TANDVÅRDS- OCH
LÄKEMEDELSFÖRMÅNSVERKET

Developed follow-ups with data from sources such as the National Service Platform

Dental and Pharmaceutical Benefits Agency, May 2021

Reference number: 1694/2020

Postal address: Box 22520, SE-104 22 Stockholm, Sweden
Visiting address: Fleminggatan 18, Stockholm, Sweden
Telephone: +46 (0)8 568 420 50
www.tlv.se

Preface

The Dental and Pharmaceutical Benefits Agency (TLV) was commissioned in the 2020 appropriation directions to continue the work of creating conditions for the follow-up of pharmaceuticals in clinical practice. The assignment is due to be reported by no later than 15 May 2021. The work is a continuation of previous follow-up assignments.

TLV's ability to follow up on the utilisation of pharmaceuticals and medical devices is a prerequisite to ensuring its ability to contribute to rapid and equal access to new innovations, and to ensuring that as many people as possible have access to treatments. Follow-ups are also a prerequisite to ensuring that the cost of using a pharmaceutical is reasonable in relation to its benefit, not only in terms of subsidy decisions but also throughout the entirety of a pharmaceutical's life cycle. Health care providers and patients expect access to innovative pharmaceuticals. Since subsidy applications for these pharmaceuticals frequently involve uncertainties about treatment efficacy and how the pharmaceutical will be utilised, TLV must be able to conduct high quality follow-ups. However, TLV's capacity for follow-ups is based on access to data.

This report provides an account of TLV's work to evaluate the practical as well as legal prerequisites for gaining access to data and how it can then be accessed for pharmaceutical products and medical devices through, for example, the National Service Platform. The work was conducted in collaboration with several external parties. Some of the pilot studies are reported in further detail as appendices to the report.

The members of the working group for this report comprised Sofie Gustafsson, Daniel Högberg, Pontus Johansson, Johan Pontén, Catharina Strömbäck, Cecilia Tollin and Anders Viberg.

It would not have been possible for TLV to carry out this work on its own. We therefore wish to thank the other agencies, regions, academic institutions and private actors that have made these pilot studies possible through their contributions of expertise, data and efforts.

Agneta Karlsson
Director General, TLV

Contents

Summary

The Swedish government has tasked TLV with analysing the conditions for following up pharmaceuticals and medical devices using, for example, data from the National Service Platform (NTjP). Although this report is a continuation of TLV's previous assignment to follow up pharmaceuticals in clinical practice, its focus is primarily on how data sources that are normally used for follow-ups could be leveraged to improve opportunities for national level follow-ups. Furthermore, this report focuses on *how* to follow up on medical devices. TLV is also engaged in another ongoing assignment to follow up pharmaceuticals and their effects in clinical practice, using alternative data sources with a focus on cancer, which will be presented in October 2022.

In recent years, ever-more pharmaceuticals products are being granted market approval at ever-earlier stages of development, due to the assessment that there is a considerable need for new pharmaceuticals products for serious diseases that lack sufficient treatment alternatives. This means that a pharmaceutical may be approved with less evidence of relative efficacy compared with previous treatments. Many cancer-treatment pharmaceuticals are used in combinations or in sequences, including prescription pharmaceuticals and pharmaceuticals that are directly administered to the patient at a hospital. Developments within the field of medical technology are contributing to ever-rising costs, as medical devices are frequently used in combination with pharmaceuticals or to monitor the effects of treatment. All of these factors are contributing to greater uncertainties about the benefits of providing treatments involving the introduction of new products.

TLV's assignment to ensure a reasonable cost for pharmaceuticals across their entire life cycle, and the combination of a lower degree of evidence and a complex cost structure, are the overarching reasons for the need to develop the use and access of health data. Developing the accessibility of health data is also a requirement of the life-sciences sector as a whole. The issues that need to be addressed by means of data on pharmaceutical utilisation in clinical practice, are: which patients are using which products and what efficacy does the treatment yield.

Prevailing uncertainties could be better managed if we know that a treatment outcome can be followed-up on over time. The agency could, with a high degree of certainty, ensure that the pharmaceutical's cost is reasonable over its entire lifecycle and in clinical practice. Enhanced accessibility to health data will provide better documentation for decision making and allow for revising decisions as needed over time. Provided that the available health data is credible, comprehensive and accessible, it will be possible to develop and apply performance-based payment models. A performance-based model could potentially manage the risk that a treatment will not be cost-efficient when utilised in clinical practice, or manage the variations in health gains between patient groups. A payment that is proportionate

to the demonstration of a specifically agreed outcome reduces the payer's risk, which in turn makes accessibility to the treatment more probable.

To perform this assignment, TLV conducted several pilot studies and also highlighted its legal prerequisites for gaining access to health data generated in tandem with health care visits.

The analysis indicates that the location of health data's storage has an impact on the legal and practical grounds for TLV to utilise the data for follow-ups at a national level. Data that is stored in the region's source system (health care register that includes medical records) or in a quality register, is generally subject to the Patient Data Act, while data that is stored at the national health data register of the Swedish National Board of Health and Welfare is regulated under the Health Care Data Register Act. In terms of data from the regions' health care registers, the regions are under no obligation to provide TLV with any data. Any such release of data is done on a voluntary basis by the regions. In terms of the health data register at the National Board of Health and Welfare, the government agencies have a well-developed process for managing TLV's access to such data. It would facilitate TLV's work if the retrieval and use of data for follow-up could be clarified and legally regulated, including health care data maintained by the regions. Moreover, TLV would have better opportunities if it had the legal prerequisites for handling sensitive personal data, since numerous analyses require the use of such data. The recently appointed government commission on pharmaceutical statistics will investigate issues such as TLV's legal basis for obtaining sales statistics.

A key component of the assignment has been to attempt to utilise data that can be obtained through the National Service Platform, which is administered by Inera, which in turn is owned by Sweden's regions, municipalities and the Swedish Association of Local Authorities and Regions (SKR) organisation. In itself, the National Service Platform does not store any data, but transfers information between various systems. Health data from medical records that are linked to the platform can be transferred and retrieved through the National Service Platform. The data that is rendered is regulated by laws such as the Patient Data Act and there is thus no clear legal support for TLV to obtain this data. The pilot that was conducted under TLV's assignment was aimed at evaluating whether data pertaining to diabetes treatments can be extracted from the service platform. However, within the scope of the pilot, no prerequisites were in place for testing such possibilities with the service platform. The follow-up that is achievable through the service platform is dependent on the availability and priority of regional resources to facilitate TLV in this regard. One way forward for evaluating the platform could be to collaborate with, for example, Regional Cancer Centres or other quality registers that have the legal prerequisites for handling sensitive data, and which are prioritised actors under Inera's governance.

The follow up of medical devices is particularly challenging, as there are no structured registers that can be utilised for follow-ups within this field. Although the Pharmaceuticals Registry contains data on the use of products prescribed through

pharmaceutical benefit schemes, known as disposable products, no nationwide data is collected for other forms of medical technology. To be able to conduct assessments at a national level, data sources must be created for medical devices. A new regulatory framework within the EU will require that all medical devices be provided with a UDI – unique device identifier. This could create the foundation for a uniform structure for the follow-up of medical devices. Creating the conditions for systematically collecting data from medical devices would increase the opportunities for TLV and other actors to follow up this important area.

The overarching challenge with medical devices is that we currently lack shared terminology for various medical devices. Furthermore, there is no national health data register that systematically receives information about the specific medical devices that health care providers prescribe or provide to patients. This means that we do not have any opportunity whatsoever to conduct national follow-ups of which particular devices are being used or which patients are using the devices. Such information is essential for enabling the assessment of usage and benefits in the next step. As a first step, the uniform and systematic coding of medical devices and opportunities to collect information in national health data registers must be reviewed.

Although there is a considerable amount of data for pharmaceuticals, even if fragmented, the data on hospital pharmaceuticals at the individual level must be supplemented, in the same manner as for prescription pharmaceuticals. The pilot studies in the present report, as well as previous TLV reports about follow-ups in clinical practice, indicate that this piece of the puzzle is a necessary component for the future follow-ups of pharmaceuticals. Knowledge about pharmaceutical utilisation as a whole also provides the basis for various payment models or agreements with the regions – a pharmaceutical's usage, regardless of whether it is through outpatient or inpatient care, or a combination of both, must be able to be systematically captured.

However, as TLV has demonstrated in its pilot studies, much can be achieved using currently available data. The glass is half full in terms of data for follow-ups. An earlier pilot project showed that it is possible to extract information about hospital pharmaceuticals from the regions' data repositories and transfer the information to the patient register. Two different pilot projects have shown that it is possible to extract laboratory results from medical record systems and present the information in an aggregated form. It is feasible to collaboratively process data from various national registers without disclosing sensitive personal data. It is also feasible to use the data to create interactive information – without disclosing sensitive personal data.

Increased access to data about hospital pharmaceuticals, primary care and laboratory results, will radically increase the prerequisites for the improved follow-up of pharmaceuticals in clinical practice.

TLV needs to have the legal prerequisites in place to receive and handle sensitive personal data. As data sources undergo development, the opportunities increase and, in turn, the need for TLV to handle sensitive personal data. Such a change would strengthen development efforts by securing reasonable costs for pharmaceuticals across their entire lifecycle, as well as early access to new pharmaceuticals. The work to review TLV's legal potential to handle sensitive personal data must proceed in parallel to sustained development work.

There are numerous actors with different interests that have similar requirements to TLV. Cooperation must be increased to develop access to data. Health data is utilised by numerous government agencies and it is urgent to increase interagency collaboration on issues concerning health data. TLV has thus taken the initiative to consult government agencies on governance through knowledge, to strengthen its cooperation regarding health data. A shared arena must be developed for continuous cooperation on health data issues aimed at strengthening interagency cooperation and, in the long-term, with regions and private companies in accordance with the Life Sciences Strategy. The goal is to identify areas in which society's actors need to collaborate more intensively to meet the need for developing access to health data.

In the absence of access to medical records via the National Service Platform, data from national health data registers are the key to the sustained development of follow-ups in accordance with TLV's objectives and purpose.

Terms and concepts

ATMP – Abbreviation for Advanced Therapy Medicinal Products: a pharmaceutical for advanced therapy that can be categorised as gene therapy, somatic cell therapy or tissue-engineered products.

Collateral agreement – a civil law agreement between a pharmaceutical company and a region. All 21 regions usually sign collateral agreements with companies. Collateral agreements regulate one or more circumstances pertaining to the utilisation of a pharmaceutical.

Combination therapy – Combination therapies may comprise several commonly used pharmaceuticals, for example, in cancer treatments. The combination may contain both procured pharmaceuticals and pharmaceuticals that are included in the high cost protection scheme, and different components in a single combination may be owned by more than one company.

Confederation of Regional Cancer Centres – The abbreviation RCC stands for Regional Cancer Centre. Under assignment by regional directors, a national cooperative group (Confederation of Regional Cancer Centres) was set up, comprising the managers of the six regional cancer centres. The Swedish Association of Local Authorities and Regions is a supporting party and is responsible for chairmanship of the group. The confederation strives to implement the intentions of the cancer strategy, such as by coordinating quality registers

The Council for Knowledge Management – the Council for Knowledge Management, which is governed by an ordinance (2015:155), deals with strategically important issues that help to ensure that the right knowledge reaches principals and professionals working in health care and social services. Nine government agencies are included in the council, and it is chaired by the National Board of Health and Welfare's Director General.

Life sciences – Life sciences contribute to the general population's improved health and quality of life, to ensuring economic prosperity and knowledge development. The life sciences sector includes the companies, universities and university colleges, as well as public actors at the municipal, regional and state level that contribute to the promotion of public health through their activities. The sector includes research, higher education and innovation, pharmaceutical development and medical devices, as well as treatment and prevention, implementation and follow-up.

Hospital pharmaceuticals – Pharmaceuticals that are procured by health care providers and administered directly to the patient during the delivery of care.

National quality registry – A national quality registry contains individualised data about patient diagnoses/problems, medical interventions and outcomes after treatment across all modes of health care delivery. There are currently just over 100 national quality registers for different diagnoses or disease areas.

The National Pharmaceutical Strategy (NLS) – the National Pharmaceutical Strategy was adopted by the central government and the Swedish Association of Local Authorities and Regions, in their capacity as partners of the National Pharmaceutical Strategy. In Sweden, some 30 public authorities and organisations are active within the strategy.

National Service Platform (NTjP) – The National Service Platform is a technical platform aimed at simplifying and streamlining information exchanges between various IT systems across all modes of health care delivery.

Non-randomised study – A non-randomised study is a study where either the intervention that is to be investigated in the study or the alternative intervention is, given to subjects, not at random. Randomly deciding (randomisation) which participants will try a new pharmaceutical is considered to be an important part of a study, in order for the study to be able to demonstrate the efficacy of the new pharmaceutical.

Prescription pharmaceutical – Pharmaceuticals that are prescribed to a patient and dispensed by prescription at a pharmacy.

PROM and PREM – the abbreviation PROM stands for Patient Reported Outcome Measures and measures functional well-being and health-related quality of life. PREM stands for Patient Reported Experience Measures and measures the patient's experience of and satisfaction with health care.

RWD – Abbreviation for Real World Data, which describes data about the efficacy of pharmaceuticals that does originate from clinical trials, for example, but from other sources, such as the patient and the health care provider.

Sensitive personal data – Data about an individual that could reveal information about the individual's health, ethnic origins, political views and sexual orientation.

Surrogate measurements – Measurable factors that are related to patient outcomes to some extent and are relevant to the patient. Examples of surrogate measurements in health and medical care are blood lipids, blood pressure and bone density.

1 Background

1.1 TLV's assignment

TLV shall, according to its instructions, contribute to the appropriate and cost-efficient utilisation of pharmaceuticals, not only in subsidy decisions, but across a pharmaceutical's entire lifecycle. In addition, TLV shall ensure proper access to these pharmaceuticals in accordance with the ethical principles for prioritisation within health care. An important prerequisite for ensuring the cost-efficient utilisation of pharmaceuticals over time is to have conditions conducive to the continuous follow up of how a pharmaceutical is being used in clinical practice and thereby evaluate what effects a treatment has on the health of patients. As of 2020, TLV has been permanently assigned to perform health-economic assessments of medical devices that are not covered by pharmaceutical benefits schemes, but procured by the regions. TLV is also permanently assigned by the government to conduct health-economic assessments of selected pharmaceuticals used within inpatient care.

Sweden has great potential in terms of leveraging health care data to follow up on how pharmaceuticals are being utilised and what benefits they bring to patients. To evaluate the efficacy of a pharmaceutical in clinical practice, there is already a range of analysis methods available today, which TLV has presented in previous reports. In its previous work with data from clinical practice, known as Real World Data (RWD), TLV reported that health care providers generate a considerable amount of data that could essentially be used for follow-ups. However, access to such data needs to be improved, via the national health data registry and other sources, such as medical record systems. To leverage the retrievable data, the opportunities for linking together various data sources must also be developed. For medical devices, their use must be linkable to the treated individuals and to relevant measurements for evaluating the benefit and value of treatments.

A structured and systematic implementation of national-level follow-ups of pharmaceutical and medical device usage, to assess whether they are being used appropriately and cost-efficiently, would result in the better leveraging of pharmaceuticals and thereby to the greater benefit for the patient. It would also result in improved control of the costs charged to pharmaceuticals. TLV requires precision tools for determining, for example, whether any pharmaceuticals are not being used in the patient groups where they would provide the most benefit. TLV's assignment to follow up its subsidy decisions is part of the objective to achieve high quality and equal care.

1.2 Government assignment to TLV

The government assignment states that: "TLV shall analyse the conditions for following-up pharmaceuticals and medical devices using, for example, data from the

National Service Platform (NTjP). Furthermore, the assignment shall be implemented in line with the government's Life Sciences Strategy on the issue of data access, the follow-up of innovative treatments and medical devices, or other initiatives that TLV deems to be relevant to the government's Life Sciences Strategy. The data that TLV analyses shall not consist of any personal data. The assignment is to be reported to the Government Offices of Sweden by no later than 15 May 2021.

In the national Life Sciences Strategy, the government's presented eight prioritised areas and set up 30 objectives. One of the prioritised areas is the Utilisation of Health Care Data.

TLV interprets the assignment to mean that it shall, in particular, analyse the conditions for following-up pharmaceuticals and medical devices using data that is currently not retrievable from national health data registers or quality registers.

Below is a general description of the National Service Platform, as well as the conditions for following up medical devices.

1.2.1 Background of the National Service Platform

The National Service Platform (NTjP) is a technical platform aimed at simplifying and streamlining information exchanges between various IT systems across all modes of health care delivery. The platform is to function as the hub between systems and e-Services that need to communicate with each other, by ensuring that information can be exchanged securely and cost-efficiently. Operations can connect their systems to the National Service Platform in order to exchange information, without setting up direct links between the systems. A system that requests information from another system queries the service platform, which then redirects the query to the right system. The platform's structure is based on structured communication between various parties and systems, pursuant to a given regulatory framework.

