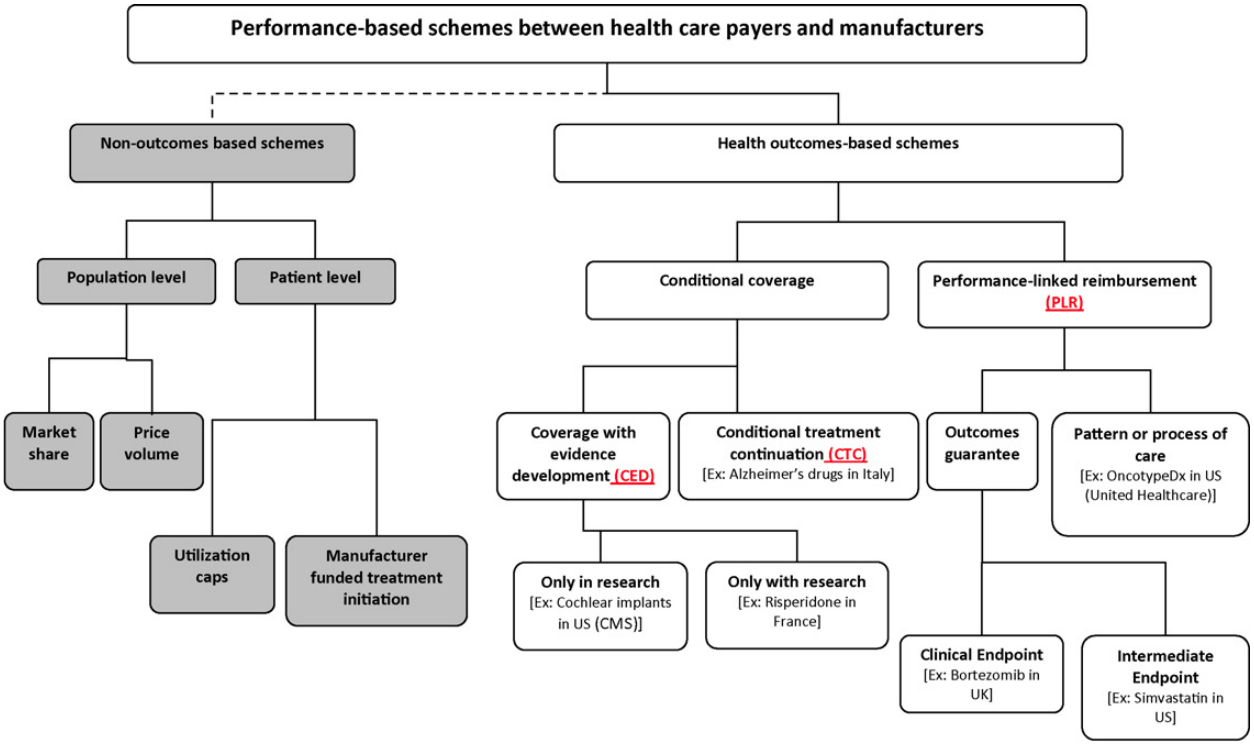
2) **Price-volume** – can be modified to incorporate different populations at different price/volume levels. Provide reduced prices as volumes of pharmaceuticals used increases. For target populations this is more innovative. There is some evidence around the effectiveness in budget management from the EU, with France reporting estimated savings of 400 million EUR for 2005; Italy saving 800 million EUR in 2006; Portugal saving 10 million EUR in 2006; and the UK saving around £15million per year between 1992-1999 (Espin and Rovira 2007)

3) **Utilization caps** – risk sharing approach, similar to price-volume approaches but are at an individual not population level; measures utilization by patients, not health outcomes.

4) **Manufacturer funded treatment initiation** – true risk sharing, since the full costs of initial treatment are paid for by industry until enough evidence is provided to convince payors (NO coverage with evidence development).

While it is important to be able to classify the approaches into this typology, it is worth noting that there are numerous examples of hybrid approaches, which will build on more than one aspect of the typology above. Figure 1 below provides a visualization of this typology.

Figure 1. Taxonomy of industry-payor agreement approaches (Carlson, Garrison, et al. 2010)



Using the wide lens – The international picture

The sale of pharmaceuticals is a global business, and the presence of international reference pricing has been one of the drivers behind creating innovative approaches to purchasing agreements – as it allows industry to maintain an international reference price while entering a market they would not be able to at that reference price (Touhmi 2010). Innovative approaches have sprung up in different ways in different jurisdictions around the world, and below we identify some of the most relevant from Europe, Asia and Australasia, and North America.

Europe

Europe has been very active in testing new approaches to industry-payor agreements, with different countries taking different approaches. The UK and Sweden have been particularly active in developing a variety of "innovative" approaches, but these vary in their scope and structure.

NICE (UK) and flexible pricing

In the UK, the PPRS has established that certain drugs can enter the market at lower cost, with the knowledge that if they are shown to be more effective in consequent NICE assessments, then their price will be increased. Roche has agreed to discount by 14.5% the price of its treatment for non-small cell lung cancer (erlotinib) in order to equalize its price to a cheaper competitor until definitive results of head-to-head clinical trials are available and a new NICE appraisal (OECD 2010).

In the UK, the new Pharmaceutical Pricing Regulation Scheme (PPRS) signed in December 2008 for five years aims to introduce value-based pricing for drugs purchased by the NHS. The government and the industry have agreed to "flexible pricing": companies can increase the price of their products after market entry provided new evidence has been produced about the benefits of their drug – as assessed by the National Institute for Clinical Excellence (NICE); *see box to the right* (OECD 2010). In addition, the UK have been involved in other approaches, such as manufacturer funded treatment initiation, where UCB agreed to provide the first 12 weeks of its treatment for moderate to severe rheumatoid arthritis (certolizumab pegol) at no cost to the NHS, with the NHS continuing to fund the treatment if the clinical response is positive for individuals (OECD 2010). The NHS is also involved in utilization capping, with a deal with Novartis on treatment for acute wet-macular degeneration with the drug ranibizumab. The NHS pay for the first 14 cycles of treatment, but any additional treatments are paid for by Novartis (OECD 2010). The UK has also been involved in outcome guarantees, with Velcade for the treatment of multiple myeloma being paid for through a risk sharing agreement based on the proportion of patients achieving partial or full response as measured through 50% reduction in serum M-protein. Should patients fail to reach this level, then Johnson and Johnson (the manufacturer of Velcade) with refund the cost of those patients (Trueman nd).

