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How should insurers assess the impact of new medicines and technologies?

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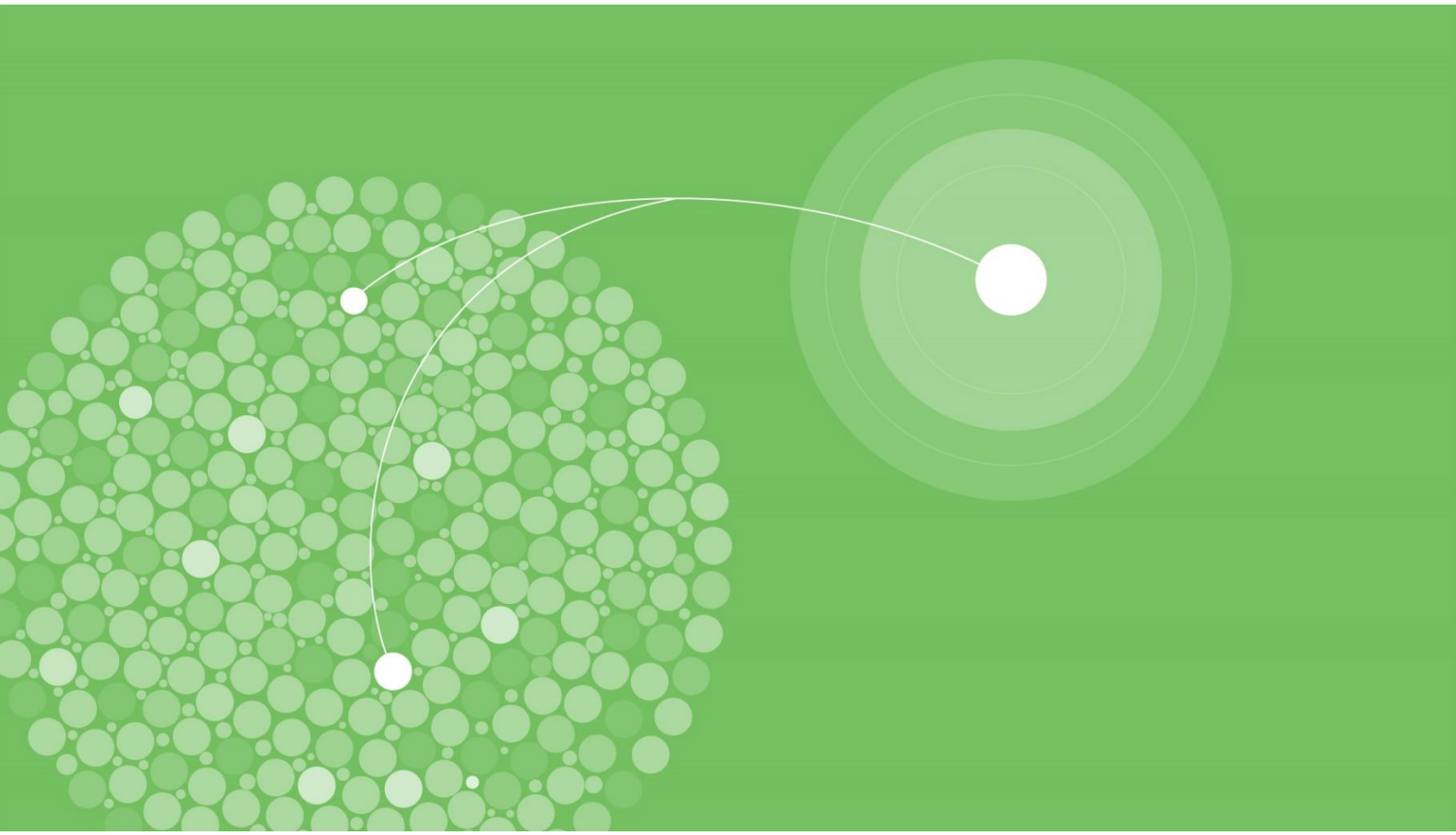

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Table of Contents

1. Executive Summary

Medical insurers globally struggle with controlling claims cost inflation, which is typically several percentage points higher than consumer or retail pricing inflation in any given year. New drugs and technologies comprise part of overall medical inflation. While patients want access to the latest drugs and technologies (in some countries, the appeal of the insurance product is predicated on its ability to allow access to new drugs not covered in publicly funded health systems), those new drugs and technologies historically have increased claims costs, and rarely led to reductions.

The Getzen[1] econometric long-term medical inflation model suggested a value for the US of 1% to 2% per year, over and above the other components of medical inflation, purely to account for the introduction of new medicines and technologies that either replaced more traditional treatment pathways, or were new treatments entirely, with an existing pathway of "no treatment." We recognise that the impact of new drugs and technologies on medical inflation will be country-specific, and depend heavily on the way that benefits are defined in each country, the maturity of the health delivery system, and the interplay between public and private systems and reimbursement mechanisms in those systems. In addition, for specific insurers, medical inflation will depend on the mix of lives in the portfolio.

This paper focuses on studying prevalent methodologies and best practices in assessing the impact of new technology on claims costs and medical inflation from the perspective of medical insurers and is primarily aimed at non-US insurers. We hope to highlight differences in practices in different insurers and to try and close the gap between existing and best practice, to allow a more consistent approach to assessment and measurement. We have based this paper on our knowledge of industry practices, and have also carried out some interviews with a small number of insurers in different countries. We also sought input from selected pharmaceutical companies to get their perspective on how payers assess and perceive value and compare and contrast this with their own approaches to demonstrating value to payers. We observe that these two key stakeholders often have very different perspectives and we hope there are some useful things in this paper to help fill gaps in understanding.

Most large insurers have some system of evaluating new technologies, either internally, or by using third parties such as Hayes.[2] However, there are differences in the methodology, robustness of application, and frequency of assessment. Smaller or less mature health insurers typically have limited horizon-scanning capabilities and, in some countries, only evaluate newer technologies at the request of the financial or consumer regulator to expand benefit coverage. Some insurers mentioned they focus on technologies and drugs that are already high-cost, such as drugs for oncology, rather than thinking about future medicines or technologies. Others mentioned specifically that robotic surgeries have been evaluated in the recent past and they expect them to have a big impact in the future.

In Appendix A, we provide some examples of potential future high-cost technologies that may increase medical inflation, such as new diabetes treatments, precision medicine and genomics, smart inhalers, and others. Payers covering these risks need to have robust systems for horizon scanning and methods to analyse and process large amounts of medical claims information. Artificial intelligence (AI) may be needed to leverage deep learning approaches to understand the potential impact of new technologies. Payers will need to understand the extent to which past experience is a good guide to future costs, or whether new approaches are required that rely less on analysis of historical experience, as even sophisticated analysis may not capture the full extent of the impact of new treatments on cost. Payers may also have to invest in understanding complex medical protocols, as well as trends in how care is provided. They may need to employ personnel who are well-versed in medical decisions, as well as increased analytics capabilities.

