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ABSTRACT

Real-world data (RWD) are an increasingly important input into the pharmaceutical R&D process as shown by countries like the USA or Finland. As the availability of and access to Swiss RWD is rather limited, the question arises whether this creates a burden for pharmaceutical R&D in Switzerland. We build on the economics of data and ideas as well as the home-market effect to analyze the importance of local RWD in the three stages of pharmaceutical R&D (pre-clinical, clinical, and post-approval research) as well as in the field of personalized medicine. We find qualitative support for a home-market effect and conclude that there is an urgent need to improve the current RWD situation in Switzerland, from the perspective of both Swiss patients and pharmaceutical R&D in Switzerland.

Keywords: Patient Data, Real-World Data, Pharmaceutical R&D, Data and Innovation, Home-Market Effects, International Trade, Location of R&D

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1 Introduction

Over the last 10 years, there has been a lively discussion in Switzerland about the state and perspective of digitalization of the Swiss health care sector. A central theme in this discussion is the limited availability of data on patients' health for doctors, hospitals, universities, pharmaceutical companies and patients themselves. It is not a lack of data per se which is the major problem; also in Switzerland, doctors and hospitals collect and record data of their patients if they become ill and are treated. However, these data exist in a very fragmented (sometimes even hand-written) form and are neither standardized, nor are they digitally available and easily transferable. In addition, data on individuals' state of health *before* they become patients and *after* they have been cured are rarely available. One can easily imagine that these data are extremely important to the health sector in its attempt to determine the causes of diseases, to optimize treatments and to develop improved cure and better medicine; even the data of a control group of people who may so far not have got or who may never get a certain disease are decisive for reliable (statistical) analyses.

It is thus hardly surprising that there seems to be broad agreement across all agents in the Swiss political spectrum – maybe except those who are very worried about data misuse and security -- that health data should, in principle, be collected and made accessible in digital, standardized and anonymized form across public and private organizations and institutions. Through better access to such standardized and harmonized data large improvements in the efficiency, effectiveness and quality of the Swiss healthcare system are to be expected. For instance, if practitioners have better access to the disease history of patients, early prevention of certain diseases is more likely. In addition to improvements in the delivery of healthcare to patients, better data access by the pharmaceutical research and development (R&D) units is likely to create better medication and new treatments. Therefore, many agents including the representatives of hospitals and the pharmaceutical industry have been urging the Swiss government for many years to do more in this respect.

In this paper, we focus on an aspect in this debate which we believe has been rather neglected so far. We study to which extent Swiss health data are important for R&D of the Swiss pharmaceutical industry, in general, and whether limited access to Swiss data may negatively affect the location of pharmaceutical R&D *in Switzerland*, in particular. Our analysis has been motivated by recent statements from industry representatives who fear a gradual location shift of

Swiss R&D to other countries if data access does not improve in the near future (see Tschan, 2022; Fulterer, 2022; Schwan, 2022). The following quote may illustrate this conviction:

> *"Switzerland is lagging behind especially in healthcare because we do not have access to big data in Switzerland. As a result, we cannot always do the research we want to do (…). [And] a number of projects are going to the U.S., which in the past would have landed in Switzerland."* (Schwan, 2021)

If this is true, the slow reaction of the various stakeholders in Switzerland to the widely recognized data problem in the Swiss health sector may not only sacrifice the wellbeing of (at least some) Swiss patients, but also endanger Switzerland's position as an attractive location for pharmaceutical research. As the Swiss pharmaceutical industry is currently very important for the standard of living in Switzerland, this would have a major negative impact on Swiss society. Note that the Swiss pharmaceutical industry contributed 5.7% of Switzerland's GDP in 2021 (FSO, 2023) and represents the strongest exporting industry of the country with 39.3% of total exports in 2022 (FOCBS, 2023). The industry is also a strong investor into R&D projects in Switzerland. Basel is the largest pharmaceutical cluster in Switzerland and one of the world's leading life sciences locations, with Roche and Novartis being two of the ten largest pharmaceutical companies in the world (Interpharma, 2022b).[1] Swiss pharmaceutical companies invested more than CHF 8 billion into R&D of new medicine and treatments in 2021, a number only surpassed in Europe by Germany (EFPIA, 2023).

Given this overwhelming current position of Switzerland in the worldwide pharmaceutical industry, one may argue that a reduction of production and R&D activities in Switzerland is unlikely. Why should it become weak, if it is currently so strong? Path-dependencies, external economies of scale and cluster-effects through linkages to other industries and access to highly qualified labour (i.e., labour market pooling) typically prevent such a change. However, it is important to note that the Swiss pharmaceutical industry is already heavily internationalized entertaining many, and relatively large, sites of foreign production and R&D. More than 50% of the R&D efforts of Swiss pharmaceutical companies are carried out outside the home country. For instance, Roche has R&D centers across the world, e.g., from San Francisco and New York (U.S.) to Welwyn (UK), and from Basel and Zurich (Switzerland), to Penzberg (Germany) and Shanghai (China). Also Novartis has over half of its R&D workforce employed outside Switzerland (Gassmann et al., 2018). Hence, the two big Swiss pharmaceutical players have

[1] Novartis and Roche are among the top 10 of the leading R&D investing companies globally. According to Statista (2021), Roche and Novartis are expected to invest $14 and $10 billion into R&D by 2026. With more than 65%, a large share of pharmaceutical research in Switzerland is financed by the pharmaceutical industry (Interpharma, 2022a).

strongly internationalized their R&D efforts which creates the floor for gradual shifts of R&D projects.

From a Swiss perspective, the question of what contributes to a successful R&D location is therefore of high relevance, since the strong R&D location of Switzerland (and Basel in particular) is in competition with others. As data availability is likely to become more important in future, access to data could play a bigger role in a company's decision where to locate single R&D projects. The increased importance of data also derives from our sharply rising capabilities to analyze big data with the help of algorithms (artificial intelligence) and quickly rising computing capacities (quantum computers). In this respect, the pharmaceutical industry bears some similarity to other industries. Our analysis may thus also provide insights for the development of other Swiss industries that seem to lag in digitalization and the use of big data (Rutzer and Weder, 2021).

Note, however, that the relationship between local data access and local R&D is not obvious. A counter-argument would be that the multinational companies in Switzerland are truly global players and have access to other countries' data that are close substitutes and even more important: why should Swiss data be important, given that the amount of data will always be relatively small and that the Swiss market for the large Swiss pharmaceutical companies is miniscule? Note that, according to Fabrizio & Thomas (2012), the Swiss home market only accounts for 2% of the two leading Swiss pharmaceutical companies' revenue.

This is how we proceed in the following and what we find, summarized in a nutshell. In Section 2 and as a background, we provide an overview of the current situation regarding data access in Switzerland and in other selected countries. We show that data access in Switzerland is generally weak due to fragmented and non-standardized data collection, a complex legal landscape concerning the secondary use of health data, and diverging views on the "correct" approach to data anonymization. Public and institutional trust towards sharing data, particularly with industry, seems limited, which currently forces companies to request data in a bilateral fashion or access data in other countries. At the same time, however, data access seems clearly better only in a few countries, mainly the UK, Finland and the United States, with regions such as the European Union making progress.

In Section 3, we ask economic theory for guidance regarding the relationship between data and the R&D process, in general, and the geographic proximity between data availability and R&D

location, in particular. It turns out that both the "economics of ideas", originating from the theory of endogenous innovation, and the "home-market effect" from international trade theory provide a good foundation for developing a simple approach to understanding how domestic (or local) data and foreign data affect the innovation process; local data may contain additional, possibly un-coded information which is not easily transferable internationally and may thus serve as an important input to the local R&D process.

Guided by this concept, the analysis in Section 4 carefully investigates how data enter each of the three stages (pre-clinical, clinical, and post-approval stage) of the pharmaceutical R&D process. In each stage we ask the question: What data are used in this stage and does it matter whether data are local or foreign for the local R&D process? We find that Swiss data are likely to be important in the pre-clinical stage of research as it may contain information on unmet needs for certain disease groups that can be captured by local R&D. The highest potential of Swiss data may, however, arise in the post-approval stage of research: they quickly inform R&D teams in Switzerland on how a treatment performs locally and how local demand reacts to it. This type of information is difficult to obtain from abroad at the same quality level and within the same time frame after the launch of a product or treatment. From this insight, we infer that the importance of Swiss data is likely to increase with the expansion of personalized medicine.

In Section 5, we discuss the path forward. We conclude that the Swiss central government in Bern should take on its leading role as a provider of a public good and push ahead much more forcefully. The target should be to create a broad pool of high-quality health data of Swiss residents (which also includes healthy people) that guarantees individual anonymity and that can be accessed by patients, doctors, hospitals, universities and research units of pharmaceutical companies. At the same time, these agents should (continue to) closely work together to create and exchange information which may not immediately be entered in the standardized data pool. We briefly provide an idea how this goal can be reached.

2 Current Access to Real-World Data in Switzerland

Following the Food and Drug Administration (FDA) and Swissmedic, we define real-world data (synonymous to "patient data" or "health data" and henceforth RWD) as information on patients' health collected from multiple sources outside of clinical research. Sources of RWD

include routinely collected health data generated during the treatment of patients in hospitals or other medical institutions and stored in electronic health records (EHRs), claims and billing data of health insurances, product and disease registries, or data collected through sensors or personal devices and health applications by patients themselves (Sherman et al., 2016; Klimek et al., 2022).[2] Key information of interest from RWD includes patient characteristics, disease status, medications used, laboratory tests, and other diagnostic tests (Zhu et al., 2023). In a broader sense, one can imagine that RWD should also include data of patients long before they became ill and after a successful or unsuccessful treatment as control groups; in addition, for some purposes it would also be helpful if they included data of people that are generally considered to be healthy.

To gather sufficient information of high quality on a patient or a patient-subgroup, multiple sources of RWD may be needed and linked together. For instance, RWD can increasingly be linked with more novel types of data such as genomic data from biobanks as well as providing data from other patients than the ones volunteering to share their data with biobanks or in clinical trials (Kalra, 2019). Evidence derived from analyzing RWD is considered real-world evidence (RWE). Further, we define *secondary* use of health data as the use of data which has been collected for some primary use (e.g., treatment) and is later re-used for research purposes (Widmer et al., 2022).

Data access and re-use in Switzerland can be discussed along (i) the fragmented nature of data collection and storage and the slow progress in the digitalization of the healthcare system, (ii) regional and national initiatives that attempt to improve the data infrastructure, (iii) structural and institutional barriers of data access for pharmaceutical companies, (iv) legal uncertainty and complexity regarding the re-use and anonymization of RWD, and (v) current strategies of Swiss pharmaceutical companies to access RWD for R&D in both Switzerland and foreign countries.

The vast majority of health data in Switzerland is collected across 26 regional health systems, with no overarching interoperability or harmonization strategy.[3] As Gaudet-Blavignac et al. (2021) show, data are collected in decentralized silos, making it costly or impossible to link

[2] Modern sensors can measure common vital signs like blood glucose, heart rate, blood pressure and blood oxygen saturation in unobtrusive form on multiple body locations via wearables in decentralized settings. And it is not only health related data, but also shopping, mobility or socio-economic data that can create valuable links to health-related parameters of a person (see Subbiah, 2023).