In Sweden, there have been numerous examples of coverage with evidence development. These include pharmaceutical companies providing additional data:

- To support the economic value of inhalable insulin in a Swedish clinical day-to-day setting.
- On the long-term effects of rimonabant and its economic value in a Swedish clinical day-to-day setting.
- On the cost-effectiveness of rasagiline versus entakapon and selegilin.
- On the long-term effects of lyophilisate (a drug for grass pollen allergy) and a new health-economic evaluation based on costs and medical effects of the drug in clinical practice.
- On the long-term effects of Champix, a smoking cessation drug.

- On ongoing and planned studies in order to determine the cost-effectiveness from a long-term perspective for the HPV drug Quadrivalent. Data to be provided every 6 months starting from 01/10/2007.
- On the effect of Neupro (for Parkinson's disease) in the Swedish clinical day-to-day setting. (All from Carlson, Garrison et al 2010)

Italy has also taken on a number of "innovative" approaches, with conditional treatment continuation, outcome guarantees and manufacturer funded initiation all used. For example, Alzheimer's disease drugs are provided free by manufacturer and assessed for short-term effectiveness during the patient's first 3 months on the drug. If treatment goals are met after 3 months, then treatment is continued for a maximum of 2 years with the drug costs reimbursed by the National Health Service. Also, Novartis has agreed to refund the cost of treatment with nilotinib for CML for every patient who does not reach an agreed hematological response after 1 month (Carlson, Garrison et al 2010).

Belgium and the Netherlands both have forms of conditional coverage schemes that take into account multiple factors relating to the value of the new therapeutic.[3] These factors can include: effectiveness in clinical practice; pharmaco-economics in clinical practice; size of the target group; sales volumes; and, reimbursement status in other EU Member States (EU 2008). In Germany, a health insurance fund signed an agreement with Novartis to obtain a refund of a patient's treatment for osteoporosis if an osteoporosis-related fracture occurs (OECD 2010).

Greece is revising its reimbursement and pricing policy to a modified *price-volume* approach that will use the three lowest prices in the European Union as benchmark for price at market entry. This will then be combined with "dynamic pricing" after market entry such that an annual increase in sales exceeding 5% will lead to a 2.5% price reduction for Greek government payors (OECD 2010).

Asia and Australasia

Australia have been one of the major countries who have taken on "innovative" approaches, with numerous non health outcomes-based approaches and a small number of health outcomes-based ones. New Zealand have yet to move towards "innovative" approaches, but their spend on pharmaceuticals is also lower than other reference countries, so they have not yet felt the need to move to value-based pricing (Sundakov and Sundakov, 2005). There are some instances when price-volume agreements can be used in NZ however (Pharmac 2010; Willison et al 2001). In Asia, Singapore has not yet moved to "innovative" pricing approaches, but they do seem ready to in the near future, with a roundtable in Singapore on the subject of innovative pharmaceutical pricing models concluding:

> *It was timely for all stakeholders to give thought on how innovation in formulary decisions could be introduced into the system and what drugs could be included under such schemes. Moving forward, if there was interest by healthcare institutions or pharmaceuticals to moot innovative pricing proposals, it would be fitting to engage in discussions with the Healthcare Finance Division at the Ministry of Health*. (SingHealth Centre for Health Services Research 2009)

[3] In the Netherlands the focus has been on expensive cancer drugs

In Australia, the Medical Services Advisory Committee (MSAC), which determines the coverage of medical devices, can allow interim funding for data collection that will help to show the effectiveness of a new therapeutic. However, this CED approach is one that must take place within an agreed research framework, and as such the data collection approaches are developed in partnership between government payors and industry (Hutton et al 2007; Klemp et al 2011). The box to the right provides an example of where CED is in use in Australia.

Australia and Coverage with Evidence Development

In Australia, Actelion pharmaceuticals have agreed to link the price of Bosentan, a drug for pulmonary arterial hypertension, to the survival of patients followed in an observational study. This is a prime example of CED using an only in research approach (Carlson et al 2010).

As an example of outcomes guarantees and conditional treatment continuation, Medicare Australia will provide conditional reimbursement to Novartis for imatinib mesylate on an assessment of short-term effectiveness evaluated at 18 months. Reimbursement will continue for patients in whom it is effective and cease for those it isn't effective. A similar approach is taken for etanercept, a drug for rheumatoid arthritis (Carlson 2010). Also, while we are not covering price-volume agreements in detail here, they are common in Australia, where they are used to manage utilization uncertainty in a country with multiple populations (Towse and Garrison 2010).

North America

In the U.S., the focus on "innovative" agreements has generally been around the medical device industry, rather than pharmaceuticals (Carlson 2010). This is likely due to differences in the level of evidence required to reach the market in the U.S. for devices and drugs. For those drugs that have been purchased through "innovative" agreements, the U.S. has a combination of coverage with evidence development, conditional treatment and performance-linked reimbursement schemes.

For U.S. CED schemes, all are funded by the health insurer CMS and cover activities undertaken as part of approved clinical trials. They include: coverage of Percutaneous Transluminal Angioplasty and Stenting of intracranial arteries for the treatment of cerebral artery stenosis ≥50% in patients with intracranial atherosclerotic disease; use of PET scans for dementia patients in trials; and, cochlear implants for those in trials (Carlson 2010). Drug agreements in the U.S. tend to be in conditional treatment and performance-linked schemes. For conditional treatment, CMS will reimburse erythropoiesis-stimulating agents until the patient achieves a hemoglobin level of 10 g per dl (Carlson 2010). For performance-linked approaches, there have been four interesting agreements identified in the U.S. These are shown in the table below:

Disease area	Product	Manufacturer	Payor	Description
High cholesterol	simvastatin	Merck	Patients and insurers	Merck promised to refund patients and insurers up to 6 months of their prescription costs if simvastatin plus diet did not help them lower LDL cholesterol to target concentrations identified by their doctors.
Breast cancer	Onco*type* Dx	Genomic Health	United-Healthcare	UnitedHealthcare agreed to reimburse the Onco*type* Dx test for 18 months while it and Genomic Health monitor the results. If the number of women receiving chemotherapy exceeds an agreed upon threshold, even if the test suggests they do not need it, the insurer will negotiate a lower price.
Type 2	sitagliptin;	Merck	CIGNA	Merck has agreed to peg what the insurer CIGNA

diabetes	sitagliptin + metformin			pays for the diabetes drugs sitagliptin and sitagliptin + metformin to how well type 2 diabetes patients are able to control their blood sugar.
Osteoporosis	risedronate	Proctor & Gamble, sanofi-aventis	Health Alliance	Two companies that jointly sell the osteoporosis drug risedronate agreed to reimburse the insurer Health Alliance for the costs of treating non-spinal fractures suffered by patients taking that medicine.