[1] Society of Actuaries (October 2018). Getzen Model of Long-Run Medical Cost Trends. Technical Manual. Retrieved 9 December 2020 from https://www.soa.org/globalassets/assets/files/research/research-2016-getzen-model-tech-manual-doc.pdf.

[2] Evidence Solutions | Hayes, a TractManager Company (hayesinc.com), retrieved 10 December 2020 from https//www.hayesinc.com/payersolutions-2/evidence-solutions/.

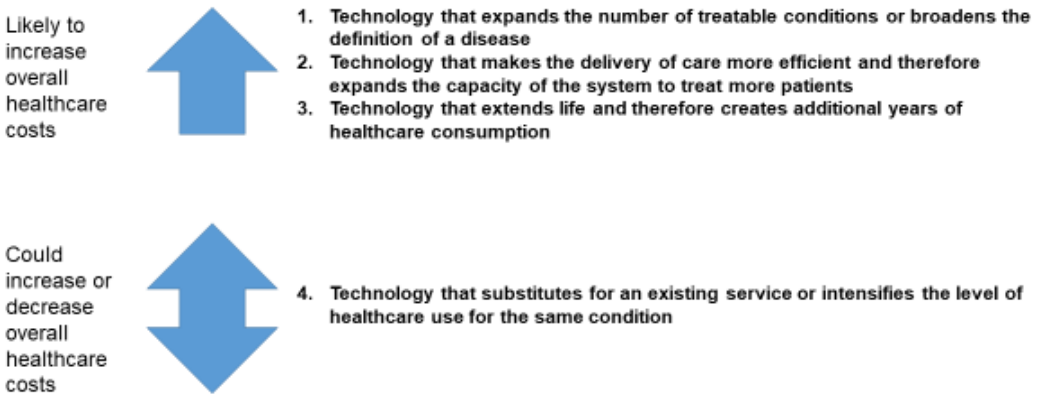
This paper outlines best practices in assessment and evaluation from a private insurer's perspective and is structured as follows:

- **Section 2** talks about different types of new drugs and technologies.
- **Section 3** offers a theoretical introduction to different assessment methods, including a discussion of actuarial return on investment (ROI) models versus cost-effectiveness analysis and outcomes-based methodologies and discusses some common government health technology assessment approaches.
- **Section 4** contains a best practice step-by-step practical guide/framework for assessment and an illustrative case study.
- **Section 5** sets out our concluding comments.
- **Appendix 1** outlines some practical examples of new technologies and medicines introduced over the last five years and some comments on their perceived impacts.

2. What is a “new” drug or technology and how do they impact healthcare delivery?

Econometric models and our own collective experience suggests a cost-increasing effect of new technology overall. However, the relationship between technological advances and healthcare expenditures is complex and changing over time with many factors that shape the effects depending on technology type, patient circumstances, and focus of reimbursement of the new technology. Figure 1 sets out some broad types of technology and the likely overall healthcare cost impact. Below we then discuss some specific examples.

FIGURE 2.1 – LIKELY IMPACT ON OVERALL HEALTHCARE COSTS



1. **Technology that expands the number of treatable conditions or broadens the definition of a disease:**
   a. Patients could not be treated previously or could not be treated effectively and therefore the new technology increases costs but improves health for a previously untreated population.
2. **Technology that impacts the delivery of care (e.g., improves the capacity of the system to treat more patients):**
   a. Some innovations that employ a new technique or procedure may lead to an increased use of medical personnel, supplies, or training, while others may reduce staff or time requirements or shift care to less costly settings of care (e.g., inpatient to outpatient).
   b. Some technologies may improve the efficiency of care delivery by reducing procedure time, length of stay, or number of hospitalisations, thereby increasing the capacity of the hospital to treat additional patients; overall costs may rise as a result, but there may be improved health outcomes for a large number of patients.
   c. Some technologies can expand access to care (e.g., in rural areas, or for people who cannot miss work to see a doctor). Telehealth is a potential example of a technology that could increase provider efficiency and capacity, but may not decrease overall costs if it expands access, even though unit costs of delivering the service may be lower.
3. **Technology that extends life and adds additional years of healthcare consumption which may increase costs:**
   a. An example of this technology is new oncology drugs, where the treatments can extend life span significantly, but the costs can be large over time.
4. **Technology that substitutes for an existing service or intensifies the level of use for the same condition:**
   a. May *increase* spending more rapidly in the beginning as those who are undergoing maintenance or conservative treatment are now treated with the new technology.
   b. May *decrease* unit costs due to treatment becoming cheaper or having fewer complications, e.g., use of percutaneous transluminal coronary angioplasty (PTCA) allows potentially reduced occurrence of restenosis, heart attacks, emergency coronary artery bypass grafting (CABG), and overall mortality.
   c. Costs may increase in the long run but not as much as initially or may even decrease as technology allows substitution for more expensive existing treatments; generic medicines are a great example, as innovation increases costs initially but the cost drops rapidly after patent expiration.

3. Assessment methods for impact

The two most common approaches to assessing impact and value are:

1. Actuarial ROI models, which tend to look purely at financial costs and benefits.
2. Health economic approaches, such as cost-effectiveness analysis (CEA), which look at incremental quality-of-life benefit metrics (for example Quality Adjusted Life Years) versus incremental costs for a new medicine or technologies relative to the existing treatment regime.

Both CEA and ROI approaches give widely varying results, depending on the timeframe, the investment perspective taken, and the range of costs and benefits accruing to the different stakeholders that are included.

Both approaches can use pre-post observational studies to gather data to parameterise their models or randomised controlled trials (RCTs). However, it is far more common for private insurers to use pre-post observational studies with real-world data to build financial ROI models, as the main question they are trying to answer is: "Will this new medicine or technology increase or decrease my claims cost?" Government payers, on the other hand, tend to favour CEA, with models parameterised from literature studies that gather data on relative quality of life and costs alongside clinical outcomes as part of RCTs. The main question that government payers seek to answer is broader than that of a typical private payer; the fundamental question is: "Is paying for this new technology or medicine going to give me more 'health' for my population relative to other ways I could spend my limited health budget?"

Some of the advantages and disadvantages of each approach are set out in the table in Figure 3.1.