[3] For instance, the same process (e.g., measuring body temperature) is measured differently across institutions, leading to inconsistency in data collection. In addition, 34% of general practitioners were still using exclusively paper health records in 2015 (Deml et al., 2022).

datasets across institutions and cantons. Data curation and sharing is thus mostly occurring in bilateral projects. As a consequence, the Swiss patient population is insufficiently described. For example, large national cohorts or biobanks are currently lacking in Switzerland.[4] This fragmentation of data collection coincides with the generally slow progress of digitalization of the healthcare system. In cross-country comparisons, Thiel et al. (2018) and Boyd et al. (2021) find that Switzerland ranks low in terms of re-use of health data and digital health data infrastructure. This issue has recently been acknowledged by the Swiss Federal Government which formulated a number of strategies to improve data interoperability and sharing for biomedical research (Swiss Federal Council, 2022; FOPH, 2022a). Already in 2013, the Swiss Federal Council had launched a so-called Masterplan to strengthen biomedical research and technology in Switzerland with, at least so far, limited success.

Following the statement of intent of the Federal Office of Public Health (FOPH, 2022a), the plan pursues, among others, to establish the best possible conditions for biomedical research and technology. The masterplan specifically focusses on the health data ecosystem, covering the whole value chain from research and development to the treatment of patients. The most recent program is "DigiSanté", where until the end of 2034, health data including the nation-wide Electronic Patient Dossier described below should be accessible for both care and research through standardization, interoperability and better legal clarity concerning data re-use (FOPH, 2023). The program is governed by the Federal Office of Public Health jointly with the Federal Statistical Office. These ambitions stand in stark contrast to the currently existing policies and infrastructure.

A prominent example of slow progress in digitalization is the Electronic Patient Dossier ("Elektronisches Patientdossier" or EPD), a national electronic health record introduced more than 15 years ago with the aim of making patient-level data accessible for research (Interpharma, 2021). The adoption of the EPD has been slow and only a small minority of Swiss citizens have opened their personal EPD (Martani et al., 2023). Hence, while the Swiss government seems to share the health sector's concerns and legislative steps have been undertaken, the digitalization of the Swiss healthcare system is still in an early development phase and so far characterized by a high degree of fragmentation and non-harmonized data collection. This fragmentation is contributing to the current challenges regarding data access. At the same time, however, the decentralized Swiss system could potentially also prove to be advantageous in the long term as

[4] There are 60 disease specific cohorts/biobanks in Switzerland registered under the Swiss Biobanking Platform, for instance the Swiss HIV Cohort or SAPALDIA for patients with lung diseases.

regional initiatives can compete to find the best solution for a national data harmonization strategy. But time may be the scarce factor here, as the following initiatives demonstrate.

2.1 Regional and National Initiatives to Improve RWD Access

A prominent national initiative to overcome the fragmented data collection system in Switzerland is the Swiss Personalized Health Network (SPHN) founded in 2017 by the State Secretariat for Education, Research and Education (SERI) and Federal Office of Public Health (Lawrence et al., 2020). The goal is to implement a national interoperability infrastructure and to establish harmonized standards for the secondary use of health data for research purposes in all university hospitals and a few cantonal hospitals -- with the aim of expanding the network to all Swiss hospitals and clinics, the Electronic Patient Dossier as well as existing and future biobanks and cohorts. Up to date, the project has been able to formulate a main dataset consisting of vital signs, laboratory results and diagnosis. Data are collected via a Data Coordination Center and analyzed on the BioMedIT platform. Data are only shared with external parties in aggregated form to ensure anonymization. The public funding of the initiative is currently limited to the end of 2024.

In recent years, the field of oncology has also experienced considerable progress in the standardization of data collection and sharing. A cancer registration hub standardizes the collection of cancer data throughout Switzerland with the goal to have a complete dataset of all cancer patients in Switzerland (FOPH, 2022b). Every clinic or medical institution in every canton and every cantonal cancer registry needs to be associated with the national registry. There is agreement on a basic set of variables that need to be collected in the same way across the country. Among the reasons for this development seems to be the agreement among many stakeholders that oncology is a field of public health interest.

Moreover, there are a number of regional, bottom-up initiatives working towards harmonized data collection and sharing. For example, BâleDat has been initiated by the so-called “Life Sciences Cluster Basel” of the Handelskammer beider Basel, a regional interest group which involves the university hospital of Basel, the canton hospital Baselland, Interpharma and representatives of Roche and Novartis. The project aims to develop interregional cooperation with other stakeholders and to identify “use cases” where and how health data can be collected and shared in a standardized way. Progress of these and other initiatives are slow due to fundamental legal and structural barriers as we show in the next subsection.

2.2 Legal and Structural Barriers to RWD Re-use

Recent surveys find that the Swiss general public is willing to share their health data for academic research purposes, but the willingness to share them with the pharmaceutical industry seems to be low (Pletscher et al., 2022).[5] Generally, there appears to be caution to share health data with others, and even more so with the pharmaceutical industry. For instance, industry access to SPHN data is currently restricted to aggregated results, mainly because data collectors (i.e., hospitals) are reluctant to share their data with the industry. Among the reasons for this reluctance is, as hypothesized by experts in the field, an uncertainty on what the industry will use the data for. Concerning legal barriers, the secondary use of health data in Switzerland is restricted and complex. As Martani et al. (2020), Scheibner et al. (2020) and Widmer et al. (2022) show, data protection laws in Switzerland follow a rather complex architecture, with 26 different data protection regulations (the Federal Act on Data Protection (FADP) and 25 cantonal data protection laws). For most cases, these laws apply when dealing with personal (i.e., individually identifiable) data.

There are generally three main strategies to re-use health data for research purposes (i.e., use data for other purposes than those originally envisaged during primary collection): (i) through explicit informed consent of the data subjects (e.g. using the general consent form)[6], (ii) through a research exemption granted by an ethics committee, or (iii) through using anonymized data (Martani et al., 2019). So far, there is no legal basis in Switzerland that allows to link datasets with personal health data because a personal identifier (such as the AHV number) has not been introduced and linking datasets is only permitted by the Federal Statistical Office (Martani et al., 2021). Transferring health data across borders is only possible with informed consent or if

[5] Pletscher et al. (2022) find that a large majority of the Swiss population (71%) is willing to share their anonymized health data for medical research. The main motivation behind sharing that data is of an altruistic nature (i.e., other people get better treatment). However, a smaller share of participants expressed trust in hospitals or universities (two thirds), an even smaller share in the government (about half) and less than a fifth of participants showed trust into the pharmaceutical industry.

[6] The "General Consent" facilitates the secondary use of health data for research purposes under the Human Research Act. This consent form has been adopted by all five Swiss university hospitals as well as the SPHN and it allows the further use of routinely collected health data for a multitude of purposes once signed by a patient. Hence, the purpose of the secondary use of the data does not need to be known at the time of the primary data collection, in contrast to an explicit consent form (Widmer et al., 2022). The data collected via the Generalkonsent can only be shared with third parties like industry in anonymized form.

anonymized data is used, and only with countries whose data protection laws are deemed adequate (such as the EU or the U.S.).[7]

In addition, while anonymization presents an opportunity to escape legal barriers to the secondary use of health data, there is legal uncertainty on the correct process of anonymization. Swiss legislation does not clearly state how to anonymize data, which leaves room for interpretation and confusion about when a dataset can be considered "anonymized" (Martani et al., 2023). According to Widmer et al. (2022), the so-called "relative approach" to anonymization is used in Switzerland, where a dataset is considered anonymized if any party has to use *disproportionate efforts* to re-identify the data. The law also lists a minimal yet not exhaustive set of indicators that need to be deleted in a dataset, namely name, address, date of birth and unique identification numbers (i.e., AHV number). Hence, while working with anonymized data falls out of the scope of the FADP and Human Research Act (HRA), the *process* of anonymization is subject to the HRA.

Overall, the complex and non-harmonized legal landscape for the secondary use and anonymization of health data in Switzerland leads to uncertainty among research institutions and pharmaceutical companies. Hence, even if health data are accessible, there are still legal barriers complicating the secondary use of these data for research purposes. The question remains how Swiss pharmaceutical companies deal with the limited and uncertain access to local and foreign data for R&D purposes.

2.3 Strategies for Local and Foreign Data Access

For access to Swiss RWD, pharmaceutical companies negotiate access in a bilateral fashion with healthcare institutions such as hospitals or registries. Typically, the governance board of a healthcare institution needs to evaluate the conditions of data sharing with the industry in a project-by-project fashion (e.g., anonymized data and the price for access). Another pathway to access data for companies is going through data brokers like EMS Health. These institutions themselves gather data from different healthcare institutions and sell them to companies. In most cases, the data is shared in an anonymized form. Whenever data becomes available through such bilateral collaborations in Switzerland, the data quality is usually very high.

[7] The General Data Protection Regulation (GDPR) of the EU and the Health Insurance Portability and Accountability Act (HIPAA) of the U.S. regulate the secondary use of sensitive personal data such as health-related data (Harrer et al., 2019).

Accessing data in foreign countries is another option for Swiss pharmaceutical companies. In most of these countries (including all neighboring countries), data access is *not* better than in Switzerland. However, a number of best practice examples of digitalized health systems exist, most of which are located in Nordic countries. Finland, Denmark, Sweden, or Estonia are seen to have set a "gold standard" for how RWD can be collected and accessed (Klimek et al., 2022) and the USA and UK are examples for countries with larger populations and good data access (Bate et al., 2016).

In Denmark, a centralized national data analytics center (DAC) collects and links patient data from national registries by using a personal identifier (CPR number) while ensuring high levels of data security (Geneviève et al., 2019). However, access to these data for industry researchers and cross-border data transfer seems to be limited and more strongly regulated than access for academic research (Martani et al., 2022).

In Finland, the Act on the Secondary Use of Health and Social Data passed in 2019 allows for the secondary use of health data for research purposes (see Ferencz & Buki, 2022). Based on this law, the national FinData database was created in 2020 to share medical data held by the public sector with research institutions, including industry. FinData combines data from several state databases and provides them to the applicants for a price in either anonymized or aggregated form via a secure hosting service. FinData is a valuable and fully accessible source of high-quality RWD for pharmaceutical companies. The comparison of Finland with Switzerland appears promising, since the high-quality data from a similarly small country like Finland could provide a blueprint for a data infrastructure in Switzerland.

Following Bate et al. (2016), the UK and the National Health Service (NHS) is a best-practice example in a larger population of how RWD can address a wide range of challenges, across drug development with its connectivity and rich longitudinal patient records. The publicly funded NHS is a near monopoly provider of primary and secondary healthcare to UK residents. Electronic health records provide a detailed record of primary care interactions and other healthcare delivery systems. These electronic health records are stored in databases and used in anonymized format by external parties for research. One such dataset is the Clinical Practice Research Datalink (CPRD), hosting data of over 15 million patients and 82 million years of longitudinal data (more than 5 years per patient on average).

Each patient has a unique NHS number which enables data linkage across the healthcare system. As Singh et al. (2018) show, research using CPRD data has resulted in more than 1700

publications since 1987 in drug safety, best practice and clinical guidelines. Another prominent example for successful health data sharing through public funding is the UK Biobank. According to Conroy et al. (2023), it is a large-scale biomedical cohort database and research resource, containing in-depth and longitudinal information on genetic, physiological, lifestyle and environmental factors of more than 500,000 UK participants, with their health followed up through linkage to electronic health records. The Biobank is globally available to all bona fide academic and commercial researchers and most suitable for cancer research.

Accessing data in the USA for a Swiss pharmaceutical company usually means buying them from commercial data vendors. The advantage of U.S. data is that it tracks patient data across medical institutions and states. As Dagenais et al. (2022) show, the cost of acquiring RWD through third parties in the U.S. varies between $100,000 to 400,000 for specific therapeutic areas and up to $5 million for curated (i.e., tailor-made) electronic health records data. Albeit expensive, the advantage of purchasing curated RWD is that the data can be prepared to the needs of the companies' research focus. In cases where companies cannot directly access or buy the data (e.g., Medicare data), they can purchase the analysis of the data while an authorized third party performs the analysis with prices up to $1 million for complex analyses across different RWD datasets. This practice of investing into institutions capable of analyzing RWD has become routine for large pharmaceutical companies.