* Table taken from Carlson et al 2009.

The final approach identified in the table, that for risedronate, is particularly interesting as it is the first identified example of a pharmaceutical company paying for disease-related outcomes that were not prevented by the drug in question (Carlson et al 2009). This is a major step for "innovative" agreements, as it is a significant departure from simply reimbursing the cost of the drug or discounting the costs of further treatment. This approach is worth watching further to see how it develops as it may change the approaches taken more widely than just the U.S.

In sharp focus – Canada and the provinces

In Canada, pharmaceutical purchasing is determined by the provinces, although with significant input from the common drug review at the national level. Each province has the ability to determine which drugs it wants to fund on its formulary, and this can include drugs that were not recommended for listing by the common drug review, if the province deems it appropriate to fund based on some negotiated arrangement. The participating provinces in the Common Drug review utilize and do not repeat a centralized cost-effectiveness assessment but are independent in terms of their policy response. There is clearly pressure for some harmonization in listing decisions and this is profiled with increased communication between provinces amongst particular patient access advocacy organizations.
For "innovative" agreements, in Canada, this means looking at primarily provincial decision-making as private payors generally provide open formularies passing on costs to plans. The federal government does run a number of major drug programs and as well is responsible for regulatory approval. As part of that regulatory or market authorization process Health Canada will occasionally identify promising drugs that are yet to provide enough evidence to warrant full notice of compliance (NOC) status, and will label these drugs as "compliant with conditions". This means that Health Canada will expect further trials and significant monitoring of the drug in circulation (Health Canada). A phased conditional regulatory approval combined with perhaps a phased conditional reimbursement approach signals a new world of evidence gathering which could occur along the entire life cycle of a product.

For the drug companies, identifying specifics around a particular agreement with a province may understandably not be transparent. There is significant secrecy around where innovative agreements have been put into practice in Canada and the terms and conditions. This has made it difficult to identify exactly who is involved in "innovative" agreements, and to what extent.

One example available is and old one from Saskatchewan, where the drug finasteride (Proscar) for benign prostatic hypertrophy, has been provided by Merck with an agreement to refund the cost of the drug in situations where a patient receiving the drug subsequently proceeded to surgery (Klemp et al 2011). Interestingly, with this example of performance-related reimbursement, the outcome was that the utilization of the agreement was lower than expected due to strict conditions on which patients were deemed eligible for the refund (Klemp et al 2011).

Ontario has been using conditional treatment approaches, with an agreement between an Ontario health authority and Pfizer, Novartis and Johnson & Johnson over Alzheimer's drugs providing for patients using donepezil, rivastigmine, or galantamine. The patients will be reimbursed for a period of up to 3 months for patients on those drugs, after which further reimbursement will be made available to those patients whose disease has not progressed/deteriorated while on this drug (Carlson et al 2010).

In Alberta, it was identified by one interviewee that there was a move towards reinvesting money saved through pharmaceutical purchasing agreements into an "innovation fund" for new drugs. This is difficult to corroborate however. Alberta, has had some experience with appropriate utilization agreements and has proposed a policy suite of a number of approaches in its new pharmaceutical strategy. These include price-volume agreements, CED (which experienced difficulties around data collection) and "listings with research capacity" (where the drug company provided the funding to research the effectiveness of the new drug, rather than performing the study themselves).

Sandoz Canada promised to reimburse individuals, hospitals and government drug plans where patients with treatment-resistant schizophrenia discontinued clozapine within six months. This was initiated to address acquisition cost concerns versus typical anti-psychotics among the Provinces (Adamski et al 2010). Sanofi-Aventis agreed to reimburse the cost of docetaxel to provincial payors if an agreed responder level was not reached in patients with cancer due to concerns about its efficacy and costs (Adamski et al 2010).

Manitoba was also cited as a location with potential for interesting "innovative" agreements, since the presence of a "utilization management agreement" between government payors and industry requires industry to provide comparative effectiveness data. However, this agreement approach currently only requires industry to show that their new therapeutic is more effective than existing approaches, and does not link payments to health outcomes. The Atlantic Provinces have yet to move to "innovative" approaches beyond some price-volume agreements. For QC it is currently unknown to what extent they are taking forward "innovative" approaches.

The Atlantic Provinces, BC and Alberta are all working on developing systematic approaches to "innovative" agreements, according to interviewees. However, since these are work in progress, and agreements are likely to be kept secret when the systems are in place, it is difficult to provide details on the systems being developed. Alberta have some information on their developing system, in that the framework being developed has four arms:

- price volume approaches;
- utilization management approaches;
- listing with evidence development approaches;
- listing with research capacity approaches (a new category in AB that speaks to agreements in which the drug company will provide value back to the province in terms of research capacity building in the area their product is focused. This is technically a sub-category of CED approaches).

One major problem with the lack of information on innovative approaches in Canada, is that there is very little information on whether they work on not in the Canadian context. While not available in the literature, there is evidence from one interviewee, that one CED approach used in Ontario for Plavix, was not hugely successful, since the length of time it took to get data on outcomes was so long compared to the need for reimbursement.

Even with a little data, we have attempted to develop a matrix of Canadian provinces and their current involvement in "innovative" purchasing agreements (table below). This will be adjusted with feedback from roundtable participants and further discussions with jurisdictions.

Provinces and existing (available) innovative arrangements[4] - *DRAFT* *(based on initial information gathering will be supplemented for final report)*

INNOVATIVE APPROACH CATEGORY	Province										
	BC	AB	MB	SK	ON	QC	NB	NS	PEI	NFL	Territories
Conditional coverage					✓						
Coverage with evidence development (CED)		✓									
Only in research		✓									
Only with research		✓									
Conditional treatment continuation (CTC)					✓						
Performance-linked reimbursement (PLR)	✓	✓		✓	✓						
Outcomes guarantees	✓	✓		✓	✓						
Pattern or process of care											
Market share											
Price-volume	✓	✓		✓	✓		✓	✓			
Utilization caps											
Manufacturer funded treatment initiation											

* Shading relating to the Atlantic Provinces represents their united approach to innovative agreements, where they are developing systems across the Atlantic Provinces, rather than in specific provinces.

The views of key stakeholders

In addition to the existing literature and documentation on this subject, the project team interviewed 25 key stakeholders in industry, government, HTA, academia, insurance and other stakeholder groups from Canada and internationally.[5] We supplemented this interview information with survey data from a short six-question web survey for stakeholders we could not access for interviews.

Interview main themes

From the interviews, there were a number of recurrent themes, regardless of the stakeholder group that people came from.