FIGURE 3.1: ADVANTAGES AND DISADVANTAGES OF ROI AND CEA

CEA/ROI	Advantages	Disadvantages
ROI	Clear focus on financial costs and benefits allows articulation of claims cost inflation impact over a defined time frame, which allows direct estimate of budget impacts. Easily understood conceptually by business-focused stakeholders.	Looks purely at financial benefits or cost savings in the core model. Any consideration of quality or outcomes is an add-on. Provides no common framework for comparing money invested in treatment options for different diseases or patient groups against each other.
CEA	Provides metrics that can be easily compared across different investments in health opportunities if a common methodological framework is applied to all evaluations.	Academic literature suggests that using certain quality-of-life metrics creates a bias against older patients.[3] Quality-adjusted life year (QALY) thresholds to determine whether or not something is cost-effective can vary significantly by country, so cross country comparison is challenging. Quality-of-life metrics are usually highly subjective and taken from small-scale studies. Does not consider budget impact or medical inflation impact as part of the core model.

The outputs of the two approaches look quite different. Some highly simplified examples are given below. In this case we have considered a new cancer drug, which replaces the existing pathway or surgery, followed by radiotherapy and chemotherapy. The new drug must be taken for a year, while the existing pathway is a six-month therapy. However, there is a lower ongoing risk of relapse with the new drug; in the second year, the risk of relapse for the patient is 20% under the existing pathway, but only 5% under the new pathway.

For both approaches, we need to specify a timeframe over which we are going to measure costs and benefits. In this case, we have used a timeframe of two years only.

The existing pathway costs £10,000 for a six-month episode of treatment, split among £4,000 of hospital facility costs, £2,000 of physician costs, and £4,000 of drugs costs.

[3] We note that the use of QALY metrics has been controversial because, among other reasons, their limitations in achieving consistent measurements and their perceived biases against older people.

The new medicine costs £10,500 for a one-year supply, but has a less intensive administration regime; therefore there are only £1,000 of estimated physician costs and £1,000 of facility costs over that year.

Under both pathways, the cost of treatment at the point of relapse is £5,000.

The new drug has far fewer side effects, and so, although the treatment period is twice as long, there is a much higher quality of life associated with the new drug. Patients were asked about their quality of life during clinical trials and, from preference questionnaires, it was established that patients under the existing pathway estimated that, in the first year of treatment, their quality of life was only half of that of a healthy person. However, under the new drug, their quality of life was only 20% lower than that of a healthy person. For those patients who relapsed, the quality of life was 80% lower than that of a healthy person during the relapse period when they were undergoing remedial treatment.

ILLUSTRATIVE EXAMPLE 1: AN ROI MODEL

The Year 1 costs for a cohort of 100 patients will be:

a) Existing pathway = £10,000 * 100 = £1.0m

b) New pathway = £12,500 * 100 = £1.25m

Incremental costs in Year 1 = £250k, or £2.5k per patient

In Year 2, for our cohort, the costs will be:

a) Existing pathway = £5,000 * 20 = £100k

b) New pathway = £5,000 * 5 = £25k

Incremental costs in Year 2 = (£75k)

If it is anticipated that the new medicine has ongoing protective benefits beyond the second year, those benefits can be incorporated and, depending on the timeframe, the total benefits may exceed the total costs and the break-even point can be estimated.

Note that the patient's quality of life does not feature in the calculation.

ILLUSTRATIVE EXAMPLE 2: A CEA MODEL

As per the ROI model, there are incremental costs in Year 1 of £250,000, offset by £75,000 in Year 2. Therefore total incremental costs are £175,000 over this timeframe.

However, there are also incremental benefits. The metric of quality-adjusted life year (QALY) is used:

Year 1

a) Existing pathway = 0.5 QALY * 100 = 50 QALYs

b) New pathway = 0.8 QALY * 100 = 80 QALYs

Incremental QALYs in Year 1 = 30

Year 2:

a) Existing pathway = 1 QALY * 80 + 0.2[4] QALY * 20 = 84QALYs

b) New pathway = 1 QALY * 95 + 0.2 QALY * 5 = 96QALYs

Incremental QALYs in Year 2 = 12

So now there is a total of 42 additional QALYs to compare with the £175,000 of additional costs over the two years. The CEA then means there are 175 / 42 = £4.12 per additional QALY.

[4] Varies according to the exact timing of the relapse and treatment time.

ILLUSTRATIVE EXAMPLE 2: A CEA MODEL (CONTINUED)

If a similar analysis was carried out for a different cohort of patients with an entirely different disease and estimated that cost and QALY, there would be a basis on which to compare investment in different treatment options for a fixed budget. The concept of "willingness to pay" becomes important in this context, as it informs the payer of the threshold cost and QALY for cost-effectiveness by linking the CEA calculation to gross domestic product (GDP). New drugs and technologies that are assessed to be above a certain threshold value of cost and QALY would be deemed as not cost-effective, i.e., the payer is not willing to pay that amount of money to produce an additional QALY. New drugs and technologies that are assessed to be below the threshold cost and QALY would be deemed as cost-effective and likely worth paying for. Cost and QALY thresholds are often set by governments to be between a range recommended by the World Health Organisation (WHO) of one to three times GDP.[5]

The illustrative examples above are designed to demonstrate the different approaches, but are over-simplified. Some of the additional factors both models would need to take into account are:

- How can the number of patients be estimated who would be eligible for treatment, both those currently eligible and those patients who might benefit or become eligible in the future? Will the patients actually selected for treatment match our assumptions or will there be an element of selection or other bias?
- Are there patients who have abandoned the current standards of treatment and therefore will incur higher incremental costs for the new treatment ("warehoused" patients)?
- Within the cohort of patients, are there sub-cohorts who may have very different costs or risks of relapse? For example, patients with comorbidities (which may be unknown to the payer)?
- How can inflation of costs be dealt with over time? How can we deal with discounting of future costs and benefits?
- Is the patient cohort large enough that we have confidence in the estimates of costs and benefits?
- Are the clinical studies relied on clear about the relative treatment pathways and their benefits? Are there other costs or benefits that we need to take into account, such as side effects, productivity, or time away from work?
- Are the clinical studies used to parameterise the models robust?
- How accurate and reliable is each of the parameters? Are they internally consistent? Do the broad conclusions of the modelling hold true under different scenarios or sensitivity analyses?
- Do the results vary by age, sex, or other demographic characteristics? Do they vary by geographical region?
- If we carry out the assessment after the new technology has been introduced, rather than before, how can we adjust for statistical issues such as selection bias, regression to the mean, small sample sizes, and different population risk profiles in our model?

[5] Cameron, D., Ubels, J., and Norstrom, F. (22 March 2018). On what basis are medical cost-effectiveness thresholds set? Clashing opinions and an absence of data: A systematic review. Glob Health Action. Retrieved 9 December 2020 from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5930346/.