A prominent example is Flatiron, a U.S. health-tech company bought by Roche in 2018 for $1.9 billion. Flatiron provides care solutions for cancer patients using RWD analyses. The company has subsidiaries in Japan, Germany and the UK that partner with hospitals and health networks. Currently, Flatiron holds more than 3 million patient records that are available for research. In the same year, Roche acquired Foundation Medicine Inc. for $2.4 billion, a U.S. based company that offers services to physicians that help them in making personalized treatment decisions for cancer patients, e.g., through genomic profiling of tumors and interpretation of such results. At the same time, the data that are generated through its services can serve as a resource for cancer research. Roche is also using these data in Switzerland to improve diagnosis and treatments for patients, for example, in the Precision Oncology Project with University Hospital Zurich and the University of Zurich. The collaboration investigates how RWD can be shared and integrated into routine clinical practice. The goal is to learn how oncology patients in Switzerland may benefit from an integration of larger and more personalized datasets in the clinical setting.[8]

[8] See: https://www.roche.ch/en/media-switzerland/informationen/med-ch-2024-01-23 (accessed March 27, 2024).

From these examples the question arises why Swiss companies cannot simply continue with the strategy of accessing datasets in countries where access is better. The remainder of this paper attempts to explore the potential of local Swiss RWD in the pharmaceutical R&D process and the value of local data access for R&D locations. The theoretical framework guiding the analysis will be discussed now.

3 Economics of Data, Home-Market Effect and Location of R&D

The international allocation of individual activities in a company's value chain is a result of a multitude of factors. The same applies to the aggregate, the individual countries, which are composed of a myriad of national, international and multinational companies. International trade theory -- whose origin goes back to David Ricardo (1817) -- provides a rich set of explanations on which industries and activities an individual country specializes in and how this pattern changes over time, for example, due to government interventions, new technological developments and new countries entering the world markets. The driving force of this process arises from companies' aim to constantly increase their productivity through better products, services, processes and forms of internationalization in order to survive in international competition. Countries benefit from an increase in aggregate productivity and societies from an increase in real income.[9]

In the following, we focus on the innovation process and show the essentials of a concept that explains a company's decision to install and maintain research and development sites in a certain location. Figure 1 simplifies the relevant environment to two groups of determinants and two agents. The government can provide favorable or unfavorable conditions and regulations for both demand conditions (i.e., local demand from customers of companies) and factor conditions (i.e., the availability of specialized inputs such as skilled labour). Companies not only operate within these conditions, but also influence them -- for example, through human capital building or technological breakthroughs. In addition, they may also affect government policies

[9] There is a large literature that contributes to our understanding of the observed international specialization of countries and regions. Widely noted contributions, accessible to a broad audience and which we build on in the following, include Porter (1990) and Krugman (1991). An application to Switzerland can be found in Borner et al. (1991).

through lobbying and their expertise in the decision making process. The direction of innovation of companies is likely to be affected by both demand and factor conditions, as many case studies illustrate and empirical analyses confirm.[10]

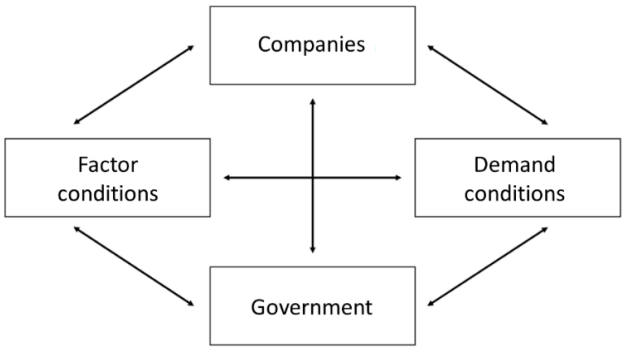

Figure 1: Factors Influencing the Location of Innovation. Source: Rutzer & Weder (2021), p. 238

For this paper, we focus on these two determinants (factor conditions and demand conditions) as being potentially impactful for the direction and location of pharmaceutical innovation in the Swiss (home) market. Specifically, we investigate the impact of local RWD access on the R&D process of pharmaceutical companies. We expect that these data contain information on local demand signals that provide the corresponding companies with a competitive advantage to pursue R&D activities. Through a circular process, this may affect local factor conditions by attracting high-skilled and specialized labour (possibly through the entry of related firms) which, in turn, may spur innovation in the field. Such dynamic, self-reinforcing processes are typical in this theme and sometimes called "cluster", "spillover" or "agglomeration" effects.

Before we can empirically analyze whether we find support for these effects, we need to study more carefully the economics of ideas as the basis for the innovation process, how data enter this process and in which way the home market relates to the location of R&D activities. This will allow us to derive a framework which serves as a basis for our empirical analysis of the relationship between Swiss RWD and R&D in the pharmaceutical industry.

[10] For example, the Swiss textile dyeing companies set the standard for the Swiss textile dyestuff companies, the Swiss chemical industry for the Swiss fire detection equipment industry which both, in turn, became highly successful in these products developed for their demanding Swiss customers. Research and teaching at Swiss universities (at the ETH in Zurich and the University of Basel) in these areas provided the human capital which was further developed through labour market pooling among related industries; see Enright and Weder (1995).

3.1 Ideas

Romer (1990) emphasized that ideas are very different from other economic goods as they are non-rivalrous in their use: After an idea has been invented, it can, in principle, be used by anybody with no additional costs. Ideas are thus a non-rival factor of production and are a potential source of increasing returns to scale in production.[11] To produce output Y -- which can be thought of as the aggregate output of an economy or the quantity of production of a drug -- rival factors of production such as labour (L) and capital and a non-rival factor such as ideas or knowledge (A) are combined. This can be illustrated with the following simple production function with A and L as an input:

$$Y = A * L. \tag{1}$$

Labour is rival, because one unit of L can only be employed by one company at a given moment, whereas other companies cannot use that unit of labour. Ideas, however, are non-rival. A can be thought of as a set of instructions (a recipe or blueprint) to produce a certain good or service. Once shared with the world, the idea can be used by all people who have knowledge of the idea simultaneously without degrading the quality of the idea. This gives rise to increasing returns to scale.[12] Importantly, while an idea itself is non-rival, the human capital required to use the idea remains rival.[13]

Another important characteristic of ideas is that they are, in principle, excludable. The creator of an idea in the innovation process may exclude others from the use of this idea, at least for some period of time, or charge a fee for its use. Patent and copyrights are forms of a (temporary) exclusion and provide incentives to those who create new ideas to invest time and effort in the innovation process. As different ideas are typically only partially excludable and to a different degree (with basic research being largely non-excludable), new ideas create spillovers or positive externalities in an economy and tend to be under-produced. Societies therefore have found ways in supporting the creation of ideas through subsidies (e.g., the financing of universities) or property rights (e.g., the granting of patents or the approval of new drugs). Given the non-

[11] Paul Romer received the Nobel Prize in Economics in 2018, together with William Nordhaus, for his fundamental contributions to the understanding of innovation as the determining factor in economic growth, an area which is now called the "endogenous growth theory". See also the recently composed Innoscape Talk #2 with Prof. Romer on innovation economics and its implication for societies and government policies (Romer, 2021).

[12] This can be illustrated by a simple example. If both A and L double in size (both inputs are doubled), the final output increases by more than twice and we have increasing returns to scale: $2L * 2A = 4AL = 4Y$. When only L is doubled in size but A remains fixed, output doubles and we have constant returns to scale: $2L * A = 2LA = 2Y$.

[13] Varian (2019) argues that both information and knowledge are indeed non-rival goods, but information is typically stored in documents and files, whereas knowledge is stored in humans. This in turn means that applied knowledge (human capital or skills that use the knowledge) is rival which is in line with our perception above.

rivalry characteristic and the increasing returns property of ideas, it is in the interest of societies as a whole that new ideas are being accessed and used as much as possible after they have been created.

3.2 Data

Following Romer (1990) and Jones & Tonetti (2020), an important set of economic goods that are non-rival can be thought of as *information*. Ideas are one example of information, data are another example. Data, like ideas, can be used by many agents simultaneously without degrading their quality. Data are frequently discussed as being "the new oil", and like oil, data need to be refined in order to be useful (Varian, 2019). The non-rival characteristic of data, however, makes them rather different from oil, which is a rival good.

Jones & Tonetti (2020) emphasize that *data* should be considered as an input into the production of ideas; they can lead to more ideas or improve the quality of ideas. Following the authors and disregarding other (rival) factors of production which are necessary to create ideas, we can simplify the relationship between ideas (A) and data (D) by the following production function:

$$A = D^{\gamma}. \tag{2}$$

The parameter γ ($\gamma>0$) captures the importance of data and thus the extent to which data affects the creation of ideas: if $\gamma>1$, twice the amount of data implies more than twice the amount or quality of ideas, and vice versa if $\gamma<1$. The exact value of γ remains an empirical question. For the purpose of this paper, we simplify and assume that $\gamma=1$, hence a linear relationship between data and ideas:

$$A = D. \tag{3}$$

This in turn implies that we can rewrite the production function in (1) as:

$$Y = D * L. \tag{4}$$

Data are thus -- through their positive effect on ideas -- an important input for the creation of output in an economy or by a firm.[14] In analogy to equation (1), equation (4) implies that there are increasing returns to scale with respect to data and labour (or, more generally, other non-rival factors of production). Moreover, data D as an intermediate input are themselves an output

[14] There are several attempts to formalize data as an input into a production function (see Jones & Tonetti, 2020; Farboodi & Veldkamp, 2021; Cong et al., 2022).

as they have to be created and collected. In Jones & Tonetti (2020), the amount of data is assumed to be positively affected by the overall quantity of production: if more is produced and consumed, more data (e.g., about consumer preferences) is being generated. This, however, creates a "circularity" or positive feedback loops: data improve the quality of ideas in production, which in turn increases output of the final good *Y*. The increased consumption of the final good generates more data, and these data can be used to extend and improve ideas and produce more or better quality products and services. And so on. This process leads to dynamic increasing returns to scale and makes data an ingredient into the innovation process even more important.

Like ideas, data can, in principle, be excluded from the use by others. The degree of excludability is the consequence of a decision by data holders to either keep data in silos, encrypted or in fragmented data landscapes or, alternatively, to share the data by making them easily accessible, standardize them or store them in compatible or interoperable systems. The decision to exclude other agents from using data may, for example, be due to privacy concerns, fear of creative destruction or technical barriers (i.e., interoperability problems).[15] As it is the case for ideas and thus due to the non-rivalry of data, it is in the interest of the society as a whole to make existing data widely accessible once they exist. Based on their model and numerical examples, Jones & Tonetti (2020) argue that, from this perspective, "giving data property rights to consumers can lead to allocations that are close to optimal" (p. 2857). The reason is that firms as owners of data may be reluctant to share them (for competitive reasons), whereas governments may be too restrictive because of concerns for privacy. By contrast, consumers individually would "balance their concerns for privacy against the economic gains that come from selling data to all interested parties".