For an information exchange to work via the National Service Platform, all actors must agree on how the communication will take place. Inera AB is the region-owned company that develops and manages the technical specifications, known as 'service agreements', which describe how the querying system should formulate its query, and how the responding system should formulate its response. In terms of pure patient data, there are several defined service agreements that were initially created, primarily through the National Patient Overview (NPÖ) project. It is important to emphasise that the National Service Platform is a federated system, which means that it is not a database containing any health data in itself, but holds information about where various types of medical records are located for specific individuals. The data remains stored in each region's medical record systems.

1.2.2 Background of data access for pharmaceutical and medical devices

When new pharmaceuticals and medical devices are introduced to the market, uncertainty may prevail about their clinical efficacy and how they will be used in clinical practice. This can create difficulties for payers and government agencies to

evaluate the product and determine whether the cost is reasonable in relation to the benefit yielded. Uncertainties are commonplace not only for pharmaceuticals used in cancer treatments, but for many orphan pharmaceuticals, as well as precision medicines and new Advanced Therapy Medicinal Products (ATMPs).

By far, the highest percentage of medical devices used in health care is locally procured by health care providers and directly distributed to patients. Information about these medical devices is not available in any health data registers. Since the products are procured at a local level, there is no national overview of the specific products and volumes used, and at what prices. This entails a serious limitation to any opportunities for follow-ups at a national level. At the same time, the opportunity to follow up on the usage of medical devices is a prerequisite to ensuring equal care throughout the country and it is also of great importance for promoting research within Life Sciences.

New EU ordinances for medical devices enter into force as of May 2021, imposing requirements on manufacturers to label medical devices with a unique device identifier (UDI). Furthermore, the new regulatory framework will entail a requirement that all medical devices be registered in the EU database, EUDAMED. These changes could potentially facilitate future follow-ups on the utilisation and costs of medical devices, by creating conditions conducive to the uniform identification of products in the data systems of various regions.

1.3 Adjacent assignments

Access to national data sources for follow-ups are crucial to several assignments that the agency has received from the government.

1.3.1 Payment models for ATMP treatments

In parallel to this assignment, TLV has also been assigned by the government to investigate how health-economic assessments can be developed for precision medicines and how payment models can be applied to ATMP treatments. For these types of treatments, the question is usually a matter of urgency. When performing the health-economic assessment, there are often material uncertainties about long-term effects, and data is required, regardless of whether the this must be followed up, to enable the review of a decision about whether a treatment cost is reasonable, or whether the problem should be addressed through payment models where the size of the payment is conditional on a specified health gain or the achievement of another outcome. [1]

[1] "How should we perform an evaluation and how should we pay?" https://www.tlv.se/download/18.6dab39ff179179457163974e/1620379890581/Rapport_atmp_20210430.pdf

1.3.2 RWD cancer assignment

TLV has an additional assignment through the 2021 appropriation directions to follow-up pharmaceuticals and their efficacy in clinical practice, using alternative data sources, with a focus on cancer, which will be presented in October 2022.

1.3.3 TLV's assignment on cost savings for pharmaceuticals covered by benefits schemes

TLV was further assigned by the government through the 2021 appropriation directions to implement cost savings of SEK 800 million over four years on pharmaceuticals covered by benefits schemes. The cost savings are to be achieved either by lowering listprice or through refunds from collateral agreements between regions and pharmaceutical companies. To achieve these cost savings, TLV will remeasure the advantages of treatments with pharmaceuticals covered by benefits schemes and whether the costs are still reasonable in relation to the benefits. The remeasurement must be based on analyses of how pharmaceuticals are used and to what efficacy in clinical practice. This requires access to data and the development of methods of analysis for generating more knowledge about the specific advantages of pharmaceutical treatments in practical usage.

1.3.4 HTx report on the use of RWD among HTA (Health Technological Assessment) bodies

Within the framework of the EU-financed Horizon 2020 project, *HTx – Next Generation HTA*, TLV has prepared a report that describes the use of RWD among several other European HTA bodies[2]. The report is based on a questionnaire distributed to HTA bodies that are members of the EUnetHTA (European Network for Health Technology Assessment), and about a dozen interviews. In its report, HTx concluded that only a few government agencies are actively working to improve access to data, although many are discussing the problem of the lack of critical evidence for relative efficacy in new pharmaceuticals. One example from Italy's pharmaceutical and HTA body, AIFA, indicates that a register can be built up with very comprehensive information, if there is determination and political support. Infrastructure is crucial, as is expertise among government agencies, but the critical factor is leadership and the will to use alternative data sources together with randomised control trials (RCT).

[2] https://www.htx-h2020.eu/wp-content/uploads/2020/12/HTx-D4.4-Overview-of-the-development-of-the-use-of-RWD-final-for-publication.pdf

2 TLV's requirement of data and the basis of its work

TLV's continued work with its assignment to make subsidy decisions and follow up on these decisions, requires that data access be developed. This is also true for TLV's other assignments to evaluate hospital pharmaceuticals and medical devices.

This chapter provides a description of the requirements for following up pharmaceutical and medical devices from a lifecycle perspective, as well as the framework that was created to specify the data sets with which TLV has worked to improve conditions for follow-up.

2.1 Lifecycle perspective – RWD and market dynamics

Upon receiving market approval, pharmaceuticals can be introduced and commence usage. For a pharmaceutical to be subsidised and included under pharmaceutical benefits schemes, TLV must make a decision on its subsidisation and price. The documentation of efficacy and safety that is available at the point of introduction and TLV's subsidy decision are usually based on hitherto conducted clinical trials. Over time, further knowledge is generated from additional clinical trials and experience collected from utilisation in clinical practice.

Medical devices encompassed by non-pharmaceutical regulatory frameworks. Instead of being subject to market approval, the manufacturer must demonstrate compliance with the applicable requirements of prevailing regulatory frameworks and CE-mark their product prior to its market release. Under the new EU ordinances within the field of medical technology, a product must fulfil the applicable general requirements on safety and performance, and proof of such fulfilment must include a clinical evaluation. On the other hand, medical devices are not required to undergo clinical trials that involve one or more test subjects to evaluate the device's safety and performance. Therefore, to ensure that the cost of using a medical device is reasonable, it is important to be able to follow up on its usage and the knowledge generated from clinical practice.

A clinical evaluation is defined under the new EU medical device regulation (MDR) as:

> *'a systematic and planned process to continuously generate, collect, analyse and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer'.*

2.1.1 Increased uncertainties about treatment efficacy upon market introduction

In recent years, ever-more pharmaceuticals products are being granted market approval at ever-earlier stages of development, due to the assessment that there is a considerable need for new pharmaceuticals products for serious diseases that lack sufficient treatment alternatives. In these cases, approval is often based on surrogate markers, i.e. measurable factors that are assumed to correlate with real clinical outcomes that are relevant to the treatment. These could pertain to, for example, measuring progression-free time since the treatment commenced to predict the life expectancies of cancer patients. Or they could also pertain to results from non-randomised clinical trials, or trials without control groups or trials with only a small patient sample size.

For serious medical conditions where no treatment options were previously available, it is important to offer patients new treatments as soon as possible. Although new innovative pharmaceuticals usually bring great potential clinical benefits to patients, they are also usually associated with high costs and significant uncertainties about their long-term clinical efficacy. Due to prevailing uncertainties about treatment efficacy, subsidy decisions are based on assumptions about long-term efficacy and assumptions about causal links between surrogate measurements and what is known as 'hard outcome data'. When making subsidy decisions, uncertainties about treatment benefits and their frequently high costs lead to uncertainties about whether the new pharmaceutical is being utilised at a reasonable cost. For the high costs and uncertainties to be acceptable, it is important to develop and compile additional information over time about how pharmaceuticals are used and to what efficacy in clinical practice, to facilitate the subsequent follow-up of subsidy decisions and new evaluations based on data obtained from clinical practice. If the assumptions or estimates made at the time of the subsidy decision do not match the usage in clinical practice, a pharmaceutical's subsidy status may require review, which in turn results in the need for a price change.

For many pharmaceuticals, early market approval is frequently based on delimited patient populations and performance indications from conducted clinical trials. Additional clinical trials are usually conducted over time, which include larger patient populations, more indicators or treatments in the early phases of a disease. When these trials are presented, the approval and subsidisation of the pharmaceutical's treatment indications may be extended. The clinical benefits of treatments based on the new indications are not necessarily the same as those of the original indication. Consequently, TLV's subsidy decision may need to be limited to encompassing one or several of the approved indications, and cost efficiency may need to be remeasured whenever new indications are created.

Many cancer-treatment pharmaceuticals are used in combinations or in sequences, including pharmaceuticals covered by pharmaceutical-benefit schemes (which are prescribed and retrieved at a pharmacy) and hospital pharmaceuticals, (which are directly administered to the patient at a hospital). The pharmaceutical subsidy may

be limited to being utilisable only after the patients have tried another pharmaceutical agent, which may be a hospital pharmaceutical. Subsidy limits could also comprise restrictions that the patient must exceed or fall below a specific measurement value. Due to the lack of a national health data register dedicated to the use of hospital pharmaceuticals or laboratory results, it is seldom possible to monitor whether subsidy limits are adhered to, which makes it difficult to ensure that the usage of any particular pharmaceutical is cost-efficient.

2.1.2 Increased uncertainties about the cost efficiency of pharmaceuticals as a consequence of added indications and market changes

A pharmaceutical's cost efficiency is always assessed in relation to another treatment alternative. Pursuant to the Dental and Pharmaceutical Benefits Agency's general recommendations (TLVAR 2003:2) on economic assessments, comparison alternatives shall comprise the most cost-efficient of the relevant and accessible clinical treatments. Consequently, the value of a pharmaceutical treatment and its cost-efficiency assessment could change over time, due to new knowledge and modifications to the usage of the pharmaceutical concerned, or to new situations for potential treatment alternatives, or to market changes.

Follow-up trials could verify assumptions about efficacy and usage based on clinical trials, or could indicate that the assumptions require remeasurement. Added indications or patient groups could result in a clinical benefit that may be either greater or less than that of the indication that was assessed at the time of the subsidy decision. Furthermore, the price for treatment alternatives could be reduced through competition by generic brands or the release of new treatment alternatives. Sweden's subsidy system is product-based, which makes it difficult to adapt prices to changing conditions and differentiated scopes of use. Collateral agreements signed between regions and companies are a tool that could be leveraged to manage risks associated with the uncertainties found in clinical documentation, on which health-economic assessments are based. Greater possibilities to perform follow-ups of pharmaceutical utilisation create greater opportunities for relevant collateral agreements that are adapted to the specific conditions of each individual pharmaceutical, at different phases of its lifecycle.

In several reports, TLV has demonstrated that the overall costs for several pharmaceuticals that have been covered by benefit schemes for several years are increasing rapidly, in pace with increasing sales volumes. In many cases, the increasing volumes signify that there are more patients being treated with the pharmaceutical than what was expected at the time of the decision. A substantially greater than expected patient sample size could also be due to the treatment of some patients who do not belong to the patient group that was evaluated when the pharmaceutical was approved for subsidisation. Consequently, it is important to be able to analyse the nature of utilisation, meaning, which patients are being treated, and what clinical efficacies the treatments are yielding.

The access and use of data from clinical practice could be leveraged to follow up subsidy decisions and to remeasure the benefits of a pharmaceutical treatment.

Knowledge from such follow-ups could then be used to form new assessments on whether the utilisation of a pharmaceutical is truly cost-efficient. This line of reasoning is primarily based on the opportunity to evaluate individual pharmaceuticals or delimited patient groups retroactively. The awareness that relevant and reliable data is being generated over time also creates opportunities to manage uncertainties and the lack of information about future outcomes.

For example, if we know that the outcome of a treatment can be followed up, we can also develop and apply performance-based payment models based on paying for the specific health gains of the treatment, or the specific patient that is receiving treatment. By using such payment models, any uncertainties that are identified in conjunction with a subsidy decision can be managed so as to increase the probability that costs will correlate with the benefits provided by the treatment.

2.1.3 Performance-based payment models

One possible way to mitigate any financial consequences that may arise in connection with uncertainties linked to treatment efficacy and market changes is to use performance-based payment models. Performance-based payment models could also be further developed to manage actual market changes in the future – known as 'market risks'. Examples of market risks are patent expirations that result in competition from generic pharmaceuticals, or the introduction of more cost-efficient treatment alternatives in the future. Market-based performance-based models could also provide companies with the opportunity to set prices that generate an amount of reasonable income in relation to the research and development work they have undertaken to develop a treatment. These payment models could be critical to the introduction and utilisation of many new advanced therapies (ATMPs), where the treatment is assumed to be curative, but there is no available knowledge about how long the effect will remain.

Uncertainty about a treatment's cost efficiency, where both clinical uncertainties and market risks are contributing factors, gives rise to a cost with a lock-in effect: as long as there is no new information, a treatment can remain in use, despite the existence of cost-efficient alternatives. The lock-in effect is strengthened by curative treatments (such as ATMPs that consist of one-time treatments), where the cost cannot be changed, even with new information about cost-efficient treatment alternatives.[3]

2.1.4 Medical technology and the lifecycle perspective

This report does not focus solely on the follow-up of pharmaceuticals but includes the follow-up of medical devices. Medical devices differ from pharmaceuticals in several ways, particularly in terms of the requirements imposed for their market approval. However, in similarity to the follow-up of pharmaceuticals, the same issues and similar data sources are relevant to the follow-up of medical devices and

[3] "How should we perform an evaluation and how should we pay?" https://www.tlv.se/download/18.6dab39ff179179457163974e/1620379890581/Rapport_atmp_20210430.pdf

they need to be addressed through RWD. With the exception of certain disposable products that are prescribed and obtained from pharmacies, there are no opportunities for a national-level follow-up of how medical devices are being used at the individual level. To be able to identify which medical devices the patient is using is the basis for proceeding to an analysis of the two questions (1) how the products are being used? And (2) what is the efficacy in clinical practice? To read more about these two questions, please refer to TLV's 2020 report[4]. Medical devices are developed rapidly and have begun to be utilised in combination with pharmaceuticals to a considerable extent. Ensuring appropriate and cost-efficient health care also requires the possibility of following up medical devices – those that are used separately and those that are used in combination with pharmaceuticals.

It is difficult to conduct national-level follow-ups of medical devices in Sweden today. Although the Pharmaceuticals Registry contains data on the use of products that are prescribed under pharmaceutical benefit schemes – disposable products – no nationwide data is collected for other forms of medical technology. The regions use a variety of systems and there is a lack of standardised identification protocols for medical devices. Furthermore, there is frequently no linkage between the utilisation of medical devices and patient data. These factors make it difficult to compile data on how medical devices are being used and what efficacy they provide.

There is no national structure available for utilising the data autonomously generated by certain medical devices, such as data about the frequency or duration that a device is used. Various medical devices can generate a range of data and access, and the ownership of data may differ from device to device. Differences in legal and technical conditions between various medical devices can make it challenging for health care providers to collect data in a structured manner. This impedes the opportunities to collect data on usage and efficacy at a national level.

This report comprises a description of what medical devices are, how they are regulated, the role of TLV and regions with regard to medical devices, as well as the specific challenges regarding the availability of data and the follow-up of medical devices.

2.2 Starting points and schematic model

The two main questions that TLV seeks to answer by means of RWD are how pharmaceuticals and medical devices are being utilised, and to what efficacy in clinical practice. The schematic model is explained in Figure 1 below, which was extracted from the report, *Follow-up of cancer pharmaceuticals and other pharmaceuticals via alternative data sources (TLV,* October 2020). In this report, TLV proceeds from the same schematic overview model, but expands it to include medical devices. As with pharmaceuticals, the same questions can be asked: How is the product utilised and to what efficacy? To answer the latter, the former must first be answered.