GOVERNMENT PAYER ASSESSMENT METHODS

While the focus of this paper is on how insurers adopt new technologies, it is worth noting that the bulk of the healthcare financing is done by governments globally. As per a survey conducted by the World Health Organization (WHO)[6] in 2015, about 80% of countries surveyed had a formal information-gathering process for decision making. The survey also found a link between the income level and focus of health technology assessment (HTA), e.g., low-income countries would use HTA for population-level health interventions, rather than for medicines, medical devices, or surgical interventions. On the other hand, several high-income countries reported using HTA for medicines, medical devices, and surgical interventions.

The table in Figure 2 is a snapshot of a few countries that have an established system of government health technology assessment.

FIGURE 2: HEALTH TECHNOLOGY ASSESSMENTS

COUNTRY	HTA PROCESS
India	An arrangement under the Department of Health Research (DHR) to collate and, where needed, generate evidence related to the clinical effectiveness, cost-effectiveness and safety of medicines, devices, and health programmes. The board meets at regular intervals and considers all proposals submitted to DHR for technology assessments and makes decisions.
France	The technical assessment is conducted by la Haute Autorité de santé (HAS, an independent scientific body with financial autonomy) which houses the Commission d'Evaluation des Médicaments (also known as the Transparency Commission). Economic evaluations are conducted by a separate committee within HAS, the Commission Evaluation Economique et de Santé Publique (CEESP).
Germany	Benefit assessments are conducted by the Institute for Quality and Efficiency in Healthcare (IQWiG). The Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA) issues benefit classifications based on recommendations by IQWiG. Although IQWiG conducts assessments, the G-BA regulates the methodological requirements for benefit assessment.
England	The National Institute for Clinical Excellence (NICE) uses a health economic cost effectiveness assessment framework to determine whether the National Health Service (NHS) should reimburse a new drug or technology. NICE does not get involved in commercial negotiations, but will evaluate submissions from drug companies and then determine whether they represent value for money compared with existing standards of treatment and whether there should be any restrictions (i.e., to certain subpopulations with specific clinical criteria). NICE publishes its assessments and they are widely used by other stakeholders. NICE takes a direct health systems perspective in assessing costs and benefits, rather than a wider societal perspective.
Poland	The technical assessment is conducted by the Agency for Health Technology Assessment and Tariffs (AOTMiT). Health technology assessments include three components: analysis of clinical effectiveness, economic analysis, and analysis of the impact on the healthcare system. It constitutes the basis of the development by the Consultative Council for recommendations regarding the public financing of healthcare services.[7]
Romania	The Romanian HTA system is not a typical HTA system, which usually involves evaluation techniques based on economic criteria, but is rather based on a scorecard which evaluates multiple types of drugs: new innovative molecules, old molecules that have newly approved indications, orphan drugs, drugs for infectious diseases, and drugs that were already on the reimbursement list. The HTA process through the scorecard can sum up to 145 points in total. For positive reimbursement, one needs more than 80 points for unconditional reimbursement and more than 60 points for conditional reimbursement.[8]

[6] WHO. 2015 Global Survey on Health Technology Assessment by National Authorities. Retrieved 9 December 2020 from https://www.who.int/health-technology-assessment/MD_HTA_oct2015_final_web2.pdf?ua=1.

[7] AOTMIT (2007). Guidelines for conducting Health Technology Assessment. Retrieved 9 December 2020 from https://tools.ispor.org/peguidelines/source/Poland_Guidelines-for-Conducting-HTA_Polish-Version.pdf.

[8] Radu, C.-P., Chiriac, N.D. & Pravat, A.M. (September 2016). The Development of the Romanian Scorecard HTA System. Value In Health Regional Issues. Retrieved 9 December 2020 from https://www.sciencedirect.com/science/article/pii/S2212109916300073.

OTHER ASSESSMENT METHODOLOGIES

A common method for government assessment is the CEA analysis described above, which aims to maximise healthcare benefit for the society as a whole. As described in detail in the illustrative examples above, it can be expressed as a number of additional years of quality life (i.e., QALY), which can be achieved in exchange for a given "willingness to pay." However the underlying assumption for the use of this method is an equal 1 QALY per patient independent of that person's age, the disease, or the stage of the disease. For the decision-making process, the cost per QALY threshold is usually set, above which a given health technology is assessed as cost-inefficient. In Poland, an assumed fixed level of cost effectiveness has been set at the level of three times GDP per capita for 1 QALY.[9] In England, NICE does not set a fixed threshold, but it is commonly assumed to be £30,000 per QALY for most treatments, and £50,000 per QALY for cancer or end-of-life treatments.

The distribution of resources based on the CEA methodology is difficult to apply to new medicines or technologies for orphan diseases or end-of-life treatment for which alternative treatments might not even exist. Coverage of therapies for patients with orphan diseases constitutes a challenge for all healthcare systems. In Europe, there is a growing trend of application of alternative measures for this purpose, including the Multi-Criteria Decision Analysis (MCDA). Apart from cost analysis it focuses on other aspects such as: severity of the disease, alternative treatments available, safety of therapy, impact on quality of life, and convenience of a drug's administration or complexity of the manufacturing process.[10]

Alternative approaches have developed as a result of limited information related to orphan diseases, high research and development costs which need to be spread over small patient populations and extreme levels of uncertainty around efficacy in clinical studies, due to the small numbers of patients involved.

MCDA provides an additional layer to NICE's core CEA methodology in England specifically for highly specialised technologies for rare diseases. Several other countries, including Scotland and Australia have developed separate schemes allowing for reimbursement of the whole rare disease therapy. In Poland, reimbursement of treatment for rare diseases can be approved off-label by the Ministry of Health or within the Emergency Access to Drug Programmes also individually approved by the Ministry of Health.

[9] See https://izwoz.lazarski.pl/fileadmin/user_upload/Choroby_rzadkie.pdf.

[10] See https://power.aotm.gov.pl/static/Materialy/16.%20Ocena%20wniosk%C3%B3w%20dotycz%C4%85cych%20lek%C3%B3w%20stosowanych%20w%20chorobach%20rzadkich%20w%20praktyce%20AOTMiT%20w%20latach%202012-2019..pdf.

4. A practical framework for insurers to assess impact

Once the horizon scanning phase has been completed, there are a number of steps that any insurer should go through in assessing the potential impact of new technologies and drugs. The issues identified below provide a framework for consideration.