3.3 Home-Market Effects

The home market effect in international trade theory goes back to Krugman (1980) who formalized an idea that was around since the 1960s, emphasized by Linder (1961): A country with a larger demand for some products tends to be an exporter of these products. The ingredients emphasized by Krugman (1980) were increasing returns to scale (or fixed costs) in the production of a good (e.g., a pharmaceutical product) and higher costs of exporting the good than

[15] Following Lehne et al. (2019), *technical* interoperability ensures basic data exchange capabilities between systems. *Syntactic* interoperability specifies the format and structure of the data. *Semantic* interoperability ensures that the meaning of specific concepts can be shared across systems (i.e., a common language).

selling it at home (i.e., additional international transaction costs). This creates a cost advantage for firms that operate in a larger home market compared to their foreign competitors as the costs of their total sales abroad and at home are lower. As shown by Weder (1995), an extension of this approach to small and large countries implies that countries end up being net exporters of those products for which they have a *relatively* larger home market, i.e. a comparative home-market advantage. The driving forces for a home-market effect are, however, much richer. Firms may, for example, become inspired in their product development by customers in their home market as emphasized in a number of case studies around the world.[16]

In addition to size, specific knowledge about domestic or local demand in a country may be important for firms and affect their direction of innovation and thus production. Data may provide the raw material and thus input to this specific knowledge. A recent study with the title "the more we die, the more we sell" is Costinot et al. (2019) that shows evidence of a home-market effect in the global pharmaceutical industry. The authors develop an expected disease burden variable to predict future disease burdens in a country based on the demographic development of the population in these countries. Demand for certain drugs is correlated with certain age groups. They find that relatively higher disease burdens in a home market of a multinational pharmaceutical company tend to increase the sales of these drugs both at home and abroad. Even though the precise mechanism through which the home-market effect affects these multinational companies' world-wide sales remains in the dark, there is a carefully estimated, statistically significant effect. Acemoglu & Linn (2004) and Acemoglu (2023) provide further support in this direction, also focusing on pharmaceuticals and disease burdens based on demographics.

Insights about the concrete linkages at work between local demand and local research in the pharmaceutical industry may be gained from the study by Fabrizio & Thomas (2012). The authors argue that the effect of local demand on innovation may be particularly large when the nature of demand is complex and intertwined with the institutional environment of the country. They argue that knowledge about domestic demand is *tacit* and is thus difficult to codify and difficult to transmit to others. Similarly, Audretsch & Feldman (2004) note that *tacit* knowledge is embedded in physical and social contexts and requires high social interaction to be transmitted and is thus highly sensitive to distance. This means that demand knowledge remains local

[16] This is a result emphasized in a number of case studies of firms in many industries; see, for example, Porter (1990), Borner et al. (1991), Enright & Weder (1995). Weder (1996) provides a taxonomy of transmission channels through which differences in domestic demand between countries may affect the pattern of trade.

and influences local innovation. Geographic proximity enables frequent interpersonal interactions and facilitates the transfer of tacit knowledge. Fabrizio & Thomas (2012) thus find that innovation in the global pharmaceutical industry responds to local demand. They conclude that most firms remain global in their sales revenue but R&D activities are oriented along local demand knowledge.

Suppose domestic demand sends out signals to nearby R&D activities; in this case, a cluster effect is likely to get sparked as implied by Figure 1 above. Innovative ideas are combined with existing knowledge. Knowledge spillovers are facilitated by the stock of patents (both within a company and within a region or country), the size of a firm (i.e., the number of employees), R&D expenditures and the presence of academic institutions. The presence of other similar or complementary companies and the proximity of academic institutions generate knowledge spillover*s* from which a specific company can benefit. The geographic space and how it is filled with different economic agents is a key factor in explaining innovation and technological change. This seems to be particularly relevant for industries that are highly concentrated in space and have high R&D outputs, such as the pharmaceutical industry.[17]

Overall, there is considerable evidence that local demand knowledge and domestic market size can influence the direction of pharmaceutical R&D. However, the *causal* links between local demand knowledge and the innovation process are weakly understood in the literature and the argument that a lack of local data access weakens a R&D location does not appear straightforward. We therefore attempt to fill this gap by qualitatively exploring the mechanism of access to local non-rival data in the pharmaceutical R&D process.

3.4 A Simple Approach to Link Data Access with R&D

We develop a simple relationship inspired by Jones & Tonetti (2020) that captures the intuition that both local and foreign data can be used as an input to the R&D process and ultimately to production. Recall equation (4) which shows that Y is the output of a linear production function generated by data D and labour L as inputs. We specify the available data for a firm, industry or whole economy by a weighted average of the amount of data available in the home country D_H (i.e., local data) and the amount of data available in foreign countries D_F (i.e., data abroad):

[17] The pharmaceutical industry is highly concentrated geographically in clusters, such as the New York-New Jersey-Philadelphia region, San Francisco, and the Rhine Valley (Zhao & Islam, 2017).

$$D = \alpha\beta_H D_H + (1-\alpha)\beta_F D_F. \quad (5)$$

For a small country like Switzerland it is typically the case that $D_H < D_F$. α is the *relative* importance of domestic data ($0 \leq \alpha \leq 1$) for R&D; "importance" means how relevant the data are for R&D. Next, β_H is the share of local data that a firm can use, while β_F is the share of foreign data the firm can use. β_H and β_F are measures for data access and depend on a number of factors such as, for example, excludability, government regulations, interoperability or harmonization. β_H and β_F take values between 0 and 1. In an extreme case, β_H or β_F can be equal to zero, which would mean no access to data at all. Hence, in order to reap the benefits of data, β_H and/or β_F need to have a positive value. We assume that data access is the same for all agents in an economy.

Data are used in R&D to generate new ideas. We will differentiate between individual steps in the R&D process below and thus allow α to take different values, depending on which step of the R&D process the data is used in. For instance, data might be more important in an earlier stage than in a later stage of the R&D process. In the next Section, we will assume that there are three main stages in a pharmaceutical R&D process: (i) the pre-clinical stage, (ii) the clinical stage, and (iii) the post-approval stage with the possibly of different values α_1, α_2 and α_3.[18] Hence, the adapted version of our approach for stage *i* in the R&D process is:

$$D_i = \alpha_i\beta_H D_H + (1-\alpha_i)\beta_F D_F. \quad (6)$$

With this approach, we can capture both the relative importance of local data and the access to local and foreign data for an individual stage in the R&D process. In an ideal world, both local and foreign data are fully accessible (e.g., $\beta_H, \beta_F = 1$) and firms choose the type of data that is most important for a certain R&D step which depends on α_i.

The goal of the analysis in the next section is to assess the values for each variable, based on an integrative literature analysis as well as qualitative semi-structured interviews with Swiss experts in the field (see Appendix A1 for further details).

[18] This intuition is not limited to the pharmaceutical industry. Any R&D process can in principle provide opportunities for varying trade-offs along the process.

4 Analysis of the Value of Swiss Data for R&D

A typical R&D process follows a series of activities targeted to reach the goal of discovering new medical drugs, devices or treatments. It involves the following *stages* over an average of 12 years and an investment of roughly $2.5 billion: (1) pre-clinical research, (2) clinical development (Phase I-III and approval) and (3) post-approval research.[19] In the *pre-clinical stage*, new synthetic compounds are developed from promising molecular structures to target a certain disease.[20] In the *clinical stage*, there are three main phases. In Phase I, drug candidates are tested for safety and tolerability in studies with healthy volunteers. In Phase II, the clinical efficacy (i.e., effectiveness) of the drug is tested on groups of carefully chosen patients. In Phase III, the drug is tested on several hundreds to many thousands of patients in large-scale randomized controlled trials (RCTs) under normal treatment conditions. These trials prove whether the drug will perform in clinical use. If successful, the new drug can be filed for approval by a national regulatory agency, which may require additional evidence to prove the safety and efficacy of the drug. After approval and authorization (i.e., which agents in the healthcare system will pay for the new treatment), a drug is on the market. In this *post-approval stage*, studies monitor the performance of the drug in a real-world setting and allow for adjustments and critical feedback to further develop the new product.

RWD present clear benefits to patients through better diagnostics, personalized treatments, and early disease prevention (Lehne et al., 2019).[21] The use of RWD in pharmaceutical R&D, however, is a relatively recent phenomenon that has received considerable attention in the literature and in practice. RWD can improve, transform or support each of the three stages in pharmaceutical R&D. Therefore, pharmaceutical companies are increasingly interested to invest into the knowledge and tools of capturing, accessing and analyzing RWD (Wise et al., 2018). Accessing and analyzing data can also benefit from artificial intelligence (AI). The use of AI in the pharmaceutical industry is a growing phenomenon and there is potential to use it in the R&D pro-

[19] This distinction is made for simplicity and supported by Roche (2023a; 2023b). One of our interview participants from Novartis used different terms for similar three stages, namely research (discovery), development (evidence generation and approval) and commercialization.

[20] The European Federation of Pharmaceutical Industries and Associations (EFPIA) estimates hat on average only 1-2 out of every 10,000 synthesized compounds will successfully become an actual medicine.

[21] One representative of the pharmaceutical industry gave an example for the benefits of early detection in healthcare systems. Kidney diseases are an increasing disease burden in many countries and often coincide with chronic diseases. Whenever patients need hospital care due to kidney diseases, it is often too late to heal the disease. Hence, detecting such diseases earlier requires RWD that go beyond hospital data. Because Swiss data is predominantly composed of hospital data, detection of those diseases is often too late. In contrast, U.S. data contains these integrated care data which better allows for an early detection of kidney diseases.

cess, both to create new therapeutic products and services as well as to improve the drug development process itself (Hird et al., 2016). As the capabilities of AI quickly increase, the importance of the availability of high quality RWD is likely to rise in future.

Figure 2 illustrates the potential of RWD in the pharmaceutical R&D process. In particular, it shows various sources of RWD, the real-world evidence (RWE) derived from that data for each R&D stage, as well as some exemplary research questions associated with each stage. Importantly, it is the same RWD that can be re-used within the whole R&D process. However, the evidence derived from that data (i.e., RWE) differs in each stage of the R&D process. We argue that this evidence is similar to ideas. Better access to RWD can improve the quality and the quantity of RWE in the R&D process.

Zhu et al. (2023) find that the importance of RWD may vary in the different stages of the R&D process. We argue, however, that the location of the data itself (i.e., whether these are Swiss or foreign data) is an additional important factor to consider. This is what we want to focus on in the following analysis for each stage of the R&D process.