[4] SOU 2021:4 page 319

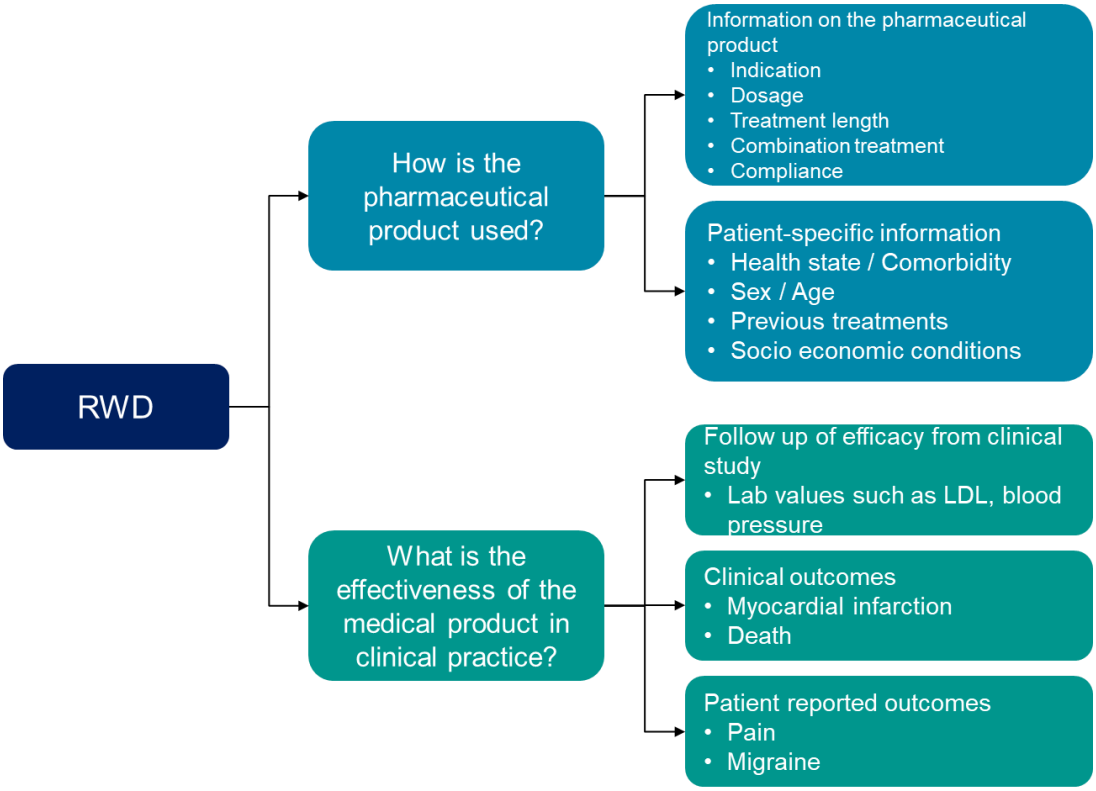

Figure1. Schematic model of the main questions that TLV strives to answer using RWD, and examples of variables that may be needed to answer questions about pharmaceutical utilisation or medical devices, and their treatment efficacy in clinical practice.

Answering the questions posed in the schematic overview model requires access to data at the individual level. For the accessed data to be usable for TLV's decision making, several prerequisites must be in place. The data must be national-level data, i.e. from all of the regions and must derived from relevant patients. TLV must also have access to the data. The time from a query to data delivery for analysis must not be protracted. The next chapter of this report will feature the legal prerequisites currently in place for TLV to obtain access to data and highlight the difficulties that arise in certain situations.

To make it realistic for TLV and other actors in the Life Sciences sector to frequently access data from health care providers, it is also important that the use of such data does not entail extra resources or costs for health care providers. Health care professionals must be able to focus on patient care and on entering generated data into existing medical record systems. The generated data should then be automatically retrievable for follow-ups or other purposes, such as research.

2.3 Data sources for follow-up

The follow-up of pharmaceutical utilisation and medical devices, as well as their efficacy in clinical practice, requires data. There are numerous types of data sources that can be used for follow-up, and data can be divided into primary or secondary data, based on the purposes for which the information is collected.

2.3.1 Primary data

Primary data is information that is specifically collected for a survey and the data would otherwise not have been compiled without the survey. Primary data can be collected through questionnaires, interviews, measurements or other types of collection methods. Primary data is generated through, for example, clinical trials, and is currently not included in any health data registers. The primary data would not have been generated, if it had not been designated for follow-up purposes.

2.3.2 Secondary data

Secondary data is information that is generated for purposes other than the specified assessment, and data is thereby independently acquired from follow-ups. The secondary usage of health data pertains to the use of information that is generated through health care providers as a result of patients receiving care. Each occasion of contact with health care providers generates health data of some and may include information about diagnoses, actions taken (such as the administration of hospital pharmaceuticals) and the results of examinations (such as laboratory results) generally found in medical records. The data may also pertain to administrative data about health care consultations with various health care departments or the retrieval of prescription pharmaceuticals at the pharmacy. Secondary data that is collected for purposes other than health care may contain health-related information and may therefore be relevant to factor into analyses of health care services. For example, Statistics Sweden (SCB) has a national register containing information about socio-economic statuses and the Social Insurance Agency has a national register containing information about long-term sickness absences.

2.3.3 Data retrieval and processing

As a rule, data must be processed before it can be utilised. This may entail the need to extract data from several different IT systems. Since different systems may use different terminology for the same items, the data must be harmonised before information from the different systems can be analysed. The collection and processing of data in preparation for analyses entails an administrative cost. Unstructured data, such as with the free-text fields of medical records, requires additional processing, which increases the administrative cost substantially.

To use secondary data – data that has already been collected for other purposes – for follow-ups means that the cost for using the data theoretically consists of the cost for the time that it takes to extract the data and utilise it. Follow-ups that require primary data require far greater efforts and costs, for example, when certain patients undergo specific tests and the results are stored in a database in a structured fashion. This means that the cost of accessing data that may be relevant to follow-ups will differ greatly depending on whether it is primary data that needs to be generated, or if secondary data can be used in its place. As a rule, the secondary usage of data entails a lower cost than generating primary data.

The overall cost of generating new evidence essentially comprises the cost of generating sufficient data from clinical practice, providing access to the data, and

processing and analysing the data. These costs constitute the overall evidence-generation cost, i.e. the costs that arise for generating new evidence. The costs can be divided into two categories:

- Costs for generating necessary data from clinical practice. These costs increase due to factors such as how much the new treatment costs and how many patients are receiving it and how long the patients need to be treated before the necessary data is generated.

Once the data is generated, costs are incurred for conducting follow-up studies.

- Cost for extracting data from various registers, processing and analysing the data, i.e. costs incurred for analyses or follow-ups when the data is available.

TLV is currently conducting work to have a closer look at evidence-generation costs, as well as the link between outcomes in clinical practice and how they can impact the health-economic assessment.

A key issue for TLV and for Life Sciences as a whole, is to create the prerequisites and infrastructure for reducing evidence-generation costs. A low evidence-generation cost stimulates follow-up studies, which could in turn help to ensure that the cost of utilising pharmaceuticals and medical devices is reasonable, in relation to the benefits generated. Much of the data that is requisite to follow-up studies is stored among care providers. If the administrative burden could be reduced for care providers to report data to, for example, the health data register, it would probably improve the opportunities for conducting follow-ups. This is because the registers would be more complete, and timelines improved as a consequence of shortened lead times in reporting. One way to reduce the administrative burden of health care providers is to reduce the requirements on how data must be reported. Once the data is reported, economies of scale could be leveraged by engaging an actor specialised in adapting the data to conform to the various format requirements of different registers.

Now that pharmaceuticals are increasingly being granted market approval at ever-earlier phases, subsidy applications are increasingly being submitted based on the documentation of limited evidence. By creating conditions conducive to the generation of new evidence in clinical practice, patients could be given early access to new innovative treatments, while reasonable utilisation costs can be ensured over time.

2.3.4 Numerous fragmented data sources in various systems.

TLV has, in previous assignments, attempted to summarise the storage locations of data related to pharmaceuticals and their utilisation[5], see Figure2. The summary indicates that the data is stored in many different systems that are frequently unintegrated.

[5] Pharmaceutical services at outpatient pharmacy (ref. no. 623/2019)

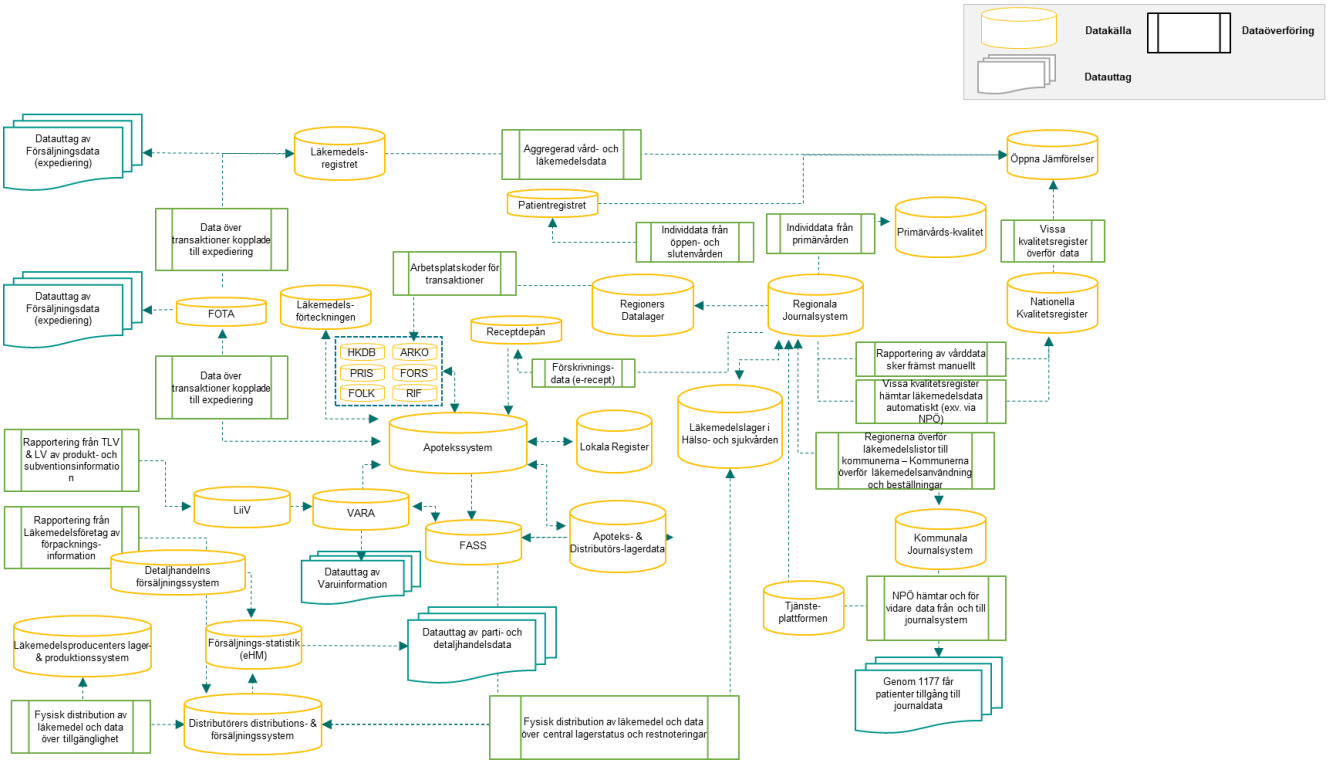

Figure2. Summary of data sources related to pharmaceuticals.

TLV has, in previous assignments, described how the Swedish National Board of Health and Welfare's health data register, primarily the Patient Register and the Pharmaceuticals Registry, often form the basis for follow-up studies to evaluate how prescription pharmaceuticals are being used, as well as their efficacy in clinical practice. What has become evident from comparisons of these two registers is that the Pharmaceuticals Registry provides an excellent overview of pharmaceutical orders via prescriptions. Prescriptions are mainly generated within primary care. Since there is no register that encompasses primary care, there are no opportunities to obtain a proper overview of the specific indications or diagnoses for which primary care patients are receiving a treatment. The opposite is true for inpatient care. The Patient Register contains useful information about diagnoses, but there is a huge gap in data about the pharmaceuticals administered to patients in hospitals. Consequently, these registers do not provide a complete picture of a patient's entire contact with health care providers. To obtain a complete picture, the national health data register must also capture data about pharmaceuticals administered within specialised care, as well as primary care treatments. If this basic data, as well as data about the utilisation of medical devices, were to be in place, the opportunities for conducting systematic follow-ups would improve substantially.

2.4 Implementation of the assignment

To implement the assignment, TLV conducted several pilot studies, sometimes solely with government agencies, and in some cases, in collaboration with other parties. The assignment includes examples of pilot studies conducted by external partners, mainly in connection with academia.

An introduction to TLV's legal prerequisites for data access is presented, followed by a description of several pilot studies that detail the challenges and opportunities in leveraging data from clinical practice. Thereafter, the report highlights TLV's specific opportunities to ensure reasonable costs for pharmaceuticals across their entire lifecycle based on RWD and the specific potential of the National Service Platform in this context. The challenges of following up medical devices are also highlighted in the report. The report concludes with several proposals from TLV's perspective, on what needs to be changed and what requires further development to enable the development of value-based pricing.

3 Legal prerequisites for TLV's data access

TLV's opportunity to systematically utilise data for national-level follow-ups and analyses with the aim of developing value-based pricing is contingent on:

(1) How data is collected and how the delivery of data is regulated.
(2) TLV's prerequisites for receiving relevant data, with or without data that comprises personal data. The latter may require that another actor process the personal data for the presentation of, for example, statistics that TLV may be privy to.

Data that is generated by health care providers can be divided into various categories based on where the data or registers are located. The classification of data that is relevant to TLV can be performed by government agencies, including data stored by care providers, i.e. by regions and private actors. Data from care providers could in turn be shared in quality registers at regional and local levels, as well as other health care data at regional and local levels. The registers are in turn governed by legal regulations, including those pertaining to the purposes for which the data may be used and whether there is an obligation to provide such data. The actual predictability of TLV's access to data in turn impacts the opportunity to systematically leverage data for follow-ups.

Under this government assignment TLV is to analyse the conditions for following-up pharmaceuticals and medical devices using, for example, data from the National Service Platform (NTjP). The data that TLV analyses shall not consist of any personal data.

The National Service Platform (NTjP) is a national platform that supports information exchanges within health care. It is administered by Inera AB, which is owned by Sweden's regions and municipalities, and the Swedish Association of Local Authorities and Regions (SKR). The National Service Platform (NTjP) is a technical platform that formalises, secures and streamlines information exchanges between various IT systems across all modes of health care delivery. Calls to various service agreements are made across the platform. More than 500 health care systems are connected and communicate with each other through the National Service Platform. The platform handles sensitive personal data and therefore, has a very high security level.

Below is a legal presentation of the regulatory components pertaining to registers, and which govern TLV's opportunities to leverage data for conducting follow-ups.

3.1 Legal framework for TLV's follow-up assignment

TLV's assignment to leverage its operations to contribute to appropriate and cost-efficient pharmaceutical utilisation and dental care, good access to pharmaceuticals in society and a well-functioning pharmaceutical market is stipulated under ordinance (2007:1206), with instructions for the Dental and Pharmaceutical Benefits Agency (hereinafter referred to as the 'Instruction'). Among other tasks, TLV shall

– monitor and analyse trends in the fields of pharmaceuticals, pharmacies, and dental care, as well medical devices,

– follow up and evaluate its decisions and the regulations adopted by government agencies,

and

– perform health-economic assessments on the question of pharmaceuticals and medical devices that are not covered by pharmaceutical benefits schemes and which are requisitioned for inpatient care or procured by the regions.

In addition to the legal foundation of the assignment as stipulated in the Instruction, TLV is also working under special government assignments and the annual appropriation directions, which are linked to TLV's assignment to follow up, evaluate and analyse developments within the pharmaceuticals domain.

3.1.1 Registry data and personal data

TLV requires data for conducting follow-ups and has access to data from other data registers. Within the framework of this government assignment, analyses are to be based on TLV's access to data but *not* personal data. At present, TLV can access data without personal data, which other actors have been able to process or analyse at a level that includes personal data (such as the Swedish National Board of Health and Welfare or researchers).

The regulatory frameworks described below and which regulate registry data pertain to the automated handling of personal data. The primary purpose of the Health Care Data Register Act (1998:543) and Patient Data Act (2008:355) is to regulate and delimit the purposes of maintaining such registers. Pursuant to the EU GDPR, personal data refers to any piece of information that pertains to an identified or identifiable natural person.[6] Once personal data has been acquired from the various health care authorities and care providers, they can be anonymised so that the information is no longer attributable to an identified or identifiable natural person. If the personal data later requires supplementation with additional data at the individual level, the data can also be pseudonymised or encrypted by, for example, using a code in place of a name or personal identity number. Pseudonymised and encrypted data still constitute personal data in

[6] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation).

accordance with the General Data Protection Regulation, while anonymised data does not.

Some sections of the EU's general data protection regulation are supplemented by national provisions, such as the Act containing supplementary provisions to the EU General Data Protection Regulation (SFS 2018:218) and the Swedish Data Protection Regulation (2018:219), containing supplementary provisions to the GDPR.

3.2 Overview of TLV's current access to data

National *health data registers*, such as the Patient Register and Pharmaceuticals Registry maintained by the Swedish National Board of Health and Welfare, are currently TLV's primary data sources. Other data is available from *national and regional quality registers*, maintained by Sweden's regions. In addition, data is available from the registers and data warehouses of various care providers, referred to below as *health care registers*. The regions have relatively extensive access to data from primary care providers in their centralised data systems. To develop the use of data, TLV collaborates with academia (such as researchers) and private actors who may in turn handle personal data and become privy to the data from these registers. TLV then receives the results at an aggregated level, without the personal data.