Theme one – Innovative agreements are ones that speak to some concept of "value": Nearly all the interviewees identified that for an agreement to be innovative, there needed to be some link to the value of a new drug to the health system. This value can be realized through evidence of real-world effectiveness, or through a way to link price to health outcomes.

[4] It should be noted that these approaches are generally kept secret in order to protect the international list price of any drug being purchased through an innovative agreement approach.
[5] See Appendix A for the list of organizations interviewed as part of this project

Theme two – Innovative agreements are sometimes seen as a "flavour of the week": In reality, innovative approaches should be considered only in specific circumstances, such as for expensive but potentially effective drugs, or for therapeutics that work well in specific populations. However, interviewees felt these approaches are often pushed where they may not be appropriate. There are other approaches to managing the use of pharmaceuticals which do not involve formal agreements (restricted listings, specialist prescribing, guideline development and dissemination to prescribers/patients).

Theme three – The benefits of moving to innovative approaches can accrue to many stakeholders: While the main benefit mentioned across interviews was improving patient access to drugs, there were also benefits identified for payors (shared liabilities; access to drugs that might not be recommended for listing by the common drug review; ability to manage drug access for specific sub-populations), industry (earlier entry to the market; increased sale of drugs that might not make it into payor systems through traditional means; chance to be reimbursed based on good performance, as well as penalized for bad), and the health system (doctors are able to provide more choice and focus drugs to populations better; chance to make sure the health system is not paying for drugs that aren't effective in sub-populations).

Theme four – Risks are as numerous and diffuse as benefits: Industry bears a risk in any agreement that speaks to outcomes or evidence, since revenues may no longer be dependent on just a reference price and product volumes. However, the risks to other stakeholders can be equally as large. For payors, adding new drugs to the formulary can be very risky without clear understanding of expected outcomes. Should a new drug not be shown to be as effective as hoped, then it becomes very difficult to remove it from the formulary, even with innovative agreements that speak to exactly that issue. For patients, having a drug removed from the formulary can create major stress and worry; this can also lead to patients suddenly being asked to pay for expensive drugs that had previously been covered.

Theme five – Putting innovative agreements in place is a costly business: On all sides, it was acknowledged that any agreement that deviates from the current approaches to purchasing drugs is going to require significant administrative and legal human resources to implement. In addition to the human resources cost of setting up agreements, there are also significant costs associated with the data on effectiveness and outcomes that underpin many innovative approaches. In general the cost of collecting and analyzing such data would be prohibitive to putting in place agreements in the current financial climate.

Theme six – Everyone needs collaboration, but not everyone wants it: One issue that came through clearly in all the interviews is that for any innovative purchasing agreement that looks at value, outcomes and evidence, the agreement would work more effectively if industry and payors work together to develop, implement and evaluate the agreement. However, perceptions from the different groups about 'motives' of the other are a significant barrier. Building trust is a major issue that will need to be effectively addressed if innovative agreements are to succeed.

Survey findings

The survey of interested stakeholders conducted to support the roundtable resulted in 38 respondents from industry, government, academia and HTA.[6] It identified that the majority of

[6] Full results from the survey are shown in Appendix B.

people in industry and all the people in government are already involved in some sort of innovative agreement. The majority of respondents considered that innovative approaches would become more important in the future, with only a single dissenting voice in the academic community feeling that these approaches will become less important.

When considering the most important values brought by innovative approaches, respondents identified "patient access" as the most important value. However, there is no clear single value brought by innovative agreements. In addition to patient access, managing real world patterns of use of drugs, and addressing effectiveness and cost-effectiveness were seen as areas where innovative agreements can add value. Issues relating to cost and budget management were less important.

The survey asked about barriers and facilitators to putting innovative agreements in place. The major barriers seen are: Capacity or expertise in government; Process of monitoring the performance of agreements (organizational capacity and structure to monitor); and, Ability to gather information on performance to assess objectives of the agreement. Interestingly, the main facilitator for innovative approaches is "Willingness in industry". Considering Industry form the largest single responding group in this survey, this would not seem surprising, however investigation of the responses by sector shows that the majority of people who considered this a facilitator were in fact from government, academia and HTA (ten responses to Industry's seven). Issues around the level of certainty of the benefits for industry, payors and patients were considered to be more neutral in terms of implementing new agreements.

When, where and why? Barriers and facilitators to implementing approaches

Since the aim of this roundtable is to better understand the need for, and appropriate implementation of, innovative industry-payor agreements, the table below summarizes the major barriers and facilitators for innovative approaches that we have identified through all the lines of enquiry in this work. We have also identified which types of innovative agreement these barriers and facilitators relate to.

Table 1. Barriers and facilitators to implementing innovative agreements

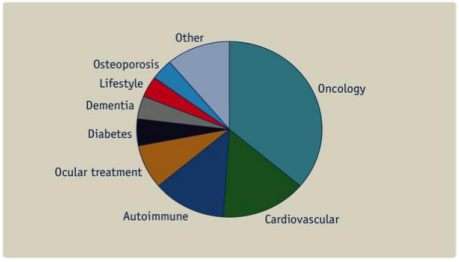
Barriers	Facilitators
Resources – For both industry and payors, innovative agreements can be resource intensive (admin, data collection, legal needs, etc.). *This barrier is applicable to all approaches, but particularly pertinent for conditional coverage and performance-linked approaches.* Trust – Since agreements have always been about negotiation, there is a lack of trust between the two sides of agreements that restricts collaboration and true sharing of risk across agreements. *This barrier is applicable to all agreements, but is particularly true for coverage with evidence development approaches, where there is a lack of comfort over who should develop the evidence on effectiveness.* Ability to monitor approaches and collect data –	Willingness of stakeholders – In general, industry and payors are interested in moving forward with innovative agreements where they add value. Clearly there are discussions over where that is, but there is a willingness on both sides to move forward with these approaches. *Willingness is stronger for agreements that show value and relate it to reimbursement, as well as for agreements that have lower development costs.* Ongoing development of frameworks to assess when to use "innovative" approaches – The development of these frameworks in multiple provinces suggests that there will soon be guidelines that provinces and industry can learn from and work within. *This is useful for all approaches.*

there is a strong level of uncertainty across stakeholders that there is the capacity to monitor effectiveness in the real world, and to collect and analyze data effectively. *This is a barrier mainly for coverage with evidence development approaches, but can apply to all approaches that require some form of post-market surveillance.*	<u>The comparative-effectiveness research (CER) movement in the U.S. is leading us to a value-based approach to drug pricing</u> – Since there is now such a focus on CER in the U.S., there will likely be a move towards more evidence-based drug purchasing decisions. *This should affect all approaches, but with an emphasis on CEDs*

Taking it forward – things to consider when developing approaches

There are a number of factors to consider when taking forward value-based approaches to purchasing agreements. However, based on the literature, interviews and survey, the following are the three main factors we consider need careful consideration.

