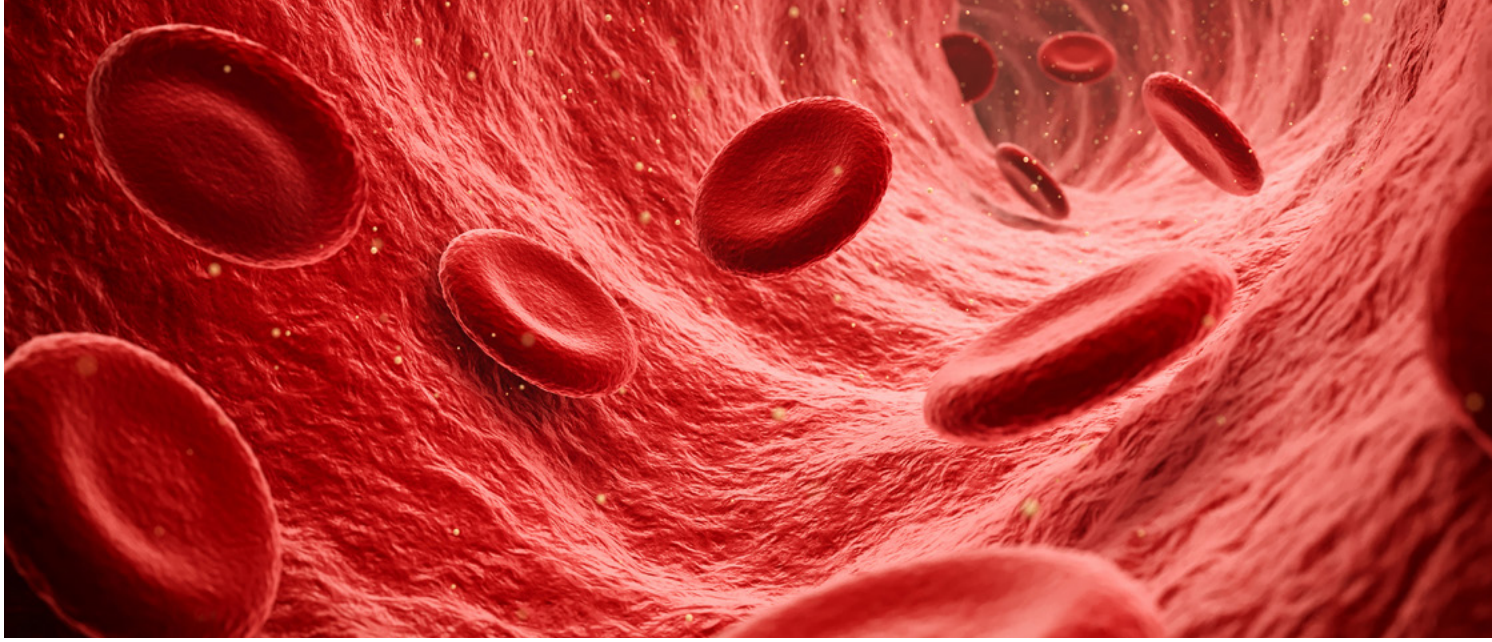

Toward the Development of a National Red Blood Cell Antibody Patient Data Exchange (RBCAX):

2023 Interim Report

U.S. Department of Health and Human Services

Office of the Assistant Secretary for Health

This report was prepared by Rose Li and Associates, Inc. (RLA), under contract to the Office of the Assistant Secretary of Health (OASH) [Contract No. 75P00122P00139]. The objective is to provide the Office of Infectious Disease and HIV/AIDs Health Policy with an interim report that summarizes the results of an environmental scan, including a literature review and relevant case studies, to determine lessons learned, best practices, and next steps toward the development, implementation, and sustainment of a national red blood cell antibody patient data exchange. RLA associates who authored this document include Christina Deuschle, Zahra Ehtesham, Kaylee Eiseman, Cecelia Garcia, Lawrie Green, Cat Thomson, and Meghan Walsh.

The views expressed in this document do not necessarily reflect those of the Office of Infectious Disease and HIV/AIDs Health Policy.

Table of Contents

EXECUTIVE SUMMARY **1**

CHAPTER 1: INTRODUCTION AND BACKGROUND **2**

Background 2

Transfusion Utilization by Blood Disorders 3

Sickle Cell Disease 3

Thalassemia 4

Obstetrics 4

Anemia, Hemophilia, and Organ Transplants 5

Health Inequities and Blood Transfusions 5

Black and African American Populations 6

Asian American Populations 6

Hispanic and Latino Populations 6

American Indian and Alaska Native Populations 6

Current State of Transfusion Tracking 7

Report Rationale 7

Report Objectives 8

CHAPTER 2: METHODS **9**

Rapid Scoping Review of Literature 9

Case Studies and Subject Matter Expert Interviews 10

RBCAX Working Group 12

CHAPTER 3: FINDINGS **13**

Established National and Provincial Systems 13

Transfusion Register of Irregular Antibodies and Cross (X)-match Problems (TRIX) 13

Quebec's Integrated Information System on Transfusion Activities and Hemovigilance 18

Canada Health Infoway 20

Established Cross-Border System 25

European Union eHealth Digital Service Infrastructure 25

Established Regional Systems 31

Kansas City Antibody Registry 31

Wisconsin Statewide Health Information Network (WISHIN) 35

Attempted Regional Systems 38

Georgia Pilot Red Cell Antibody Exchange: Lessons Learned 38

Santa Barbara County Care Data Exchange: Lessons Learned 39

Table of Contents (Continued)

CHAPTER 4: DISCUSSION 41
Elements of a Successful Exchange 41
Unanswered Questions 44
Next Steps 44
Recommendation of Pilot Options 44
CHAPTER 5: CONCLUSION 47
APPENDICES 48
Appendix A: Acronyms and Abbreviations 48
Appendix B: Glossary 51
Appendix C: Question Bank 54
Appendix D: RBCAX Working Group Presentations 57
Appendix E: TRIX Register Patient Profile 58
Appendix F: References 59

TABLES

Table 1. Scoping Review of Literature: Inclusion and Exclusion Criteria, 10
Table 2. Subject Matter Experts: Interviews and Email Communications, 11
Table 3. Implementation Investments of EHR Solutions in Quebec and Saskatchewan and Canada Health, 22
Table 4. MyHealth@EU Governing Bodies, 26
Table 5. Kansas City Antibody Registry User Access Levels, 33
Table 6. RBCAX Pilot Options, 45

FIGURES

Figure 1. TRIX Register Timeline, 14
Figure 2. Infoway Evaluation Framework, 24
Figure 3. Kansas City Antibody Registry Timeline, 2006–2022, 32
Figure 4. Overarching Barriers and Facilitators, 41
Figure 5. RBCAX Strategic Implementation Plan, 44

EXECUTIVE SUMMARY

The United States lacks a national red blood cell (RBC) antibody patient data exchange, resulting in fragmented access to patient transfusion data. Consequently, patients are at an increased risk of receiving incompatible blood during a blood transfusion. Furthermore, these risks have clear implications for the provision of equitable health care within the United States, as underserved communities are among the most impacted by blood disorders and pregnancy complications that often require transfusion. Although the benefits of such a system are clear, no guidelines exist, and information is lacking about how such a system should be structured. In this interim report, researchers systematically explore the barriers and facilitators to the development of a national red blood cell antibody patient data exchange (RBCAX) in the United States and suggest examples of pilot opportunities for such a system.

The bulk of this report examines case studies of existing and attempted red blood cell antibody exchanges and registries as well as other health information exchanges (HIEs), nationally and internationally. The goal is to provide a more nuanced understanding of the considerations required for the development, implementation, and sustainment of a successful national exchange. Case studies were selected by convenience sampling, and sources used to develop them included published and unpublished literature, expertise drawn from the RBCAX working group, and semi-structured interviews. The case studies include established national data systems, cross-border exchanges, established regional and provincial systems, and attempted exchanges that did not come to fruition. Each case study features experiential lessons, which inform the key considerations for a national RBCAX that are presented in the Discussion chapter.

Common patterns emerged across the case studies, revealing recurrent elements integral to the success of a health data exchange. The establishment of a comprehensive plan for pilot testing, implementation, and evaluation is a foundational requirement to facilitate the development of a system with inherent adaptability and scalability. Another key element of a successful exchange is a defined governance structure. In instances where governance was inadequately established, there was often a lack of accountability for critical milestones, resulting in delayed progress and increased costs. Furthermore, systems that emphasized stakeholder engagement were more successful, while those with less emphasis on end user engagement, for example, experienced frequent obstacles that, in some cases, resulted in project discontinuation. Finally, it is essential that the system be constructed to enable iterative system evaluation and improvement and demonstrate system value to end users and other stakeholders.

Several common barriers were identified across case studies, and solutions to these barriers should be integrated into the planning and implementation of an RBCAX. Interoperability, the ability to utilize and exchange data between different computer systems or software, was an overarching barrier. Developing an exchange that enables the connection of different health data systems is a challenge, but one that several existing patient data systems have been able to achieve with careful planning and adequate resources. Additionally, mandated interoperability measures have been difficult to achieve, resulting in differing standards as well as varying applications and interpretations of data laws and regulations. Pre-defined solutions to address this barrier should be established prior to exchange implementation.

Finally, the knowledge gained from the case studies was used to inform three pilot option examples presented for consideration. Each option was developed with the intention of determining the feasibility of the implementation of a national RBCAX. Advantages and rationale of each pilot option are outlined in the Discussion.

This report delineates key considerations for the development of a national exchange of patient antibody data in the United States. While there are several barriers to overcome, meticulous planning measures and comprehensive system testing can facilitate the successful development and implementation of such an exchange. Subsequent efforts should focus on solidifying a pilot implementation strategy, one that anticipates and addresses the key considerations as part of the planning process. The successful implementation of a national RBCAX would be a critical instrument in the equitable treatment of all patients. Such a system holds the potential to enhance health outcomes in all transfused patients, including those in underserved populations, while also serving as an avenue for patient education. Additionally, a national RBCAX would provide researchers with a valuable data set to better understand disease complexities, including sickle cell disease (SCD) and thalassemia, and clinical phenomena, such as evanescent antibodies.

CHAPTER 1: INTRODUCTION AND BACKGROUND

A national red blood cell antibody patient data exchange that provides **access to real-time transfused patient data** is a critical step in preventing adverse patient outcomes and ensuring equitable access to care.

Background

Recognition of the need for RBC antibody patient data exchanges in the United States and internationally has grown in recent decades, as such systems can be used to capture and track data associated with patient transfusion histories, including adverse reactions, alloantibodies, antigens, and special transfusion requirements. Although patients are pre-screened for antibodies prior to each transfusion, previously produced antibodies can evanesce (i.e., decrease or disappear over time), making them difficult to detect during screening prior to treatment. Without historical patient information, the risk of using incompatible blood in transfusions increases, potentially putting patient lives at risk (van Gammeren et al., 2019; Williams et al., 2016). Providers with access to current test results, previously identified antibodies, and records of adverse events, including delayed hemolytic reactions (DHTR), are better able to match patients with blood that will not interfere with transfusion effectiveness (van Gammeren et al., 2019).

Blood transfusions occur for various reasons, both emergent and routine. They are often required to replace blood loss due to injuries, surgeries, or conditions that cause hemorrhage. They are also used as therapies for anemia, blood disorders, and cancer, as well as for surgical procedures where blood loss is anticipated. Both adults and infants who experience complications during childbirth may require transfusion, and individuals with blood disorders such as sickle cell disease and thalassemia often need regular transfusions to alleviate painful symptoms and prolong their lives. People of Sub-Saharan and South Asian descent are at increased risk of inheriting a blood disorder that requires frequent transfusion and so are more likely to develop antibodies and experience adverse events (CDC, 2022). These patient outcome disparities are further compounded by structural racism and health care inequities, contributing to disproportionately high morbidity and mortality within these groups (Lee et al., 2009).

"So, a lot of the times I will have to go to [a hospital] . . . but they don't necessarily know anything about me, and my record. And if it's late at night I can't get in touch with my doctor, you know, something like an app or something where you do have your medical history on hand is very important." –A patient with thalassemia

Patterson et al., 2022

Currently, patient transfusion histories are often inaccessible to providers because they exist in disconnected hospital systems and blood bank registries. This shortcoming decreases the ability to prevent incompatible transfusions and DHTRs, especially for patients who seek transfusion treatment from more than one health care facility or system. One study investigated 63,973 patients with blood antibodies, comparing patients treated by more than one facility or by a single location, and found that patients treated by more than one treatment facility have a significantly higher chance of developing antibodies (7.11% vs. 3.97%, $p < 0.005$) (Delaney et al., 2013). Patients with SCD generally seek care from multiple hospitals, which has caused this population to have the highest RBC alloimmunization prevalence rate and higher RBC antibody evanescence rates when compared to others who receive frequent transfusions (Harm et al., 2014; Hendrickson, 2020).

A national RBCAX that provides access to real-time transfused patient data is a critical step in preventing adverse patient outcomes and ensuring equitable access to care. Additional benefits of a national exchange include opportunities to track the implementation of evidence-based guidelines as well as the establishment of clinical data sets for patient outcomes research to better understand, for example, antibody evanescence and the epidemiology of SCD in specific populations.

If successful, the U.S. national patient data exchange would be only the second in the world. In 2007, the Netherlands established the first national transfusion antibody registry, known as the Transfusion Register of Irregular Antibodies and Cross (X)-match, or TRIX system. Over a 10-year period, the registry database captured 80,164 alloantibodies in 62,110 individuals (van Gammeren, 2019). A localized registry was successfully created in Kansas City, USA, in 2008. During a 1-year period, it made 5,000 patient alloantibody records accessible and prevented four possible DHTRs (Schwickerath et al., 2010). However, successfully implementing a national RBCAX is a large undertaking, fraught with challenges.

To learn from the experience of other governments and organizations, this report includes case studies of several existing and attempted patient data exchanges and registries. The focus is on systems that track RBC antibody data; however, other successful systems are also included as they share similarities with the desired national RBCAX and because so few RBC exchanges and registries exist. The case studies report progress and setbacks others have experienced while implementing health data exchanges at regional, provincial, national, and cross-border levels. This information can be used to help anticipate challenges that may be encountered during the development and implementation of a national RBCAX.

Transfusion Utilization by Blood Disorders

Sickle Cell Disease

In the United States, SCD is the most prevalent inherited RBC disorder, affecting approximately 100,000–120,000 people (Kanter et al., 2020; L. Lee et al., 2019; Migotsky et al., 2022). SCD primarily affects Black and African American populations, with an incidence rate of roughly 1 in every 365 newborns diagnosed with SCD and 1 in every 13 diagnosed with sickle cell trait (CDC, 2022). Hispanic American populations have the second highest incidence rate in the country, with SCD occurring in 1 out of every 16,300 Hispanic American births (CDC, 2022). American Indian or Alaska Native populations are the third largest group affected by SCD with an estimated incidence rate of 36.2 per 100,000 live births (Prabhakar, 2009).

RBC transfusions are a crucial part of SCD therapy and have been shown to reduce the risk of disease complications, such as strokes, organ damage, and acute painful episodes (Lauridsen & Campbell-Lee, 2022; Migotsky et al., 2022). The incidence of RBC alloimmunization is particularly high among patients with SCD, surpassing that of most other populations (Tormey & Hendrickson, 2019). In a study of 150 patients with SCD, 66 people (44%) were alloimmunized. Of these 66 people, 63.6% of patients had one or more evanesced alloantibody. Additionally, patients with one or more evanesced alloantibody visited a median of three hospitals for blood transfusions over a lifetime (Harm et al., 2014). Without an accessible centralized database housing patient antibody history, patients with known alloantibodies are at risk for receiving incompatible blood and experiencing poor, and potentially fatal, health outcomes.