1. Decide on overall assessment methodology (ROI, CEA, etc.).
    a. The choice of assessment methodology is a starting point to build a transparent decision-making process and determines the point of focus for final conclusions. Depending on the overall goal the assessment might be used to compare the new drug or technology with an analogous different technology or the pathway as a whole. Consider how to deal with any methodological limitations in the chosen methodology, e.g., statistical biases.
2. Identify benefits and costs clearly and a time horizon over which to measure costs and benefits.
3. Identify stakeholder perspective. For insurers this would normally be clear, in that it would be the direct financial or claims impact of a drug or technology, but there may be other perspectives that could be included, such as savings of patient time, quality impacts, patient access impacts, or even employer absence costs.
4. Definition of clinical target group is crucial from the perspective of technology assessment. The target patient group needs to be clearly defined, along with any limitations or exclusions, from both a clinical and a claims algorithm perspective.
    a. For example the use of health technologies related to Alzheimer's disease depends, among other aspects, on age. Incidence rate increases with age and it is four times higher for people aged 75 to 84 (13.78/1,000) than those aged 65 to 74 (3.43/1,000) and even 10 times higher for people older than 85 (35.74/1,0000).[11] A wider approach to defining the target clinical group (for example: general population, or different assumptions on the level of risk sharing) might significantly understate the assessment.
5. Develop an algorithm to identify existing members in historical claims data that may be subject to the new medicine or technology.
    a. The new drug or technology, especially when related to rare disease, might bring difficulties in reliable assessment of the number of claims we would expect after its introduction. There are multiple aspects that should be taken into account to ensure proper management of potential bias embedded in incidence rates developed from claims data, but even after minimising these biases we might still underestimate the members subject to the new medicine or technology.
6. Pull the claims and assess historical episode costs and distribution of costs. Identify sub-cohorts as necessary, depending on clinical criteria. A literature search may be necessary to supplement internal historical claims data. For example, a single insurer may not have sufficient credible data in its historical claims databases. Or it may not have enough clinical granularity of data to identify sub-cohorts, and so would need to use assumptions derived from the clinical literature and apply some clinical judgement. External claims benchmarks from other countries may be another potential source of additional data.
    a. Even the best defined and detailed database on episode costs in one market might not translate easily to other markets, so there is potentially a high level of uncertainty around any historical claims statistics. We also need to be careful about the different sub-cohorts that may receive approval for the drug or technology in different markets, as this could influence the defined clinical population for which the drug is intended.

[11] H. Niu, I. Álvarez-Álvarez, F. Guillén-Grima, & I. Aguinaga-Ontoso (October 2017). Prevalencia e incidencia de la enfermedad de Alzheimer en Europa: metaanálisis Neurología, Volume 32, Issue 8, pp. 523-532.

b. For example, indications of lurasidone use in the US, under US Food and Drug Administration (FDA) supervision, are much broader than in Europe, under EU Medicine Agency (EMA) supervision, and cover not only schizophrenia but also depressive episodes associated with bipolar depression. In Europe, indications for lurasidone use are limited to schizophrenia.[12,13] Thus any aggregated usage estimates coming from a US database in Europe may be, by definition, overstated if the whole lurasidone usage were applied to Europe. Other determinants playing a role in distribution of costs include access to other technologies, indications, and prior treatment regimes.

c. When applying results from literature searches to an individual insurer's population, there are significant difficulties in estimating the difference that might come from insurance product design, the differences between the general population, the study population and our insured population, and additional biases from anti-selection and moral hazard in some insurance portfolios. We note that very few insurers have robust internal literature search and evidence-grading capabilities and those that recognise the need tend to outsource these functions.

7. Build Markov chain or similar model of the existing pathway and identify flex points where the new medicine or technology will affect the pathway. Will it just replace one drug with another, or change all the ancillary costs? Will it affect costs outside the current benefit package? What is the downstream impact—will it also reduce readmissions? Consider risk adjustment as necessary and a priori trend factors for the existing technology.
8. Calculate incremental costs and benefits relative to the status quo.
9. Project out the impact for a number of years, understanding how the prevalence or incidence might change in your portfolio over time.
10. Carry out sensitivity testing on key assumptions.

For any new drug or technology, it is difficult to build a robust and accurate assessment of the number of additional patients and overall incremental cost. There are multiple aspects that should be taken into account to ensure we deal with any potential statistical biases, but we are unlikely to be able to eliminate these biases entirely and there will be high levels of uncertainty with any assessment.

CASE STUDY OF INCIDENCE RATE ASSESSMENT FOR NEW DRUG TECHNOLOGIES USED IN TYPE 2 DIABETES TREATMENT

We consider a new generation of drugs for type 2 diabetes: Incretin drugs and SGLT2 inhibitors. Incretins are hormones made in the intestine that stimulate the pancreas to secrete insulin before the blood sugar level rises. SGLT2 inhibitors also lower blood sugar level by causing the kidneys to remove sugar from the body through the urine. Both drug treatments are relatively new, but some public health systems will reimburse some specific incretin drugs, while others would not be covered. So from an insurer's perspective, the question of incremental cost of the newest drugs will be based on not only what is covered by the existing benefit package, but also the coverage available from any government or public health system for the existing and newer drugs.

We take an insurer perspective and consider only the direct claims cost to the insurer of the newer drugs and technologies over a one-year time frame. We do not consider nonfinancial costs or benefits. We assume that the insurer has some limited historical data and therefore must rely primarily on literature searches to understand the potential incidence and prevalence rate and appetite or market for the new drugs in its insured population.

The model will need to include a pathway costing of existing treatment, with the identification of triggers and decision points where the existing treatment and costs can be compared with the new treatment and costs. All utilisation and costs will need to be taken into account in all service settings, inpatient, outpatient, and physician office, as well as the cost of the drug itself. Depending on the assessment of the clinical impact of the drug and the empirical data available, we may want to take into account diabetes complication reductions due to better insulin control.

[12] FDA guidelines for lurasidone use are available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/200603lbls10s11.pdf.

[13] EMA guidelines for lurasidone use are available at https://www.ema.europa.eu/en/medicines/human/EPAR/Latuda.

One of the key assumptions will be the incidence rate of diabetes in our population and in many insurer populations, which is difficult to observe directly due to lack of data on chronic conditions. We consider the following sources and assessment provided for type 2 diabetes incidence rates and prevalence. We can see that assessment of incidence rates might significantly differ depending on the study, region, sex, race, and ethnicity. This points to a high level of uncertainty in any estimation of costs and benefits. There is no clear distinction whether the incidence rate would be higher for men than for women as there are two separate sources of data with opposite results. Due to significant reliance of incidence rate on age, reliance on estimates for global population might lead to an underestimation.