TLV has regulated continuous access to data structured for its dental-health and supervisory assignments, which are summarised below.

3.2.1 Access to data for the supervisory assignment

TLV has been tasked with a supervisory assignment since the pharmacy reregulation of 2009. Sect. 1a of TLV's Instructions stipulates that TLV has supervisory authority over matters of compliance with Act on Pharmaceutical Benefits (2002:160) (hereinafter referred to as the 'Benefits Act'). Sect. 25 of the Benefits Act stipulates that TLV has supervisory authority over matters of compliance with the Act and regulations, as well as terms and conditions announced in connection with the Act. It further stipulates that TLV is entitled to, upon request, obtain information and documents requisite to such oversight.

The eHealth Agency collects all of the data pertaining to dispatches of pharmaceuticals and disposable products at all outpatient pharmacies throughout the country, which they maintain what is termed a prescription registry. Sect. 18 of the Act on prescription registries (1996:1156) (hereinafter referred to as the 'Prescription Registry Act'), stipulates that the eHealth Agency has a duty to report information to TLV. The eHealth Agency is to issue a range of data about utilised pharmaceuticals per outpatient pharmacy (such as product, volume, cost and so forth) to TLV. The stated purpose pertains to TLV's supervisory authority over the exchange of pharmaceuticals.

3.2.2 Access to data for the dental-health assignment

Pursuant to Sect. 1 of the Instruction, TLV is responsible for decisions about the formulation of national dental care subsidies. TLV's fulfilment of this assignment requires in-depth data documentation. Under Sect. 19a of the Ordinance on National Dental Care Subsidies (2008:193), the Swedish Social Insurance Agency has an obligation to provide TLV with non-aggregated data where the patient's and care provider's identities are subjected to a one-time encryption by means of an algorithm. The rendered data is categorised as sensitive personal data, since the information is indirectly attributable to a natural person by the Social Insurance Agency. For TLV's operations pertaining to national dental care subsidies, Ordinance (2011:306) on the Handling of Personal Data, governs TLV's handling of these data sets and provides an adapted form of protection of personal privacy, as a well-defined legal basis for handling sensitive personal data. Data privacy is provided through the amendment of Sect. 7 of the Public Access to Information and Secrecy Ordinance (2009:641), which provides the data with a level of protection corresponding to that of statistical confidentiality pursuant to Chap. 24 Sect. 8 of the Public Access to Information and Secrecy Act (2009:400). Processed and aggregated database content that is used pursuant to the agency's priorities or in the calculation of future changes to dental care subsidies are published. Under Sect. 1a of the Instruction, TLV is also responsible for providing information as part of a price-comparison service for dental care, which is rendered under the national dental care subsidies. The data is delivered to TLV by the Social Insurance Agency subject to a duty to report as stipulated in Sect. 19b of the Ordinance on National Dental Care Subsidies (2008:192). The data set contains no links to individual patients, but consists of factual data about care providers and clinics. Data from the price-comparison service that is delivered pursuant to Sect. 19b is not covered by any privacy protection by the Social Insurance Agency, since only an individual's health condition or other personal circumstances are protected under Chap. 28 Sect. 1 par. 5 of the Public Access to Information and Secrecy Act

3.3 Legal regulations for health data registers

Nationwide registers provided by government agencies within health care, known as health data registers, are currently maintained by the Swedish National Board of Health and Welfare, Medical Products Agency and Public Health Agency. Health data from these registers is used for generating official statistics and in consideration of its scope of use, the registry content must be of a high quality. Health data registers are based on personal identity numbers and provided in a structured format that can be utilised for various follow-up purposes.

National health data registers are regulated under the Health Care Data Register Act (1998:543) and several other ordinances. The Act regulates issues of particular importance common to all health data registers, based on the automated handling of personal data. Pursuant to legislative history, the idea was for the issues common to all health data registers to be regulated by law, while fine-print regulations for individual health data registers would be announced by the government within the

subsequent legal frameworks. Health data register operations are not subject consent by individuals, due to the well-defined purposes stipulated in the Act, which is applicable at a national level and serves to regulate key issues.[7] Health data registers are thus based on the principle that the information in each register is associated with private individuals and is added to the register without being subject to the individual's consent. Those who conduct health care operations – health care providers – have an obligation to submit information to a health data register for the purposes as stipulated by law.[8]

3.3.1 Permissible purposes for the handling of personal data

Th personal data in a health data register may be processed for the following purposes: [9]

- Presentation of statistics
- Follow-up, assessment and quality assurance of health care, and
- Research and epidemiological surveys

The legislative history of the Health Care Data Register Act explains that statistics, as defined by the Act, refer to both official statistics and other statistics. The latter refers to statistics used primarily for the follow-up, assessment and planning of proprietary operations.[10] The data in a health data register may also be accessed for the *follow-up*, *assessment and quality assurance of health care*. This is linked to health care and, the Act's legislative history states that follow-up refers to the continuous and regular measurement and description of requirements, operations and resource availability in terms of, for example, demand coverage, productivity and key metrics. Follow-ups are aimed at providing an overview of operational performance. *Assessment* refers to the analysis and valuation of quality, efficiency and results of an operation in relation to its set objectives. *Quality assurance* is the process of continuously and systematically describing, measuring and evaluating the quality of proprietary operations in relation to its set objectives.[11]

The Act's legislative history stresses the importance of following up, evaluating and quality assuring health care, and that is it an urgent assignment that is becoming increasingly relevant at a centralised level in a situation that requires the stringent economising of available economic and personnel resources.
It was emphasised that the handling of information in health data registers is well justifiable for following up, assessing and quality assuring health care at a centralised level.

3.3.2 About the Patient Register and Pharmaceuticals Registry

As explained above, issues common to all health data registers are regulated under the Health Care Data Register Act, while fine-print regulations for individual health

---

Prop. 1997/98:108 Health Data Registers and Health Care Registers p. 44 Sect. 6 of the Health Care Data Register Act.[7]
[8]
[9] Sect. 3 of the Health Care Data Register Act
Prop. 1997/98:108 Health Data Registers and Health Care Registers [10]p. 49
[11] Prop. 1997/98:108 pp. 49-50

data registers are supplemented by the government through ordinances. The following is thus a brief description of the regulations governing the Patient Register and Pharmaceuticals Registry.

In addition to the Health Care Data Register Act, the Patient Register is regulated by several ordinances, such as the Ordinance (2001:707) on the Swedish National Board of Health and Welfare's Patient Registers. The listed purposes for handling personal data in the Patient Register include the compilation of statistics, follow-up, assessment and quality assurance for connected health care providers and within sections of outpatient care that do not pertain to primary care, as well as for research and epidemiological surveys. In addition, the Swedish National Board of Health and Welfare has published its regulations (SOSFS 2013:35) on the duty to report to the Swedish National Board of Health and Welfare's patient register. Consequently, it is a statutory obligation to enter information into the register. The Swedish National Board of Health and Welfare may share personal data from the register with other statistics agencies.

The Pharmaceuticals Registry is subject to Regulation (2005:363) on pharmaceutical registers maintained by the National Board of Health and Welfare and the Prescription Registration Act (1996:1156). These regulate the specific information that may exist in the register, as well as the eHealth Agency's obligation to share information with the Pharmaceuticals Registry. Personal data in the Pharmaceuticals Registry may be accessed for epidemiological surveys, research, statistics compilation, follow-up, assessment and quality assurance within the field of health care.

3.4 Legal regulations for health care registers and quality registers

The Patient Data Act (2008:355) entered into force in 2008, replacing the Patient Record Act (1985:562). The Act is applied to the handling of personal data within health care by health care providers. The Act contains provisions on the obligation to maintain patient records. The Patient Data Act is a framework legislation that specifies which fundamental policies are applicable to the processing of patient data across all modes of health care. Consequently, health care registers are primarily regulated by the Patient Data Act. The Act stipulates the special regulations for national and regional quality registers, which are thus subject to some individualised regulations.

As mentioned, the Patient Data Act is applied to the handling of personal data within health care by health care providers. In Chap. 2 Sect. 1 of the Health and Medical Services Act (2017:30), the term "health and medical service" is defined as intervention to medically prevent, investigate and treat diseases and injuries, medical transports and the management of deceased persons. On the other hand, the Patient Data Act does not apply to the handling of personal data, which occurs among government agencies that are definitely active within the health care sector, but who do not provide personalised patient care per se, such as the Swedish

National Board of Health and Welfare, the Medical Products Agency and the Medical Responsibility Board.[12]

Sweden's regions have relatively comprehensive access to data from primary care providers in their centralised data systems. Data maintained by the regions' medical record system includes personal data linked to patients. The information consists of, for example, information about the patient, health care provider, date of visit, diagnoses and actions. The handling of data in such health care registers that are not quality registers, is essentially obligatory and may be transferred without the consent of the individual.[13]

Quality registers, national and regional, are to enable comparisons in the field of health care at national and regional levels.[14] Consequently, the regulatory framework provides support for a special form of operational follow up for care-provider delimitations. One thing in common to all quality registers is that data entry occurs is as a result of voluntary commitments on the part of health care providers. A quality register contains data based on individual patient diagnoses/problems, medical interventions and the treatment outcomes across all modes of health care delivery. The data is acquired through several health care providers. Registers are frequently administrated at a clinic or institution within a hospital. The region usually takes the role of Data Controller Agency. To register data in a national quality register further requires that the patient has no objection to such an action.[15] The health care provider, i.e. the region, municipality or private company is responsible for informing the patient about the register.

3.4.1 Permissible purposes for the handling of personal data

The Patient Data Act stipulates the purpose for handling personal data in the registers of health care providers.[16] There are several overarching purposes for handling personal data under the law, and they are mainly linked to the patient and to follow-up activities. It is stipulated, for example, that personal data may be accessed as needed for creating a patient's medical records, patient administration, the systematic and continuous quality development of operations, the planning, follow-up and assessment of operations, as well as the generation of health care statistics. Personal data may also be handled for *other purposes*, provided that the data is not handled in a manner that is incompatible with the purpose for which the data was acquired.[17]

The quality registers are subject to special provisions on what are permissible purposes for handling personal data, which are unambiguously linked to 'systematically and continuously developing and ensuring care quality'.[18]

---

[12] This is clarified in the government inquiry, *Data Transfer within Health Care* (SOU 2021:4) pp. 144-145
[13]Chap. 2. Sect. 2 of the Patient Data Act (2008:355)
[14] Chap. 7 Sect. 1 of the Patient Data Act (2008:355)
[15] Chap. 7 Sect. 2 of the Patient Data Act (2008:355)
[16]Chap. 2. Sect. 4 of the Patient Data Act
[17]Chap. 2. Sect. 5 of the Patient Data Act
[18]Chap. 7. Sect. 4 of the Patient Data Act

Personal data in national and regional quality registers may be accessed for

- Statistics generation
- Research within health care services
- Transmission to parties who will utilise the data for these purposes
- Fulfilment of a statutory or regulatory duty to report other than what is encompassed by Chap. 6 Sect. 5 of the Public Access to Information and Secrecy Act (2009:400, hereinafter referred to as the 'OSL')[19].

Personal data in national and regional quality registers may be accessed for other purposes than the ones stated here.

3.5 The legal prerequisites have an impact on TLV's opportunities for follow-up

The issue of TLV's access to data for its assignment to follow up pharmaceuticals and medical devices involves many complex parameters, such as who and what should administrate the registers: government agencies, regions or other actors. The matter is further compounded by the various regulatory frameworks with various objectives and purposes governing access and opportunities to utilise the data in the registers. A comprehensive regulatory framework was also created primarily to handle personal data, protect personal privacy and ensure compliance with secrecy legislation.

As mentioned above, TLV regularly requests and obtains aggregate-level information from health data registers maintained by the Swedish National Board of Health and Welfare, primarily from the Pharmaceuticals Registry and Patient Register.

When ordering such data from registers, the Swedish National Board of Health and Welfare reviews confidentiality parameters to ensure the data that it delivers is anonymised. The data can take up to two weeks to render and TLV pays for this on a cost-plus basis. The Patient Register and Pharmaceuticals Registry are updated on a monthly basis, which makes it appropriate for TLV to use the data for follow-up purposes. One of the reviews conducted by TLV on subsidies for pharmaceuticals for the treatment of haemophilia indicates that the Pharmaceuticals Registry can be utilised to follow up the use of pharmaceuticals in clinical practice. Consequently, data from the Pharmaceuticals Registry could support TLV's decision-making processes when reviewing pharmaceutical subsidies.

However, the lack of a national register comprising data from primary care has long been highlighted as a problem. In early 2021, the Swedish National Board of Health and Welfare submitted the report, Sub-assignment 1 – *National collection of register data from primary care*. The report proposed that the National Patient

[19] Chap. 6 Sect. 5 of the OSL stipulates that an agency, when requested by another agency, shall deliver information at its disposal, unless the information in classified as secret or it would prevent the progress of work

Register be expanded and emphasised that the uniform and appropriate registration and reporting of data could generate higher contribution margins and quality for the proposed data that is to be acquired. A National Patient Register for primary care would in turn generate a broader basis for statistics and research, follow-up, assessment and quality assurance. The Swedish National Board of Health and Welfare was recently assigned to submit proposals on constitutional amendments pertaining to the Patient Register, requisite to the register's acquisition of data comprising information about all patients who receive non-primary outpatient care. TLV is optimistic about the assignment and has also emphasised the need to develop the Patient Register to create a more complete health data register, particularly by automating the supply of information from the regions' basic data sets.

The data in health care registers, as well as national and regional quality registers, is highly complementary to the data existing in national government registers, such as the health data register. These other health care registers are regulated by the Patient Data Act, which could also be applicable the registers that are linked to the National Service Platform. The National Service Platform is administrated by Inera AB, which is owned by Sweden's regions, municipalities and the Swedish Association of Local Authorities and Regions (SKR). The platform handles the sensitive personal data in health care systems and therefore, has a very high security level. However, the above description of the legal prerequisites indicate that these data sources do not support TLV's more systematic approach to data extraction. In terms of the governance of regionally owned companies such as Inera AB, it is noteworthy that the ultimate responsibility for corporate governance at a municipal or regional level rests with the council assemblies, who decide on which corporate governance policies to apply.

A schematic diagram of where data is stored and which section of a law governs the asset is presented in figure 3.

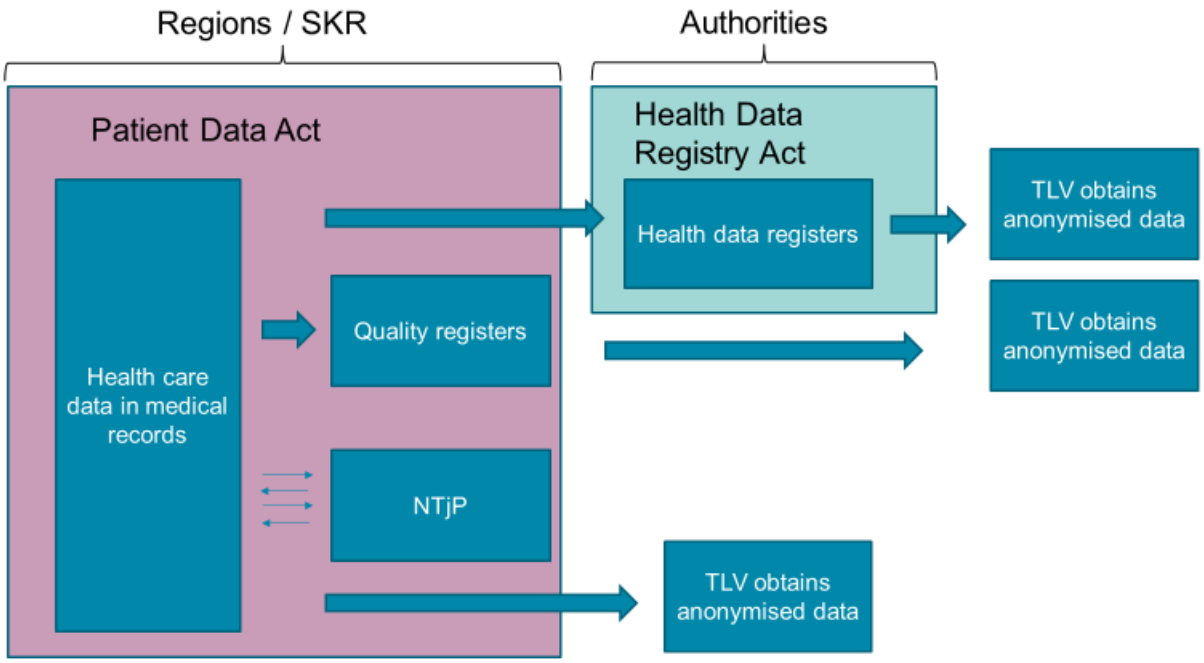

Figure3. Schematic diagram of the data storage location and the section of law that primarily governs the data's access.