Apheresis exchange transfusions are a consistent part of life for many living with sickle cell disease (SCD). Without transfusions, untreated SCD leads to chronic pain, organ damage, and even stroke. However, transfusions also carry inherent risks, such as delayed hemolytic reactions and symptoms of hives, fever, and sepsis. Often, SCD patients are not given adequate, comprehensible information about the fundamental aspects of transfusions, in particular the factors that can lead to adverse reactions. A national RBCAX would increase patients' receipt of successful transfusions and initiate discussions that can enhance patient education about their disease.

Brennan-Cook et al., 2019; McClure et al., 2016

Thalassemia

Thalassemia is an inherited anemia for which regular transfusions are essential for survival and physiological function (Lal et al., 2018). In the United States, nearly 3,500 people live with thalassemia, with about 1,200 (35%) of those being transfusion-dependent (Lal et al., 2018; Boston Children's Hospital, n.d.). Thalassemia primarily impacts individuals of Middle Eastern, Southeast Asian, and Indian Asian descent (Betts et al., 2020; Lal et al., 2021). With increasing migration from these regions to the United States, there has been a 7.5% increase in prevalence of thalassemia over the last five decades (Chapin et al., 2022; Sayani & Kwiatkowski, 2015). While there is limited data on nationwide incidence, there is an estimated incidence in California of 1 in 10,000 and 1 in 55,000 for alpha- and beta-thalassemia,[1] respectively (Baird et al., 2022).

> Navdeep—father of three, nurse practitioner, and thalassemia patient—has a deep love for travel. Yet with thalassemia, he must continually consider the risks of doing so. Should he need a transfusion while away from his home health care center, he would be treated by providers without access to his transfusion history, increasing his risk of receiving mismatched blood and experiencing an adverse event. A national patient data exchange that provides every clinician in every hospital and blood bank with reliable access to Navdeep's information would greatly reduce these risks. Navdeep could finally travel with peace of mind for the first time in his life.
>
> *Adapted from Singh, 2023*

Between 64% to 89% of patients who carry two beta-thalassemia mutations require regular transfusions—every two to four weeks. Nearly half of these patients experience transfusion reactions, and the risk of reactions increases the longer they receive regular transfusions (Betts et al., 2020). In a study of 314 patients who received chronic or intermittent transfusion for thalassemia, 12.4% had alloantibodies, and over half of the patients received blood at multiple hospitals within or outside the United States (Lal et al., 2018). The same study found that one of the most significant barriers to providing quality care reported by providers is the lack of a centralized database for multi-transfused patients. Many of their complications could be prevented if providers had consistent and reliable access to each individual's transfusion history (Patterson et al., 2022).

Obstetrics

Several complications can occur before, during, and after childbirth that may necessitate transfusion, putting pregnant people and infants at risk of adverse events. Postpartum hemorrhage (PPH) refers to a significant loss of blood during childbirth and often requires blood transfusion. Individuals who are Asian, Native Hawaiian, or other Pacific Islander are more likely than Whites to experience PPH (Harvey et al., 2017), and PPH is the leading cause of pregnancy-related maternal mortality for American Indians and Alaska Natives (Heck et al., 2021). The higher rates of maternal morbidity in American Indian women are largely due to blood transfusion complications (Linder & Ipe, 2022).

Comorbidities, such as SCD and von Willebrand disease (VWD, a bleeding disorder), increase the risk of complications during pregnancy (Linder & Ipe, 2022). Individuals with SCD are more likely to experience SCD-related complications during pregnancy (Adesina et al., 2023; Linder & Ipe, 2022), and patients with VWD suffer higher rates of PPH than the general population (Linder & Ipe, 2022). In addition, unborn babies with serious forms of thalassemia can develop fetal anemia and require transfusion before birth (National Institutes of Health National Heart, Lung, and Blood Institute, 2022).

[1] "Alpha" and "beta" represent the part of the hemoglobin chains that are reduced or not being synthesized (CDC, n.d).

Fetomaternal hemorrhage (FMH) occurs when fetal blood enters maternal circulation before or during childbirth, which can cause maternal alloimmunization if the fetal blood is incompatible (Linder & Ipe, 2022). To anticipate this potential complication, the American College of Obstetrics and Gynecology recommends all pregnant people undergo an antibody screen at the first prenatal visit (Linder & Ipe, 2022). However, ensuring compatible blood is available at the time of birth can be a challenge, especially for people with rare blood types or complex antibody profiles.

A national RBCAX could significantly improve health outcomes for people at risk of experiencing complications associated with pregnancy and childbirth. Researchers have previously suggested the creation of a national FMH registry to increase recognition and reporting of complications and to identify potential factors that may contribute to FMH (Wylie & D'Alton, 2010). An RBCAX could respond to that need while also allowing clinicians to determine the correct blood type and antibody profile to transfuse, thus preventing further negative outcomes.

Anemia, Hemophilia, and Organ Transplants

An analysis of data from the National Health and Nutrition Examination Surveys from 2003 to 2012 reported 1.5% of the U.S. population meets the criteria for moderate to severe anemia. Pregnant people, older adults, women of reproductive age, Black or African American persons, and Hispanic or Latino populations were identified as high-risk groups for this condition (Le, 2016). Researchers report a doubling of prevalence from 2003 to 2012 for both moderate and severe anemia (4% to 7.1% and 1% to 1.9%, respectively) (Le, 2016). In 2020, there were 623,000 emergency room visits with anemia as the primary diagnosis (National Center for Statistics, n.d.-a). RBC transfusions are used to quickly treat patients with severe anemia by increasing the number of RBCs in their blood.

Based on data from 139 federally supported hemophilia treatment centers between 2012 and 2018, researchers estimate between 29,761 and 32,985 males live with hemophilia in the United States (Soucie et al., 2020). Three-fourths of this population were diagnosed with Hemophilia A, and over 40% suffer from severe forms of this disease (Soucie et al., 2020). Hemophilia is an X-linked disorder, resulting in a much higher occurrence of the disorder in males compared to females. Hemophilia presents primarily in White populations (Soucie et al., 2020).

In 2022, 42,887 organ transplants were performed in the U.S. (United Network for Organ Sharing, 2022). The ability to identify compatible donor organs and blood is critical to successful transplantation and prevention of graft rejection. A national exchange would significantly improve blood type matching and donor selection and enhance coordination between clinicians by providing a centralized database of antibody information, expediting the processing of donor matching and timely transplantation.

Health Inequities and Blood Transfusions

Blood disorders such as SCD and thalassemia, along with childbirth complications, disproportionately impact historically underserved and marginalized populations in the United States. Employing an intersectional approach to assess health outcomes is useful to identify how an individual's multiple identities and social positions are embedded within systems of inequality, and how individual, institutional, and structural levels of power provide context for advancing health equity and social justice (Gadsden, 2016). Statistics on minority populations' health outcomes demonstrate the impact of social status on quality of life. For instance, Black or African American populations, Hispanic or Latino people, and Asian Americans reported significantly more perceived provider discrimination and poorer health when compared to the non-Hispanic White population (Lee et al., 2009). Additionally, they are less likely to receive adequate treatment for acute and chronic pain associated with blood disorders due to implicit bias and underrepresentation (Goree & Jackson, 2022). Subsequent sections discuss the consequences of health disparities on health outcomes for several underserved populations.

Black and African American Populations

SCD predominately affects individuals with Black or African American backgrounds. This population has a long history of marginalization in the United States that impacts quality of life and health outcomes. In a cross-sectional comparative analysis of data from the National Hospital Ambulatory Medical Survey from 2003 through 2008, researchers reported that identifying as African American and having a SCD diagnosis contributed to patients with SCD experiencing longer wait times in emergency rooms (Haywood et al., 2013). Another study found that patients with SCD who reported daily chronic pain, fewer good days during a typical week, and more severe pain on their good days also reported higher levels of perceived disease-based discrimination from health care providers (Haywood et al., 2014). This disorder receives limited public attention, pharmaceutical investment, and research funding. This funding discrepancy has far-reaching implications, from limited pharmaceutical therapy options to shortages in specialized providers and treatment centers (Kavanagh et al., 2022).

> "Sickle cell disease is a microcosm of how issues of race, ethnicity, and identity come into conflict with issues of health care." –Dr. Keith Wailoo, Medical Historian
>
> *National Academies of Sciences, Engineering, and Medicine, 2020*

Asian American Populations

Thalassemia primarily impacts individuals with Asian or Middle Eastern backgrounds. In recent decades, the prevalence of thalassemia has increased significantly in the United States, but research on how social determinants of health affect health outcomes for this population is limited. Qualitative studies have reported that parents of children with thalassemia often encounter a widespread lack of understanding and experience with the disease among health care providers. They also face difficulties in comprehending and communicating with health care providers due to language barriers or limited health literacy. These challenges persist even when parents feel confident speaking English in everyday conversations (Liem et al., 2011; Punaglom et al., 2019).

Hispanic and Latino Populations

The Hispanic and Latino population is the second largest group affected by SCD in the United States (Valle et al., 2022). One study reported that the mean age of Latinos with SCD is significantly lower than that of their non-Latinx counterparts, and the presence of Hispanic and Latino individuals in the SCD population is expected to grow (Valle et al., 2022). However, with no national system capturing data on SCD prevalence and incidence, there is limited knowledge regarding the epidemiology of the disease among this population. A national exchange would help promote further education and research into the differences between these populations and could potentially aid in data disaggregation to highlight variations in epidemiology in the Hispanic and Latino populations, a large and heterogenous group.

> A national exchange would allow for the disaggregation of sickle cell disease data to reveal variations between the Hispanic and Latino populations' epidemiology.

American Indian and Alaska Native Populations

American Indian and Alaska Native populations represent the third largest minority group affected by SCD, yet there is a dearth of research examining the impacts of the disease on the community. This issue is exacerbated by the grouping of people with different genetic, cultural, political, and social backgrounds and needs into a single category (Rangi & Terry, 2014). The "American Indian and Alaska Native" category in research is a proxy for homogeneity that does not allow deeper and generalizable understanding of the complexities surrounding these populations (Knerr et al., 2011; Rangi & Terry, 2014). Additionally, these communities may avoid participating in

genomic and genetic research for several reasons, including distrust of researchers and the government due to historical trauma, previous studies portraying them in a negative light, and lack of clarity about the motivations behind genetic research and about the direct benefits to their tribes and communities (Hiratsuka et al., 2020; Kruse et al., 2022; Rangi & Terry, 2014).

Current State of Transfusion Tracking

Approximately 12–16 million RBC units are transfused each year in the United States (Garcìa-Roa et al., 2017). Currently, there is no standard clinical practice for health care providers to check patient history prior to RBC transfusion; each facility manages the process differently, although hospital consortiums may share the relevant data among themselves (Unni et al., 2014). The variability and ambiguity inherent in the current state of transfusion tracking can have serious implications for patients. A study of data from the centralized transfusion service database for the Puget Sound Blood Center (now known as Bloodworks Northwest) from 1997 to 2010 revealed that 10.9% of patients had been tested for, or received, blood transfusions at more than one hospital, and 8.82% of the total sample had positive antibody screenings (Delaney et al., 2013). When compared to patients with only one system record, people who sought care at multiple hospitals had a significantly higher proportion of antibodies (13.2% vs. 8.26%), had clinically significant antibodies more frequently, and were more likely to experience transfusion reactions (2.41% vs. 0.49%) at a level that was statistically significant (Delaney et al., 2013).

Examples of Patient Safety Concerns

- Getting "lost in the system" when transitioning from pediatric to adult care

  Source: SCD Patient Representative

- Needing a transfusion while traveling and on-site clinicians being unable to access historical antibody data

  Source: Thalassemia Patient Representative

Individuals with diseases that require frequent transfusions are particularly at risk for dangerous outcomes, and they are more likely than other transfusion recipients to have antibodies and previous experience with adverse transfusion reactions. For example, those with SCD are likely to have received transfusions at several different hospitals. This high frequency of transfusions at different hospitals and the current state of transfusion tracking places individuals in danger of experiencing potentially fatal adverse transfusion reactions.

Report Rationale

Establishment of a national RBCAX poses complex implementation challenges, including those related to data privacy and safety, system fragmentation and data standardization, stakeholder engagement and buy-in, as well as governance and sustainability. Despite these hurdles, some regional, provincial, and cross-border exchanges have been successfully established. Currently, a single nationwide registry exists; thus, there is minimal source information regarding process knowledge. Additionally, multiple barriers to the development of such a system have been identified but not systematically investigated. The primary goal of this environmental scan was to gain insights into the optimal structure, governance, housing, and long-term sustainability of such an exchange and to inform the strategic planning process toward the establishment of a national patient data exchange.

> A study of thalassemia centers in the United States found that health care providers reported the "absence of a centralized database for multiple transfused patients" as a major barrier to providing quality care.
>
> *Lal et al., 2018, p.9*

Report Objectives

- Explore possible approaches to the development and implementation of a national system to exchange RBC antibody patient data between treating hospitals, blood banks, and other health care facilities associated with transfusion medicine.
- Outline the barriers, lessons learned, and best practices from regional, national, and international patient RBCAX, registries, and other health data systems.
- Provide foundational knowledge to aid in the development of a pilot roadmap for a national antibody patient data exchange.

CHAPTER 2: METHODS

In 2022, with guidance from the Office of Infectious Disease and HIV/AIDS Policy (OIDP), Office of the Assistant Secretary for Health, Rose Li and Associates, Inc. (RLA) conducted an environmental scan of the challenges, knowledge gaps, successes, failures, and scientific and data processes required to establish and sustain an RBCAX in the United States. The goal of the investigation was to produce a report of the results, including options for developing a pilot feasibility study. Three data collection methods were used to conduct the scan: 1) a rapid scoping review of existing published and unpublished, national and international literature regarding antibody exchanges, registries, and relevant cross-border data health systems up to December 2022; 2) semi-structured stakeholder interviews with leaders from established and attempted antibody registries and other health data exchange systems; 3) guidance and expertise from the RBCAX Working Group. Data was collected on logistical, economic, structural, and clinical information pertaining to barriers and successes that could be encountered when developing and implementing a national antibody patient data exchange in the United States.

The environmental scan incorporated Castillo and Harris's equity framework (2021) to ensure all aspects of the project were considered through an equity lens. The initial rapid scoping review was informed by Arksey and O'Malley's framework (2005), which was further refined by Daudt et al. (2013). However, it yielded scant available literature about HIEs in general and RBCAXs or registries specifically. To compensate for the limited available research, RLA developed case studies of existing and attempted RBCAX and other HIEs to provide a more complete understanding of the actions required for the development and sustainment of a successful national exchange. To elucidate unique aspects of the case study exchanges, RLA conducted multiple semi-structured interviews with the leaders involved in their establishment and implementation. Interview questions were developed using both the Castillo and Harris (2021) and Kaillo and colleagues (2015) frameworks. In addition, OIDP formed the RBCAX Working Group, the members of which offered their expertise and insights during a series of presentations and question and answer sessions. The data collected throughout the environmental scan serve as the basis for exchange development best practices and for the pilot feasibility options presented in the Discussion chapter. The needs and concerns expressed by the working group's patient representatives were foundational in developing the options. The following sections provide detailed methods and limitations for each data collection method.