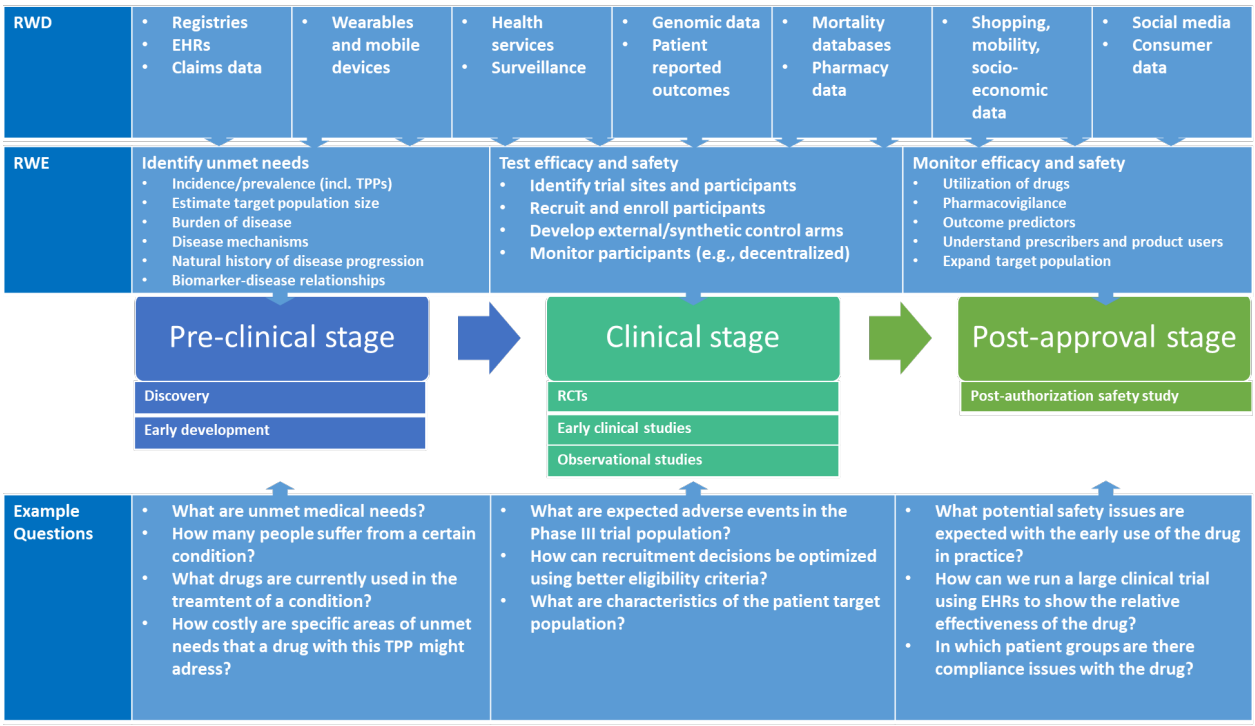

Figure 2: Use Cases for RWD in Pharmaceutical R&D. Sources: own illustrations based on Bate et al. (2016), Zhu et al. (2023), Khosla et al. (2018)

4.1 Pre-Clinical Stage

As Khosla et al. (2018) note, earlier stages of drug discovery[22] and drug development are now starting to use RWD to support important strategic decisions regarding the direction of innovation. RWD have the potential to be used in drug development to identify diseases or indications that hint at significant, unmet needs or burdens in populations. Put differently, RWD collected in high volumes have the potential to permit *hypothesis generation* regarding new research questions (Singh et al., 2018). For instance, RWD can be analyzed to develop Target Product Profiles (TPPs)[23] to provide insights into the disease prevalence and incidence to help predict how the total patient population may change over time (Dagenais et al., 2022). Since many populations are incompletely described, it is crucial to know how large a certain population is in a given disease area and country, first and foremost to inform in which areas the innovation effort should be concentrated (Bate et al., 2016). As one representative of the pharmaceutical industry said:

> *"For early decisions, it is about to know where we want to play and uncover unmet medical needs. For these questions, the location of the data is important."*

The empirical evidence on the extent to which pharmaceutical companies use RWD in drug discovery is growing. Whereas Singh et al. (2018) found little evidence that pharmaceutical companies use RWD in drug discovery, Eskola et al. (2022) detect that more than 98% of 111 medicinal products approved by the European Medicines Agency in 2018 used RWD in drug discovery, primarily to identify the right patient target population or to understand disease features and burdens of disease.

In Section 3, we presented existing empirical evidence that pharmaceutical companies seem to take into account local needs (derived from local demand conditions) in their R&D activities even if their sales are global. Even though there is ambiguous evidence in the literature whether this applies to Swiss pharmaceutical companies,[24] we argue that local demand knowledge is valuable in the pre-clinical stage of pharmaceutical R&D for the following reasons: since the

[22] Drug discovery involves finding new molecule candidates that target a specific disease and this step involves data that goes beyond RWD as one participant of Roche mentioned. In addition to working with patient data, AI and ML techniques can be used in novel target identification, drug candidate selection, protein structure predictions, molecular compound design, or understanding of disease mechanisms (Kolluri et al., 2022).

[23] A TPP outlines the desired 'profile' or characteristics of a target product that is aimed at a particular disease. TPPs state intended use, target populations and other desired attributes of products, including safety and efficacy-related characteristics.

[24] While Fabrizio & Thomas (2012) support the idea that local demand influences the direction of R&D by drawing on the notion of tacit local demand knowledge (and hence an advantage for local firms to tap into this knowledge), Woerter & Roper (2010) argue that Swiss pharmaceutical companies are more likely to respond to export market demand rather than local demand for the direction of R&D.

direction of innovation has to be decided early on based on rather incomplete information, access to local RWD presents an opportunity for pharmaceutical companies to derive demand signals that influence the direction of innovation. Firms may be inspired in their product development by customers in their home market. From this perspective, α_1 (the importance of Swiss data in pre-clinical research) is likely to have a relatively large positive value.

Note that the relative size of the home market includes both the disease burdens in terms of number of people affected by a disease (i.e., disease incidence and prevalence) as well as the willingness and ability to pay for a corresponding treatment. It may well be the case that the Swiss home market may not be very different from other markets regarding the former. If the willingness to pay in Switzerland is much larger than abroad, the Swiss home market may nevertheless be relatively large for treatments against certain diseases (see Appendix A2 for an example). Two of our interview participants highlighted the value of Swiss data in a pre-clinical setting for (i) hypothesis generation (i.e., in which areas to launch new R&D activities) and (ii) identifying sub-populations that suffer from certain diseases (i.e., how large the Swiss market is for a specific disease or burden). As one representative of the pharmaceutical industry described it:

> *"Swiss data would be invaluable to describe patient populations, to understand needs in Switzerland that may differ from global needs. We have a tendency of working with large markets like the U.S., but the question is whether that information is meaningful in the early phase of development for our country."*

The value of local data for pre-clinical research (α_1) can also be linked to the location of the R&D facilities in Switzerland. Since data is mobile, Swiss RWD could be analyzed in any country, as long as the *factor conditions* (e.g., data scientists) are favorable. We argue, however, that geographic proximity of R&D to local data collectors in medical institutions is an advantage. Being close to data collectors allows for influencing the quality of the data collected through face-to-face interactions and early inputs. Another argument brought up by our interview participants is that being close to medical institutions may be beneficial to recruit key opinion leaders for the R&D process, both to attract the best researchers but also to market a new product.

4.2 Clinical Stage

Clinical development presents the largest cost fraction in the R&D process with up to 60% of the total R&D costs (Simoens & Huys, 2021), and with Phase III trials taking up two thirds of

the cost of the clinical stage (Martin et al., 2017). Since the costs of performing randomized controlled trials are expected to rise even further without any expected rise in quality, strategies are needed to reduce both the time and costs of these trials. RWD is regarded as *complementary* rather than a substitute to randomized controlled trials, as the latter sets the standard for clinical evidence generation (Bolislis et al., 2020). However, the controlled and specialized environment in which clinical trial evidence is collected to test certain hypotheses on the efficacy and safety of a drug does not adequately reflect the performance of the drug in a larger real-world setting.[25] This is where RWD are expected to provide additional information.[26] Recently, regulators such as the Food and Drug Administration,[27] the European Medicines Agency or Swissmedic have stated ambitions for greater use of RWD to support applications for new medicines, while aiming to formalize standards and expected methods to use RWD.[28] For the case of Switzerland, Swissmedic (2022) accepts the complementary use of RWD to randomized controlled trials in the case of new approvals, for instance when RWD is used to build control arms (i.e., control groups) in a trial.

In clinical trials, RWD can potentially improve the process in three main ways: (i) improve the recruitment and enrollment process, (ii) support or replace primary data collection during the trial, and (iii) improve monitoring possibilities.

For the *recruitment* process, RWD can help to assess the population size of and information on patients suitable for recruitment (Khosla et al., 2018). The ability to recruit suitable participants is directly linked to the quality and origin of RWD.[29] Following Harrer et al. (2019), every clinical trial poses requirements on participating patients and the medical history of a specific patient might render them unsuitable. Finding the right participants and incentivizing them sufficiently is a major hurdle and more than 80% of all trials do not meet enrollment timelines and

[25] For instance, highly controlled clinical trial environments can lead to overestimation of drug efficacy, whereas the use of digital technologies can provide data that better reflect real-world performance (Hird et al., 2016).
[26] Bruland et al. (2016) find that medical history, adverse events, laboratory, disposition and vital signs of patients are the information stored in electronic health records most commonly used in clinical trials across Europe.
[27] In the U.S., the 21st Century Cures Act of 2016 was one of the first policy attempts to formalize and accept the use of RWD in regulatory processes of the Food and Drug Administration and it has been recently extended by the Advancing Real-World Evidence Program (Zhu et al., 2023).
[28] As Bolislis et al. (2020) show for the case of the Food and Drug Administration, the European Medicines Agency, Health Canada and Japan's Pharmaceuticals and Medical Devices Agency, the use of RWD for approval cases has not been restricted to any specific therapeutic area. The major share of new approvals is observed in oncology; and most new drug applications using RWD have been assigned an orphan designation, suggesting that there is still a predisposition toward accepting the use of RWD in cases where they address a rare unmet medical need or where they are used as an alternative method of clinical development.
[29] As a representative of Novartis described, in Switzerland, RWD used to recruit trial participants is often based on hospital data. This may bias the trial population towards patients with potentially late stage progressions of certain diseases, whereas other patients may benefit from a new drug in earlier stages of disease progression.

about 30% of Phase III trials terminate early due to enrollment challenges. Information from electronic health records and other RWD can potentially facilitate this recruitment "bottleneck".

Concerning the role of RWD in *supporting or replacing primary data collection* during a trial, there is large cost-saving potential. When a drug candidate is tested on participants, RWD can help deliver vital signs and other information about a person from existing electronic health records. In Phase III, using *synthetic* control arms[30] based on RWD, where participants get a standard treatment, is increasingly discussed as an option. If certain patients are getting treated with the standard treatment anyway at the point of care and their RWD is stored in electronic health records, these people would not need to be recruited and the control arm is built with RWD only. Hence, only suitable candidates for the experimental treatment would need to be found. Such pragmatic or synthetic approaches have already been applied in the U.S., but are still a rather new concept. Martina et al. (2018) find in a case study that including RWD in control arms can reduce the sample size and hence the costs in Phase III studies by up to 40%. As one representative of Novartis pointed out, the development of synthetic control arms is only possible in locations with local RWD access.[31]

Finally, the *monitoring* of the trial site could be optimized by conducting decentralized trials using digital technology to collect patient data (see Harrer et al., 2019). AI techniques in combination with wearable technology offer new approaches to developing such efficient, mobile, real-time, and personalized patient monitoring systems. Collaborations with tech companies can facilitate data collection during clinical trials. These technologies can improve participant drop-out rates, by reminding participants to follow the exact procedure of the trial. About 85% of all trials experience patient dropout at some point. In addition, trial participants can be monitored in follow-up trials for possible long-term side effects using RWD.

Overall, the empirical evidence of RWD being used in clinical development remains scarce, however. Eskola et al. (2022) find that only in about a third of 111 medicinal products approved

[30] Randomized controlled trials require a control intervention arm (i.e., a control group) where participants receive a standard treatment to accompany the experimental intervention arm where participants receive the novel treatment (Zhu et al., 2023).

[31] A prominent example for a clinical study using RWD is the Salford Lung Study (SLS) in the UK by GlaxoSmithKline to test a novel agent to treat chronic obstructive pulmonary disease and asthma, as described by Bate et al. (2016). Patients were selected for the trial based on their electronic health record and after giving informed consent, some patients were prescribed the experimental drug and some would take the standard treatment. After a year, during which the patients would regularly visit their general practitioner, information on the outcomes was extracted from the computer systems and a statistical comparison was made to inform the recommendation on coverage and effectiveness.

by the EMA in 2018 RWD was used to inform study design or efficacy. There is a slight bias towards using more RWD in clinical development for oncology and hematology products.