4 Pilot studies within the scope of the assignment

To implement the assignment, several pilot studies were conducted. The aim of the subproject was to investigate what data is available and under what conditions an actor such as TLV can be granted access to it. Once the data becomes available, TLV aims to conduct two pilot studies to demonstrate how it can be utilised.

The pilot studies are aimed at identifying what type of data is available in various systems and whether this data is in turn available at a national level for potential utilisation in follow-up activities. One of the purposes is also to analyse what methods are available for assessing pharmaceuticals. Some pilot studies focus on data that is available via the national health data register maintained by the Swedish National Board of Health and Welfare, while others focus on data stored in regional health care data systems, or both. A special focus of this report is to analyse opportunities to utilise data from regional health care systems for follow-up activities through the National Service Platform, which is administrated by Inera AB and owned by Sweden's regions municipalities and the Swedish Association of Local Authorities and Regions (SKR).

TLV has used the pilot studies described in this section to research various aspects of how TLV can gain access to health care data from medical records and from health data registers. One objective of the pilot studies was to illustrate that health care data comprises structured data, such as laboratory values, which are frequently central to the follow-up of pharmaceuticals. If the information could be utilised in a structured manner for national-level follow-ups, the conditions for follow-up activities would improve substantially, even for unstructured source data. For example, such data should be rendered through the National Service Platform. Another objective was to illustrate the need for uniform nomenclature for medical devices and thereby achieve the fundamental conditions for identifying the presence and use of medical devices at the individual level. Figure 4 below shows the laws that regulate the data used by the pilot studies.

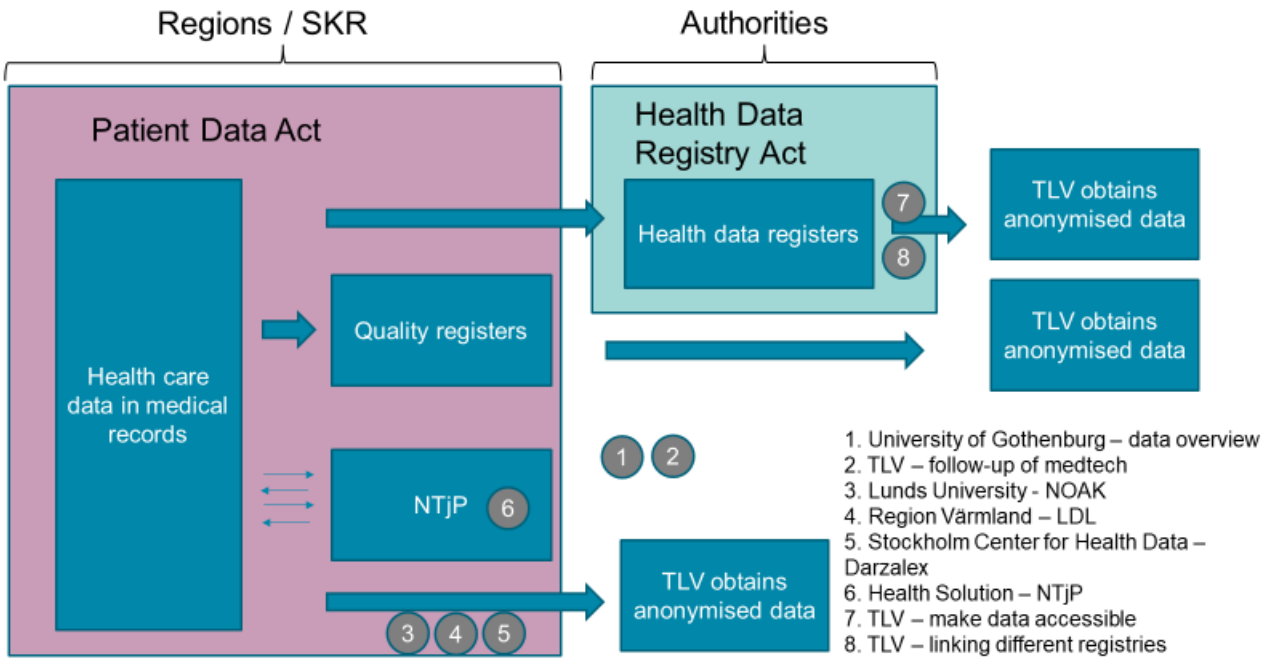

Figure4. Schematic diagram of data storage locations and the section of law that primarily governs the data's access. The figures show the specific data source from which the pilot studies obtained/assessed the data. Some pilot studies utilised data from several data sources, and in such cases, the most used data source determined where the number is placed.

4.1 Pilot study 1 – University of Gothenburg data overview of health data register

Purpose: To identify available data that can be used for updating health-economic assessments.

Conducted by: University of Gothenburg

Method: Identification and assessment of the usability of data sources for routine health-economic assessments of pharmaceuticals.

Results: The fundamental usability of the health-data sources described in the study is generally high or extremely high when it comes to studying health-related issues, although the usability varies depending on the field of therapy. The Swedish National Board of Health and Welfare's health data register may need to be supplemented with other types of data for numerous fields of therapy. The various quality registers are highly significant to opportunities to satisfactorily analyse issues related to health and health outcomes that are linkable to medical interventions. At present, quality registers are showing some degree of heterogeneousness in terms of the data that is acquired and when it pertains to published register descriptions. To further increase the usability of health data registers, the proposal is to shorten the time between data acquisition and publication of the data, to shorten lead times for data extraction and improve the reporting of certain key variables. It is particularly important that information about hospital pharmaceuticals be improved. Other deficiencies are the lack of

national-level information about primary care and laboratory diagnostics, and information about sick leave periods of less than 14 days.

Link to the interim report here

4.2 Pilot study 2 – TLV's report on the follow-up of medical devices

Purpose: This pilot study comprises a report issued by TLV to provide a brief description of what medical devices are, how they are regulated and how the market then works to focus on the conditions and challenges for following up medical devices. The report provides a summary of the issues that urgent to investigate going forward, to enable the improved follow-up of medical devices.

Conducted by: Dental and Pharmaceutical Benefits Agency (TLV)

Method: TLV has proceeded from the experiences gained from its work with medical devices, including medical devices and disposable products that are encompassed by pharmaceutical benefits schemes. The reference point is the regulatory framework that governs the market for medical devices, a brief description of the new European ordinances for medical devices that come into force in May 2021 and May 2022.

Results: TLV reported that medical devices in health care are processed differently by different regions. One factor that further complicates centralised follow-up is the lack of a uniform nationwide identification system for medical devices. Certain regions use the manufacturer's serial numbers in their goods management systems, while others use their own descriptions or identification numbers.

Data is available in the Pharmaceuticals Registry for (disposable) products that are prescribed within the scope of pharmaceutical benefits. Consequently, analyses of their utilisation and costs can be compiled at a national level by government agencies and other decision-making bodies. By far, the highest percentage of medical devices used in Swedish health care is procured and distributed without any coverage by pharmaceutical benefits, and therefore, does not allow for follow up using data from the Pharmaceuticals Registry. The lack of a nationwide overview of specific products used, and their specific prices and volumes, and what their utilisation costs, is an obstacle to the analyses of the present situation and the trend over time. This entails a serious limitation to any opportunities for follow-up at a national level.

In distinction to pharmaceuticals, numerous medical devices do not undergo clinical trials and thus do not allow for meeting the requirement for efficacy data. On the other hand, the number of data streams are rapidly increasing within health care, and the utilisation of medical devices is generating large volumes of data with considerable potential to meet the data requirements on efficacy and resource

usage. Large volumes of data are also being generated through the use of medical devices by the patients themselves, outside of the health care system, for example insulin pump systems connected to mobile apps. This type of data could potentially be used to assess the efficacy generated by the use of medical devices, as well as for evaluating pharmaceutical treatments, for example. However, a range of different problems, particularly the ownership of data generated in a medical device, must be resolved before the data can actually be used.

The new EU ordinances impose requirements on manufacturers to label medical devices with a unique device identifier (UDI). Furthermore, the new regulatory framework will entail a requirement that all medical devices be registered in the EU database, EUDAMED. These changes could facilitate future follow-ups on the utilisation and costs of medical devices, by creating conditions conducive to the uniform identification of products in the data systems of various regions. A prerequisite for using UDI for follow-up activities at a national level is that it must be registered in the data systems of relevant actors in a structured manner. To enable the follow-up of the products' efficacy and costs, their usage must also be linkable to individuals.

There is a clear need for an organised nationwide introduction, structured data acquisition and the sustained development of methods to assess medical technology. This need is further driven by the trend of products utilising a combination of pharmaceuticals and medical devices. Developed and appropriate cooperation between relevant government agencies and regions provides key opportunities and conditions for achieving equal care in Sweden. The follow-up of medical devices can also help to attain the objectives of Sweden's national Life Sciences Strategy.

Link to the interim report here

4.3 Pilot study 3 – initiatives by the Lund University to study the introduction of new oral anticoagulants (NOACs) using data from national registers and primary-care data from three regions

Purpose: This pilot study focuses on applying and testing methods for assessing the efficacy of pharmaceutical utilisation in clinical practice, as well as highlighting the need for following up primary care at the individual level. For this purpose, the introduction of NOACs is being studied.

Data sources: Swedish National Board of Health and Welfare health data register: Pharmaceuticals Registry, Patient Register and Cause of Death Register. Statistics Sweden: The Income and Tax Register, the Total Population Register and the

Education Register. Primary-care data from the Skåne Regional Council, Region Östergötland and Region Västra Götaland.

Conducted by: Lund University

Method: The clinical efficacy of NOACs is followed up by examining the differences in efficacy between patients in different regions, by staggering the rollout of NOACs in the different regions. The analysis is based on patients who got warfarin and/or NOAC pharmaceuticals dispensed, and who have received one of the selected diagnostic codes. The clinical efficacy is measured in stroke-related hospitalisations and primary care visits, as well as mortality. The analyses are adjusted for patient characteristics such as age, education and marital status. To demonstrate the importance of additional data, an analysis is performed, based on data from national health data registers and Statistics Sweden, and an analysis where the same data is supplemented with primary care data from three regions.

Results: The study could not demonstrate superior health for patients who were treated in regions or district health care centres that were faster at introducing NOACs to prevent stroke. The method did not show any causal links between the early introduction of NOAC treatments and effects on the health of patients. Additional analyses are required to demonstrate such potential connections.

Other experiences: The pilot study demonstrates that it is possible to assess clinical efficacy at a group level by having different regions and health care providers stagger the rollout of new pharmaceuticals. Since patient are treated in both primary care and inpatient care, it is necessary, at the individual level, to process data from the Pharmaceuticals Registry together with the Patient Register and with regional primary-care data.

Link to the interim report here

4.4 Pilot study 4 – Region Värmland's work to extract individual data on laboratory results from medical records

Purpose: To investigate the possibility of using data from structured medical records to assess compliance with subsidy limits and the efficacy of a pharmaceutical treatment. TLV's utilisation of structured medical records is dependent on the possibility of generating anonymised individual data for laboratory values, before and after a treatment is begun. This pilot study focuses on identifying specific data that can be extracted in an anonymised format from medical record systems, for the subsequent assessment of compliance with subsidy limits and clinical efficacy.

Data sources: Data from Region Värmland's medical record system.

Conducted by: Region Värmland and TLV

Method: Jointly with Region Värmland, TLV identified relevant variables for the follow-up of treatments with one of the PCSK9 inhibitors, Repatha or Praluent. Region Värmland then extracted from the medical record systems:

- Date and time treatment commenced with Repatha or Praluent
- Whether a diagnosis of familial hypercholesterolemia is registered
- Whether the patient has tried using another cholesterol reducer before the introduction of a PCSK9 inhibitor
- Laboratory values for LDL (blood lipids) before and after the introduction of a PCSK9 inhibitor

Usable anonymised data was then delivered to TLV for analyses.

Results: A total of just over 30 patients were identified, who had initiated treatment with PCSK9 inhibitors. Most of the patients had values of higher than 2.5 mmol/l prior to treatment (Table1).

Table1. LDL values before commencing treatment with PCSK9 inhibitor

LDL values before commencing treatment	<2.5 mmol/l	2-5–4 mmol/l	>4 mmol/l
No. of patients	2	12	14

The availability of data on LDL values before and after the introduction of a PCSK9 inhibitor allows for the percentage of change in lab values to be calculated. After treatment has begun, LDL levels are reduced for most of the patients (figure 5).

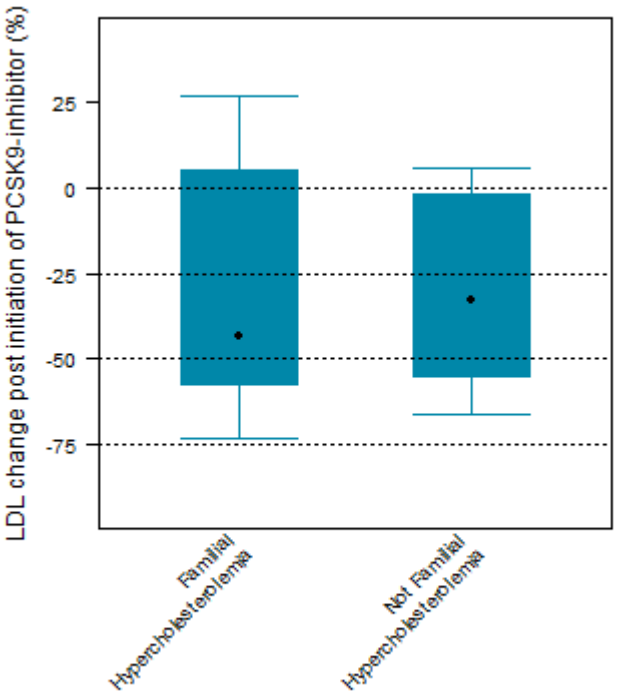

Figure 5. Change in LDL after the introduction of PCSK9 inhibitor.

Other experiences: With relatively few resources, Region Värmland was able to extract data that was crucial to the follow-up of subsidy limits and to analyse the extent of efficacy generated by the pharmaceutical's utilisation. More comprehensive lab data from other regions would substantially increase the opportunities to follow up treatments used in clinical practice.

4.5 Pilot study 5 – Region Stockholm's utilisation of laboratory data for follow-ups (M component)

Purpose: To generate data about patients treated with Darzalex and data about the temporal development of the M component in laboratory results. However, the pilot study was not tasked with assessing the possibility of utilising the M component as a surrogate measure for the efficacy of treatments involving Darzalex.

Data sources: Extracts from health data register maintained by Region Stockholm.

Conducted by: Region Stockholm, Stockholm Center for Health Data.

Method: Partnering with the Center for Health Data provides TLV with access to an actor authorised to handle sensitive personal data, and the opportunity to obtain data from several different health care providers within Region Stockholm, without

requiring that TLV maintain separate contact with each health care provider. Confidentiality reviews do not need to be conducted for each individual health care provider, but can be centralised to a single point within the region. The pilot project is being conducted based on ethics approval procedures, whereby each owner of information reviews confidentiality parameters before delivering the data to the Center for Health Data. Data from several different sources are compiled by analysts at the Center for Health Data and presented to TLV as aggregated data, so that no personal data is disclosed.

Results: Data from the region's medical record system was compiled, proving that data specific to individual patients treated with Darzalex can be merged with the M component in laboratory results, to be graphically visualised as shown in figure 6. Additional work and data is required to further assess whether the M component can be utilised as a surrogate measurement Darzalex treatment outcomes.