Rapid Scoping Review of Literature

The environmental scan began with a rapid scoping review, which revealed a scarcity of literature on RBCAX and registries. The inclusion and exclusion criteria summarized in Table 1 were developed to meet the parameters of the overall environmental scan. The scan included literature referring to antibody exchanges, registries, and repositories that are currently or have previously been operational. It also included similar human HIEs, such as those pertaining to electronic health records (EHR). To meet the inclusion criteria, articles had to report on the governance, funding, structure, barriers, health equity, or similar of an HIE program. Regional, national, and international programs were included in the review. Studies sought would report on program effectiveness, interoperability, procedures, evaluations, and legal documentation. Unpublished literature included information hosted on websites as well as strategic and operational plans (SOP) and government or organizational reports. Literature related to non-human data, exchanges, or registries was excluded, as were articles that did not inform the pre-selected categories.

An initial scientific search of literature with no date restriction was conducted using the bibliographic database PubMed. Search terms were adapted for targeting specific and nonspecific transfusion registries, patient data registries or exchanges, and patient data health systems worldwide. The search strategy identified a total of 90,999 articles, which were screened for eligibility. Review of the title and abstract resulted in the elimination of almost all articles with a total of three publications being eligible for use. The scientific search of literature revealed little information specific to the exchange of patient RBC antibody data. There are few examples of such a system in the United States and internationally.

Table 1. Scoping Review of Literature: Inclusion and Exclusion Criteria

Inclusion Criteria
Articles which describe successful or unsuccessful antibody exchanges, registries, and repositories or data health systems
Any article that discusses the development, implementation, or maintenance pertaining to antibody exchanges, registers, or data health systems
Any article that describes information related to governance, funding, structure, barriers, and health equity challenges of antibody exchanges, registries, or data health systems
Any article which describes an antibody exchange or registry that has been implemented and crosses state, regional, or national borders
Articles describing similar types of exchanges or registries which include human health information (e.g., organ transplant registries)
Published: Case studies, case reports, guidelines, systematic reviews, legal documentation, notices of award, and journals
Unpublished: Websites, SOPs, annual hemovigilance reports, government reports, press releases, business reports, presentations, letters, annals of medicine, audit reports, executive summaries
Exclusion Criteria
Any article describing registries, exchanges, or repositories not limited to human health data
Articles limited to discussing rare blood programs

Grey literature was identified to provide a comprehensive representation of antibody exchanges, registries, and data health services, including implementation, maintenance, and expert opinions. Searches of key terms were performed in Google; Google scholar; local-, state-, and federal government–hosted websites; and sites hosted by programs of interest. The nonprofit corporation Transfusion Antibody Exchange Inc.'s website (alloantibody.org) also provided numerous research articles investigating the importance of a widespread antibody data exchange. Search terms replicated those used in the published literature review, with appropriate modifications to identify grey literature—such as "patient data registry," "data system implementation," or "patient health data system"—to identify relevant systems and models. Sources were excluded when they did not directly inform the review objectives. Additional records identified through grey literature searches included government reports and reported financial information.

Case Studies and Subject Matter Expert Interviews

Given the limited available research about RBCAX or registries, the Findings chapter is composed primarily of case studies describing previously attempted or existing HIEs, repositories, or registries, with a focus on those that capture RBC antibody data. The case studies provide detailed descriptions of each data system in terms of its development, implementation, and maintenance across regions, states, territories, and countries. Information captured for each system relates to governance, structure (including patient safety and security measures), evaluation, barriers and limitations, health equity challenges, and other considerations, such as user buy-in and perceived benefits.

Convenience sampling was performed to identify systems that would reveal insights into the process of developing and implementing a national RBCAX. Existing RBCAX or registries and other health information

systems that would require similar planning and execution strategies were included. Two systems that did not come to fruition were investigated to glean information on the obstacles.

Sources for the case studies include published articles, case reports, and legal documentation, as well as websites, SOPs, annual hemovigilance reports, and government reports. As a complement to this information, virtual semi-structured interviews were held with representatives from the organizations featured in the case studies. Using the framework from Kaillo and colleagues (2016), researchers developed a series of informed questions that would elicit information not available in published and unpublished literature and aligned with data collection goals. The question bank (Appendix C) was developed with the intent of obtaining similar data across multiple interviews while providing flexibility to support gaps in knowledge identified by the environmental scan. When minimal information was needed, representatives responded to questions by email. Table 2 presents the names of these individuals, the case study registry or exchange they represent, and their position (past or current) within the organization involved in implementing it.

Table 2. Subject Matter Experts: Interviews and Email Communications

Name	Case Study Registry or Exchange	Position/Role (Past or Current) as Related to the Case Study Registry or Exchange
Cassandra Josephson, MD	Georgia Pilot RBC Exchange	Director of Clinical Research and Associate Director for Transfusion Therapies at the Emory School of Medicine
Shay Jones, MLS (ASCP)^{CM}, BB^{CM}	Kansas City Antibody Registry	Administrator Kansas City Antibody Registry
Perry Kjargaard	Canada Health Infoway	Senior Regional Account Director
Fredrik Linden, MS	European Union eHealth Digital Service Infrastructure (MyHealth@EU)	Project Coordinator epSOS
Adriaan J van Gammeren, PhD	Netherlands TRIX Register	President & Clinical Chemist Sanquin & Amphia Hospital
Charles Veldhoven, PhD	Netherlands TRIX Register	Operations Engineer Sanquin

Note: Information for the Canadian provinces, the Wisconsin Statewide Health Information Network (WISHIN), and the Santa Barbara County Care Data Exchange was obtained through sources available online; therefore, direct contact with a representative was not initiated.

RBCAX Working Group

The RBCAX Working Group played a crucial role in the development of this RBCAX report by providing guidance and expertise on topics relevant to the implementation of an RBCAX. This working group was developed by identifying relevant subject matter experts and representatives of impacted patients. These included multiple government agencies within the U.S. Department of Health and Human Services (HHS), including Indian Health Service (IHS), the Office of Minority Health (OMH), the U.S. Food and Drug Administration (FDA), the Office of the National Coordinator for Health Information Technology (ONC), the Centers for Disease Control and Prevention (CDC), and the National Institutes of Health (NIH). Also participating in the working group were representatives from the SCD and thalassemia patient communities, clinician representatives, and representatives from the American Red Cross, the American Society of Hematology (ASH), the Association for the Advancement of Blood & Biotherapies (AABB), the Kansas City Antibody Registry, and Transfusion Antibody Exchange.

A total of ten bi-weekly working group meetings were convened, during which working group members shared relevant research, experiences, and program information through presentations and question and answer sessions. External subject matter experts (SME), including representatives from the TRIX register, the Department of Veterans Affairs (VA), and the Department of Defense (DoD) also delivered presentations. See Appendix D for a full list of presentations. The data and insights from these presentations and discussions were used to inform this report.

CHAPTER 3: FINDINGS

Case studies were created to describe—through a health equity lens—how different models were initiated and sustained in terms of governance, funding, structure, evaluation, and barriers. Established national systems, national and cross-border health data systems, established regional systems, and attempted regional systems are reviewed. The following case studies inform the Discussion chapter, which outlines best practices common to successful data exchanges as well as major obstacles that should be anticipated in the establishment of a national exchange.

Established National and Provincial Systems

Transfusion Register of Irregular Antibodies and Cross (X)-match Problems (TRIX)

Introduction

In 2007, the Netherlands launched the TRIX register, establishing a network between the Netherlands blood supplier, Sanquin, and the transfusion laboratory information systems in hospitals (van Gammeren et al., 2019). The register began with the inclusion of one hospital laboratory and eventually grew into a nationwide system. Laboratory professionals now have quick access to accurate and up-to-date information about a patient's RBC antibody history within a system of linked hospital laboratories. The laboratory professionals can report this data to treating clinicians to ensure they have the correct blood for patient transfusions. According to the Transfusion and Transplantation Reactions in Patients (TRIP) national bureau of hemo- and biovigilance, "TRIX is a tool for reducing transfusion of incorrect blood components in the presence of antibodies, previous stem cell transplantation, or other transfusion problems" (TRIP Foundation, 2007). Currently, the TRIX register is the only national registry of RBC antibody data, serving as an exemplar for the efficient exchange of patient antibody data, resulting in improved patient care. Since its establishment, TRIX has successfully reduced the risk of negative transfusion reactions in patients (van Gammeren et al., 2019).

The TRIX register is the only national registry of RBC antibody data, serving as an example of the efficient exchange of patient antibody data that results in improved patient care.

Background

Developed and owned by Sanquin, a private not-for-profit organization and the sole supplier of blood in the Netherlands, the fully operational TRIX register was launched in May of 2007. TRIX developed into a nationwide system over an 11-year period, as hospital laboratories that regularly provided transfusion information joined. By 2013, 78 hospital laboratories (out of 98 reporting hospital laboratories) were connected to TRIX (TRIP Foundation, 2013). As of 2018, "all Dutch laboratories that need TRIX in daily practice are connected to the system" (Sanquin, 2021b, para. 1). Figure 1 outlines the timeline of the TRIX register development and implementation, from 2004 to 2019.

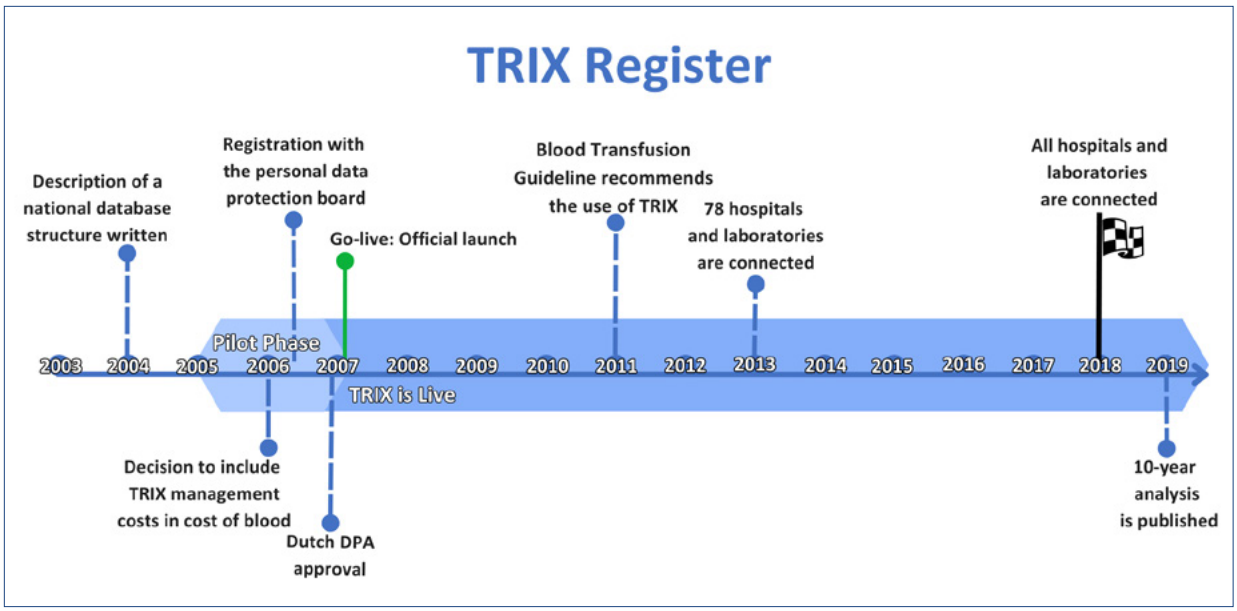

Figure 1. TRIX Register Timeline

In 2004, Sanquin began to plan for the TRIX register. In 2006, a pilot phase of the registry was initiated, and in 2007 implementation for full system use began with the first hospital laboratory. By 2018, all hospitals and laboratories were connected and regularly using the register. Success of the register was promoted by the 2011 *Blood Transfusion Guideline*, which recommended the consultation of TRIX prior to all transfusions.

TRIX contains information on any patient who has tested positive for an RBC alloantibody—regardless of its clinical significance—or who requires reports on allogeneic stem cell and bone marrow transplants. This includes administrative data, RBC antibody data, reports of TRIX "hits," and in some cases, historical data. RBC antibody data is manually entered into the TRIX register by the identifying laboratory. Hits in the TRIX system are "notifications on antibodies in a patient record that were registered in the database by [an entity] other than the consulting laboratory" (van Gammeren et al., 2019, p. 2560). The system also features a "free text" field for each entered antibody where TRIX users can input additional relevant patient data (Sanquin, 2017). Administrative data includes patient name, initials, prefix, gender, date of birth, patient identification number of the institution, citizen service number (BSN), partner of the patient (if applicable), place of residence, and the laboratory where the screening and typing occurred and was entered (Sanquin, 2017). See Appendix E for an example of a patient profile. Laboratory professionals can search for patients by their BSN, name, and date of birth (Veldhoven, 2016).

Clinically relevant antibodies are denoted in the system with a red exclamation mark to ensure that they are easily identifiable to the system user. Each antibody is entered into TRIX only once (Sanquin, 2017) and is saved in the register for the entire lifespan of the patient (Dutch Institute for Healthcare Improvement, 2011). TRIX hits are then used as a metric of system use. Hospital laboratories record TRIX hits manually, and only Sanquin can record the number of hits that have been registered (van Gammeren & Veldhoven, personal communication, March 31, 2023). A TRIX hit falls into one of three categories:

1. The antibody reported in TRIX by another institution is also found and confirmed by one's own institution through antibody typing;
2. The antibody reported in TRIX by another institution is not found in one's own institution because no screening or typing has been conducted; and
3. The antibody reported in TRIX by another institution is not found in one's own institution despite screening or typing.

The third case represents a potential evanesced antibody. In this case, consulting TRIX provides critical RBC alloantibody information, preventing potentially life-threatening transfusion reactions. Documentation of the

third case provides data on the frequency at which potentially evanesced antibodies are detected through TRIX consultations.

Governance

Legal/legislative

Hospital laboratory participation is voluntary and not legally mandated. However, the register and its participants must follow all data protection laws and regulations (van Gammeren & Veldhoven, personal communication, March 31, 2023). Prior to its launch, TRIX received approval from the Dutch Data Protection Authority (DPA), an independent administrative body legally appointed to oversee the processing of personal data. Each participating institution must be registered with the DPA (Jansen, 2007). The DPA's Personal Data Protection Board (CBP) oversees certification, ensuring that TRIX meets the requirements of the Personal Data Protection Act. This act requires that data be only used for patient care, that access is restricted to authorized personnel, and that patients are properly informed of their data use and retain their right to withdraw consent (Jansen, 2007).

The TRIX register must also comply with the Dutch Medical Treatment Contracts Act, which regulates patients' rights to provide informed consent and use of confidential patient data. While patients have the right to withdraw their data from TRIX, few do (Gevers, 2001; van Gammeren & Veldhoven, personal communication, March 31, 2023; van Gammeren et al., 2019). TRIX also must be compliant with the EU's General Data Protection Regulation enacted in 2018. Sanquin's legislation experts worked with the Ministry of Health and participating laboratories to adapt TRIX to ensure regulation compliance (van Gammeren & Veldhoven, personal communication, March 31, 2023). These regulations ensure strict monitoring of the exchange of patient data (van Gammeren & Veldhoven, personal communication, March 31, 2023).

The *Blood Transfusion Guideline*, published by the Dutch Institute for Healthcare Improvement (CBO), includes recommendations for the use of the TRIX register by hospital laboratories. The guideline specifies that irregular antibodies be registered in TRIX upon identification, data be retained for the entire lifetime of the patient, and that TRIX be consulted prior to each transfusion (Dutch Institute for Healthcare Improvement, 2011).