1. **What types of drugs?** It is important to note that the literature strongly points to "innovative" agreements being most useful for drugs that relate to high cost or high importance (however it is defined) diseases and conditions. The chart to the right shows the conditions that innovative agreements are currently used for, indicating the relative importance of the two major causes of death in Canada (cardiovascular diseases and cancer). When entering into any new agreement, it is clear that the benefit for patients must outweigh the costs of implementing the agreement and the risks associated with developing evidence in clinical practice.



Taken from: Sheppard A 2010

2. **Where is the uncertainty?** "Innovative" approaches all relate to uncertainty around new drugs. It is important to understand where the uncertainty for the new drug lies before creating some form of conditional listing agreement. Uncertainty may be in the effectiveness of the drug, it may be in the epidemiology of the condition for which the drug works, it may be in the value of the health gain from the drug. Where the uncertainty lies will be key to developing the correct approach to funding the drug. For uncertainty over effectiveness, CED approaches may be effective. For uncertainty in epidemiology, outcome guarantees may be more appropriate.
3. **Collaborate early in developing approaches.** The key message from interviews and in the literature has been that for "innovative' approaches to be truly successful, they require strong levels of communication and trust between both sides of the agreement. By beginning the conversations about the need for "innovative" agreements early on in the development of the drug, industry and payors can benefit from a shared understanding of the need for the drug and where likely uncertainty will be in the system.

Where to now? How should we take on this information

In conclusion, there is a significant level of information now on "innovative" approaches, albeit with little of it in Canada. The need for these approaches has been stated in every continent, and there is now a definite movement towards linking health outcomes to the cost of drugs purchased.

For Canada to move forward in this brave new world, there are a number of steps to take:

- A definite need to develop good approaches to evidence development for therapeutics in the real world;
- A need for better understanding of when and where particular categories of “innovative” agreements can add value to the health system(s) in Canada;
- A set of defined characteristics for “innovative” agreement components in provinces or even nationally;
- A need for early dialogue between industry and payors to create a shared understanding of the new therapeutic and a shared vision of how to bring it to the patients that need it;
- An acceptable way for payors to adjust reimbursement criteria if evidence shows a new product isn’t cost-effective in the particular population.

The first step on this journey is to bring all of the stakeholders together and to then decide on: a) the needs for these approaches; b) the people to involve in developing strategies to address those needs; and c) the road map for bringing these approaches to life where appropriate. The aim of the IHE roundtable is to do just that through stimulating thinking on the issue and providing a forum for open and frank discussion across stakeholder groups.

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Appendices

Appendix A: Interviewee organizations

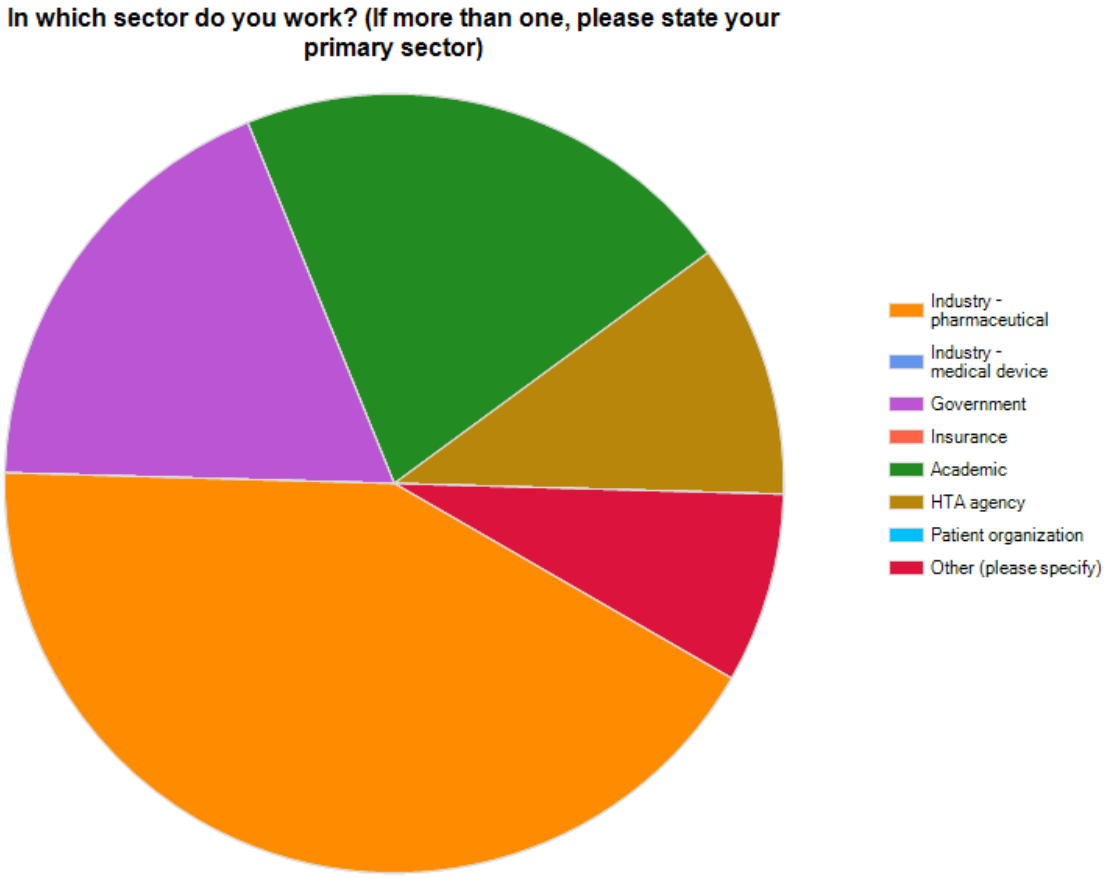
Below we identify the organizations that were represented in the interview process for this work.