Regarding R&D locations, clinical trials have experienced strong internationalization in recent years with a shift towards emerging economies or so-called non-traditional countries (Bignami et al., 2020). Most clinical trials are multicenter trials that are conducted in many different countries to ensure representativeness of the results. The USA are the leading country involved in 40-50% of trials conducted globally while Switzerland ranks 17th globally in terms of frequency of being a clinical trial location (Haeussler & Rake, 2017). In line with Gassmann et al. (2018), both factor conditions (supply-side drivers) and demand conditions influence the decision to internationalize (i.e., relocate) pharmaceutical R&D facilities. *Factor* conditions for clinical trials include the availability of specialized personnel, know-how sourcing, regional infrastructure, proximity to universities, easier coordination with local hospitals during clinical phases, the availability of sufficient and suitable trial participants or the R&D environment.[32]

Our interview participants confirmed that geographic proximity to qualified clinicians performing clinical trials is an advantage. Establishing close connections with the data collectors is important in this stage of the R&D process, as it allows knowledge spillovers. Hence, local RWD access directly improves the factor conditions for clinical trials. *Demand* conditions include the attractiveness of a location being shaped by the size and quality of the local demand. The need to adapt products for local markets may drive the location of R&D facilities. Accordingly, countries with large or fast-growing markets may have advantages in attracting R&D.

Haeussler & Rake (2017) show that both factor and demand conditions influence the gradual shift of clinical trials from traditional countries like the U.S. or Western European countries towards non-traditional countries like India, China or other Asian countries. Concerning factor conditions, the authors find that it is not cost-factors that primarily drive this development, but rather knowledge-intensive factors. They show that for the period of 2002-2012, more knowledge-intensive Phase I and II trials have been growing in these countries rather than data-intensive and costly Phase III trials. Concerning demand conditions, the authors find that non-traditional countries are able to address disease burdens that are particularly important in their

[32] The R&D environment includes local content rules, technology acceptance and public approval times (Gassmann et al., 2018).

local environment, especially infectious diseases that are addressed to a lesser degree by Western pharmaceutical companies.[33]

The literature presented above indicates that RWD has large cost-saving potential for the clinical phase and that trial locations have experienced internationalization. However, it remains unclear how the location of data may influence clinical trials and the location of these trials. In the last 15 years, the number of clinical trials performed in Switzerland has decreased by approximately 43% partly due to relatively higher costs of conducting trials (Interpharma, 2023).[34] By including RWD in the different phases of clinical trials, the total cost of performing a trial can be reduced and the attractiveness of the Swiss location would increase compared to the status quo. If control arms can be generated based on available RWD, many participants would not have to be recruited in the first place. Hence, this could be a major factor increasing the attractiveness of the Swiss location, and representatives of the pharmaceutical industry speculated that this might lead to relatively more clinical trials in Switzerland as compared to the status quo.[35] In other words, the Swiss factor conditions would experience a direct improvement through better local RWD access.

This supports the circularity introduced in Figure 1 in Section 3: local demand conditions may influence local factor conditions. An additional argument for the importance of the Swiss clinical trials location is that clinical trials provide an opportunity for certain participants to get a novel treatment when a standard treatment is not effective, which is the case for some cancer cases. An extreme case would be where a single patient is subject to a clinical trial ("N-of-1"), as in the case for fatal rare diseases (Subbiah, 2023). One interview participant highlighted this "last resort" as an argument to ensure the presence of clinical trials in Switzerland. The connection to RWD access in these cases is apparent, since better RWD access may facilitate the identification and recruitment of patients in need of clinical trial treatment.[36]

Interestingly, however, Swiss patient data are not required as part of the evidence base for approvals by Swissmedic. Randomized controlled trials and RWD collection can be performed in

[33] Typically, Western pharmaceutical companies prioritize the development of drugs that address diseases with a worldwide prevalence and high demand in Western markets, such as cancer, cardiovascular, and metabolic diseases (Haeussler & Rake, 2017).
[34] The costs are high due to higher labour costs but also recruitment costs. The latter entails a general reluctance of Swiss patients to participate in trials, high bureaucratic hurdles for individuals (up to 30 pages of informed consent), and difficulties to recruit sufficiently many participants for a trial.
[35] This however assumes that data access will be better in Switzerland than other countries.
[36] Other representatives from the pharmaceutical industry challenged this statement, since this may be the case for only a few cases whereas for most diseases, access and availability of treatments is generally high in Switzerland as compared to other countries where clinical trials are a viable opportunity to get treatments in an otherwise underserved healthcare system.

other European and North American countries. The assumption is that Swiss patients do not react pharmacogenetically different to treatments than patients from the mentioned regions.[37] A participation of Swiss patients in the clinical evidence generation is thus not required.[38] Due to this assumption of interregional similarity, there are a number of collaborations between regulatory agencies involving Swissmedic to facilitate and accelerate the approval of drugs in many markets simultaneously, such as the project Orbis or the Access Consortium. In addition, approval for the Swiss market might be faster if the same drug has been approved by a recognized regulatory agency elsewhere, such as the Food and Drug Administration.

We conclude that the geographic proximity between medical institutions and industry is generally of high relevance due to knowledge spillovers in collaborations; but these collaborations can relatively easily be re-located to other countries. Both factor and demand conditions are important factors determining the location of clinical trials and especially factor conditions derive direct benefits from better RWD access. At the same time, however, the trials experience relatively high levels of internationalization due to their standardized procedure. Given the above arguments, we conclude that the importance of Swiss data in the clinical phase (i.e., α_2) is positive but lower in comparison to α_1.

4.3 Post-Approval Stage

In the post-approval stage, the pharmaceutical industry uses RWD to describe populations, to gain knowledge on patient safety and to evaluate the effectiveness of drugs (Khosla et al., 2018). In recent years, a new model of approval has been implemented in a majority of approval cases, especially in oncology.[39] New drugs receive an initial *conditional* approval[40] for marketing based on fewer evidence than required in a traditional approval, but firms are required to deliver more data about the efficacy and safety of the drug in a real-world setting. One reason is that evidence collected in randomized controlled trials has certain limitations regarding real-world performance. These post-approval studies (sometimes also called pragmatic trials) may cover safety, efficacy or optimal use of a drug over longer periods of time.

[37] For drugs developed South East Asia, Japan or China, additional evidence will be required due to differences in metabolism and diets.
[38] One representative of the pharmaceutical industry agreed on this point but highlighted the possibility that Swissmedic may change this position in the near future.
[39] To put this statement into perspective, about 50% of all approvals by Swissmedic concern the area of oncology.
[40] Swissmedic calls it conditional approval, while the European Medicines Agency calls it conditional market authorization and the Food and Drug Administration calls it accelerated approval.

For instance, a study tracks a large group of patients receiving the new medicine over a long time period. With good data access, all patients treated with the drug could be tracked and hence their health outcome.[41] In other cases, special registries are set up to track the performance of a certain drug. This in turn informs physicians on how to best use the new treatment in the broad patient population as opposed to the restricted clinical trial sample. Hence, RWD allow for outcome-based information, an often lacking type of information in current health systems.

This information has direct feedback effects to earlier stages of the R&D process, to adapt dosages or find new areas of usage of the drug. Put differently, access to RWD can provide such information at much lower cost and the authors expect the usage of RWD for post-marketing safety surveillance will further evolve in the future. Eskola et al. (2022) provide strong empirical evidence and show that 100% of 111 medical products approved be the European Medicines Agency in 2018 used RWD in post-approval settings, supporting the claim that RWD is predominantly used in this stage of the R&D process to gain insights into safety and efficacy of a new product.

Overall, interview participants agreed that *currently* the post-approval stage is the R&D step in which RWD are of highest relevance in Switzerland. As access to RWD is improving, more insights into post-approval performance of drugs and treatments are possible which inform R&D. From a regulatory perspective (i.e., Swissmedic), better access to Swiss patient data would facilitate the approval process for new drugs. It would be easier, faster and more effective to monitor the performance of a drug in a real-world setting, ideally with real time RWD. This would facilitate the faster approval of new drugs using the conditional approval approach with requirements to deliver more evidence from a real-world setting. This in turn would automatically inform the R&D process about possible adjustments of the doses or treatments. Hence, from the perspective of a pharmaceutical company, it may be of high interest how a drug performs regarding safety and efficacy in Switzerland and in the Swiss healthcare sector that prescribes the drug in a certain way.

Industry representatives supported this view, as the performance of a new drug also depends on how it is applied by practitioners in the health system and how the treatment is reimbursed by the insurance system. Since the Swiss healthcare system operates differently from foreign systems such as the EU (reimbursement is organized through the FOPH and approval through Swissmedic), the Swiss market may provide unique insights into the performance of the drug

[41] As one representative of Roche mentioned, tracking patients and their long-term responses to a treatment is possible in the USA through tokenization, where health data travels wherever the patients go.

and health outcomes in general. As representatives of the pharmaceutical industry mentioned, health outcome data in Switzerland is incomplete, with predominantly hospital data providing such insights while outcome data from (potentially) earlier phases in disease progression are mostly lacking. This provides an opportunity to fill this knowledge gap in the Swiss market.

Another factor is the excellent standard of care under which new products are accessible and used as treatments. As one representative of a pharmaceutical company explained, Switzerland often represents a best-practice example of how a new drug is applied and used in a real-world setting. In some cases, Switzerland may be one of few countries where a certain medicine is available and in such cases, the Swiss market is a prototype for the global application of this product.[42] Returning to our simple model, we expect the importance of Swiss data in the post-approval phase (α_3) to have (currently) the relatively largest value compared to α_1 and α_2.

Concerning the location of post-approval research, similar arguments can be made as for the pre-clinical stage. Geographic proximity to data collectors such as hospitals or practitioners can help to influence the data quality and the usefulness of the data for research purposes, but also influence the method of how a certain product is applied at the point of care. Representatives of the pharmaceutical industry mentioned that in some cases, a medicine is applied differently by practitioners than intended by the producers and being close can help to intervene early or learn quickly. This in turn requires RWD access to monitor how products are used in a real-world setting. Hence, RWD access and geographic proximity can potentially create positive circularity effects between demand conditions (i.e., demand responses) and factor conditions (i.e., researchers and data collectors).

4.4 RWD in Personalized Medicine

Pharmaceutical markets are currently turning from mass treatment based on population averages (i.e., blockbuster drugs) towards personalized medicine, where treatment and prevention take into account patient heterogeneity (Wadmann & Hauge, 2021).[43] A much-discussed topic is the potential for RWD to better inform R&D of individual needs of personalized medicine. Following Jakka & Rossbach (2013), the concept of personalized medicine based on RWD

[42] An example is Gilenya (Fingolimod), a drug treating multiple sclerosis. As described by a representative from the pharmaceutical industry, Gilenya is approved by Swissmedic to be a first line treatment, whereas in other countries, patients are first treated with another product. Hence, Switzerland provides a unique case study to monitor the application of Gilenya in the post-approval stage.

[43] Other terms used synonymously with personalized medicine are: precision, individualized and stratified medicine (Barazzetti et al., 2021).

promises to increase the quality of clinical practice and targeted care pathways as well as lower healthcare costs through early-detection and prevention, and should enable medical interventions even *before* symptoms are visible with the help of new sensors tracking a person's health continuously.[44] Using RWD shows an opportunity to retrieve, update and provide real-time access to individualized patient records, including (digital) biomarkers and genetic-based diagnostics.[45] This can give insights into patient responsiveness to therapies in specific disease states and enable cost-effective and personalized treatments to reduce the share of patients receiving inefficient treatments.

For pharmaceutical companies, investing into personalized medicine appears lucrative. To date, personalized medicine can target either (i) drugs for a certain phenotype,[46] (ii) drugs for a very small and specific patient population, and (iii) one drug for one patient ("N-of-1"). The overall structure of the R&D process retains the three stages introduced above. However, target populations for new drugs are becoming smaller and more specific. Due to this, a first step in preclinical R&D entails identifying the amount of potential patients in a given country and access to RWD facilitates this. Many regulatory agencies, including Swissmedic, increasingly accept conditional approvals for personalized medicines. Agencies must determine whether a drug is of high quality, safe, and effective. If an increasing share of new, personalized treatments are developed, approval processes will face new challenges and more data (Vokinger et al., 2019).