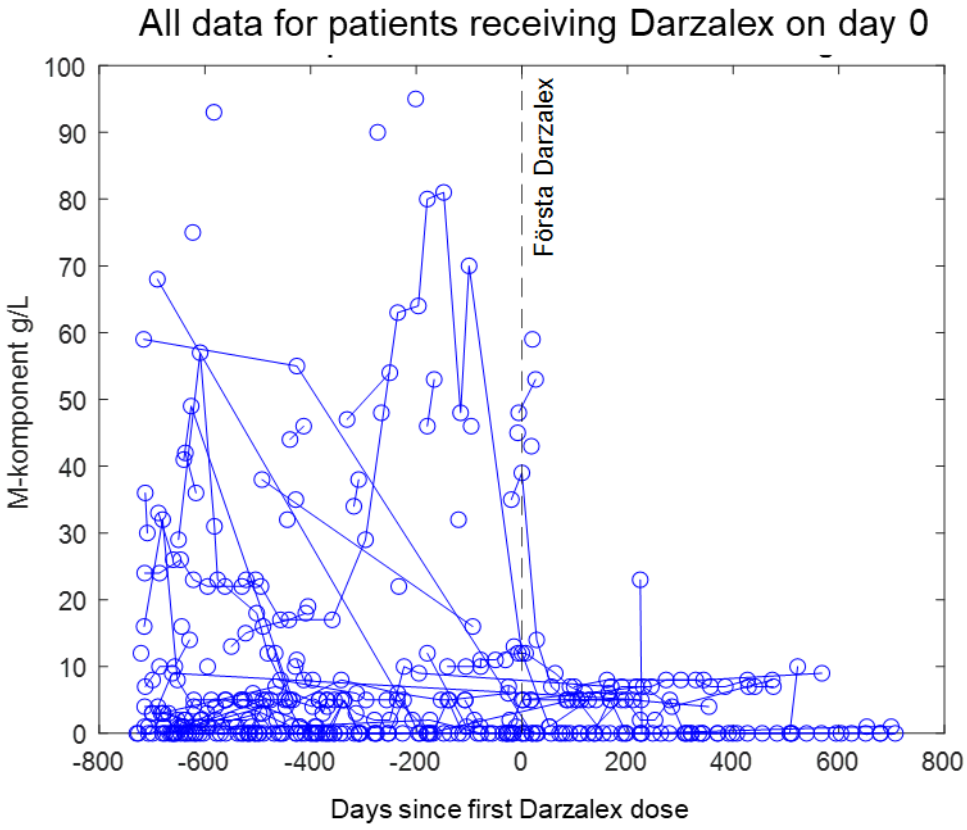

Figure 6. Visualisation of changes to the M component following treatment with Darzalex.

Other experiences: It can be quite challenging to extract data, even when the analysis of data is performed within one and the same region. Each owner of information must provide their approval for the data to be used and, in this case, the M-component data was stored as text files, which require additional processing.

Link to the interim report here

4.6 Pilot study 6 – Health Solution's work to acquire data from the National Service Platform

Purpose: The pilot study was aimed at testing whether TLV can gain access to data from the regional platforms and the National Service Platform to conduct national-level follow-ups.

Data sources: Patient medical data via national service agreements.

Conducted by: Health Solution.

Method: Obtaining aggregated information about insulin pumps to indicate the usability of the service platform as a data source.

Results: In 2018, a data order for descriptive statistics about diabetes pumps was made to Inera AB through the partner, Health Solution. Following several interactions with Inera, it became evident that the company exclusively initiates work prioritised by its owners, i.e. Sweden's regions and SKR. The more regions that consider the work to be a priority, the higher the priority assigned to the work by Inera. At present, more than two years after the order, Inera is yet to provide a response to the request, which shows that a government agency is not automatically prioritised, but that Inera's priorities are governed by the regions and its owners.

Other experiences: A survey of the National Service Platform indicates challenges to using it for follow-up activities from a national perspective and TLV's perspective. The National Service Platform was not designed to allow for general data queries. Generating any data requires advance knowledge of the specific individuals whose data is to be queried. This allows for the National Patient Summary (NPÖ) to function according to its intended purpose. Doctors know the specific individual and personal identity number when querying for their information, and data is displayed solely for the specific individual. Similarly, a quality register can utilise the National Service Platform to furnish the register with data, since quality registers already hold the personal identity numbers of the individuals whom the data pertains to. The system is simply not designed for queries where the user does not know which individual to extract data for, such as when querying for the number of people who are receiving a particular treatment.

Link to the interim report here and application for data extract here

4.7 Pilot study 7 – TLV's work to make data accessible for follow-up activities

Purpose: To show how data from health data registers can be made accessible for use as an interactive tool, where the user can autonomously choose the analyses

that are to be illustrated. This type of tool could be used to continuously follow up TLV's decisions.

Data sources: The Swedish National Board of Health and Welfare health data register: Pharmaceuticals Registry and Patient Register.

Conducted by: Dental and Pharmaceutical Benefits Agency, TLV

Method: Data from the Pharmaceuticals Registry is used to illustrate how data can be utilised to follow up TLV's subsidy decisions. JAK inhibitors are subject to subsidy limits, which entails that a TNF alfa inhibitor must have been attempted before beginning treatment; CGRP inhibitors are subject to subsidy limits, which entails that at least two other migraine prophylaxis medications must be attempted before treatment begins. The Pharmaceuticals Registry contains data about the retrieval of other prescription pharmaceuticals. Therefore, the prerequisites are potentially in place for assessing compliance with subsidy limits. The Pharmaceuticals Registry's monthly updates allow for the continuous monitoring of the number of patients linked to the respective treatment. The Patient Register comprises diagnostic codes for treatments within inpatient care and outpatient specialist care. The Patient Register is also continuously updated every month. Although no information about the reason for the prescription is provided in the Pharmaceuticals Registry, by combining information from the Patient Register and Pharmaceuticals Registry, approximate assessments can be made of the particular diagnosis a pharmaceutical was prescribed for. Using this data, TLV has developed two different portals where the user can choose to look at different data slices regarding JAK inhibitors and CGRP inhibitors.

Results: You can access the portal for CGRP inhibitors here https://tlvanalys.shinyapps.io/cgrp/ and the portal for JAK inhibitors herehttps://tlvanalys.shinyapps.io/jak_hammare/. A visualisation of what the applications will illustrate is provided in Figure 7 and Figure 8

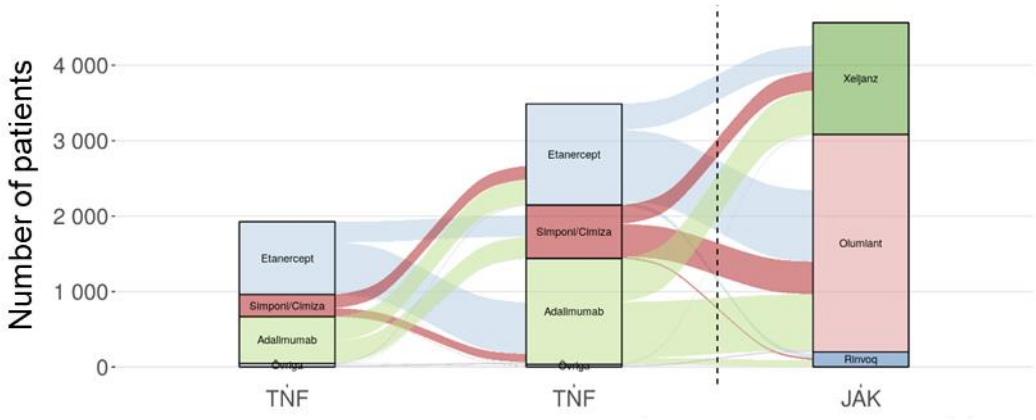

Figure 8.

Figure 7. Screen dump from the portal for following up CGRP inhibitors. The image shows the number of patients who account for the treatment over time in all of Sweden and in Uppsala-Örebro.

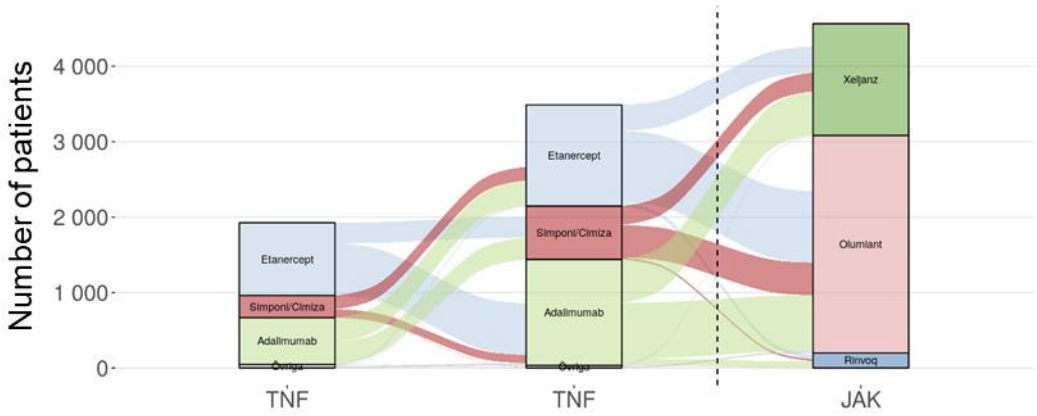

Figure 8. Screen dump from the portal for following up JAK inhibitors. The image shows whether, and if so, which TNF inhibitors were used prior to treatment with JAK inhibitors.

Other experiences: For JAK inhibitors and CGRP inhibitors, information about previous treatments is crucial. For JAK inhibitors it is of interest to know whether infliximab was previously used and for CGRP inhibitors, it is of interest to know whether Botox was previously used. Since both of these products are hospital pharmaceuticals, no information is available about them in the Pharmaceuticals Registry. To obtain a complete picture, this information must be available in a nationwide health data register.

4.8 Pilot study 8 – TLV's work to link the national registers of the Swedish National Board of Health and Welfare, Statistics Sweden and Swedish Social Insurance Agency

Purpose: To demonstrate that data from the Swedish National Board of Health and Welfare's health data register can be combined with other agency registers to perform analyses linked to pharmaceutical utilisation and efficacy.

Data sources: The Swedish National Board of Health and Welfare's health data register: Pharmaceuticals Registry. Statistics Sweden: monthly income, education level The Swedish Social Insurance Agency: sickness benefits.

Conducted by: TLV

Method: The Swedish National Board of Health and Welfare's health data register contains data about pharmaceutical treatments and various diagnoses, but frequently lacks data about health-related outcomes such as sickness absence and earned income. One possible health-related outcome for prophylactic migraine treatments could be the improvement of a patient's health, and the requirement for sickness absence could be reduced if the pharmaceutical treatment reduces the number of days the patient suffers from migraine. Information about reduced sickness absence could in some cases be measured as a reduction in sickness allowances, which are registered by the Social Insurance Agency. A reduction in sickness absence could also entail increased earned income as a consequence of fewer days of illness. If the capacity for work increases, it is also probable that employers will pay a higher salary since a smaller portion will consist of sickness allowances. Since employers have begun reporting salary payments on a monthly basis to Statistics Sweden in 2019, this information could be utilised to study the changed patterns in earned income in conjunction with the commencement of a new treatment.

This project combined information about commenced treatments with CGRP inhibitors (Aimovig, Ajovy or Emgality) with data from Statistics Sweden and the Social Insurance Agency. The Swedish National Board of Health and Welfare generated data on specific patients who had retrieved CGRP inhibitors from pharmacies at least twice, and who had received treatment for at least six months. The personal identity numbers of the patient population and the data on the pharmaceutical retrievals from pharmacies was then forwarded to the Social Insurance Agency and Statistics Sweden. The Social Insurance Agency then performed an analysis to calculate how much sickness allowance was paid per month for each individual, for the 12 months prior to and after the start of pharmaceutical treatments. The aggregated data, without any personal data, was then forwarded to TLV. In the same manner, SCB analysed data based on the monthly salary payments of employers to the individuals who received a CGRP

inhibitor. Data was generated for monthly payments 12 months prior to and after the start of treatment. The data was then forwarded to TLV as aggregated data. SCB also generated statistics on the education level of recipients of CGRP inhibitor treatments, which could be utilised to follow up equal care opportunities.

Results: With some minor investments, it is possible to collaboratively process data from different registers. Data for sick leave is shown in figure 9 and data for employers' monthly salary payments are shown in Figure 10. Data for those with the highest education levels upon receiving CGRP inhibitor treatments is shown in Figure 11. Although this pilot study demonstrates the potential of utilising multiple registers, the potential of drawing conclusions using data from other government agencies requires complementary analyses beyond the current scope of TLV, as the agency has no legal possibility of handling sensitive personal data.

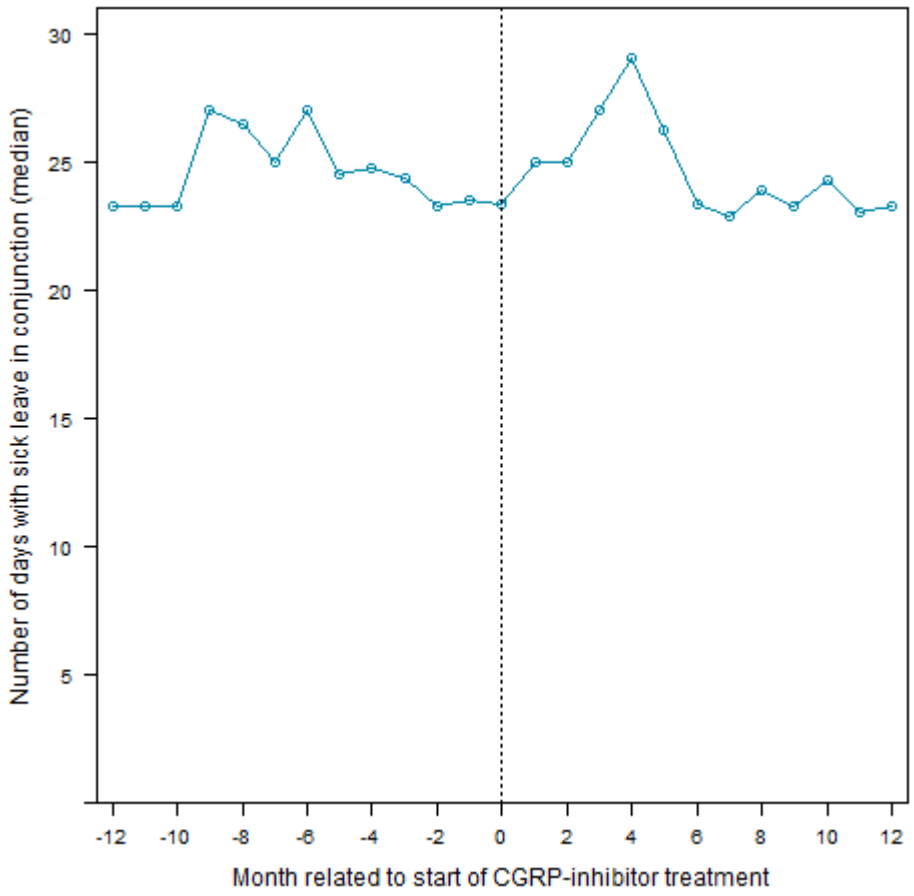

Figure 9. Days of sick leave in conjunction with CGRP-inhibitor treatments, based on data from the Swedish National Board of Health and Welfare and the Social Insurance Agency.

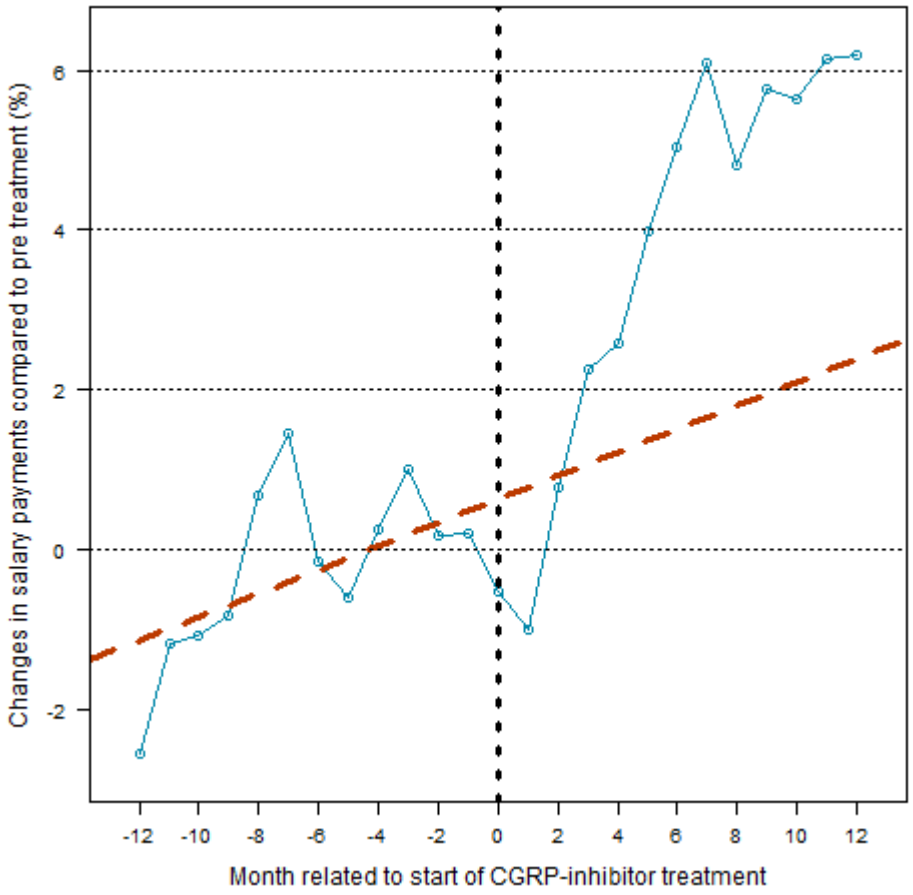

Figure 10. Changes in salary payments in conjunction with CGRP-inhibitor treatments, based on data from the Swedish National Board of Health and Welfare and SCB. The dotted red line indicates a linear regression of the 12 months preceding treatment and corresponds to the natural trend in salary payments.