Interviewee organization	Stakeholder group
Alberta Ministry of Health	Government
BC Ministry of Health	Government
CIHR	Academic
Eli Lilly Canada	Industry
Eli Lily and Company (International)	Industry
EVIDEM	Industry
GlaxoSmithKline Inc.	Industry
Hill & Knowlton	Industry
I3 Strategies	Intermediary between payors and industry
Janssen Inc.	Industry
Mercer consulting	Represent insurance and employers
New Brunswick Ministry of Health	Government
NICE (UK)	Government
OECD	Data experts
Ontario Ministry of Health	Government
Pfizer	Industry
Pfizer Canada Inc.	Industry
Saskatchewan Ministry of Health	Government
University of Montreal	Academic
University of Saskatchewan	Academic

Appendix B: Survey findings

The online survey of interested stakeholders on the issue of industry-payor agreements was circulated through the IHE's networks and to a selection of those invited to participate in the roundtable and interviews. In response, there were 38 people who participated, with 31 completing the survey. Questions and responses are shown and explained below.

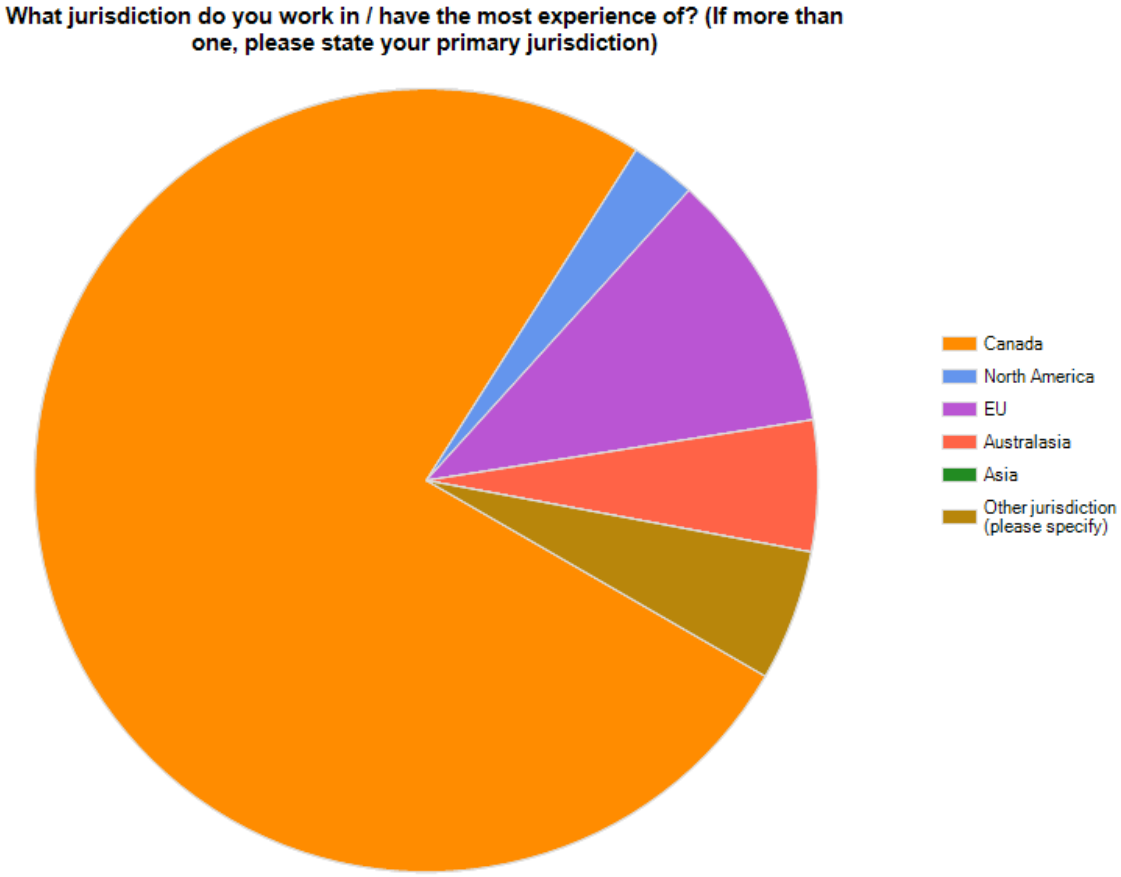
Question 1. In which sector do you work?



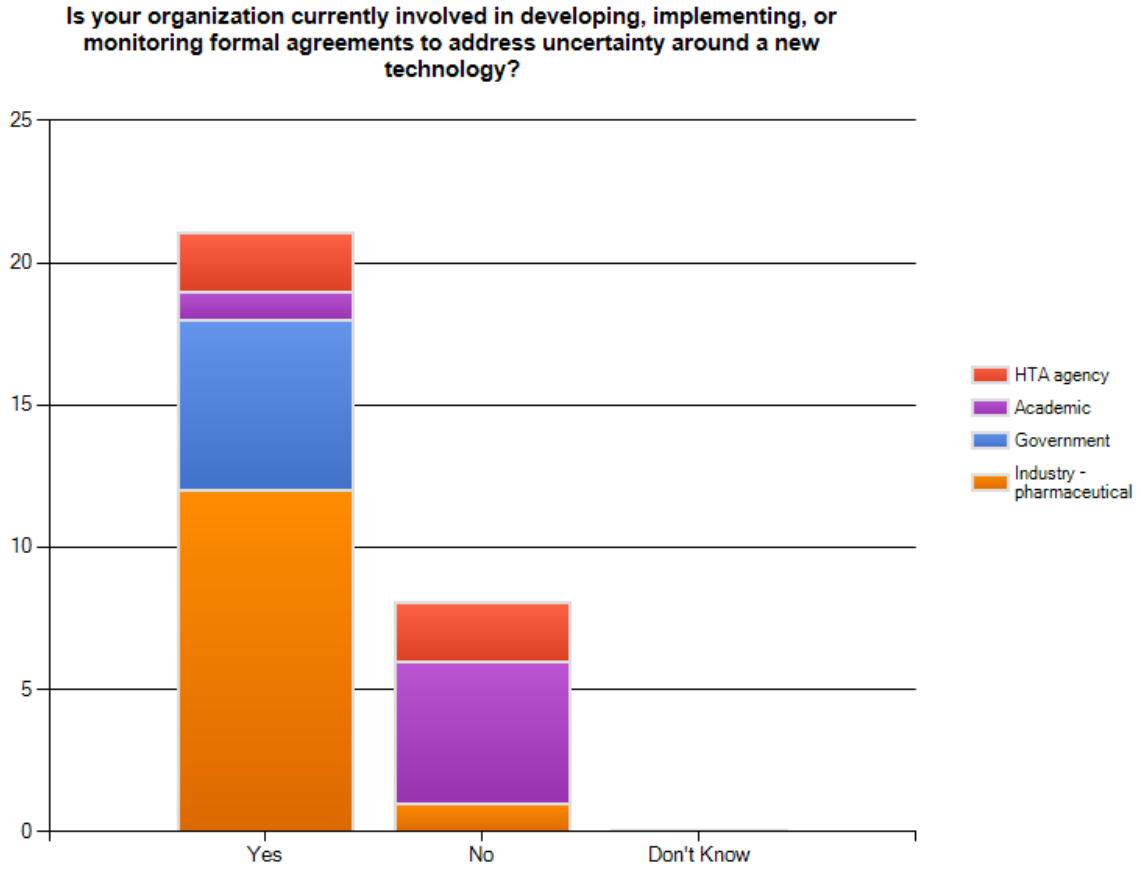
Although the most represented group in the survey was the pharmaceutical industry, government, academia and HTA also were represented substantially.