Oncology is currently the field with most applications of personalized medicine; this also applies to Switzerland (Barazzetti et al., 2021).[47] For instance, in 2017, the Food and Drug Administration approved the first cancer immunotherapy (Keytruda) to be used in the case of the presence of a specific genomic biomarker (Pulini et al., 2021). RWD is also included in the molecular tumor-profiles generated by the Tumor Profiler project (Schweizerischer Ärzteverlag, 2020). One main reason why oncology is pioneering personalized medicine is the nature of the disease. As one representative of Roche described it:

> *"In oncology, there is almost always tissue available that can be analyzed. As cancer is a genetic disease, genetic alterations can be detected much easier compared*

[44] For instance, insulin pumps with integrated blood sugar tracker or ear-sensors that collect data such as blood pressure, electrocardiogram (EKG) or heart rate (Schweizerischer Ärzteverlag, 2020).
[45] *Biomarkers* are any measurable quantity or score that can be used as a basis to stratify patients, such as genomic alterations, molecular markers, or lifestyle characteristics. *Gene therapy* aims to treat or even prevent diseases by directly targeting the genes that cause the disease (e.g., by replacing malfunctioning genes).
[46] "Phenotype" refers to an individual's observable traits, such as height, eye color and blood type.
[47] Each person has a unique genome and cancer is caused by alterations of those genomes, making cancer unique in each case and in certain cases extremely rare.

to other diseases. Such genetic alterations are often drug targets and treatment can be tailored to such genetic profiles."

To which extent large global datasets – such as the "100,000 Genomes Project" by Genomics England or the already-mentioned datasets by Flatiron – may have contributed to the development and rise of personalized medicine in oncology is an open point which would have to be further investigated. It is, however, not unlikely that it has or will do in future.

A second area of applied personalized medicine are *rare diseases* (Kalra, 2019). Rare diseases affect between 260 and 450 million people globally and are increasingly becoming a large public health burden (Subbiah, 2023). Using RWD for rare disease research is of particular interest since more and more medical areas experience "orphanisation",[48] where low incidence rates (i.e., small target groups) make the use of randomized controlled trials impossible or unethical, for instance when the eligible patient pool is too small (Zhu et al., 2023).[49] In these cases, the only option for the patients are experimental trials using RWD to test a treatment directly on the patient. Eskola et al. (2022) provide empirical evidence that RWD plays an especially important role in the R&D process of orphan drugs approved by the European Medicines Agency in 2018.

Switzerland provides an interesting case study for the emergence of personalized medicine. Following Barazzetti et al. (2021), a strong public narrative has developed around promoting personalized medicine as a gateway to improve public health through the development of data infrastructure which aims to enable nationwide accessibility and sharing of health data. In a certain sense, the discourse regarding the use of RWD for pharmaceutical R&D introduced in the beginning of this paper culminates in the vision of personalized medicine in Switzerland. The focus on personalized medicine and the associated circulation of data and knowledge blurs the divide between research and healthcare. As one representative of Novartis described it:

"In personalized medicine you need to be closer to the patient and the primary and secondary use of real-world data is more integrated."

The national and regional initiatives introduced earlier, exemplified by the SPHN, show how the Swiss biomedical research community is driven by a strong institutional commitment to a paradigm of personalized medicine. The willingness of the Swiss general public to share their personal data for personalized medicine research, however, seems to remain limited (Brall et al., 2021). While Swiss patients may not differ from European or North American patients on

[48] An orphan drug is a medicinal product that is developed to treat, diagnose or prevent a specific rare disease.
[49] In the case of some fatal rare diseases, the eligible patient pool is just one patient (Subbiah, 2023).

average, differences on a subgroup or even individual level may be of relevance when personalized treatments are developed and applied, as pointed out by an interviewee. This gains even higher importance for personalized treatments under limited time, as in late cancer stages. The argument here is, the better the (demand) knowledge about the single patient, the better the treatment can be "programmed". Hence, for Swiss patients only their own data can help for the development of targeted, personalized treatments. Put differently, demand conditions are country-specific and dependent on RWD access.

According to two interview participants, the Swiss market is particularly interesting because its relative high ability and willingness to pay for personalized treatments, which tend to be costly and require highly technical equipment (see Statista, 2023).[50] Good data access appears to be one missing piece of this *potential* home market advantage in terms of high quality, personalized treatments. Other factors such as access to treatments and equipment to implement the treatments are already in place. Another argument brought up in an interview concerns the approval of personalized medicines of the future. To get approval, evidence for the target population, which might be located in Switzerland only, would become necessary. Access to RWD may be critical to gather this evidence, for instance in the clinical stage to find suitable participants.

Future potential for personalized medicine are, apart from oncology, neurodegenerative diseases like Parkinson's or Alzheimer's, which will ultimately require patient data availability due to a highly heterogeneous target population (Stucki et al., 2023). There is also potential to address large burdens of diseases like cardiovascular diseases using personalized treatments. Especially in terms of preventative interventions, *before* people become patients, RWD can help across the entire R&D process: to identify and describe patient populations, better understand (unmet) burdens, causes and mechanisms of diseases in pre-clinical research (α_1), to develop preventative treatments through clinical phases on selected, local populations (α_2) and ultimately apply and monitor the personalized treatments in a post-approval setting (α_3).

In personalized medicine, the R&D process is, overall, more strongly integrated and Swiss data increases in value (α_i) in *each* research stage compared to our analysis above. Hence, working towards improving data access for pharmaceutical R&D (i.e., increase β_H) means working to-

[50] A recent example is the approval of HEMGENIX by Swissmedic in December 2023, the "world's most expensive drug" ($3.5m per dose) treating adult patients with hemophilia B using gene therapy. Swissmedic is one of only three regulatory agencies to fully approve the new drug, besides the FDA and Health Canada. Reimbursement of the drug through Swiss health insurances is unclear at the time of writing.

wards a home market advantage for personalized medicine. Thus, the lack of Swiss RWD access for pharmaceutical R&D is likely to yield the largest negative consequences in the field of personalized medicine.

4.5 Discussion

What does this all mean for the pharmaceutical R&D process and the location of R&D in Switzerland? With our simple framework presented in Equation (6), we can capture the importance of local data (α_i) vs. foreign data (i.e., the importance of the home market) as well as the access to these data (β_H and β_F). As analyzed above, RWD contains information about local demand (i.e. specific information on local patients) that is highly relevant for R&D. If RWD positively affects local R&D, a whole cluster effect may be initiated: collaboration between (geographically close) health institutions and pharmaceutical companies can improve RWD access and quality which boosts research with the data, creates experiences in data analysis, and in turn benefits the locally available specialists in data science, also available for local R&D sites. The availability of RWD creates a re-enforcing process between domestic demand and supply conditions.

Our findings in Section 2 imply that data access (β_H) in the Swiss home market is impaired by multiple barriers. Data collection is fragmented and non-standardized across 26 health systems. Various national and regional initiatives are engaged to find interoperable and national solutions, with limited progress to date. Public and institutional trust to share data with industry research seems generally low. A complex legal landscape regarding the secondary use of data for R&D as well as uncertainty about the correct approach to anonymization present additional barriers to data access. This implies that β_H (a proxy for local data access or local excludability from using data) has a relatively low value. As a consequence, pharmaceutical companies currently access data through bilateral negotiations with data holders or brokers in foreign countries where access is better (e.g., Finland, the UK or USA). Importantly, data access for pharmaceutical companies is only better in a few countries (hence, β_F is only larger than β_H in those countries). The amount of data collected in Switzerland (D_H) is smaller than the amount collected in foreign countries (D_F), which is not surprising for a small country. However, per capita data collection and the quality of the data, if it exists, seems relatively high.

Regarding the importance of Swiss data for R&D (α_i), we argue that depending on the step in the R&D process, local data varies in importance. Figure 3 captures our main findings:

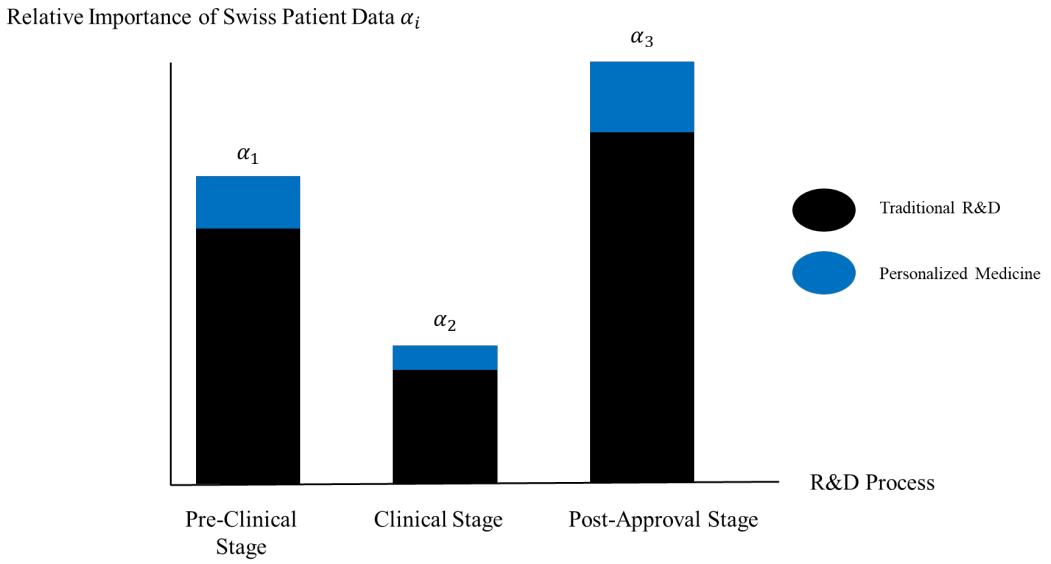

Figure 3: Relative Importance of Local Data in the R&D Process

We find that local data access has a positive effect in each of the three R&D stages. Based on our analysis, we conclude that local data is more important in the pre-clinical stage than in the clinical stage but less important than in the post-approval stage $(\alpha_2 < \alpha_1 < \alpha_3)$. These interpretations need to be treated carefully, as the relative value of α_1 may differ depending on the specific R&D project.

α_1 is strictly positive because access to local RWD may improve local demand knowledge and thereby identify new unmet or significant medical needs in the local population. Hence, demand factors are directly derived from RWD access. This would be in line with empirical evidence that pharmaceutical companies direct their R&D efforts towards local needs (e.g., market size) as found by some studies we mentioned in Section 3.

The value of Swiss data in the clinical stage (α_2) is, according to our analysis, relatively low in comparison to α_1, but still positive. Access to local RWD can improve trial design and costs and increase the attractiveness of a trial location. This in turn would benefit local factor conditions employed in performing these trials. Geographic proximity between pharmaceutical companies and health institutions involved in the trials can lead to knowledge spillovers. However, there are other factors that weaken the Swiss trial location and better RWD access may not compensate for those weaknesses. In addition, Swissmedic does not require new products to contain Swiss data as part of the evidence base.

The value of Swiss data in the post-approval stage (α_3) is currently providing the largest value in the R&D process, since RWD produces direct feedback effects concerning local demand

responses to a product in the Swiss market as well to the overall performance of the product. Put differently, demand factors are strongly visible in RWD in the post-approval stage.