FIGURE 3: SOURCES

Source	Assessment
World Health Organisation[14]	"The number of people with diabetes rose from 108 million in 1980 to 422 million in 2014. The global prevalence of diabetes among adults over 18 years of age rose from 4.7% in 1980 to 8.5% in 2014. Diabetes prevalence has been rising more rapidly in low- and middle-income countries than in high-income countries."
Agency for Health Technology Assessment and Tariffs (AOTMiT)[15]	"According to the World Health Organization (WHO), average prevalence amounts to 3.5% and incidence rate amounts to 200/100,000 per year. In Poland, prevalence of type 2 diabetes stays within the range of 1.6-4.7%."
Agency for Health Technology Assessment and Tariffs (AOTMiT)[16]	"Type 2 diabetes constitutes 90 to 95% of all cases of diabetes."
National Diabetes Statistics Report 2020, Estimates of Diabetes and Its Burden in the United States[17]	"Total diabetes prevalence at the level of 13% (12.0-14.1% 95%CI). Among US adults aged 18 years or older, crude estimates for 2018 were 1.5 million new cases of diabetes—or 6.9 per 1,000 persons—were diagnosed. The incidence rate varies based on race and ethnicity."
Incidence of diabetes in the Polish population, Results of the Multicenter Polish Population Health Status Study – WOBASZ, Maria Polakowska, Walerian Piotrowski[18]	"According to WHO, the number of diabetics in Poland will increase to 2.2–2.5 million by 2030. The aim of the study was to conduct an epidemiological analysis of the incidence of diabetes and impaired fasting glucose (IFG) in the Polish population. Diabetes was diagnosed in 6.8% of the study population. We observed a slightly higher incidence in men than in women (518 [7.4%] vs. 482 [6.2%]."
National Health Fund (NFZ)[19]	"It is estimated that currently over 2 million people in Poland suffer from diabetes, of which approximately 25% do not know about it. The incidence of diabetes is approximately 6.54% (including 5.81% men and 7.25% women). In people over 18 years of age, this ratio is 8% (including 7.15% men and 8.9% women), while among children under 15 the estimated number of diabetics is 17.7 cases per 100,000 residents. Forecasts predict that the number of diabetics in Poland will double in the next 15-20 years."

The sources above show the variability of incidence rate data for a high prevalence disease and illustrate the importance of sensitivity testing, no matter what methodology for assessment is used.

[14] WHO (8 June 2020). Diabetes. Retrieved 9 December 2020 from https://www.who.int/news-room/fact-sheets/detail/diabetes.

[15] See http://bipold.aotm.gov.pl/assets/files/zlecenia_mz/2017/080/REK/RP_53_2017_Victoza.pdf.

[16] See http://bipold.aotm.gov.pl/assets/files/zlecenia_mz/2013/254/REK/RP_157_2013_galvus.pdf.

[17] US Centers for Disease Control and Prevention. National Diabetes Statistics Report 2020. Retrieved 9 December 2020 from https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf.

[18] Polakowska, M. & Piotrowski, W. (2011). Incidence of diabetes in the Polish population. Retrieved 9 December 2020 from https://www.mp.pl/paim/en/node/1047/pdf.

[19] See https://www.nfz.gov.pl/nfz-blizej-pacjenta/cukrzyca/.

5. Concluding remarks

There are defined assessment methods for calculating the impact of new medicines and technologies on an insurer's portfolio, but in our experience few insurers outside the US have a robust assessment process and a significant minority have no defined process at all. While some insurers are purely reactive—either to provider, regulatory or consumer market pressure—there are a few notable examples of sophisticated horizon-scanning methodologies which translate into defined assessment models. In those markets where insurers cover new technologies at insurance regulator request or mandate, it is not clear that the insurance regulators themselves have the tools or capabilities to assess the market impact, which leads to some widely varying estimations. A few insurers also leverage the fact that newer technologies are generally not covered or have limited coverage in the existing benefit plan, and they have introduced enhanced products that cover some of these technologies with an extra premium. We note that these new benefits and products would also require similar pricing studies on impact.

In this paper, we have tried to highlight some theoretical points for insurer consideration, but also to provide a practical step-by-step framework for insurers trying to improve their capabilities and capacity in this area. We also provide some examples of new drugs and technologies that, in our conversations with insurers, arose as having potential large claims cost impacts, although we note that the impact on any specific market will vary significantly.

Appendix 1: Examples of new drugs and technologies with potential high cost impact

This section contains some examples of new technologies or drugs introduced in the market in the last five years which we believe anecdotally have had, or insurers expect to have, significant impacts on overall medical costs. In some markets, the main bulk of the cost will have been borne by public health systems, while in others, it will have been felt mainly by private payers.

DIABETES AND INCRETIN MIMETICS

Insulin is a protein that helps control blood glucose levels by signalling the liver, as well as muscle and fat cells, in order to take in glucose from the blood. Diabetes is a disease that impairs the body's ability to process blood sugar levels, and is related to levels of insulin within the body, and the body's ability to utilise insulin. In type 2 diabetes, the tissues are resistant to the effects of insulin increasing blood sugar level. If diabetes is not carefully managed, and consistently high levels of sugar are found in the blood, it can lead to increased risk of complications, including stroke and heart disease.

Therefore, the goal in diabetes treatment is to prevent these outcomes by maintaining tight glycaemic control and minimising vascular risk factors. Usual therapies to maintain blood glucose control usually fail after several years, according to a study by the American Diabetes Association, and clinicians should use treatments that are less likely to fail in type 2 diabetes. Nonpharmacologic therapy as well as oral anti-hyperglycaemic agents eventually result in patients having histories of uncontrolled hyperglycaemia which can be extremely costly in terms of treating downstream complications.

According to the International Diabetes Federation,[20] 463 million people globally were living with diabetes in 2019, and this is projected to be 700 million by 2045. In Canada for example, glucose-lowering medications represent the second-largest drug spending category. Reimbursement costs for glucose-lowering medications through public or private insurance or out-of-pocket payments, are growing more quickly than the number of people living with diabetes. Diabetics' drugs are an example of a medication that is relatively low-cost and low-severity but high-frequency. Because of ubiquitous and increasing use, they have the potential to increase the cost of medical care materially.

Incretin mimetics are a class of anti-diabetes drugs and they involve modulation of the incretin system. They bind to and activate receptors on pancreatic beta-cells, which results in insulin secretion and synthesis. These compounds have also been associated with beneficial effects on cardiovascular risk factors such as weight loss, decrease in blood pressure, and changes in lipid profile, as well as lower risk of hypoglycaemia. Discussions regarding their therapeutic value, and their place within treatment algorithms for type 2 diabetic patients, will continue in future years.