Data Ownership

Sanquin houses and maintains the TRIX data; however, the participating institutions own the data. As stated in the "TRIX procedures: Methods of Use" document, "Each institution is responsible for its own variable data . . . The institution is regarded as the holder and processor of its 'own' data" (Sanquin, 2017, p. 13). Only the laboratory that originally entered the patient data can make alterations or corrections; all other laboratories are authorized to view the patient data.

Structure

TRIX is an HCL Technologies web-based application that connects participating institutions' server data to a central server at Sanquin (Sanquin, 2021c). To initiate interconnection, Sanquin technical experts worked with information technology (IT) staff at each hospital to install HCL Domino server software. Each hospital server has a fixed IP address that links to the TRIX application, enabling the hospital lab information system (LIS) to access, enter, and receive data within the register. All data included in TRIX is manually entered into the system by hospital laboratories. The database is synchronized every two hours to keep up to date (Sanquin, 2021c). Notably, TRIX can share an interface with all commercially available hospital LISs in the Netherlands (van Gammeren et al., 2019; Sanquin, 2021c; van Gammeren & Veldhoven, personal communication, March 31, 2023). Sanquin is responsible for maintaining the Domino server software while the hospitals must ensure their hardware, operating systems, and backups are functioning properly. Sanquin is currently modifying the structure of the register from a system whereby each hospital laboratory has its own server to a single shared online network where users will access and input patient data via a single shared website. This new structure will eliminate the delays required to synchronize data from participant servers (van Gammeren & Veldhoven, personal communication, March 31, 2023).

Importantly, a verification and authorization process occurs prior to data access. If edits are required, the user who originally entered the data makes the changes, and re-authorization occurs (Veldhoven, 2016). To ensure accountability of system users, the register includes a built-in tracing system that records each instance a patient's data is requested and/or edited. When data is removed from the register, it is viewable but labeled "invalid" (Sanquin, 2017).

Staffing and Resource Requirements

Sanquin is responsible for maintaining the central database, system development, management of rights to the system, and agreement documentation, via the user council and committee, and IT manager. The user council, which consists of representatives from each participating institution, monitors data safety, identifies ways to improve procedures and data quality, and elects TRIX committee members (Sanquin, 2017). The user committee is responsible for policy application, data protection, evaluation and improvement of system functionality, and user procedures (van Gammeren & Veldhoven, personal communication, March 31, 2023). Laboratory professionals who need assistance with the register can work with their institution's helpdesk or acquire support from Sanquin through its TRIX Application Management department (Sanquin, 2017). Additionally, a hemovigilance staff member is responsible for checking data and lab results prior to incorporation into the TRIX database (van Gammeren & Veldhoven, personal communication, March 31, 2023). Resource requirements for participating hospital laboratories are minimal. Participating institutions are required to maintain the servers, hardware, and software necessary to access the TRIX register.

Funding Mechanisms

Sanquin estimated that the cost of sustaining the TRIX system is approximately 300,000 euros per year. Higher costs were incurred during the early implementation stages and involved server system set-up and patient data entry. Although exact implementation costs are unknown, Sanquin provided initial funding of approximately 100,000 euros to hospital laboratories (van Gammeren & Veldhoven, personal communication, March 31, 2023). In 2006, it was decided that the cost of managing the register would be added to the per-unit cost of blood, at an addition of 0.50 euros per unit. This method is more cost-efficient than charging separate licensing fees (Sanquin, 2021b). Additionally, an annual TRIX budget is developed in consultation with participating institutions. The Ministry of Health, Welfare, and Sport must approve this budget. If not approved, or only partially approved, costs outside of Sanquin's budget are taken on by the participating institutions (TRIX contract version 2.0).

Hospital costs include the servers and software needed at each hospital laboratory to connect with TRIX. In 2007, Lotus Notes and the Microsoft Windows server each cost approximately 400 euros annually (Jansen, 2007). The exact costs of other required hardware, software, and connectivity tools at each institution were not identified in the current review.

"Front loading" the register allowed for immediate stakeholder engagement. Within the first week of operation, a patient who required a transfusion following a hospital transfer was successfully treated using data accessed from the TRIX network.

van Gammeren & Veldhoven, personal communication, March 31, 2023

Stakeholder Engagement and Cooperation

At the outset, Sanquin engaged with hospitals to encourage stakeholder buy-in. Hospitals were receptive to system utilization due to the cost-saving and patient-safety benefits. However, there were concerns regarding the system's utility if too few patient data points were included. In response to this feedback, historical data from 20,000 patients, collected from 1998 to 2007, were incorporated from the Sanquin National Reference Laboratory for Erythrocyte Serology, making it a more attractive data source for participating institutions (van Gammeren & Veldhoven, personal communication, March 31, 2023; van Gammeren et al., 2019). This early stakeholder engagement process demonstrates the importance of "front

loading" a new system with data to reduce skepticism about implementing a system with minimal data. The value of the system came swiftly: within the first week of operation, a patient who required a transfusion following a hospital transfer was successfully treated using TRIX network data (van Gammeren & Veldhoven, personal communication, March 31, 2023).

Decision and Implementation Processes

Throughout the pilot and implementation stages, between 2005 and 2007, decisions were made and refined regarding data inclusion and protection, patient consent and education, and other essential elements of the register. In 2006, pilot testing of system resilience (no system downtime), data entry and authorization performance testing, and data accuracy were assessed at five hospital laboratories (van Gammeren & Veldhoven, personal communication, March 31, 2023). TRIX representatives identified several challenges during the pilot phase, including programming and patient identification issues. Prior to implementation, the pilot team also addressed interoperability issues related to the various lab systems used by different hospitals. For example, in some instances, hospitals utilized different versions of the same lab systems, causing delays and operability challenges (van Gammeren & Veldhoven, personal communication, March 31, 2023). Due to the rigor of the pilot phase, the transition to system implementation in 2007 was successful.

Standardization and Data Quality

To ensure standardization, TRIX utilizes the nomenclature established by the International Society of Blood Transfusion (Sanquin, 2017). To secure current and historical data quality, three qualifications must be met for alloantibody data to be included in the register:

1. The antibody identification must have been performed in accordance with the Netherlands' 2011 (or most recent) CBO *Blood Transfusion Guideline*.
2. The identifying hospital/laboratory must be accredited by an independent accrediting body (e.g., the Dutch Accreditation Council).
3. The antibody identification test must be done according to the Fisher Exact test. (Sanquin, 2017).

In some cases, and only with approval from the Sanquin user committee, unaccredited laboratories can enter irregular antibodies in the register if they engage in a "quality system for blood transfusion" and follow CBO guidelines for blood transfusion and alloantibody identification (Sanquin, 2017).

Evaluation

The third "hit" category represents potentially evanesced antibodies. The ability to access this information is especially important for measuring the register's value because it provides information that cannot be obtained through crossmatch testing. However, not all participating hospital laboratories report hits in the TRIX register. In a 2019 study, only half of the register's users were reporting this information (van Gammeren et al., 2019). Without a comprehensive report of TRIX hits, the full benefit of the register is unknown.

There is a correlation between the implementation of TRIX and a decrease in the number of DHTRs.

van Gammeren et al., 2019; the Dutch Institute for Healthcare Improvement [CBO], 2011

System Successes

TRIX value can be estimated by the number of potential DHTRs prevented. Between 2005 and 2014, a total of 1,014 evanesced antibodies were recorded in TRIX (van Gammeren et al., 2019), a finding that aligns with a 2012 and 2016 report of a downward trend in the occurrence of DHTRs in the Netherlands (TRIP Foundation, 2012; TRIP Foundation, 2016). This trend was attributed both to the

use of TRIX and to a TRIP Foundation recommendation for preventative matching in the 2011 Dutch transfusion directive (van Gammeren et al., 2019; the Dutch Institute for Healthcare Improvement [CBO], 2011). Additionally, between 2010 and 2019, the register recorded 80,164 identified alloantibodies in 62,110 patients, providing a large pool of patient data critical to the care of transfused patients (van Gammeren et al., 2019). While TRIX is intended primarily for treatment purposes, researchers can obtain de-identified data registered in TRIX via a request from the Sanquin user committee (Sanquin, 2017).

System Challenges

One TRIX shortcoming is the lack of complete historical RBC alloantibody patient data. Hospitals were asked to enter historical patient data into the system when they joined the register; however, not all hospitals did. Archival alloantibody data is most commonly entered only if patients return to the hospital for treatment (van Gammeren & Veldhoven, personal communication, March 31, 2023; Sanquin, 2021a). Additionally, the TRIX register system is susceptible to human error. Ongoing evaluation has identified several examples of data errors, data entry delays, and occasions when providers failed to consult TRIX prior to treatment, though such cases are rare. Additionally, as recording TRIX hits is voluntary, it is difficult to determine if all hits since TRIX's inception have been reported, making it challenging to fully evaluate the register.

Conclusion

The TRIX register in the Netherlands is an example of how RBC alloantibody patient data can be exchanged in an efficient, accurate manner, resulting in the improvement of patient safety at a national scale. Since its inception, the register has reduced adverse transfusion reactions, and it continues to provide near-universal access to secure RBC patient antibody data across the Netherlands. While not fully generalizable to the United States, this system provides a proof of concept confirming that a national system is achievable.

Quebec's Integrated Information System on Transfusion Activities and Hemovigilance

Introduction

Quebec is the only identified Canadian province to successfully create an antibody patient data exchange program. The Integrated Information System on Transfusion Activities and Hemovigilance (SIIATH) exchange system features two different software applications, SIIATH-GS and SIIATH-ST. The SIIATH-GS web application is used by blood collection organizations such as Héma-Québec and public laboratories to manage blood product information and track laboratory analysis findings (TI MSSS, 2016b). The SIIATH-ST web application facilitates information exchange, providing provincial health care providers patient laboratory results, including patient antibody data and transfusion history. Together, the applications work to "ensure traceability of all blood products and contribute to the integrated monitoring system" (Quebec Ministry of Health and Social Services, 2017b). To prevent DHTR occurrence, the exchange also warns providers of conflicts between patient blood, patient antibody history, and pending blood to be transfused (TI MSSS, 2016c). The co-existence of the two SIIATH applications allows for information exchange throughout each step of the blood transfusion process from blood bank to patient.

Background

In 1997, findings from the Commission of Inquiry on the Blood System in Canada, also known as the Krever Inquiry, called for the creation of legislation and a new governing body, now Canadian Blood Services, which would establish a safer national blood system. Opting to create its own provincially based system, the Quebec Ministry of Health and Social Services (MSSS) developed a plan to establish a system for reliable blood product safety, management, and data information. Drawing from the data elements and case definitions of the French system (Robillard et al., 2004), this initiative led to the development of SIIATH, and in 1998 Héma-Québec and

the Biovigilance Committee were entrusted to facilitate this new program (Quebec Ministry of Health and Social Services, 2017d). Within the first 2 years of implementation (2000 and 2001), hospital participation represented 80% and 82% of transfused products, respectively (Robillar et al., 2004).

Governance

The MSSS heads the Quebec blood system and is responsible for making executive decisions on creating and validating necessary changes to SIIATH. The MSSS Biovigilance Committee's mandate is to provide an opinion annually on the risks related to the use of blood and other related products, and to also provide opinions on questions submitted to the committee by the Minister (Quebec Publications, 2013; Quebec Ministry of Health and Social Services, 2017a). The committee is composed of 21 members representing system subject matter experts such as hematologists, health departments representatives, and transfusion safety officers (TSO) (Quebec Ministry of Health and Social Services, 2017b). The Quebec blood system also collaborates with the nonprofit organization Héma-Québec, which manages and distributes transplanted organs, tissues, and blood products through the SIIATH application (Quebec Ministry of Health and Social Services, 2017d). Héma-Québec board of directors is made up of 13 government-appointed members, who also identify and report issues with SIIATH or the overall blood system (Quebec Ministry of Health and Social Services, 2017b).

Legal and Legislative

The core legislation for Quebec's blood system is based on the Gélineau Report (Quebec Ministry of Health and Social Services, 1999). This document outlines the responsibilities and expectations of developing and implementing SIIATH. Much of the developmental role falls to the MSSS (Quebec Ministry of Health and Social Services, 2017e). As stated in proposal 29 of the Gelineau report, "there is to be an integrated information system developed and maintained to allow for sharing of all information regarding blood transfusion from blood bank to patient" (Quebec Ministry of Health and Social Services, 1999). This proposal allowed for SIIATH-GS and SIIATH-ST to be implemented and is unique legislation to the province of Quebec. MSSS and Héma-Québec continue to make legislative revisions to improve the overall goal of providing safe and easy blood transfusions within the public system through SIIATH.

Funding Mechanism

SIIATH is publicly funded by the Quebec government. Canadian provinces fund their health care systems through provincial tax revenue and federal government funding (Laberge et al., 2022). The costs for implementing and sustaining the SIIATH system are charged to the Quebec Transfusion Safety and Blood Products Activity Center, which covers workforce costs, SIIATH maintenance and support, and transfusion medical needs along with other miscellaneous charges (Quebec Management Standards and Practices, 2005).

> SIIATH's goal is to "connect all the components of the health and social network and thus contribute to maximizing the safety of the blood system."
>
> *Fonctionnement- Biovigilance-professionnels de la santé- MSSS, 2017*

Structure

SIIATH are MAK-SYSTEM applications that allow for data exchange between Quebec's public health care system and blood distribution centers. The SIIATH-ST application is called eTraceLine, and the SIIATH-GS application is named eProgesta (MAK-SYSTEM, n.d.). Together, they are structured to allow easy access to blood transfusion information. These tools trace all blood products, aid in blood inventory, and provide patient blood transfusion history. Thus, SIIATH connects all components of the blood system in Quebec (Quebec Ministry of Health and Social Services, 2017c). The SIIATH-ST web application enables providers to access to important patient information, including patient blood type, previous transfusion history, past transfusion reactions, and patient antibodies. SIIATH is easily accessible to all hospital systems integrated within the Health and Social Services Network (RSSS). For SIIATH-ST access, providers must navigate to the extranet site on a workstation that is

connected to the Integrated Multimedia Telecommunications Network (RITM) or have remote token access (TI MSSS, 2016a). Through this site, health care providers have access to 22 separate health care assets, including both SIIATH-GS and SIIATH-ST applications.

System Challenges and Successes

Due to the lack of publicly available information regarding SIIATH, it is difficult to obtain details about the successes and barriers of the system. However, its continued use for over a decade is indicative that the program has been a success overall.

Conclusion

The universal access and utility of SIIATH throughout the Quebec health care system make it a useful model for how a RBCAX might be developed in the United States. SIIATH highlights the need for developing an integrated blood information system. Selecting a web-based application that is secure and easily accessible to health care providers, and selecting a data exchange application that is compatible with other blood data systems, are necessary to create an integrated exchange. Providing space for constant stakeholder feedback and engagement during each step of the exchange process will also ensure success.

Canadian Provincial Blood Coordinating Offices

While Quebec is the only identified province to have an RBCAX, other Canadian provinces have systems in place that collect blood data as part of hemovigilance protocols (BC Provincial Blood Coordinating Office, 2021). These systems are not used to provide clinicians data regarding patient clinical histories for treatment purposes, however, as their primary function is to inform officials of how to optimize Canadian blood resources (Shih, 2023). For example, the British Columbia Provincial Coordinating Office's (PBCO) Central Transfusion Registry (CTR) collects "blood disposition data" and acts as a large archive for transfusion and blood product records (UBC Centre for Blood Research, 2023). Its records include blood product type, blood product ABO, blood product Rh, recipient identifying information, recipient ABO, recipient Rh, institution information, adverse event type, adverse event description, and transfusion history (BC Provincial Blood Coordinating Office, 2020). This data warehouse then disseminates the information to provincial health departments to inform improvements in blood inventory management protocols. The provinces of Alberta, British Columbia, Manitoba, Nova Scotia, Newfoundland and Labrador, Ontario, and Saskatchewan all have PBCOs that act as liaisons between provincial partners, stakeholders, and government officials. While the PBCOs form a national collaborative network for blood information (UBC Centre for Blood Research, 2023), they do not function as provincial, territorial, or national patient blood information exchanges for treatment purposes.