Question 2. What jurisdiction do you work in / have the most experience of?

As obvious from below, the survey respondents were overwhelmingly from Canada, although the EU, North America and Australasia were also represented (the "Other" category contained individuals who identified with the USA).



Question 3. Is your organization currently involved in developing, implementing, or monitoring formal agreements to address uncertainty around a new technology?

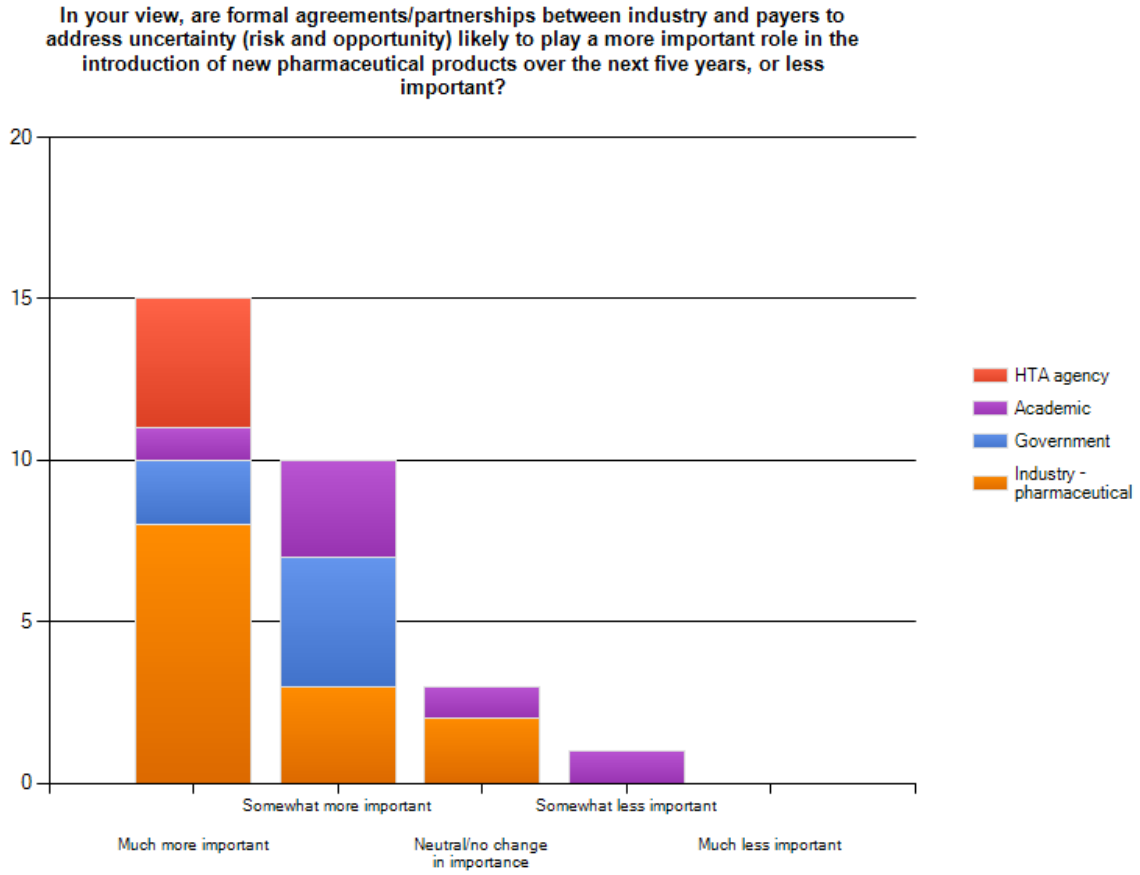


Since one of the issues that we are interested in addressing is how different stakeholders in the pharmaceutical reimbursement system view innovative approaches, we have split the responses to this question by stakeholder group.

From this analysis, it is clear that around ¾ of respondents were involved in some sort of innovative agreement. Interestingly, all of the government respondents are involved in some sort of innovative agreement. Unsurprisingly, the majority of those not involved are in academia or HTA.

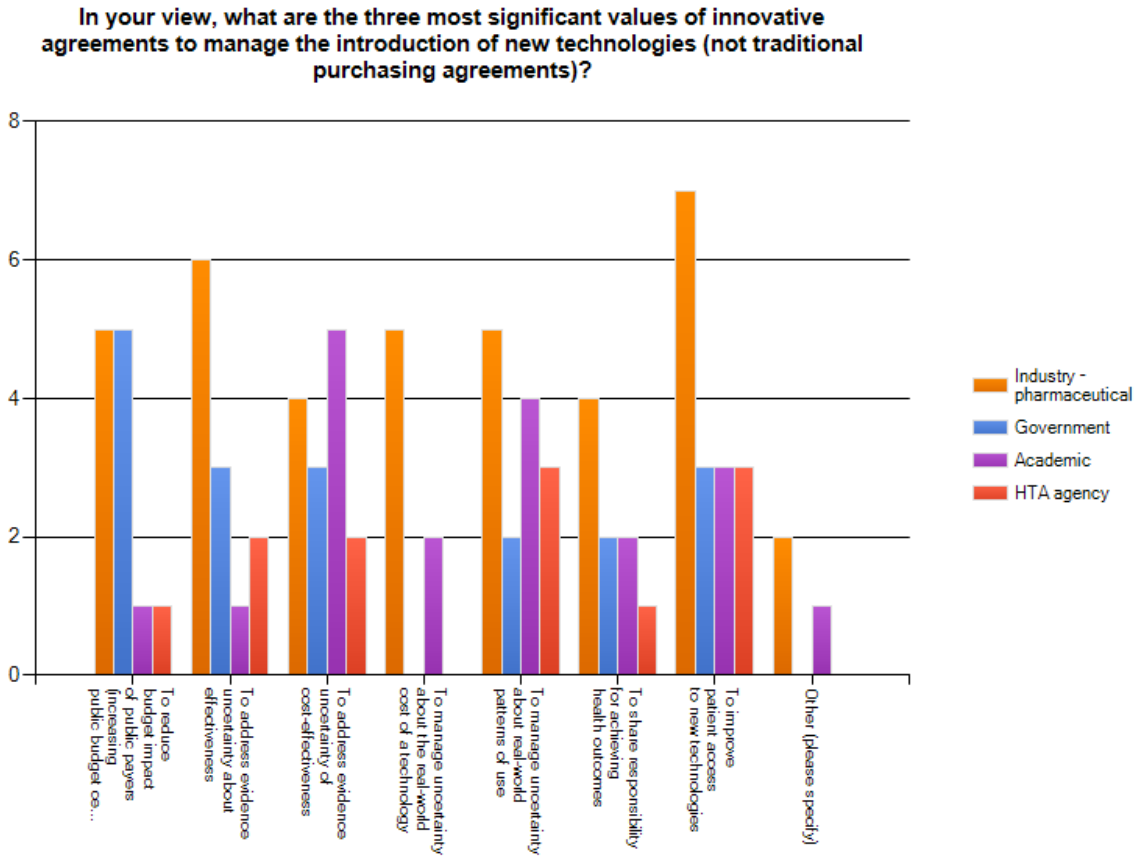
When assessed against the country of stakeholders, there is no major difference between countries for their participation in innovative agreements (the proportions of regions are the same for those in innovative agreements and those not in).