These new compounds are expensive, with potential to impact cost of claims upwards, both due to their inherent cost relative to the existing standards of care, but also because, if they are used ubiquitously to treat diabetes, then they could be used for significant numbers of people. On the other hand, this therapy may not be covered by insurance plans, leaving patients to potentially pay for it out-of-pocket. Studies also do not necessarily show cost-effectiveness when taking into account common CEA thresholds. For example, one study published in the UK showed that one type of incretin mimetics does not appear to represent a cost-effective treatment option for patients with type 2 diabetes when compared to insulin, considering UK NHS prices.

Up to 2020 incretin mimetics (GLP-1) were available only as a pre-filled pen used for daily injection. With the introduction of Rybelsus, with an active substance of semaglutide, approved by the FDA in 2017[21] and EMA in April 2020, the GLP-1 treatment started to be available in an oral form.[22]

[20] International Diabetes Federation (2 February 2020). Diabetes Facts and Figures. Retrieved 9 December 2020 from https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html#:~:text=In%202019%2C,low%2D%20and%20middle%2Dincome%20countries.

[21] RYBELSUS®. Highlights of Prescribing Information. Revised and issued, September 2019. Retrieved on 17 December 2020 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/213051s000lbl.pdf.

[22] European Medicines Agency (31 January 2020). First oral GLP-1 treatment for type 2 diabetes. Retrieved on 17 December from https://www.ema.europa.eu/en/news/first-oral-glp-1-treatment-type-2-diabetes.

ASTHMA/COPD AND SMART INHALERS

According to WHO,[23] the Global Burden of Disease Study reports a prevalence of 251 million cases of chronic obstructive pulmonary disease (COPD) globally in 2016. It is estimated that 3.17 million deaths were caused by the disease in 2015 (5% of all deaths globally in that year). About 339 million people globally suffered from asthma in 2016.[24] Patients suffering from such chronic respiratory ailments need to adhere to strict treatment schedules, which include daily medications that are needed to keep the symptoms in check.

Asthma is a complex chronic disease, which presents acute exacerbation periods with dyspnea and bronchospasm. Patients with asthma need short-term treatment for exacerbations and long-term treatment to obtain and maintain asthma control. Long-term treatment is important to reduce future asthma attacks, which can cause lung function deterioration. Patients who are not managed well typically access large amounts of unscheduled emergency care, mainly due to reduced compliance with asthma management, severe asthma that may not be responsive to the prescribed treatment, lack of access due to high out-of-pocket costs, and patient exposure to trigger factors. Although the number of COPD hospitalisations may be relatively stable between 2002 and 2010[25] (and between 2005 and 2014[26]), associated costs may not be, with over 50% increases in cost of COPD between 2010 and 2020 (USD 49 billion[27] in the US alone), making this an expensive disease to treat.

One of the most important therapies in the care of asthma and COPD is inhalation therapy. The inhaler has been used as effective therapy for many years. Inhalers for asthma are effective for 90% of patients if taken correctly. However, research shows that only about 50% of patients have their conditions under control and as many as 94% don't use inhalers properly.[28]

Only recently, the smart inhaler reinforced with technology has been introduced to the market. This inhaler is designed to connect with a mobile application through Bluetooth. This smart inhaler has the potential to help patients adhere to a medication schedule, maintain treatment, and help with compliance, while collecting relevant patient data that can help physicians track treatment and efficacy, and can even predict and circumvent attacks before they occur. This is archived by recording the time, date, and location of each dosage administered, which can be used to schedule a reminder for the subsequent dosage. Additionally, it can help asthma patients identify triggers and connect and share information with their medical providers. Some digital inhalers can even track high levels of pollution or pollen and alert patients.

Smart inhalers for asthma are an example of technology which may decrease the cost of care, by reducing complications of disease. Cost reductions are, however, potential and will be situation-specific depending on reimbursement mechanisms, prevalence, and current treatment. On the other hand, ubiquitous use of inhalers can lead to intensification of the level of use of the technology for the same condition, which may increase cost.

According to an Allied Market Research report, the global smart inhalers market size was valued at circa $34 million in 2018, and is estimated to reach $1,406 million by 2026, growing at a compound annual growth rate (CAGR) of 58.4%. As more and more people demand it, despite reductions in complications, it may drive up the overall costs of care.

[23] WHO (1 December 2017). Chronic obstructive pulmonary disease (COPD). Retrieved 9 December 2020 from https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd).

[24] WHO (20 May 2020). Asthma. Retrieved 9 December 2020 from https://www.who.int/news-room/fact-sheets/detail/asthma.

[25] Jinjuvaida, C., et al. (February 2017). Trends in outcomes, financial burden, and mortality for acute exacerbation of chronic obstructive pulmonary disease (COPD) in the United States from 2002–2010. COPD. Retrieved 9 December 2020 from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5626565/.

[26] Goel, K., et al. Trends in chronic obstructive pulmonary disease hospitalization and in-hospital deaths in the United States by sex: 2005 to 2014. Annals of the American Thoracic Society. Retrieved 9 December 2020 from https://www.atsjournals.org/doi/full/10.1513/AnnalsATS.201807-488RL.

[27] US Centers for Disease Control and Prevention COPD Costs. Retrieved 9 December 2020 from https://www.cdc.gov/copd/infographics/copd-costs.html.

[28] Jahedi, L., et al. (1 February 2017). Inhaler technique in asthma: How does it relate to patients' preferences and attitudes toward their inhalers? J Aerosol Med Pulm Drug Deliv. Retrieved 9 December 2020 from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5278803/.

The economic burden of asthma may be decreased with improved management of asthma with the use of smart inhalers. In 2019, a Cleveland Clinic study[29] revealed that COPD patients who were provided with electronic monitoring devices for maintenance and rescue inhalers for one year were considerably less at risk of hospitalisation, and saw significant reduction in COPD-related healthcare utilisation compared to the year prior to enrolment, from an average of 3.4 trips to the hospital to 2.2, a decrease of 35%.