Canada Health Infoway

Introduction

Canada does not have a national RBCAX; however, it has been developing a national EHR system since the early 2000s. The federal government aided this initiative by establishing an independent, not-for-profit corporation, Infoway, with an initial investment of CAD 500 million (Canada Health Infoway, n.d.-a). Core EHR components include patient registry, provider registry, diagnostic imaging system, drug information system, laboratory information system, and interoperability (Office of the Auditor General of Canada, 2010).

Background

Canada Health Infoway began operations in March 2001 (Canada Health Infoway, n.d.-a). The corporation's mission is to improve the health of Canadians by fostering national collaboration between the provinces and territories and accelerating the development, adoption, and use of innovative digital health solutions (Canada

> Canada Health Infoway primarily serves as coordinating center, investor, and knowledge exchange facilitator for all province and territory EHRs.
>
> *Gagnon, 2022*

Health Infoway, n.d.-a). Infoway's history can be divided into two phases: From its inception to 2010, the corporation focused on establishing national standards and supporting provinces and territories in the digitalization of their health records and in EHR implementation. In 2016, the focus shifted to advanced electronic medical records (EMR) and information system features, with investment in provider solutions and patient-centric systems, such as scheduling, e-prescribing, and patient summaries (Gagnon, 2022).

Infoway primarily serves as a coordinating center, investor, and knowledge exchange facilitator (Gagnon, 2022). In its role as a coordinating center, Infoway provides data standards, security, and privacy for EMRs to realize the goal of a national interoperable EHR system. These "base standards" are the building blocks of interoperability that localities can build upon to meet their own unique needs (Kalra & O'Reilly, 2022).

Governance

Infoway's governance structure includes provincial and territorial Deputy Health Ministers and the federal cabinet, whose appoints the Board of Directors (Gagnon, 2022). The Board includes representation from the federal government, the five regions of Canada, and the private sector (Gagnon, 2022). Infoway does not mandate a centralized governance structure for EHRs but rather allows provinces and territories to develop a structure that best meets their needs (Canada Health Infoway, 2021). For example, many provinces and territories adopted a role-based model of data governance in which "parties must determine what 'role' they play under the relevant privacy legislation to establish the applicable rules for collections, uses, and disclosures" (Canada Health Infoway, 2021). Unfortunately, this role-based data governance model poses challenges to developing interoperable solutions. This is discussed in greater detail later.

Legal/legislative

One significant challenge to the establishment of the national EHR system is the differences in health privacy legislation, which complicates interprovincial data sharing. For example, both Alberta and the Northwest Territories refer to "information managers" in their legislation, but these definitions are not identical so any agreements between the jurisdictions requires terminology clarification, which can be complex, expensive, and time-consuming. Additionally, the varying health privacy laws are complex to navigate, and stakeholders tend to conservatively interpret them for fear of unauthorized disclosures, financial penalties, and damaging patient trust (Canada Health Infoway, 2023).

The consequence of varying privacy laws and data governance structures across the country has increased the burden on stakeholders as they attempt to develop a national EHR system. In an interoperable environment, more than one custodian may be responsible for the data or play multiple roles. Lack of standardized data agreements, unclear roles and responsibilities for vendor management, and varying data residency policies also further complicate the development of an interoperable environment (Canada Health Infoway, 2023).

The passing of the Personal Information Protection and Electronic Documents Act (PIPEDA) in January 2021 marked a significant milestone in the legal framework in the development of national interoperable EHRs in Canada. While PIPEDA is primarily focused on personal information protections, it has established crucial infrastructure for EHR system development. All entities that collect, use, or disclose personal information of any kind are subject to PIPEDA, unless the province or territory in which the business is based has its own "substantially similar" legislation. However, any organization that operates interprovincially must comply with PIPEDA regardless of whether its jurisdiction has substantially similar privacy legislation (Office of the Privacy Commissioner of Canada, 2019).

Structure

Infoway and the Expert Advisory Group for the Pan-Canadian Health Data Strategy proposed a shift from a custodian-based privacy structure to a data stewardship model in an attempt to deal with the challenges. The new model shifted from health care providers as data custodians to a patient-centered data access authorization (Canada Health Infoway, 2023; Canada Health Infoway, 2021). However, while the stewardship model will ease some implementation hurdles, legislative changes may still be required. Currently, the concept of data stewardship is not addressed or defined in Canadian legislation or policy as most health data privacy laws were not created for the current digital age (Canada Health Infoway, 2021). Consequently, transitioning from a custodian-model of data governance to a patient-centered stewardship model will require the federal, provincial, and territorial governments to agree upon definitions and collaborate to standardize data privacy and governance structures.

Funding Mechanisms

Infoway funds a majority of EHR planning and implementation with provinces responsible for maintenance or ongoing operations costs (Bell Browne Molnar & Delicate Consulting Inc., 2021). Infoway and provinces initially split the costs of planning and implementation equally, and money was not tied to meeting milestones. However, provinces were unable to shoulder 50% of the costs, causing significant delays (Arksrez, 2010). Infoway now invests up to 75% and 100% of provincial and territorial projects, respectively, if the EHR Solution Blueprint interoperability framework is followed. Infoway uses a gated funding model, wherein the release of funds is linked to the achievement of mutually agreed-upon milestones. Infoway's investment is fixed, and provinces and territories assume any risk of paying in full for costs above the initial budget (Canada Health Infoway, 2016). Table 3 depicts implementation investments in two provinces and corresponding Infoway monies.

Table 3. Implementation Investments of EHR Solutions in Quebec and Saskatchewan and Canada Health Infoway

Province/Territory	Total Cost	Province/Territory Investment	Infoway Investment
Saskatchewan	CAD 32.5 million	CAD 10 million[1]	~CAD 24.4 million
Quebec	CAD 563 million	CAD 259 million[2]	CAD 303 million

[1] Does not include development of additional system components.
[2] Does not include local implementation costs, security framework developments, physical infrastructure updates, and staff training.
Sources: Gagnon, 2022; Canada Health Infoway, 2015

There is limited available information regarding ongoing maintenance costs. However, in 2010, the Office of the Auditor General in British Columbia estimated that the maintenance costs for its EHR solution would be CAD 727.4 million (Office of the Auditor General of British Columbia, 2010). In the province of Alberta alone, from FY 2016/2017 through FY 2018/2019, the total costs for maintenance and ongoing operations of the EHR solution was CAD 296.1 million (Ernst & Young LLP, 2020).

> Engagement of infrastructure users, such as clinicians, patients, and vendors, is key to the successful implementation of new information exchange software.
>
> *Buckeridge, 2021*

Stakeholder Engagement and Cooperation

In the early stages of the integrated EHR process, Infoway and jurisdictions did not engage end users (e.g., clinicians, patients, the public, and vendors) in the development and implementation of their solutions (Buckeridge, 2021; Gheorghiu & Hagens, 2016; Rozenblum et al., 2011; Salzberg et al., 2012; Zimlichman et al., 2012; Zinszer et al., 2013). This oversight led to low uptake of EHR solutions, stalling interoperability (Almoaber & Amyot, 2020).

Infoway has since engaged a variety of stakeholders to develop the EHR Solutions Blueprint, which provides priorities, measurable goals and targets, and a roadmap for development of the various components of an EHR (Canada Health Infoway, 2016). Additionally, Infoway has released toolkits and guidance on how jurisdictions should engage stakeholders (Canada Health Infoway, 2012b). Infoway also conducts annual surveys, such as the Canadian Digital Health Survey, to understand and engage various stakeholders. The corporation also launched the Digital Health Learning Program to improve digital health literacy among providers and the public (Canada Health Infoway, 2021).

> The Infoway initiative did not have a well-formulated strategic plan or planning process before launching. Important stakeholders, such as health care professionals, were also not engaged in the planning process to ensure the EHR system would meet their needs.
>
> *Electronic Health Records in Canada: An Overview of Federal and Provincial Audit Reports, 2010*

Decision and Implementation Processes

Implementation plan

While Infoway developed two EHR Solutions Blueprints, one in 2006 and an updated version in 2016, jurisdictions must refine and develop their own implementation strategies. In a review of federal and provincial audit reports, the Auditor General of Canada reported that most of the provinces that had been reviewed struggled to develop an implementation plan (Canada Health Infoway, 2016). Several provinces also found monitoring costs and timelines a challenge. The audit concluded that the EHR initiative did not have a well-formulated strategic plan or planning process before launching. Important stakeholders, such as health care professionals, were also not engaged in the planning process to ensure the EHR system would meet their needs.

Data standardization

Prior to the release of the Solution Blueprints, Infoway provided certification services to ensure health information solutions met their privacy, security, and interoperability standards. Infoway also offers pre-implementation certification of various EHR components, such as drug information systems and diagnostic imaging systems (Schmidt, 2016). These data standards for interoperability are released through their InfoCentral website. However, standard adoption is not mandatory, which is an ongoing barrier to implementation. Provincial health care systems often prioritize achieving provincial interoperability over national interoperability, which has hindered the latter due to incompatibility (Ministry of Health and Long-Term Care and eHealth Ontario, 2016; Gagnon, 2022). Initially, vendors saw no demand for health information solutions that met Infoway's standards, which stalled standards-based solutions development (TECHNATION, 2021). However, progress is being made: in March 2022, Infoway held the first Pan-Canadian Projectathon for the pan-Canadian Patient Summary (Canada Health Infoway, 2022b), a collaborative effort to validate Infoway data standards. These base standards will allow different components of the patient summary, such as radiology, cardiology, and pathology, to be interoperable (Farkas, 2022).

Evaluation

Infoway and provincial and territorial governments utilize the Infoway Evaluation Framework (Figure 2). This framework is made up of three quality dimensions (system, information, and service). All quality dimensions focus on two system usage dimensions (use and user satisfaction) that impact three net benefit dimensions (quality, access, and productivity) (Canada Health Infoway, 2012a). This framework aims to establish the relationship between Infoway's investments and its resulting benefits. The published technical report contains a complementary framework tool that includes detailed measures, indicators, and methodology, and which allows provinces and territories to choose the methods that best fit their evaluation goals (Canada Health Infoway, 2012a).

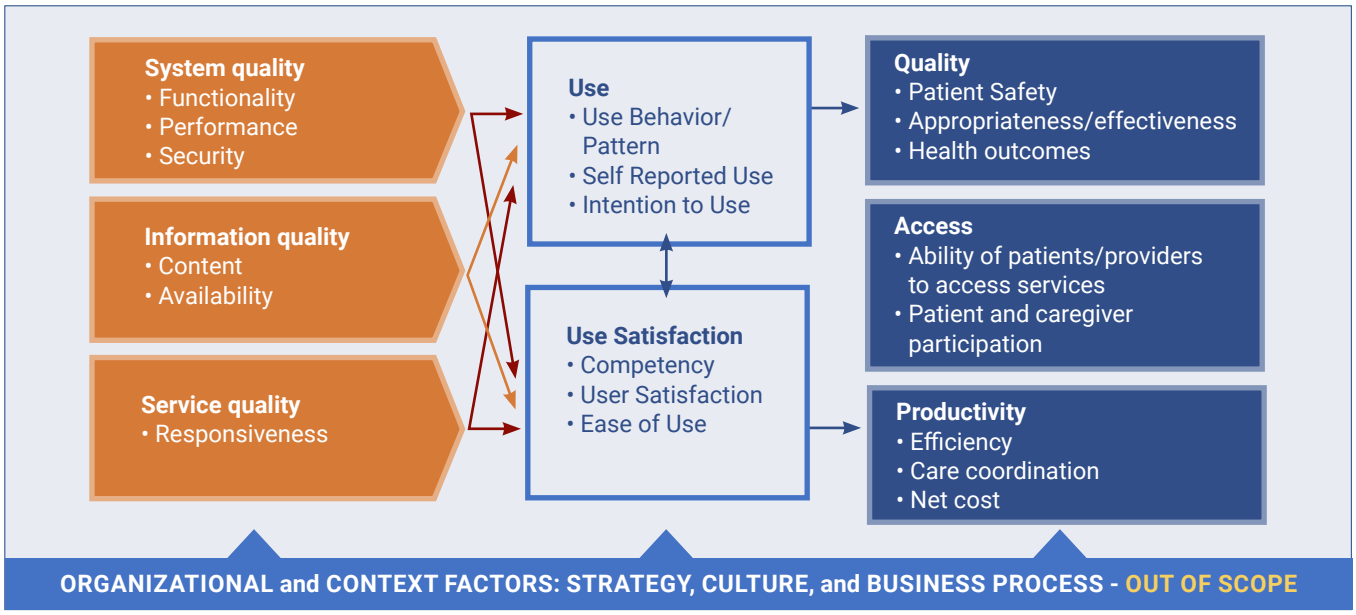

Figure 2. Infoway Evaluation Framework

The methodology for three examples is summarized below.

- In 2018, Infoway released evaluation findings reporting on the cost and time-saving benefits of successfully implemented provincial and territorial EHRs (Canada Health Infoway, 2018). The results were based on key informant interviews, literature reviews of published research, and previous benefits evaluation studies conducted by Infoway.
- In 2022, Infoway utilized a mixed methods approach to release a report that aimed to confirm the need for improvement of interoperability in health care. It investigated current infrastructure and how it could be improved, potential gaps in interoperability and care, and how Canada stands relative to international initiatives (Canada Health Infoway, 2022a).
- In 2019, a time and motion study was conducted to assess the Panorama Immunization module in Quebec (Canada Health Infoway, 2019). It utilized a mixed methodology and had a similar approach to the other two reports. Objectives include stakeholder perceptions of the module implementation and benefits, end users' experience with the module, and the module's impact on productivity.

Infoway is not perceived as a policy-setting authority. Instead, it provides suggested EHR standardizations that act as foundational "building blocks" when developing the national system.

Kalra & O'Reilly, 2022; Rozenblum et al., 2011

System Successes

Since incorporation in 2001, Infoway has utilized institutional knowledge and feedback to adapt its approach to system implementation. This adaptability is illustrated through its increased stakeholder engagement. Infoway, criticized in the past for its poor engagement of clinicians and patients, collaborated with a diverse group of stakeholders during its development and deployment of PrescribeIT, a nationwide e-prescribing service, to ensure this product would meet the needs of its end users (Canada Health Infoway, 2022c). PrescribeIT is now live in six provinces, and memorandums of understanding have been signed with the remaining jurisdictions (Newfoundland & Labrador Centre for Health Information, 2020).

Infoway has played a significant role in the successful digitization of health care for many Canadians. In March 2018, Infoway attained an average pan-Canadian EHR availability of 95.3% with an estimated 191,000 monthly users of two or more clinical domains (Bell Browne Molnar & Delicate Consulting Inc., 2021). Infoway, through its EHR standardization efforts, established a comprehensive national approach that set the foundation for interoperability and collaboration across provinces and territories.

System Challenges

There are variations in data privacy regulations across Canada, and navigating these is a significant challenge to full implementation of a national EHR system. The lack of clear guidance and education regarding permissible use and disclosure of patient health information has led to a "data freeze," in which stakeholders conservatively interpret data privacy laws and regulations and are risk-adverse, restricting access to authorized individuals and inhibiting clinical care, decision support, and research (Canada Health Infoway, 2023).