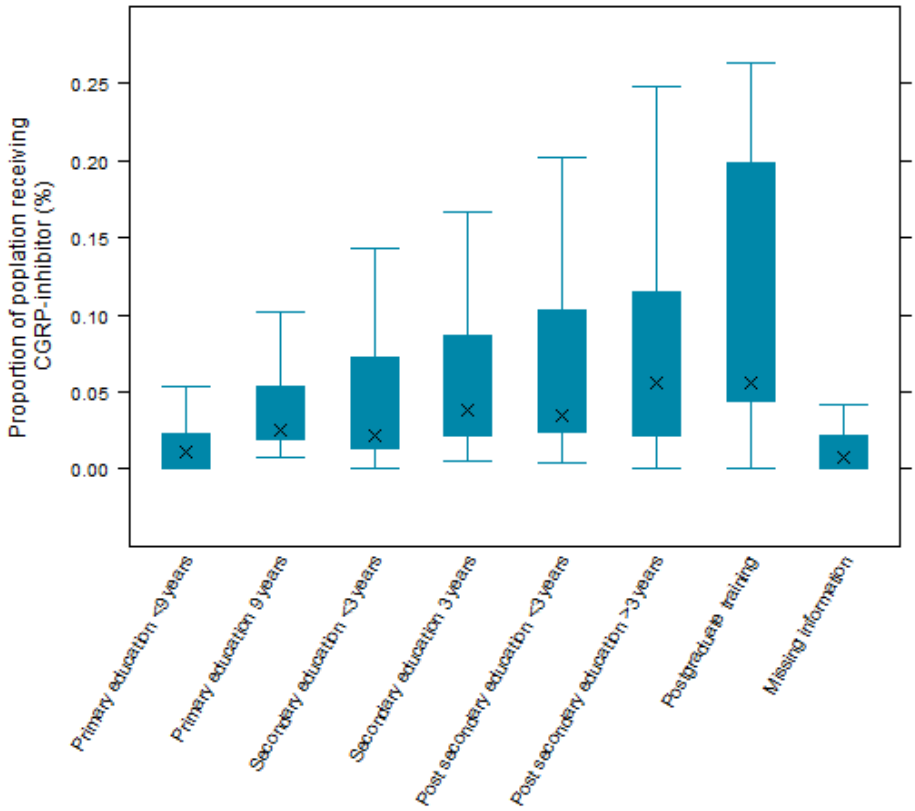

Figure 11. Highest education level for patients who commence with CGRP-inhibitor treatments, based on data from the Swedish National Board of Health and Welfare and SCB.

Other experiences: It is important to note that no data is available from the Social Insurance Agency about sickness absences of less than 14 days.

5 The result of TLV's own work and pilot studies

TLV is to follow up its subsidy decisions as part of its assignment to ensure that pharmaceutical utilisation is appropriate and cost-efficient over a pharmaceutical's entire lifecycle. Pharmaceuticals and medical devices that are categorised as disposable products can be encompassed by pharmaceutical benefits schemes, provided that the cost for their use is deemed to be reasonable in relation to their efficacy. A decision must be followed up in cases of uncertainty about utilisation and/or efficacy that have a major impact on health-economic assessments. Such follow-ups could result in TLV reviewing its subsidy, which in turn could lead to the subsidy being limited or expanded to encompass additional patients. Developing these follow-up opportunities could help patients to gain early access to innovative pharmaceuticals and medical devices, despite the uncertainties. Improving the conditions for follow-up entails that TLV has greater opportunities to do so and to review its decisions on benefits with the aim of ensuring that pharmaceutical utilisation is appropriate. Improved conditions for follow-up could also stimulate the usage of various payment models, where the cost for utilisation is partly contingent on the outcome of the treatment. The concept of leveraging payment models as a tool for handling uncertainties in a health-economic assessment are discussed in detail in TLV's government report, *How should we perform an evaluation and how should we pay?* However, these purposes are requisite on access to data for continuous follow-up.

In this capacity, a brief account is first given of the pilot studies' results on how TLV can gain access to data to conduct follow-ups and studies that allow for ensuring a reasonable cost for pharmaceuticals. The extent to which TLV can legally be given access to data for follow-ups at a national level are impacted by where the data is stored in the health care system. This is described in detail in the next section of this chapter. It is followed by an account of the conclusions reached on how the National Service Platform maintained by Inera could be utilised to provide TLV with access to data, and a review of the outlook in terms of availability of data within the field of medical technology. Finally, a general conclusion is presented on how data access could be developed.

5.1 Where the data is generated and stored has an impact on its accessibility

The pilot studies presented in the preceding chapter and TLV's continuous work to develop data sources demonstrates that there is data in the health care system that could potentially be utilised for follow-ups at a national level. However, the data's storage location in the health care system has an impact on how TLV can access the data, in terms of content and frequency of access.

To ensure a reasonable cost for a pharmaceutical's entire lifecycle and to handle uncertainties when introducing new pharmaceuticals, TLV needs data for follow-ups at a national level. Many other government agencies and actors require similar data for various purposes. However, TLV's work in this assignment and previous government assignments to identify existing data sets demonstrates that the systems are fragmented and in some cases, national registers are burdened with deficiencies in quality and drop-outs. Data about a patient's health is generated and registered differently in all sections of health care. The medical record system contains all the information that is critical to a patient's care. Information about and access to such data is regulated by the Patient Data Act. Actors who provide health care services are obligated to forward certain information to national health data registers. This does not require the consent of the patient. Once the data is available in a national register, all stakeholders can legally gain access to the data. This could occur within the scope of the statistics generation, whereby all personal data is reduced to anonymise it and no single individual is identifiable, or data delivery could fall within the framework of a research project following a successful customary ethics review.

Data that is available in medical record systems, but which is not transferred to a health data register, could also be utilised in various ways. In distinction to working with the national health data registers described above, actors who provide health care services are under no obligation to submit information to national quality registers. Furthermore, this involves the free will of the patient. Consequently, a patient who does not wish to have his/her data entered into a quality register can opt not to share it or to have it deleted. Similarly, a health care provider may voluntarily submit the data to the register. These are the factors that risk impacting the coverage rate of quality registers[20]. Some, but far from all quality registers, utilise automated direct transfers from medical record systems. If the data transfer were not automated, there would be a greater risk of data drop-outs and deficiencies in quality. When the data is ready for use from a quality register, it may be unclear who is entitled to request and access the data. This means that it cannot be guaranteed that the data will be available to, for example, TLV.

Data that is not forwarded to health data registers or quality registers could also be used for follow-ups or quality assurance. The region has the opportunity to utilise the data for its own follow-up operations and also to share it with other actors. However, the sharing of data is completely on a voluntary basis by the region. The only route to ensuring that data is available for other parties such as TLV within the scope of applicable legislation, is through the national health data registers.

5.2 Access to health care data via National Service Platform and other systems

Data from health care systems is required for national-level follow-ups. As described above, the National Service Platform is a technical platform aimed at simplifying and streamlining information exchanges between various health care IT

[20] https://www.vardanalys.se/rapporter/lapptacke-med-otillracklig-tackning/

systems. Since the National Service Platform has a digital infrastructure in place that enables data transfers between many different health care systems, TLV has conducted a pilot study within the scope of the government assignment, aimed at assessing how TLV could utilise the National Service Platform for follow-ups. The pilot study focuses on opportunities to gain access to aggregated data linked to the use of insulin pumps. Medical technology is a field for which there are currently no structured databases, which is also the case for prescription pharmaceuticals in the Pharmaceuticals Registry or diagnoses in the Patient Register maintained by the Swedish National Board of Health and Welfare. More about medical technology is presented in the next section. However, there is also a need for data from medical record systems for the general follow-up of pharmaceuticals, and for the national registers need to be developed.

In the course of a pilot study, TLV submitted an application to Inera AB via the consultancy firm Health Solutions, to extract health care data via the National Service Platform. The application has not resulted in any delivery of data, which means that TLV has not been able to assess whether the National Service Platform is utilisable for national-level follow-ups for TLV's purposes. From the agency's experience in working with the pilot study and dialogues held with Inera in conjunction with the application, TLV has concluded that under its current governance structure, the National Service Platform is not designed to provide government agencies such as TLV with data. The National Service Platform is administered by Inera, which in turn is owned by Sweden's regions, municipalities and the Swedish Association of Local Authorities and Regions (SKR). In brief, Inera prioritises assignments that are broadly supported by the regions. Projects that are not crucial to all the regions face tougher conditions in terms of extracting health care data from one or more regions via the National Service Platform. Since TLV did not receive the requested data delivery, it was unable to assess whether the National Service Platform could be utilised to meet the requirements for follow-up it has been tasked with.

It is worth noting that the National Service Platform itself does not contain any data in itself, but uses service agreements to transfer data between various systems. This entails that the health care data from medical records, which are online and transferable via the National Service Platform, are regulated by laws such as the Patient Data Act. This is no clear legal support for TLV to systematically and continuously obtain data from these sources. However, individual health care providers may, upon request, provide information (without any personal data) to TLV. It is highly probable that the legal prerequisites for TLV to obtain data are the same, regardless of whether the data is to be obtained directly from a health care provider or via the National Service Platform. The lack of legal support for TLV to systematically obtain data, entails that the delivery of data from the National Service Platform to TLV currently requires that care providers disclose data after reviewing each such request. Although the principle of public access applies to opportunities for government agencies to request information and data, the alternative is barely a long-term solution for TLV to obtain data systematically and more regularly.

In the pilot study conducted by Health Solution within the framework of this assignment, TLV has not been able to assess whether there is data linked to the use of insulin pumps or to test the function of data transfers via the National Service Platform. However, TLV has succeeded in identifying examples where Inera and the National Service Platform are more generally utilised for analyses at a national level.

5.2.1 Service under 1177 Vårdguiden – example of national follow-ups via Inera

One example of how aggregated data from each region can be utilised is the Service, 'Hälsoläge' (state of health) which was developed by the Public Health Agency. The 1177 Vårdguiden telephone service is jointly financed by the country's regions, and inhabitants can use the service for telephone consultation on health care matters. Each region is responsible for the service within its own region. 'Hälsoläge' is a tool created by the Public Health Agency to monitor and assess outbreaks or health risks based on anonymised data derived from telephone consultations. It may provide early signals for Sweden's state of health, such as indicating when a seasonal flu has begun. The data obtained by 'Hälsoläge' is acquired via separate infrastructure provided by Inera and thus bypasses the National Service Platform.

However, obtaining the data in a structured manner has required considerable work. For each region to be able to deliver anonymised data requires that agreements be signed between each region and the Public Health Agency. The handling of personal data has been regulated through personal data-processing agreements (hereinafter referred to as a 'PuB Agreement') between each region and Inera, and are requisite to Inera's handling of personal and aggregated data, which is then forwarded to the Public Health Agency as anonymised data. In this case, 42 agreements were required for the anonymised nationwide data to be rendered in a usable format for generating knowledge about the state of health in Sweden, and construction took four years. Although lessons can be learned from these efforts, the risk is that it will not be practically feasible to scale up this solution in general. Further work is required to assess the opportunities.

5.2.2 *Vården i siffror* (Health Care Statistics) – examples of national-level usage

Another example of the use of Inera's infrastructure is SKR's web application, *Vården i siffror* (Health Care Statistics). *Vården i siffror* is managed and developed by SKR on assignment by the regions collaboratively, and is the regions' shared gathering place for the continuous publishing of data about the quality and efficiency of health care. *Vården i siffror* provides indicators and measurements of waiting times, various specific treatment initiatives and the experiences of patients with regard to care. It also contains information about the costs, care utilisation and resource usage within health care. The information originates from numerous sources, such as quality registers and databases that are acquired via the National Service Platform, and is used to generate a status report for all health care at a regional and nationwide level. The information is retrieved from source systems and databases such as the Medical Care Event Database and Health Care Waiting Times, maintained by SKR, and *1177 Vårdguiden* maintained by Inera.

Vården i siffror demonstrates that the National Service Platform can be utilised for transferring data for global operational follow-ups.

5.2.3 Quality registers, Individual Patient Summaries and the National Service Platform

In the field of cancer treatments, the Confederation of Regional Cancer Centres (hereinafter referred to as the 'RCC') works collaboratively with regions to create more equal high-quality cancer treatment opportunities, which includes improving the opportunities for follow-up, and developing a knowledge base for cancer treatments. The assignment is based on the government's long-term focus on national-level initiatives with cancer treatments.
Within the scope of the assignment, development work is being conducted to improve the follow-up opportunities of various treatments, including cancer pharmaceuticals, from national and regional levels to specific local clinics. The introduction of Individual Patient Summaries (hereinafter referred to as 'IPÖ') has enhanced the opportunities for more patient-centric care within clinical practice, and provided vigorous support for the planning and follow-up of health care, particularly with regard to the introduction of new treatments. Data from IPÖ can be automatically transferred (with the possibility of patients to opt out) to the national quality register for diagnoses, where data can be extracted for national-level follow-ups.

To avoid burdening health care systems unnecessarily, RCC is working to enable automatic data transfers from various health care information systems to the IPÖ system and quality registers. Much of the data in patient medical records is not structured in accordance with a national standard, which means that the data cannot be conveniently retrieved from the systems. Structured data can potentially be transferred automatically via the National Service Platform. The National Service Platform has a nationwide service agreement for laboratory tests and the agreement allows for data to be transferred to health care providers who are signatories to this agreement.

CytoBase and Cytodos are the two primary IT systems used by care providers to register information about cancer treatment pharmaceuticals administered to hospitalised patients. However, the National Service Platform has no nationwide service agreement to support information exchanges with CytoBase or Cytodos. Data transfers to IPÖ and national quality registers will instead utilise service agreements linked to CytoBase and Cytodos.

5.2.4 Summary of conclusions pertaining to the use of the National Service Platform for national-level follow-ups

In summary, TLV has determined that it is not a matter of course how a national actor such as TLV can utilise the National Service Platform for its purposes. This is demonstrated by the legal overview presented above and work conducted under TLV's pilot implemented through the consultancy firm, Health Solutions. Since the pilot has not resulted in any delivery of data, TLV has not been able to assess whether the National Service Platform is utilisable for national-level follow-ups within TLV's purposes. TLV's needs in terms of conducting national-level follow-

ups are essentially needs that are shared by other government agencies and actors. Other agencies would thus be able to implement their assignments better, if they could gain access to data in the same manner as illustrated by TLV above. However, there are examples of Inera and the National Service Platform being utilised at a national level to some extent.

As described above, RCC is currently collaborating on efforts to automate the transfer of laboratory tests from health care providers to the national cancer quality register via the National Service Platform. If the National Service Platform were to be used more systematically to automate data entries to various national health-related registers, opportunities for national-level follow-ups would be improved. However, this requires that care providers link up their systems to relevant modules of the National Service Platform.

In terms of national follow-ups at the individual level based on data from various health care providers – data which is not available through national registers – TLV's experience is that with its current structure, the National Service Platform is not designed to facilitate access to health care data by government agencies such as TLV. However, to more concretely assess existing opportunities with the platform based on TLV's follow-up requirements, further work is required on several levels. It would be ideal to look closer at the legal aspects concerning the delivery of health care data from the regions to TLV, as well as clarify the opportunities for agencies to receive such data.

5.3 Data for the national-level follow-up of medical devices

As described in the pilot study section of this report, the market for medical devices is different from that of pharmaceuticals and is not processed in the same manner by health care providers. However, the need for national-level follow-ups matches the structure of pharmaceuticals, where the questions 'who is receiving the product?' and 'what is the efficacy?' are relevant. There is currently no uniform system for following up individual medical devices at a national level, except for the disposable products prescribed through pharmaceutical benefit schemes. These disposable products can be partly followed up using the Pharmaceuticals Registry, but since health care providers can also bypass the pharmaceutical benefits route and procure corresponding products directly, the picture tends to be incomplete.

When the new EU regulatory framework for medical devices comes into force, the EU database, EUDAMED, will be established, in which all medical devices will be registered in conjunction with their market introduction. The new EU regulatory framework also requires that all medical devices be designated a unique device identifier, UDI, which potentially creates the basis of a uniform structure for the follow-up of medical devices. However, one critical prerequisite for achieving the potential benefits is that UDIs must be stored and maintained in a structured manner, so that the information is convenient to extract and analyse at a national level.

The use of medical devices can change how health care services are provided, for example, by moving care services outside of specialised health care. This, combined with the fact that clinical trials to demonstrate efficacy are not always required prior to the market launch of a medical device, means that there is a considerable need to be able to follow up the utilisation of medical devices. Further knowledge about such utilisation would create a more knowledge-guided health care system, and is requisite to ensuring equal care opportunities.