Overall, we argue that the potential rise of personalized medicine would increase the value of Swiss data (α_i) proportionally by the same factor in each stage of the R&D process. The Swiss healthcare system has existing infrastructure already in place for high-tech personalized treatments and a relatively high ability to pay for expensive treatments. Hence, access to RWD appears to be one missing link to realize both research and treatment on personalized medicine. Potentially, a home market advantage in personalized medicine could arise with better access to RWD, especially because data access for companies is better in only a few other countries.

Beyond using local RWD for R&D purposes, we argue that local data access also has an important positive effect on the Swiss R&D location. This connects with the innovation environment and determinants presented in Section 3: improved demand conditions through better data access also impact local factor conditions. In both the pre-clinical and post-approval stage, geographic proximity facilitates the influence of pharmaceutical companies on data collection and quality through short communication pathways between industry and data collectors. In the clinical stage, geographic proximity is a well-established factor contributing to successful trials. This is the "circularity effect" described in Section 3: Through better demand conditions (i.e., data access), local factor conditions (i.e., high-skilled and specialized labour) benefit as well. As one representative of the pharmaceutical industry described it:

> *"It is important to collaborate and interact with data vendors to tailor the data to your own needs. We have symmetric collaborations with hospitals and universities. If Switzerland would be de-prioritized as a research location, academic and clinical research in Switzerland would suffer as well. The more data available, the more activity there will be around that data."*

5 Conclusion and Path Forward

Governments around the world have learned that new ideas and thus invention and innovation are essential ingredients of development and prosperity of societies. From economists they also know that these activities have the characteristics of a public good: without support from the government, they tend to be under-produced as the benefits of new ideas can typically only partially be captured by their originators. At the same time, new ideas can be used by anybody without that the use by others is negatively affected. Societies thus have an interest to create incentives for creators of new ideas, but at the same time to make sure that as many agents as

possible have access to them. This is why governments heavily invest in human capital building, subsidize R&D and grant patents and copyrights. Data are a crucial input into the R&D process and have, in principle, the same characteristics as ideas.

The unsatisfactory situation regarding the availability of and access to patient data in Switzerland considerably limits inventions and innovations in the whole life sciences sector as emphasized in this paper. It not only limits the quality and efficiency of treatments patients have access to in Switzerland. As we have shown in our analysis, it also tends to negatively affect the quantity and quality of R&D pursued by pharmaceutical companies in Switzerland. We find that the limited access of the Swiss pharmaceutical industry to Swiss real-world data (RWD) is particularly negative in the pre-clinical as well as in the post-approval stage of the R&D process. We expect that the associated locational disadvantage of Switzerland – particularly in comparison with countries such as the U.S., the UK and Finland – is magnified in the field of personalized medicine. As our capabilities to work with big data through artificial intelligence will increase in future, this locational disadvantage of Switzerland in pharmaceutical R&D is likely to rise.

What can be done? The awareness of the issue is high on all levels and across stakeholders. Discussions have been taking place for at least a decade. Memoranda of understanding (e.g., by the Swiss Federal Council) and many initiatives have been articulated over the years. Pilots such as the Swiss Personalized Health Network have been run and analyzed in many subfields, in individual cantons and regions. As the issue is of high relevance for both the health sector, which provides health services to the Swiss patients, as well as for the R&D activities of pharmaceutical companies and universities in Switzerland, progress now has to be made quickly and forcefully. There is still a chance for Switzerland to become a high-quality RWD hub. We see two policy steps on the path forward that could make a difference.

First, we propose that RWD collection and re-use should follow an opt-out system or, in other words, be subject to a change in the allocation of property rights: whenever health data are collected in medical institutions, patients automatically agree that their data are stored in the Electronic Patient Dossier and that they can be used for research purposes. If patients choose not to share the data, they can actively opt-out, but may in some cases also incur negative effects on their treatment. In this system, patients retain the right to decide whether their data is re-used, but the default option is that their data is shared widely, which is in the interest of the society as a whole. It is crucial to communicate clearly what these sensible data are used for in the R&D process and what ultimately the benefit of using these data is: the development of new

medicines and treatments that respond to local medical needs to improve the lives and well-being of patients in Switzerland – and beyond.

Second, we propose that a Swiss governmental agency – we suggest the Federal Statistical Office (FSO) -- becomes an important gate keeper of RWD that should also include longitudinal data of people that may or may not have been subject to a certain disease burden. Data protection, security and privacy (or anonymity) of Swiss patients and, more generally, Swiss people have to be guaranteed. The FSO has extensive experience in handling sensitive data (e.g., unemployment data or firm data), in linking data and making sure that data are not misused. To assign data to an independent government institution as the FSO has a big advantage in that all research-oriented agents in an economy are, in principle, granted access to the data if they fulfill certain standards. Alternatives such as providing companies, associations or patients with data tend to limit the potential of the public-good characteristics of data by transforming them to merely a club good residing in silos.

Progress is urgent. If, alternatively, stakeholders in Switzerland continue to do what they did in the past, they are likely not only to create a burden for patients in Switzerland, but also for R&D activities performed in Switzerland by the various companies of the pharmaceutical industry. A de-clustering effect may arise more quickly than expected, given that the large Swiss pharmaceutical companies show a relatively large degree of internationalization of their R&D already today.

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Appendix

Appendix A1: Semi-Structured Expert Interviews

We use semi-structured expert interviews with experts in the pharmaceutical industry and the healthcare system. We conducted 7 interviews and 2 roundtables with a total of N=14 representatives of Novartis (n=3), Novartis Foundation (n=1), Roche (n=3), Biotronik (n=1), the Swiss Data Alliance (n=1), the Life Sciences Cluster Basel (n=2), the Institute for Biomedical Ethics at the University of Basel (n=1), the Swiss Personalized Health Network (n=1), and Swissmedic (n=1). The interviews lasted between 45 and 90 minutes, were transcribed and analyzed in MAXQDA. Table 1 below shows the experts, their role and the institutions they represent:

Participant	Function/role as expert	Institution
Arzt, Michael	Lead Early Medical	Novartis
Bentele, Marc	Manager Clinical Safety and HEOR	Biotronik
Bolte, Claus	Chief Medical Officer	Swissmedic
Brauchbar, Mathis	Partner and Senior Consultant; Head of Knowledge Transfer NRP 77 "Digital Transformation"	Swiss Data Alliance and Advocacy
Crameri, Katrin	Director Data Coordination Center SPHN	Swiss Personalized Health Network SPHN
Erismann, Jürg	Location Manager Roche Schweiz (Basel, Kaiseraugst)	Roche Pharma Switzerland
Hofstetter, Philippe	Project Manager BâleDat	Life Sciences Cluster Basel, HKBB
Kiermaier, Astrid	Personalized Healthcare (PHC) Leader	Roche Pharma Switzerland
Martani, Andrea	Researcher in Law and Bioethics	Institute of Biomedical Ethics, University of Basel
Prieto-Rodriguez, Luis	Director Health Data Partnerships	Novartis
Rebhan, Michael	Translational Research & Data Science	Novartis
Schnurbein, Barbara von	Head Communications, Public Affairs, Operations	Roche Pharma Switzerland
Speyer, Peter	Head of Data & Analytics	Novartis Foundation
Strub, Deborah	Head of Department "Cluster and Initiatives"	Life Sciences Cluster Basel, HKBB

Table 1: Interview Participants

Appendix A2: Relative Market Size

This example shows how access to RWD may reveal market sizes for certain disease burdens in Switzerland. Swiss disease burdens may be average for most diseases. The Institute for Health Metrics and Evaluation IHME (2023) Database allows insights into temporal *disease burdens* until 2019 for most countries. Disease burdens are harmonized by the Global Burden of Disease (GBD) classification, which classifies diseases on three major levels. Level 1 makes a broad distinction between communicable diseases (like nutritional deficiencies), non-communicable diseases (like neoplasms) and injuries. Level 2 distinguishes between major diseases within level 1, such as cardiovascular diseases or neoplasms in non-communicable diseases. Level 3 then classifies single diseases within major diseases, like lung cancer.

For Switzerland, the disease burdens with the highest prevalence are neurological disorders (43.3%), unintentional injuries (39.9%), skin diseases (34.6%) and musculoskeletal disorders (32.4%). In comparison with similar countries (Denmark, Germany, Finland, UK, USA), Switzerland has relatively average prevalence per 100,000 inhabitants in most disease categories as shown in Figure A2 below for selected Level 2 diseases:

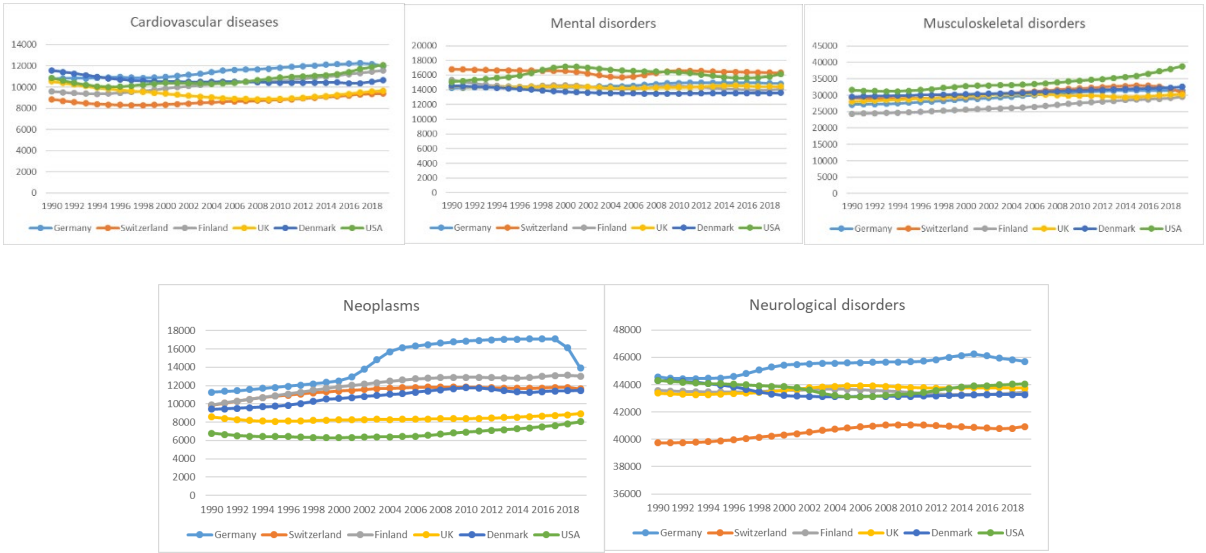

Figure A2: Disease Burdens Based on Prevalence per 100'000 Inhabitants. Source: own illustrations based on IHME data

This indicates that there may not be a relatively large market (even on a per capita basis) for disease areas and hence no apparent home market advantage. However, this may change if we take into account a higher willingness and ability to pay and differences in health insurance coverage. A recent example of new insights into spending patterns and relative market sizes for certain disease categories is provided by Stucki et al. (2023), who collect RWD from insurance claims data, hospital inpatient registries and population surveys to estimate spending patterns

and drivers for certain disease burdens in Switzerland from 2012-2017. They find that mental diseases account for the highest share of spending in major disease categories (14.3%), followed by musculoskeletal disorders (13.8%) and neurological disorders (8.5%). The single disease with the highest spending share was depression (4.1%). A substantial part of spending on mental disorders occurred in inpatient long-term care. Demographic trends lead to increases in spending on neurological disorders like Alzheimer's. Almost half of the effect in changes in spending patterns over the time period was ascribed to changes in spending per capita. This study indicates that the relative market size may be large in Switzerland for mental and neurological disorders. These elaborations lack a cross-country comparison of relative market sizes for disease categories. However, the study strengthens the argument that local RWD access can further improve insights into significant as well as unmet medical needs in the Swiss population and influence the direction of innovation through *demand conditions* signaled in the data.