PRECISION MEDICINE

Precision medicine has been defined by the Precision Medicine Initiative as "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person."[30] This type of medicine involves expensive research for drug creation as well as testing of disease markers. Analysing the genome in disease state may reveal rich information about how to diagnose and treat the patient, but to personalise care even more and explain disease mechanisms, precision medicine also involves research and analyses in the field of "–omics," a term describing the study of the biological components of cells at the molecular level. Here is some information on the "-omics" fields and how they can affect patient care:

1. The first such "–omics" field is genomics. Through genomics, one can determine complete DNA sequences to help understand the disease better for diagnostic or therapeutic decision-making. DNA sequences are used to build proteins, which play a significant role in cell functions, including cancer cells. In a diseased state, protein function can be impaired because of changes occurring at the genetic level or because of the direct impact on a specific protein.
2. Another "-omics" field, proteomics, is the study of the complete set of proteins in an organism and can provide information about how to treat the patient.
    - Even though all cells in an organism have the same set of genes, the proteins that are made from those genes are produced in different tissues and are different and dependent on gene expression. The genome is therefore constant, but the proteome not only varies within an organism, but can be modified after translation (after protein synthesis). Therefore, although the genome can provide a blueprint of disease, the way a disease manifests itself depends on many factors besides the genome, including the proteome.
    - An example of how proteomics can offer opportunities to advance treatment on cancers is provided in the context of triple-negative breast cancers which are not sensitive to anti-hormone therapy used for other types of breast cancers. A reverse phase protein array, a technology for the quantitative measurement of signalling proteins, has found that a subset of triple-negative breast cancers has elevated levels of certain proteins which could serve as potential therapeutic targets for these patients.
3. Another "-omics" example is proteogenomics or the study of genetic data, transcriptomic data (the sum total of all RNA sequences and proteomic data), and proteomics studied together can provide a more comprehensive map of disease and can better match a disease to individual therapy. Technologies such as liquid biopsies, which can analyse cells, DNA, RNA, and proteins, can be used in precision medicine by helping to acquire information reflecting the biology of tumours and metastatic tissues differentiating among cohorts of patients and thus personalising care.
4. Another area impacting precision medicine is phenotyping.
    - Phenotype represents the observable characteristics resulting from gene expression, such as, for example body weight, or the clinical presentation of someone with a particular genotype, for example, blood sugar levels or insulin secretion and response to blood sugar levels in diabetes. Precision medicine requires breakdown of diseases into subtypes according to their pathophysiologies, which implies understanding of the relationship between genes and phenotypes. Discovery of subtypes of diseases for purposes of precision medicine depends largely on capturing phenotypic data and integrating it with genomics data.
    - For example, there are different genes that are responsible for particular subtypes of diabetes, and there are many steps between the genetic mutation and the phenotype. Therefore, to understand diabetes better, it may also be important to understand not only the genetic mutations, but also how they translate to the resulting phenotype.

[29] Cleveland Clinic (11 June 2019). Electronic inhaler monitoring reduces hospitalizations, ER visits in patients with COPD. News release. Retrieved 9 December 2020 from https://newsroom.clevelandclinic.org/2019/06/11/electronic-inhaler-monitoring-reduces-hospitalizations-er-visits-in-patients-with-copd/.

[30] What is precision medicine?: MedlinePlus Genetics, retrieved on 15 December 2020.

- Although perhaps not used on routine basis, phenotyping can also be used in drug design and to improve health outcomes by reducing adverse drug reactions and associated costs of managing them. A drug called azathioprine used for autoimmune conditions such as rheumatoid arthritis can cause adverse drug reactions like significant neutropenia. Not all patients develop this adverse drug reaction, depending on the activity of an enzyme called TPMT. Identifying mutations in the gene that codes for TPMT (genotyping) or measuring the levels of TPMT (phenotyping) can be used to identify patients at high risk of severe neutropenia.

5. Precision medicine can also help drug administration further in a process called pharmacogenomics or the study of how genes affect a person's response to drugs.

   - Patients who have a condition such as atrial fibrillation, may be predisposed to blood clots which can cause heart attacks or strokes. Patients are usually prescribed Coumadin, which is an anticoagulant, but it is difficult to determine the best dose, as excess Coumadin causes bleeding and too little does not prevent clot formation. The drug's activity is closely monitored through a blood test called INR and the dose adjusted as needed. There are two genes that influence Coumadin's effectiveness. One of them is called CYP2C9 and deactivates the drug. The other, VKORC1, activates vitamin K, which is necessary for blood clotting. Variations in these genes will affect how a person responds to this drug. Pharmacogenetics can be used to dose the drug in order to incorporate the person's genetic profile to better predict the dose that the person may need.
   - Accurate dosing will not only help patients' health, but may help insurers better predict the cost associated with disease treatment and will prevent insurers from paying for treatment for possibly longer periods of time due to poor drug dosing and prolongation of disease.

The research underlying precision medicine is costly and is likely to impact future medical inflation. Even though there are companies already starting to provide genetic sequencing at much lower cost than previously envisioned, in order to further develop targeted therapies based on genetic profiling the research can be very costly, as it includes screening and treating patients with tailor-made treatments and drugs that target only narrow groups of patients.

ROBOTIC-ASSISTED SURGERY

The da Vinci Surgical System is an example of a minimally invasive surgical alternative to provide a numerical reference point for the individual system supporting robotic-assisted surgeries. Da Vinci Surgical Systems are used primarily in general, gynecologic, urologic, and cardiothoracic surgeries, as well as head and neck surgeries.

Da Vinci solutions were used over 7.2 million times over the last 20 years (approximately 1.3 million in 2019), with over 39,000 surgeons trained and 18,000 peer-reviewed published articles.[31,32] At the end of the year 2015, robotic-assisted procedures could be recognised in the US under a new set of ICD-10-PCS codes, which together with the increase of electronic health documentation allows better data analysis, boosting the number of clinical studies and research.

At the end of June 2020, the company had an installed base of 5,764[33] da Vinci Surgical Systems in 66 countries, including over 3,500 in the US and 1,000 in Europe. Intuitive Surgical, Inc. estimates that every 26 seconds a surgeon starts a da Vinci procedure. The product revenue reached the level of $3.8 billion in 2019 with 22% and 20% increases observed in years 2019 and 2018, respectively.

While the market growth in 2020 has been significantly disrupted by COVID-19, capacity limitations due to COVID-19 and shortages in blood bands and availability of beds and intensive care has underlined the importance of less invasive alternatives. However, in some countries, the development of the market is still limited by the fact that surgeries with the assistance of da Vinci systems are not reimbursed within the public healthcare system.

[31] Intuitive Surgical, Inc. Annual Report 2019. Retrieved 9 December 2020 from https://www.annualreports.com/HostedData/AnnualReports/PDF/NASDAQ_ISRG_2019.pdf.

[32] Intuitive Surgical, Inc. Intuitive for Patients. Retrieved 9 December 2020 from https://www.intuitive.com/en-us/patients/patients.

[33] Intuitive Surgical, Inc. (21 July 2020). Intuitive Announces Second Quarter Earnings. Retrieved 9 December 2020 from https://isrg.intuitive.com/news-releases/news-release-details/intuitive-announces-second-quarter-earnings-0.

How Milliman can help

Milliman has vast and deep technical experience in understanding evaluation frameworks of all kinds. Whether you want to understand more about the impact of a specific drug or technology on your market, or just want to improve your overall assessment framework and approach, we can bring our global experience of best practices combined with local knowledge.

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