Infoway is not perceived as a policy-setting authority (Rozenblum et al., 2011). Infoway has approached standardization by suggesting EHR "building blocks" that are foundational to developing a national system; provinces and territories can then build upon this foundation to meet their specific needs (Kalra & O'Reilly, 2022). As previously mentioned, Infoway also offers certification services for vendors that confirm their solutions and meet Infoway's standards (Canada Health Infoway, n.d.-a). However, Infoway does not require jurisdictions to adopt these standards, leading to jurisdictions selectively choosing which standards they adhere to. Infoway does not have the capability to mandate standard adoption, which has stalled progress towards a national interoperable system.

Conclusion

Several measures can help ensure successful implementation of an EHR system. Using a gated funding approach and involving vendors and end users in the early stages of development can generate stakeholder interest in the system's progress. To ensure accountability and governance, clear structures should be established to track expenditures and the timeline of implementation. Since privacy laws can differ in small but significant ways across jurisdictions, it is helpful to institute standard terms and definitions to facilitate data system interoperability and scalability. A coordinating body, such as Infoway, can help with data standardization, but it is essential that this entity be able to enforce standards for the achievement of full-scale interoperability.

Established Cross-Border System

European Union eHealth Digital Service Infrastructure

Introduction

Currently, the European Union (EU) is working toward EU-wide expansion of MyHealth@EU, a cross-border eHealth digital service infrastructure (eHDSI). The pilot program, Smart Open Service for European Patients (epSOS), took place from 2008 to 2014, and its deliverables were used as the foundation of MyHealth@EU. In 2014, the EXPAND project was launched to secure the epSOS services and assist with transferring governance to the Connecting Europe Facility (CEF), which funded and implemented the program between 2014 and 2020 (Bruthans & Jiráková, 2023; European Commission, 2014; Regulation [EU] No. 1316/2013, 2013). In 2021, EU4Health was created as a means to support national health systems. It provides funding to support the implementation of MyHealth@EU, to assist in the ongoing expansion of the eHDSI (European Commission, n.d.-b). The European Commission (EC) aims for every member state to have implemented MyHealth@EU by 2025, for use by all EU citizens (European Commission, n.d.-a; Nalin et al., 2019).

Background

When launched in 2008, the epSOS pilot initially included 12 member states, then expanded to include 25 member states and 50 beneficiaries (European Commission, 2014). By the end of pilot testing, 16 sites had successfully tested live operations (Liden, 2014). Efforts to implement sustained system operations began in 2014, and as of 2023, 11 member states have established operational MyHealth@EU services (European Commission, n.d.-a). Expansion efforts to all EU member states continue at the time of this report's publication.

MyHealth@EU offers cross-border health care services including ePrescription, eDispensation, and Patient Summaries (European Commission, n.d.-a). ePrescription and eDispensation allow patients to obtain their prescription medications while located in a participating EU country outside of their home country. Patient summaries provide general patient information, such as allergies, current medication, previous illness, and surgeries, with plans to include additional information, such as medical images, lab results, and hospital discharge results (European Commission, n.d.-a). Included in this eHealth data exchange are patients who have consented to the inclusion of their data and who use facilities that employ MyHealth@EU services. Notably, the guidelines on patient consent to MyHealth@EU services currently varies by member state (European Commission, 2022b), although the cross-border directive 2011/24/EU specifies that sensitive information within the patient summary remain confidential and used in the patient's best interest (European Commission, 2022b).

Governance

As implementation efforts progressed during the pilot phase, several governing bodies and decision-maker groups were established. Table 4 summarizes these groups, their roles, and important contributions.

Table 4. MyHealth@EU Governing Bodies

Governing Body/Group	Roles and Contributions
eHealth Network (eHN)	Coordination, coherence, and consistency in eHDSI services • Created application guidelines for patient rights digital health domain decision-maker • Approves member states joining of MyHealth@EU
Joint Action to Support the eHealth Network (JASeHN)	Stakeholder collaboration resulting in recommendations for MyHealth@EU • Manages patients and HCP identification[1] • Limits access to patient data to HCPs • Use of National Contact Point for eHealth (NCPeH) as communication gateway between countries[2]
eHealth DSI EU Countries Expert Group (eHMSEG)	Nomination of managers from participating countries and NCPeH representation[3] • Implements eHDSI, including NCPeH coordination and operation, ensuring interoperability • Provides recommendations for member states to implement MyHealth@EU[4]
eHealth Operational Management Board (eHOMB)	Representation of the European Commission internal services • Oversees internal services • Makes operational decisions on the eHDSI, based on advice from eHMSEG members[4]

Table 4. MyHealth@EU Governing Bodies, continued

Governing Body/Group	Roles and Contributions
Digital Health Authorities (Designated by each member state)	Implementation and enforcement of eHDSI rules at a national level[5] • Safeguards citizens related to data sharing[5]

[1] Following Electronic Identification, Authentication and Trust Services (eIDAS) regulation (Regulation [EU], No 910/2014, 2014)
[2] Nalin et al., 2019
[3] Representation includes the legal working group, requirements working group, service desk community, key performance indicator (KPI) task force.
[4] Coyne & Jirakova, 2022; European Commission, n.d.-a
[5] Horgan et al., 2022

Legal/Legislative

The epSOS pilot operated under Directive 95/46/EC, which protects the processing and free movement of personal data, though the directive is not specific to the cross-border exchange of health data (Regulation [EU] No 1882/2003, 2003). Additionally, a framework of contractual agreements at the national level holds member states to the technical and legal requirements in place for epSOS operation (epSOS, 2014). Pilot deliverables included recommendations on legislation and regulation for the sustained operation of eHDSI services (epSOS, 2014). Therefore, the laws and regulations governing eHDSI services continue to evolve in conjunction with the development of the system.

In 2011, Directive No. 2011/24/EU, known as the Cross-Border Healthcare Directive, established EU citizens' right to patient health care in EU member states outside of their home country (European Court of Auditors, 2019; Palojoki et al., 2021). Recently, the EC proposed a regulation for "The European Health Data Space" (EHDS), which would involve a shift from the voluntary model of MyHealth@EU expansion to a mandatory one. For example, the EHDS regulation would require member state conformance to interoperability and security requirements for EHR systems and the appointment of a digital health authority in each member state (Bruthans & Jirakove, 2023). The proposed legislation is undergoing refinement (Horgan et al., 2022).

Data Ownership

Data included in MyHealth@EU services are owned by the data's origin location. Data sharing is intended to occur between EU member states; however, data is not meant to be modified by member states outside of the data's origin. It is recommended that patient data received from out-of-state sources not be stored for longer than required for treatment (Nalin et al., 2019).

Structure

The structure of MyHealth@EU was developed during the epSOS pilot (European Court of Auditors, 2019). Each participating member state has a NCPeH, which forms the communication gateway between all other participating member states (Staffa et al., 2018; Nalin et al., 2019). The NCPeH in each member state is connected to regional health information from the national and regional EHRs. Nalin and colleagues (2019) provide an example of this structure in Italy, where each region has a node that enables patient information sharing to the interregional contact node. The interregional node then connects to Italy's overarching NCPeH, which connects to all other countries with operational NCPeHs.

Staffing and Resource Requirements

The staffing and resource requirements for both the epSOS pilot and the MyHealth@EU implementation are substantial. Staffing is required to improve the structure and interoperability, as well as ensure the function of the services and assist in implementation, as described in the legal/legislative section. For these requirements, staff are needed at the EU level and within the member states, as described in Table 4.

Funding Mechanisms

Pilot and Implementation costs

The epSOS pilot program was partially funded by the Information & Communication Technology Policy Support Program, part of the EC's Competitiveness and Framework Program (Nalin et al., 2019). The total epSOS project budget was 38,111,769 euros. EU and industry partners both contributed about half of the budget funds (European Commission, 2014; Digitalhealth, 2009).

From 2015–2020, implementation of MyHealth@EU was partially funded by the CEF Telecom Program, with funds specifically designated for NCPeHs set-up, per a 2013 regulation (Regulation [EU] No 1316/2013, 2013). Historically, CEF covered 75% of the costs for member states to build National Contact Points for eHealth. This had a maximum subsidy of 1 million euros; additional costs were acquired by the member state. However, some member states reported that the maximum subsidy funding was inadequate (Piha et al., 2022). From 2021 through 2027, the EU4Health Program is providing partial funding for National Contact Points for eHealth, per a 2021 regulation (Regulation [EU] 2021/522, 2021). The exact amount of funding provided by EU4Health was not identified. Member states are also responsible for the connection of hospitals to the eHDSI services within their country, but costs for this were not identified (Piha et al., 2022).

The implementation of MyHealth@EU at the EU level has proven costly, with estimates for a partial completion of MyHealth@EU ranging between 165–414 million euros for full deployment and operation of services, including investments and maintenance costs, for over 10 years (European Commission, 2022a). Slow implementation has been identified as a key contributor to high costs (European Commission, 2022a). Furthermore, considering the varying levels of EHR development among member states, some member states may require funding to enhance health digitalization, facilitating the establishment of NCPeHs.

System Development and Maintenance Costs

Member states are responsible for the maintenance costs related to NCPeH operation, but it is unclear if the maintenance costs are uniform across member states (Piha et al., 2022). In Portugal, the maintenance of the ePrescription service was estimated to be about 1 million euros annually between 2016–2020 (European Commission, 2022a). Additional costs of cross-border eHDSI services include system development project costs, such as KONFIDO and EXPAND. The KONFIDO project is designed to ensure that patient health data is exchanged securely across borders, adhering to all legal, ethical, and regulatory requirements, and protection of personal data (Coppolino et al., 2017). KONFIDO alone cost the EU 4,992,077.50 euros over 3 years, highlighting the high costs associated with the development of cross-border HIEs (European Commission, 2020).

Stakeholder Engagement and Cooperation

Stakeholder engagement and cooperation from market partners, member states, and end users were critical to the success of the epSOS pilot. Over 30 companies within the eHealth market contributed their knowledge and expertise to the project and did so for free (epSOS, n.d.-b). A dashboard was created to communicate project progress to stakeholders.

End users, including physicians, pharmacists, and patients, provided system use feedback during the pilot phase (Moharra et al., 2015; epSOS, n.d.-a). Patients whose data was included in epSOS services completed a questionnaire, and clinicians were asked to complete a questionnaire following each interaction with an epSOS

> EU member state stakeholder engagement and cooperation continue to be critical for the actualization of the European Commission's implementation goals.
>
> *Nalin et al., 2019*

patient. Interviews with health professionals were also conducted to evaluate their feedback regarding the availability, usability, and semantics of eHDSI services. Physicians reported that they felt that epSOS services could be implemented successfully into everyday clinical practice. They also identified areas for improvement: system response time, ease of use, and local system integration. Data reliability and service access difficulties were identified as barriers (Moharra et al., 2015). Additionally, "the patients testified positively towards using the epSOS services and thought it was a useful tool for the health professional" (epSOS, n.d.-a).

In the current implementation and expansion stage of MyHealth@EU, stakeholder engagement and cooperation continue to be critical to the realization of the European Commission's implementation goals. For instance, the success of a cross-border HIE relies on the participation of each member state. This includes compliance with international standards and digital health policies. Differing adherence and interpretation of standards and policies has been a barrier to implementation, but the EHDS proposal attempts mitigate these issues. Researchers suggest that end user feedback be used to construct an iterative process of service improvement; however, it is unclear if this has been instituted in the expansion process to date (Nalin et al., 2019).

Decision and Implementation Processes

Implementation Plan

> Differing interpretations and adherence to standards and policies has been a barrier to implementing a cross-border health data exchange system.
>
> *Nalin, 2019*

Both the epSOS pilot and the implementation of MyHealth@EU have received criticism related to insufficient planning. For instance, the epSOS pilot did not adequately account for the scope and scale of testing required to establish a robust proof of concept, resulting in limited live data exchanges. In 2018, the European Commission adopted a new eHealth strategy to include the expansion of eHDSI services, but this strategy lacked an implementation plan that included expansion timelines, expected results, and assigned responsibility for expansion milestones (European Court of Auditors, 2019).

Evaluation/Assessment

Upon epSOS pilot completion in 2014, the EC evaluated pilot success, including weighing program approach for interoperability and functionality (specific outcome measures for evaluation are unknown). Forty-three data set transfers (patient summaries and ePrescriptions) were carried out from 16 pilot sites. Although the number of live data exchanges was not considered robust, the European Commission accepted it as a valid proof of concept (European Court of Auditors, 2019; epSOS, 2014).

Additionally, the EC produced an impact assessment report on the expansion of MyHealth@EU in 2022 to accompany the EHDS proposal. The authors provided a list of proposed measurement outcomes for the expansion of eHDSI services. Those to be determined every 5 years were the percentage of citizens who have access to their EHRs and a measure of citizen satisfaction with services. Those to be determined annually were the number of member states operating MyHealth@EU routinely; the percentage of pharmacies utilizing MyHealth@EU services; and the percentage of hospitals using MyHealth@EU services.

Beginning in 2019, the European Commission has tracked several key performance indicators (KPI) for each member state with operational eHDSI services (Bruthans & Jirakova, 2023). Displayed in a publicly available dashboard, the KPIs include the number of member states with operational NCPeH; number of transactions between member states; number of ePrescriptions, eDispensation, and Patient Summaries exchanges; hospitals and pharmacies operational with MyHealth@EU services; laws and regulations affected and amended to enable

cross-border services interoperability; NCPeH uptime and downtime periods; and number of citizens who are potentially able to benefit from my MyHealth@EU services.

Data Standardization and Data Quality

The epSOS project involved the development of standardization and interoperability approaches for cross-border eHDSI services. This process involved mapping the coding system of each member state onto the coding scheme used by epSOS, an exacting and time-consuming task (Nalin et al., 2019). In 2019, a draft of the international patient summary standard (*prEN 17269 – The Patient Summary for Unplanned, Cross-border Care*) was approved with the goal of formalizing the data included in patient summary services and so facilitating standardization (Nalin et al., 2019). Implementation guidance *prTS 17288 – The International Patient Summary: Guidance for European Implementation Technical Specification* was also released to provide guidance on how to deploy the standard Patient Summary in Europe (Nalin, 2019). Other guidance includes the *eHealth Network Guideline on the Electronic Exchange of Health Data Under Cross-Border Directive 2011/24/EU, Patient Summary*, which provides guidance on coding to be used within patient summaries (European Commission, 2022b).

Data Security

To ensure that member states meet all nationally agreed upon standards and data security requirements, NCPeHs must undergo audits and compliance checks for information security and data protection. Audits are completed prior to operation and then every 3 years to remain in operation (Coyne & Jirakova, 2022).

Additionally, for a member state to implement MyHealth@EU legal background preparation, technical implementation, testing of technical function, a compliance check, "go-live" approval from eHMSEG, and other steps are required (Coyne & Jirakova, 2022). To continue operation, member states must also continue to fulfill several requirements, such as timely upgrades to new specifications, educating end users, testing communication with other member states, and maintaining involvement in eHMSEG (Coyne & Jirakova, 2022). These stringent requirements help ensure the security of the system and appropriate use of data.

System Successes

The epSOS pilot phase played a pivotal role in the establishment of the cross-border eHDSI structure, later developed into MyHealth@EU. This pilot phase served as a foundation for the subsequent implementation and expansion of cross-border patient information exchange. As of 2022, all member states that commenced MyHealth@EU operations in 2019 have successfully continued their operations. The dashboard of MyHealth@EU KPIs demonstrates many successful data transfers across several member states. Nevertheless, the implementation and expansion of MyHealth@EU encountered significant challenges along the way, and it has room to improve on EU-wide implementation.