Question 4. In your view, are formal agreements/partnerships between industry and payors to address uncertainty (risk and opportunity) likely to play a more important role in the introduction of new pharmaceutical products over the next five years, or less important?



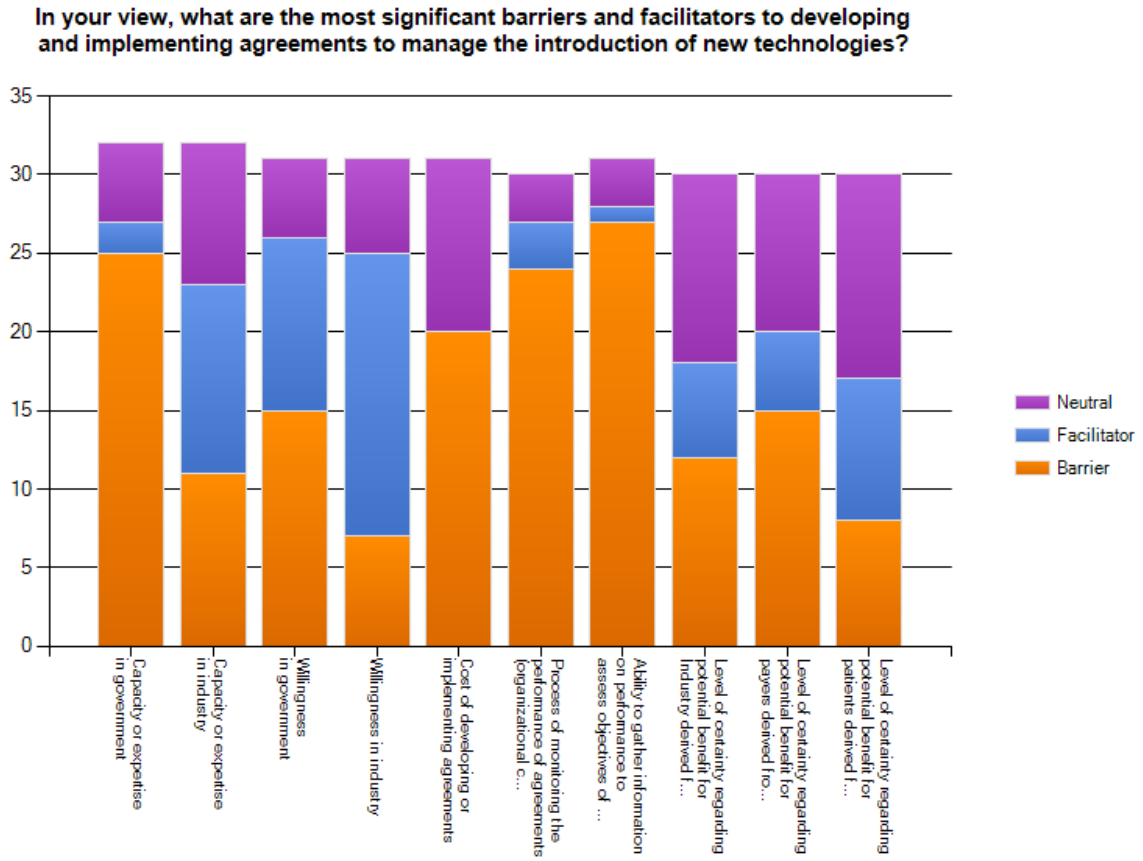
As we can see, the majority of respondents consider that approaches to address uncertainty are going to become more important in the next five years. It is only from the academic community that there is any concept that agreements might become less important.

Question 5. In your view, what are the three most significant values of innovative agreements to manage the introduction of new technologies (not traditional purchasing agreements)?



We asked respondents to identify the three most important values brought by innovative approaches. Patient access is seen as the most important value, but there is no clear single value brought by innovative agreements. However, the idea of new approaches "managing uncertainty about the real-world cost of a technology" was only half as popular as the other responses. There is no clear difference between the different stakeholders in responses. However, "reducing budget impact of public payors (increasing public budget certainty)" was seen to be more important by those in government and industry than by those in academia or HTA.

Question 6. In your view, what are the most significant barriers and facilitators to developing and implementing agreements to manage the introduction of new technologies?



As with many new technologies and approaches, the general consensus around innovative approaches is that they seem to face many barriers. The major barriers seen are: Capacity or expertise in government; Process of monitoring the performance of agreements (organizational capacity and structure to monitor); and, Ability to gather information on performance to assess objectives of the agreement. All of these have around 80%+ response rates as barriers.

Interestingly, the main facilitator for innovative approaches is “Willingness in industry”. Considering Industry form the largest single responding group, this would not seem surprising, however investigation of the responses by sector shows that the majority of people who considered this a facilitator were in fact from government, academia and HTA (ten responses to Industry’s seven).

Issues around the level of certainty when it comes to benefits for industry, payors and patients were considered to be more neutral in terms of implementing new agreements.

Overview

Overall, this survey suggests that innovative approaches are already fairly common and will become increasingly so. The main drivers of this have not been around cost, but around

benefits to patients and improving effectiveness information on new drugs. Barriers stopping these approaches taking hold tend to be around capacity to put agreements in place (both in terms of government capacity to enter into agreements, and the capacity to collect data as part of agreements).