5.3.1 Differences and similarities between following up pharmaceuticals and medical technology

One of the clearest differences between pharmaceuticals and medical devices is how the various markets work. The differences in the regulatory frameworks of pharmaceuticals and medical technology has consequences, such as the absence of any clinical trials for medical devices upon market launch, which in turn lead to insufficient knowledge about their clinical efficacy. Another difference is that a pharmaceutical substance is constant over time, even when new forms of preparation and new indications are added. On the other hand, medical devices are frequently subject to continuous development, with new-generation releases of essentially the same product.

One of the consequences of these differences in regulatory processes and the markets, is that for pharmaceuticals, while there are shared systems and categories from a national perspective, the same cannot be said of medical technology. For example, pharmaceuticals have ATC codes, goods numbers and NPL pack IDs. There are currently no equivalent national systems for medical devices. For disposable products covered by pharmaceutical benefits schemes, TLV assigns each product a goods number. However, there is no corresponding system for other medical devices. If, moving forward, UDIs should be registered within health care, it could result in a more uniform method for handling medical devices, which in turn could enable access to structured data at a national level.

The need to create conditions for systematically collecting data from medical devices is similar to the need for acquiring data from primary care. In both cases, it would make a considerable difference if the data for medical devices and primary care could be stored in national health data registers, such as the Patient Register.

A major difference between pharmaceuticals and medical devices is that some medical devices can autonomously generate data. While a medical device that continuously measures the values or symptoms of a patient and makes the data visible through, for example, an app, could help the patient to manage his/her health, it could also potentially be used by health care providers and researchers. This data is usually data that would not otherwise have been available. There are varying legal conditions for utilising data generated by various medical devices, and there is the issue of the liabilities health care providers may assume, if they were to gain access to data from medical devices. Data that is generated by medical devices creates numerous opportunities, but to be able to utilise these opportunities in

practice, there are many issues that must first be resolved, particularly the ownership of data generated by a medical device.

However, the overarching challenge for medical devices is to be able to monitor the specific individual who received such a device. The uniform and systematic coding of medical devices and their storage in national registers must be reviewed, to allow for the next step: following up and assessing utilisation and efficacy.

5.4 Great possibilities for data exist today – is the glass half full or half empty?

TLV's previous experience and work with this government assignment demonstrates that considerable amounts of data are already available today from various data sources. On the other hand, TLV has conditions for accessing and utilising such data, depending on where in the system it is stored. TLV is demonstrating through various pilot studies that the opportunities already exist. However, there are obvious deficiencies in TLV's accessibility to data and a lack of data requisite to national-level analyses. A crucial piece of information that is missing pertains to pharmaceuticals that are requisitioned directly for hospitalised patients. Another critical piece of information that is missing pertains to the care that patients receive through primary care. Data from laboratory results could also be important for following up and assessing the efficacy of numerous pharmaceuticals, but such data is currently missing from national registers.

Although the data is missing at a national level, it frequently exists, fragmented throughout various systems maintained by Sweden's regions and various health care providers. To systematically assess and ensure that the pharmaceuticals that are utilised within health care are contributing toward our best possible health for the money, the fragmented data that is stored across various systems must be linked together and made available to the relevant actors in a cost-efficient manner, without unnecessary delays.

The pilot study that TLV conducted jointly with Region Värmland demonstrates that the region, through its data stores, can identify the individuals who received prescription PCSK9 inhibitors for the treatment of elevated blood lipids, and identify how their laboratory values for LDL change over time. The region can also remove sensitive personal data through data processing and deliver anonymised data to TLV. If other regions could deliver data to TLV in the same manner as Region Värmland, TLV could better follow up its decisions and ensure that the cost of utilisation is reasonable, given the efficacy in clinical practice. Such information needs to be generally available via national registers.

As with the pilot study with Region Värmland, the Center for Health Data is also examining laboratory values. In this pilot study, changes of the M component are tracked over time in individuals treated with the anti-cancer pharmaceutical Darzalex in hospitals in Region Stockholm. The pharmaceutical-treatment data and laboratory data was derived from patient medical records. In the long term, this

type of data could be utilised for many different purposes. It could potentially be used to assess the efficacy of pharmaceutical treatments. Such information could provide the basis for various decisions by government agencies and regions. It could also provide documentation for utilising payment models based on clinical responses. Information about treatment efficacy is of considerable value to the industry. However, such information is not available for systematic access at a national level.

The pilot study with Lund University is aimed at assessing how the introduction of new oral anticoagulants (NOACs) impact health and whether there is data to support such analyses. In addition to data from national registers such as the Patient Register, the study also has access to primary-care data from three major regions. The study shows that primary-care data may be needed to assess the efficacy of NOACs – a group of pharmaceuticals frequently prescribed within primary care. Information about primary care is needed in national registers, in order to gain a cumulative summary of pharmaceutical utilisation and potential efficacy.

TLV's own work to link the Swedish National Board of Health and Welfare's data on the retrievals of CGRP-inhibiting pharmaceuticals, with data from Statistics Sweden and the Social Insurance Agency, demonstrates the potential of combining various data sources. Such analyses not only allow for assessing pharmaceutical utilisation, but potential efficacy at a society level, by using data from fields other than health care. TLV has linked information from the data sources of the Social Insurance Agency and Statistics Sweden, with data from the Pharmaceuticals Registry and Patient Register maintained by the Swedish National Board of Health and Welfare. The information pertains to sickness absences from the Social Insurance Agency's database, MiDAS, and data about employers' monthly salary payments from Statistics Sweden. Information about the education level of patients was also available from Statistics Sweden. TLV has received aggregated results that were anonymised, which impacts its ability to assess and analyse the data at this stage. Further work is needed with this data. However, TLV's work indicates that data from national registers that was acquired for primary purposes other than health care, may be of significance to the assessment of pharmaceutical efficacy. This is because pharmaceutical utilisation may impact health, which may in turn impact an individual's capacity for work and patterns of sick leave.

Efforts to develop visualisation tools prove that knowledge about how pharmaceuticals are being utilised can be conveniently rendered through the application of user-friendly tools. The insights that such data could provide must be made available for TLV's purposes, as well as for other actors. These tools could simplify and facilitate more systematic follow up by TLV on its subsidy decisions throughout a pharmaceutical's entire lifecycle. The tools could also be utilised by the regions to monitor operations and thereby the governance of prescription pharmaceuticals in order to ensure that their utilisation involves a reasonable cost over time.

In general, it is necessary for data about a patient's utilisation of hospital pharmaceuticals to be available in order to generate relevant knowledge about pharmaceutical utilisation. For example, in cases where a pharmaceutical covered by a benefits scheme ('benefit pharmaceutical') is subject to a limited subsidy until after the use of a hospital pharmaceutical (which is usually the case, particularly for anti-cancer pharmaceuticals), TLV needs to obtain a comprehensive summary of a patient's pharmaceutical utilisation to follow up compliance with subsidy limits. Information about hospital pharmaceuticals is also needed for assessing a benefit pharmaceutical's effects on health in clinical practice, since the results can be misleading if the study cannot control for any utilisation of hospital pharmaceuticals. If the regions are to develop payment models that take pharmaceutical utilisation or efficacy into consideration, data about hospital pharmaceuticals will also be required.

All of these examples demonstrate that much can be accomplished using currently available data. The glass is half full in terms of data for follow-ups. Filling up the cup further will require addition data. The information that is potentially available and which would yield the greatest immediate benefits are:

- expanded information about a patient's complete pharmaceutical treatments – obtained by adding information about *hospital pharmaceuticals* to the Patient Register
- additional information about *primary care utilisation*, and
- data extracts from *laboratory results*.

With this information, the glass would be fuller.

6 Conclusions and requirements for further work

The assignment was to develop the follow-up of pharmaceuticals and medical devices by utilising data sources such as the National Service Platform.

The overarching purpose of the assignment and other TLV assignments was to identify and develop data sources, in order to ensure reasonable costs for pharmaceuticals throughout their entire lifecycle by means of developed follow-up methods. This includes managing the challenges of the increasingly early introductions of pharmaceuticals, and ever-higher costs alongside a high degree of uncertainty. Improved follow-up opportunities can strengthen TLV's possibilities of subsidising potentially efficacious pharmaceuticals and thereby promote early access to pharmaceuticals for patients. To further develop follow-up tools, TLV needs to systematically access the relevant and up-to-date health data and other data that it requires.

6.1 TLV was unable to assess the National Service Platform

TLV has established that it could not test whether data can be extracted from medical record systems by means of the National Service Platform. However, TLV has also determined that no data is stored on the platform itself, but that it is linked to medical record systems. This means that data access is governed by the same legislations as those for other medical records. Consequently, there is no legal obligation for the regions to provide TLV with such data in an anonymised form. TLV has established that the possibility of gaining access to data from medical record systems is dependent on the regions voluntarily providing such data, which in turn is dependent on the regions' willingness and ability to prioritise resources toward TLV's follow-up operations.

TLV is of the opinion that any future assessments of how to make data accessible for national-level follow-ups through the National Service Platform is contingent on collaboration with other actors. These could be, for example, Regional Cancer Centres and quality registers with legal support for the prioritised management of access to data, since they are prioritised actors under the governance of Inera. Within the scope of the government assignment with a focus on cancer, for which TLV will submit a report to the Ministry in 2022, TLV intends to continue to cooperate with RCC and the Swedish National Board of Health and Welfare, and thereby collaboratively improve opportunities for follow-up.

6.2 Follow-ups of medical technology

Medical devices are integral to health care and span across a broad product range that includes everything from simple adhesive dressings to advanced robots that assist with surgery. There is considerable activity in the medical-device market and moving forward, usage will probably increase and medical devices that are used in combination with pharmaceuticals may become increasingly prominent. There is currently no uniform method of registering which medical device a patient has received. Medical devices can be followed up using the same framework that TLV has set up for pharmaceuticals, where the two fundamental questions are: 'How is the product used?' and 'What effect on health was achieved?' To answer the latter, we have to first know how the product is used. The basic question is then: who has received treatment with which product. That question cannot be answered today, with the nationwide data available.

As a first step, health care must, in a structured and systematic manner, register which product is being used on a patient. The new EU regulatory framework for the field of medical technology prescribes that health care providers store and maintain UDIs for class III implants that they have delivered or received. EU member states are also being encouraged to require that health care institutions store and maintain the UDIs of medical devices other than class III implants which have been delivered to them. One way of achieving more structured and systematic registration would thus be to start using UDI numbers and registering them in medical record systems. To make the information accessible at a national level, one possible solution is to report a task code in the Patient Register, in the same manner as hospital pharmaceuticals are reported. What is problematic with medical devices is that many of the disposable products are prescribed within primary care. Consequently, TLV is positive about the Swedish National Board of Health and Welfare's proposal to expand the Patient Register to include primary care[21].

TLV deems that further work is required to make information about medical devices available for follow-up operations. Although the data exists today, it is neither structured nor accessible for use. Access to data must be improved to be able to meet the trend that is already unfolding, where medical products are being used together with pharmaceuticals to an ever-greater extent. Using medical devices will in some cases allow for continuous monitoring of a patient's health outcome in clinical practice. Sustained efforts could occur within the framework of the National Service Platform and/or the development of the Patient Register maintained by the Swedish National Board of Health and Welfare.

[21] https://www.socialstyrelsen.se/om-socialstyrelsen/pressrum/press/socialstyrelsen-foreslar-att-patientregistret-utvidgas-for-battre-uppfoljning-av-varden/

6.3 There are considerable opportunities within the Swedish system, if some critical problems could be resolved

As TLV has shown through its pilot studies, there is a considerable amount of data available in numerous systems. Laboratory diagnostics can be extracted from medical record systems and the information rendered in an aggregated form. It is also feasible to collaboratively process data from various national registers without disclosing sensitive personal data. It is also feasible to use data to create interactive information – without disclosing sensitive personal data.

However, it is also evident that in many cases, there is no access to comprehensive national-level data. What is important, as a first but insufficient step, is to make individual data pertaining to hospital pharmaceuticals accessible. Knowing which patient has received which pharmaceutical treatment is fundamental to the follow-up of pharmaceuticals.

Knowledge about the utilisation of hospital pharmaceuticals also provides the basis for various payment models or agreements signed by the regions regarding hospital pharmaceuticals, whereby pharmaceutical companies receive payment based on health outcomes, and not solely on sales. If information about the specific patient and specific treatment is unavailable, payments cannot be linked to predefined health outcomes. TLV's report on ATMPs highlighted the need for such knowledge**.** Solving this problem is the key to developing payment models for new costly therapies. It is also critical to managing cases of treatments with combination pharmaceuticals.

In TLV's opinion, one of the key measures that could be put in place very quickly and which would benefit many actors, is to increase the coverage rate of reporting of hospital pharmaceuticals in the Patient Register. In addition, the Patient Register needs to be expanded to include information about pharmaceuticals administered to patients by medical staff who are not doctors, primarily nurses, within specialised outpatient care. This was presented in TLV's RWD report of October 2020. In conjunction with its work on the October report, TLV contacted several regions and established that other regions with relatively limited funds, as is the case with Region Värmland, could also render the equivalent data for their region. In the view of TLV, it is *necessary* for the data to be available from the national health data register, and it must be developed relatively quickly, since we are already facing challenges with processing the data.

TLV's work also indicates that the lack of information about *primary care* in national health data registers makes it impossible to systematically assess and follow-up pharmaceuticals and medical devices. This is an area that the Swedish National Board of Health and Welfare is working on, to enable the acquisition of data at a national level**.** A national health data register that contains data about primary care is of the greatest importance, not only to TLV. The pursuit of knowledge-based management within health care requires a holistic view of the care

that is being offered. When the gaps in knowledge about which pharmaceuticals are being used within inpatient care and what is happening within primary care are filled, it will be possible to gain a more complete view of how health care is being offered in Sweden. The prerequisites will then be in place for assessing efficacy within clinical practice.

Access to *Laboratory data* is a key aspect of following up the utilisation and efficacy of pharmaceuticals. These key metrics can serve as a measurement of the patients being treated, as well as a measurement for treatment outcomes. There are currently no methods for gaining access to nationwide laboratory data that can be linked the utilisation of pharmaceuticals. In TLV's view it is highly important for its own operations and for many other actors, to develop national registers to include laboratory results or to develop other means of extracting data from medical records at a national level.

The work has proceeded from determining what forms of data TLV can process at an anonymised level. To fully assess who is receiving a product and the degree of treatment efficacy requires considerable amounts of data about each individual, which makes anonymised data inadequate. One conclusion is that TLV needs to have the legal prerequisites in place for handling detailed and thereby, sensitive, personal data, to further develop its work pursuant to the assignment: to ensure that pharmaceuticals have reasonable costs and prices across their entire lifecycle, while ensuring early access to new pharmaceuticals. This requirement also encompasses the developed data access that TLV deems to be necessary. TLV currently uses other actors to perform analyses that require sensitive personal data, in order to gain access to the aggregated results. TLV's work with pilot studies indicates that much can already be accomplished at present, based on the prevailing conditions. In pace with the development of data sources pursuant to the proposals submitted by TLV, opportunities are increasing and, in turn, the need for the TLV to handle sensitive personal data. This should in turn improve TLV's opportunities to feed the data to various actors, such as the regions. Efforts to review TLV's legal potential to handle sensitive personal data needs to proceed in parallel with future development work – under the present conditions.

Health data is utilised by numerous government agencies and it is urgent to increase interagency collaboration on issues of health data.

TLV has thus taken the initiative to provide government agencies within the framework of consultation on governance through knowledge, strengthen its cooperation regarding health data. A shared arena must be developed for continuous cooperation on health data issues, aimed at strengthening interagency cooperation and, in the long-term, with regions and private companies, in accordance with the Life Sciences Strategy. The goal is to identify areas where society's actors must collaborate more intensively on the need to develop access to health data.

In the absence of access to medical records from the National Service Platform, data from national health data registers are the key to the continued development of follow-up in accordance with TLV's objectives and purpose. TLV has an ongoing assignment to develop alternative data sources, as a continuation of the assignment that was debriefed in October 2020. The report for the new assignment is to be submitted in October 2022.

Appendices

Separate reports for the pilot studies

https://www.tlv.se/download/18.6dab39ff17917945716b0037/1620736284867/pilotstudie1_svenska_halsodata.pdf

https://www.tlv.se/download/18.6dab39ff17917945716b0038/1620736284914/pilotstudie2_medicintekniska_produkter.pdf

https://www.tlv.se/download/18.6dab39ff17917945716b0039/1620736284938/Pilotstudie3_effects_of_clinical_practice.pdf

https://www.tlv.se/download/18.6dab39ff17917945716b9797/1620798302856/Pilotstudie5_darzalex_m-komponent.pdf

https://www.tlv.se/download/18.6dab39ff17917945716b003a/1620736284973/Pilotstudie6_nationella_tjansteplattformen.pdf

https://www.tlv.se/download/18.6dab39ff17917945716b003b/1620736285008/Pilotstudie6_appendix_arendebeskrivning.pdf