System Challenges

The initial significant hurdle in the successful implementation of EU-wide eHDSI services emerged during the transition from the pilot phase to full-scale implementation, as there had been a failure to adequately plan for barriers (European Court of Auditors, 2019). Technical interoperability barriers due to differing EHR systems resulted in varying levels of system implementation success among member states. For example, in early 2019, some member states could send ePrescription information, while others could only receive it. Furthermore, certain countries could receive patient summaries but were unable to send them (European Court of Auditors, 2019). A lack of mandated interoperability between member states also proved to be a major barrier to expansion efforts. A 2019 paper reported that not all member states are aligned with the JASeHN agreement and eIDAS regulation (Nalin et al., 2019). In 2021, some member states did not have legislation to promote interoperability and had a lack of implementation guidelines and frameworks (European Commission, 2021). A 2022 report

revealed that there was no legislative support for the access and sharing of health-related patient data in almost one-third of member states (European Commission, 2022a).

Furthermore, member state participation in MyHealth@EU has historically been voluntary, contributing to slow implementation rates. According to the European Commission, the EHDS proposal will help to support increased interoperability by enacting appropriate legislation, potentially including required member state participation and implementation in eHDSI services (European Commission, 2022a).

Conclusion

Although not specifically an RBC antibody data exchange, the EU's epSOS pilot and implementation of MyHealth@EU services offer valuable insights that can be applied during the development of a national patient data exchange in the United States. This case study suggests that even when a project is well-funded, barriers such as the failure to develop a thorough implementation plan and mandated interoperability between EHR systems can dramatically hamper expansion and increase costs. By considering both the barriers and facilitators encountered, planners gain valuable knowledge to anticipate and address potential issues prior to implementation.

Established Regional Systems

Kansas City Antibody Registry

Introduction

Established in 1955, the Community Blood Center (CBC) of Greater Kansas, a Division of New York Blood Center (NYBC), Inc., currently serves more than 40 hospitals in over 70 counties in Missouri and Kansas (Community Blood Center, n.d.). In June 2008, CBC launched a service-area-wide registry to link patients and antibodies detected at CBC's immunohematology reference laboratory (IRL). The goal of the Kansas City Antibody Registry was to "assist transfusion services by providing information about patients with a history of antibodies, thereby reducing likelihood of DHTRs" (Schwickerath et al., 2010). Upon inception, 73[1] hospitals were included in the registry.

The Kansas City Antibody Registry links patient antibodies detected at CBC's immunohematology reference laboratory to hospitals located throughout Kansas and Missouri.

Background

Prior to initiating the registry, hospitals had been using CBC's IRL to run and confirm antibody testing; however, IRL staff observed transfusion delays caused by repeat testing and confirmation of known RBC antibodies. CBC, therefore, sought to create a patient registry to make historical antibody data readily available to practitioners (Schwickerath et al., 2010). The blood center staff worked with the local hospital relations staff, a web design company, and legal counsel to design and implement an antibody registry for the Greater Kansas City region (Schwickerath et al., 2010). A registry administrator performed overall project management. Figure 3 outlines the timeline of the registry's development and implementation.

[1] This number is larger than the number of hospitals currently being served by the CBC. This may be due to hospital consolidation or closures of rural hospitals.

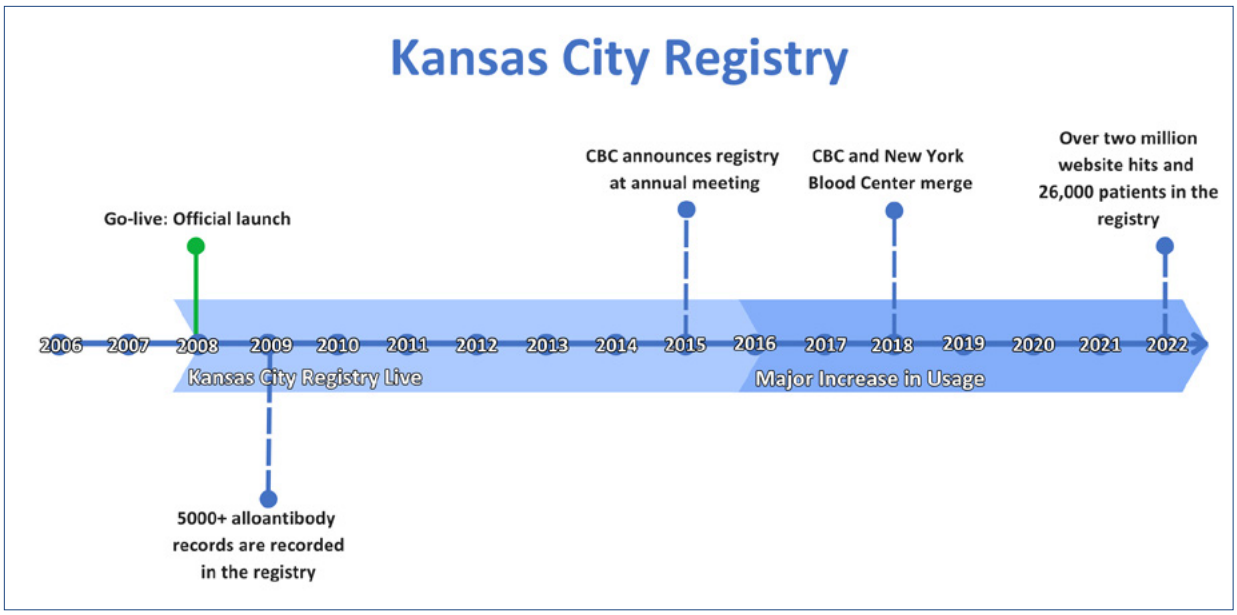

Figure 3. Kansas City Antibody Registry Timeline, 2006–2022

The Kansas City Registry was officially launched in June of 2008. In just 1 year more than 5 thousand alloantibodies were recorded in the registry. In 2015 the CBC announced the use of the registry system, which resulted in a major surge in usage starting in 2016. Then in 2018 the CBC was purchased by NYBC. By 2022 the Kansas City registry had over 2 million website hits and is still successfully allowing data exchange in Kansas and Missouri hospital systems.

Governance

Legal/Legislative

Several measures were established to ensure Health Insurance Portability and Accountability Act (HIPAA) compliance. All participating hospitals and partner entities, including the initial web design company and Hot-Spot Interactive, LLC (current registry host), signed a business associate agreement. Users are assigned IDs and complex passwords, and a monitoring system enables daily and weekly usage tracking. Furthermore, blood center staff undergo HIPAA training, and the web company has implemented policies and procedures to adhere to HIPAA security regulations (Schwickerath et al., 2010). For example, users must sign a HIPAA disclaimer when registering for an account and every time they log in to view or edit patient records (Jones, 2023).

Data Ownership

Data stored in the registry were originally owned by CBC. However, in 2018, NYBC acquired CBC and its registry (Community Blood Center, 2018). Following the sale, data ownership was transferred to Hot-Spot Interactive, LLC, which hosts and manages the registry site and holds a non-exclusive software license. While NYBC does not currently use the registry, it is still in operation in the greater Kansas City area and is increasing in patient numbers every year (Jones, personal communication, 2023).

Structure

The Kansas City Antibody Registry enables providers to search patient records—using last name and first name or data of birth, if available—for relevant blood screening information, including the date of testing, blood type, antibodies, antigens, special transfusion requirements (e.g., washed, irradiated), and relevant notes in the comment field. If available, genomics testing information and date of service may be provided. Search results also include the user who entered the data, their facility, and the time and date of entry. All data is logged and tracked in perpetuity. In addition, the registry enables information sharing among users, including technical bulletins, memos, and conference notes (Jones, 2023).

The registry has multiple tiers of access, enabling different types of users to view and/or change data, depending on their roles (Table 5). Protections, such as time and record limits, have been put in place to prevent unauthorized users from accessing data and to restrict the overall number of users. At the end of the time limit, users must enter their login credentials to regain access to the registry. An annual audit is conducted to verify registry users and remove inactive accounts (Jones, 2023).

Table 5. Kansas City Antibody Registry User Access Levels

User Type	Capability	Record/Time Limit
Super Admin	Add/edit/delete all content and users	Unlimited records/60 minutes
IRL User 1	Add/edit/delete all patient data and view reports	Unlimited records/60 minutes
IRL User 2	Add/edit/delete all patient data	Unlimited records/60 minutes
Hospital Admin (limited to about 3/facility)	Add patient data, edit facility information, view memos and forms	20 records/60 minutes
Hospital User	Search and view patient data, view memos and forms	5 records/15 minutes
Conference User	View conference notes only	
Hospital Accounting User	View and process (mark viewed) invoices	
CBC Accounting User	View and manage invoices	

Source: Jones, 2023

Users have 24/7 Internet access to the registry. Data entry is daily as new patient samples are evaluated. To ensure correct data entry, each step in data entry requires confirmation before progressing to the next screen and antibody information is entered in duplicate (Schwickerath et al., 2010).

> The Kansas City Registry ensures patient privacy by complying with HIPAA, requiring signing of business associate agreements, assigning patients unique IDs and complex passwords, training staff on security, and consistently monitoring website usage.
>
> *Jones, 2023*

Staffing Requirements

The registry administrator was responsible for overseeing the implementation process, including onboarding hospitals and processing access request forms for all users. The early implementation phase required nearly 100% of their time. As the number of users stabilized, the administrator dedicated 5–10% of their effort toward managing the registry (Jones, 2023). Additionally, an IRL technologist was hired, contributing approximately 5% of their effort to the project (Schwickerath et al., 2010).

Funding Mechanisms

Until its sale to NYBC, CBC funded the registry. The one-time start-up fees totaled around $22,000 (in 2010 dollars), in addition to the salary of the administrator. Web development is estimated to have cost $11,000, legal fees $3,000, and registry development $8,000. As of 2010, annual maintenance fees were approximately $900, not including the salaries of the administrator or IRL technologist. The monthly hosting fee at that time was $50 (Schwickerath et al., 2010).

Stakeholder Engagement and Cooperation

Engagement with the registry was influenced by word of mouth and marketing by CBC. There was an increase in users from 2016 to 2017 following an announcement at an annual workshop (Jones, 2023). Hospital staff sharing registry benefits and sharing instances when they did not check the registry prior to a transfusion, leading to negative health outcomes, also increased engagement (Jones, 2023).

Decision and Implementation Processes

Standardization and Data Quality

The registry relies on manual data entry. To ensure data quality, antibody information is entered in duplicate, and each data entry step requires confirmation before moving to the next screen (Schwickerath et al., 2010).

Evaluation

During the registry planning phase, a failure modes and effect analysis was undertaken to determine potential problems with the design and validation testing needs and to ensure data could be shared across hospitals and vendors (Schwickerath et al., 2010).

To assess the effectiveness of the registry, CBC analyzed unique user usage, hospital usage, and the number of DHTRs. During the registry's first year of operation, antibody records were entered and accessed more than 3,900 times by unique users; unique users accessed more than one patient record per week; and no incidents of HIPAA regulation misuse or abuse were reported (Schwickerath et al., 2010). By 2022, there were over 2 million website hits and 26,000 patients in the registry. Some patients had as many as nine antibodies listed at four different facilities. There were no security breaches from 2010 to 2022, but there was one HIPAA violation involving an administrator who shared unique login credentials with multiple laboratory technicians (Jones, 2023).

> While implementation of the Kansas City Antibody Registry provides patient safety benefits, it has also substantially reduced the volume of blood samples for laboratory evaluation. This has streamlined the transfusion process not only for patients but laboratory organizations as well.
>
> *Schwickerath et al., 2010*

System Successes

The Kansas City Antibody Registry has been successful in terms of ongoing operations, consistent funding, and stakeholder engagement. Its implementation has led to an overall increase in transfusion safety by identifying false-negative pre-transfusion serologic testing results and has prevented potentially fatal DHTRs. In its first year, the registry identified four cases among 1,766 patients (0.0023% of transfused patients) (Schwickerath et al., 2010). In addition, the volume of blood samples required for laboratory evaluation has decreased thanks to the registry, as has the turnaround time for providing compatible blood (Schwickerath et al., 2010).

System Challenges

The registry's primary challenge is scalability from regional to national. Much of the registry's daily operations are managed by one employee and are largely manual. This drawback may have played a role in current owner NYBC's decision not to expand the registry to the New York region (Jones, personal communications, 2023). It would be beneficial to integrate the antibody registry with the hospitals' laboratory information systems to enable seamless sharing of information and reduce the amount of manual labor required for data input (Jones, 2023). This integration could also allow additional patient information to be shared (e.g., medications, relevant patient histories, etc.), which would increase the value of participating in the registry.

Kansas City Antibody Registry System Successes

- Ongoing operations
- Consistent funding
- Stakeholder engagement
- Overall increase in transfusion safety
- Reduction in the volume of blood samples required for laboratory evaluation

Kansas City Antibody Registry System Challenges

- Scalability
- Antibody registry not integrated with the hospitals' laboratory information systems

Conclusion

The continued success of the Kansas City Antibody Registry, and the word-of-mouth promotion from stakeholders after avoiding adverse health outcomes, is promising for the future development of a national registry or exchange. The factors that contribute to its success include consistent leadership of a reputable organization, sustained funding, and stakeholder engagement. Although the registry's reliance on manual procedures limits its scalability, the case study serves as a positive indication that the involvement of a credible stakeholder can affect stakeholder participation and the registry reputation.

Wisconsin Statewide Health Information Network (WISHIN)

Introduction

WISHIN Pulse is an HIE program that enables data transference for a wide variety of health care providers and facilities. The program is operated by the Wisconsin Statewide Health Information Network (WISHIN), a nonprofit organization founded by the Wisconsin Hospital Association, Wisconsin Medical Society, Wisconsin Collaborative for Healthcare Quality, and the Wisconsin Health Information Organization (WISHIN, n.d.-f). WISHIN Pulse is used by over 2,000 health care providers located throughout Wisconsin, parts of Minnesota, Illinois, and Michigan, including cancer centers, clinics, community-based providers, correctional facilities, emergency medical services, hospitals, and pharmacies. There is also a connection to a site in New York and one in Virginia (WISHIN, n.d.-i). The system has enabled the collection of billions of patient records, including admit, discharge, and transfer notes, patient data reports and results, and Public Health Syndromic Surveillance data. Providers can also access Wisconsin's prescription database through this system, and its direct messaging solution allows for the exchange of patient information between health care providers, regardless of affiliation (WISHIN, n.d.-c.; WISHIN, n.d.-d.).

Background

Wisconsin's statewide HIE program was conceptualized in 2009 after receiving an award granted to Wisconsin Relay of Electronic Data for Health (WIRED for Health) to encourage and support the use of EHRs among providers in an efficient and secure manner (HealthIT.GOV, 2019; WISHIN, n.d.-a). During WISHIN Pulse's development, the Wisconsin Department of Health Services (DHS) selected it as the designated entity for implementing statewide HIE (Wisconsin Legislative Council, 2010; WISHIN, n.d.-a). The WISHIN Pulse plan was approved by the federal ONC in December of 2010 and remains in operation (WISHIN, n.d.-a). The system enables health care providers to communicate, store, and transfer patient data through a HIPAA-compliant platform (WISHIN, n.d.-e).

Governance

Legal/Legislative

James E. Doyle, former governor of Wisconsin, formed the WIRED for Health board by signing Executive Order #303 and obtaining approximately $9.4 million to develop and implement SOPs for a statewide HIE (Wisconsin Department of Health Services Office of the Secretary, 2010; Doyle, 2009). After enacting Wisconsin Act 274,

the nonprofit organization WISHIN was selected to be the state-designated entity to govern the HIE (Wisconsin Legislative Council, 2010). In addition to support from ONC for WISHIN Pulse development, 2019 Wisconsin Act 185 enabled health care providers to receive incentives sufficient for a 2-year subscription to WISHIN Pulse services (Wisconsin Legislature, 2020; WISHIN, 2023). Act 185 both encouraged provider participation in the statewide EHR service and improved WISHIN's sustainability (ProPublica, n.d.; WISHIN, 2023).

To maintain patient data, WISHIN Pulse must meet certain standards, including federal and state laws (WISHIN, n.d.-b). These include HIPAA and Wisconsin statutes 146, 51, and 252, which require patient consent, the protection of sensitive information, and patient confidentiality, with few exceptions (WISHIN, n.d.-b). The WISHIN Board is required to report annually to the Wisconsin DHS Secretary and submit yearly SOP updates to ONC (WISHIN, 2012a; WISHIN 2012b). Furthermore, the State Health IT Coordinator continually verifies that WISHIN Pulse is compliant with state regulations (WISHIN, 2012b).

Data Ownership

Patient data stored in WISHIN Pulse is considered the property of the health care provider (WISHIN, 2014). Patients serviced by WISHIN Pulse participants are automatically enrolled into the WISHIN system and may opt-out of the system at any time by completing a Patient Choice Form (WISHIN, n.d.-g). Opting out prevents health care providers from sharing patient information via WISHIN Pulse; however, it does not remove previously uploaded patient data, which may be accessed in emergency situations or reported to public health departments (WISHIN, 2014). Additionally, to ensure privacy, security, and confidentiality, health care providers that utilize Direct+ (direct messaging through WISHIN Pulse) are assigned direct addresses, and communications are managed by Health Information Service Providers (WISHIN, n.d.-d). Account access also requires two-factor authentication and data security that abides by federal and state laws.

> WISHIN patient data is considered the property and responsibility of the health care provider.
>
> *WISHIN, 2014*

Funding Mechanisms

WISHIN was initially supported by a $9.441 million award granted as part of the American Recovery and Reinvestment Act of 2009 (Office of the National Coordinator for Health Information Technology, n.d.). These funds were distributed from 2010 through 2014 to assist with the implementation of statewide HIE (Department of Health and Human Services Office of the Secretary, 2010).

As part of the 2012 SOP update, WISHIN proposed different pricing structures for physicians, hospitals, and health care payers (WISHIN, 2012b). Under these structures, physicians paid a monthly subscription fee of $100, and non-clinical users employed by the physician were provided access at no additional charge. The pricing structure proposed for hospitals was variable to account for differences in hospital size and patient turnover. In this model, hospital subscriptions were determined based on net patient revenue, including both inpatient and outpatient procedures. Finally, health care payer pricing was dependent upon the number of members they serviced, with each member costing a flat rate of $1–$2 per year. At the time of the 2012 SOP update, WISHIN identified potential support mechanisms through the Medicaid Federal match program and the Department of Employee Trust Funds, as it met criteria required by both mechanisms (WISHIN, 2012b).

Increases to program services occurred in 2020, correlating to the enactment of the 2020 Wisconsin Act 185, which required the Wisconsin DHS to initiate a pay-for-performance (P4P) incentive program to support hospitals participating in WISHIN Pulse (WISHIN, 2023). The support provided by the program is based on the volume of Medicaid claims, with a maximum incentive of $120,000 per hospital per year, potentially supporting more than 6 years of a hospital WISHIN subscription (WISHIN, 2023). As of January 2023, approximately 120 hospitals have benefitted from the P4P program.

Stakeholder Engagement and Cooperation

Initial stakeholder engagement was driven by including various entities during SOP development. Representatives from other HIE organizations, network plan board members, health care providers, higher education, Wisconsin government, federal government, and more were included when developing the initial SOPs, and many remain involved in the WISHIN board (WISHIN, n.d.-a, 2012b). WISHIN has now formed 18 partnerships with various companies spanning from technology to health care (WISHIN, n.d.-j).

Initial uptake of WISHIN Pulse appears to span the entirety of the state, with over 43 counties and 90 organizations having subscribed to the HIE by November of 2013 (*WISHIN Pulse Pioneers*, 2013). As of 2023, WISHIN Pulse has expanded to include several locations in Minnesota, Michigan, Illinois, and Iowa, one location in New York, and one location in Virginia, and involves a wide variety of health care professionals and payers (WISHIN, n.d.-d; WISHIN, n.d.-i).

Decision and Implementation Processes

The original Wisconsin HIE implementation process was designed by WIRED for Health and implemented by WISHIN beginning in 2010 (WISHIN, n.d.-a). Implementation was divided into two phases (Office of the National Coordinator for Health Information Technology, n.d.). Phase one of the implementation plan prioritized uptake of the WISHIN Direct+ messaging system. Leveraging the Wisconsin Medical Society provider directory, WISHIN worked alongside regional entities to identify, train, and provide technical assistance to providers interested in WISHIN Direct+. Additionally, this phase expanded upon the Wisconsin Medical Society provider directory to include additional types of providers. Phase two continued to build the foundation of WISHIN Pulse services by expanding the provider registry to include patients and payers (Office of the National Coordinator for Health Information Technology, n.d.). This phase also involved strengthening security features, providing gateways to federal partners, and supporting public health connectivity.

System Successes

WISHIN has overcome several barriers, including lack of support and trust in HIE programs, initial investment costs that could be burdensome for smaller health care providers, and lack of internet connectivity for some providers attempting to join the WISHIN network (WISHIN, 2012b). WISHIN gained trust in the HIE network through stakeholder meetings and inclusion in the WISHIN board (Wisconsin Legislative Council, 2010). Pricing models accommodated organizations of all sizes by offering different structures based on requirements and patients served (WISHIN, 2012b). Additionally, state incentives provide support to health care clients with Medicare patients, further enhancing the affordability and accessibility of the pricing model (WISHIN, 2023). Finally, while WISHIN is still limited to clients with internet accessibility, connectivity continues to expand across the state. Thanks to these efforts, WISHIN Pulse has experienced rapid growth and is now serving diverse types of client sites, including those across state lines and several Veterans Administration health care sites. This self-supporting system continues to incorporate new services and client sites.

System Challenges

Despite these successes, there are several barriers yet to overcome. Currently, one of the largest hurdles preventing WISHIN from becoming a national service is state variations in laws dictating patient data privacy and data security measures (Wisconsin Legislature, 2020; WISHIN, n.d.-b). While Wisconsin has been able to accommodate variations in Minnesota laws, expanding interoperability to additional states would require additional security features. This issue also presents a challenge to expanding to include national organizations such as the Red Cross, which recently identified the lack of patient data transference as a factor increasing the time required to obtain blood transfusions (Narayanan et al., 2022).

Conclusion

In conclusion, WISHIN Pulse provides an example of a statewide HIE that has accommodated a variety of communities and is beginning to navigate additional state requirements to expand its service nationally. It provides health care providers with safe, secure, and fast access to patient information to improve patient care and health care management. While it does not function as an RBC information exchange and is not yet coordinated with national blood suppliers such as the Red Cross, it can serve as a positive example of HIE implementation and sustainability.

Attempted Regional Systems

Georgia Pilot Red Blood Cell Antibody Exchange: Lessons Learned

Introduction

In 2015, the Georgia Health Policy Center at Georgia State University received a CDC grant to study transfusion-related complications in patients with SCD and thalassemia (Georgia Health Policy Center, 2015). One of the purposes of the grant was to demonstrate the feasibility of an RBCAX in Georgia (Josephson, personal communication, April 14, 2023). The pilot program began with several hospitals, health systems, and blood banks in the metro Atlanta area, including Emory University Hospital, Grady Health System, and Augusta University Health, which serves the eastern part of Georgia. The goal was to expand the exchange to other health systems in Georgia after the pilot program was completed. However, stakeholder buy-in proved difficult to obtain, and the pilot was not implemented.

Background

A third-party vendor, the National Patient Antibody Registry (NPAR, n.d.), was brought in to complete the technical work of creating the exchange. The exchange was designed for the uptake of historical patient transfusion data from any hospital in the network to a remote server. This would allow all other hospitals within the exchange to access and retrieve the relevant information. Blood banks and blood centers would also be able to add patient data to the cloud. Initially, the exchange was only going to include antibody data and patient identification information, but some stakeholders identified a need to capture phenotype and genotype data. The third-party vendor was open to adding more fields given that the data could be properly validated.

Stakeholder Engagement and Cooperation

User hesitancy was the primary obstacle to the exchange reaching the implementation phase. Significant effort was made to obtain buy-in from the hospitals and health systems that would be involved in the pilot. The CDC grant provided substantial funding for pre-implementation activities, which included multiple meetings with stakeholders. Physicians and administrators were supportive of the pilot exchange; however, there was hesitancy due to set-up costs, even with the grant funding. Moreover, hospital IT staff expressed uncertainty about security safeguards needed to protect patient information (Josephson, personal communication, April 14, 2023).

> The primary obstacle that prevented implementation of the registry was user hesitancy. Utilizing bottom-up program implementation has historically led to program success.
>
> *Josephson, C., personal communication, April 14, 2023*

User Perspectives

The Georgia pilot planners interviewed patients with SCD to gather their perspectives regarding an RBCAX (Lawrence et al., 2020). Most participants expressed that they would find a data exchange helpful, particularly in situations where they require care at a new hospital during a health crisis. While the participants identified data security as a concern, they stated that the current patient cards with their antibody information could also be stolen or lost. Many patients were interested in having their data available on a smartphone app that could be taken to new medical settings (Josephson, personal communication, April 14, 2023).

Conclusion

Despite funding from the CDC and support from physicians and patients, the pilot RBCAX in Georgia was unable to progress beyond the initial buy-in phase. The technical challenges with the hospital IT departments could not be overcome at that time. Hospital IT staff are important stakeholders and are responsible for the safety of patient data. As EHRs become more commonplace, it may be possible to alleviate their concerns and transmit transfusion data safely, securely, and correctly between hospital systems.

Santa Barbara County Care Data Exchange: Lessons Learned

Introduction

The Santa Barbara County Care Data Exchange, also known as the "Santa Barbara Project," was a public-private HIE project designed to connect three hospital systems in Santa Barbara, Santa Maria, and Lompoc to improve health care for Santa Barbara County's 400,000 residents. With a 3-year $10-million grant, the project was initiated and funded in late 1998 by the California HealthCare Foundation (CHCF) to facilitate the sharing of patient data among hospitals, physicians, ancillary centers, health plans, public health entities, and consumers. Data to be exchanged in the system included personal health information; reports and results reporting; findings and treatment advisories; test orders; eligibility, enrollment, and authorization; as well as case reporting and population reporting (Brailer et al., 2003). Although implementation was briefly achieved, the project faced several challenges and was shut down in December 2006.

Governance

The Santa Barbara Project was initially governed by the Care Data Exchange Council, which received counsel from advisory committees of technical experts and clinical leaders. CareScience was engaged by CHCF to lead program management efforts, which included disbursing funds, organizing participants, setting up and staffing governance structures, certifying, and contracting software vendors, and addressing barriers. In 2003, Quovadx acquired CareScience, and in 2004, the Santa Barbara Project nonprofit was created to assume governance and administrative functions (Miller & Miller, 2007).

Key Constraints

An early obstacle involved ensuring that the proposed exchange would comply with all relevant privacy laws. A legal firm specializing in health law was engaged to make this determination; however, the task proved to be more complex than anticipated. The necessary privacy assurances were made but only after the expenditure of significant time and expense (Fried, 2007).

Vendor-related technology delays proved to be a major challenge throughout the process. Many of the provider organizations' systems were not capable of joining the network. An early attempt to use off-the-shelf software failed, and adapting existing technology to accommodate these older "legacy" systems was more difficult than anticipated. As these issues arose, CareScience took on the role of software developer and vendor, in consultation

with experts who could help develop a prototype of key software elements. However, development took place largely by trial and error, creating significant delays.

Funding and vendor limitations were another key constraint. While the exchange was developed with CHCF grant money, there was no clear plan for how to sustain the system. More than half of the $10 million was applied to the development of interfaces between the Santa Barbara Project and the legacy systems. Separate from the CHCF funds, it is estimated that CareScience's net investment ranged from $5–11 million. The company's lack of profitability became a concern to its investors, forcing CareScience to scale back on the Santa Barbara Project's software development efforts midway through the process. The company was acquired by Quovadx, who improved the repository's interface, consistency across organizations, data integration, and confidential data screening.

By September 2005, the system was able to share 10 types of data among eight organizations; however, confidence in the project was waning. The transition from CareScience to Quovadx necessitated the creation of new participant and vendor contracts. Obtaining agreement was challenging because none of the stakeholders wanted to assume liability in the event of improperly exchanged data. For example, the dominant lab (Quest Diagnostics) would not sign an agreement (Miller & Miller, 2007).

Lack of community leadership was another hindrance to the project. There was no community development prior to the system's implementation, and participants were not expected to bear any of the cost, making their involvement passive. Although the initial grant had stimulated substantial stakeholder interest because it lowered the burden of participation, this lack of up-front investment by health care providers and labs also lowered their tolerance for risk as challenges arose (Miller & Miller, 2007).

By the time the system was implemented, the community's health care organizations no longer perceived enough benefit to justify involvement. At the outset, providers had expected the exchange to enable viewing of data they could not already access. Yet when the system finally went live, the shared data was largely available to providers through other outlets. As challenges mounted, time passed, and the benefits of participation became unclear, the credibility of the project came into question (Miller & Miller, 2007).

Santa Barbara Summary of Key Constraints

- Unanticipated legal complexities involving patient privacy
- Lack of sustained funding
- Vendor-related technology delays
- Liability concerns
- Failure to establish an agreement with the dominant lab
- Lack of community leadership
- Lack of momentum and credibility
- Lack of compelling value proposition to stakeholders

Conclusion

In December 2006, the Santa Barbara Project was shut down due to several mounting problems, including lack of sustained funding, difficulties determining liability, technology delays, and lack of community leadership. Despite these, the project created the infrastructure and agreements to exchange limited data and tested the exchange of additional data. Its failure highlights the importance of addressing key constraints during pre-implementation to ensure the success of future HIE projects.

CHAPTER 4: DISCUSSION

The benefits of establishing a national RBCAX are clear. In addition to the improvement of individual health outcomes, particularly among those in underserved communities, an exchange would enable the creation of an important data set for clinical research to develop a deeper understanding of blood disorder epidemiology and clinical phenomena such as antibody evanescence. An exchange would foster opportunities to inform caregivers and patients about the impacts of RBC antibodies on their treatment, enabling them to make informed decisions about their own care. Furthermore, by having the ability to verify their own transfusion histories and antibody data, patients from underserved or marginalized communities could be taken more seriously by medical professionals who are new to them.

It is important to acknowledge the substantial work that has already been undertaken in other countries and in the United States to enable clinician and patient access to historical RBC data and other types of patient information that improve health outcomes and empower patients. Thanks to the pioneering work initiated in the Netherlands, the EU, Canada, Quebec, Kansas City, Wisconsin, Georgia, and Santa Barbara, the following discussion of the elements of a successful exchange can take place. In addition to these existing or attempted HIEs, another initiative that has laid important groundwork in the United States is the Transfusion Antibody Exchange, a non-profit organization created "to enable blood banks to electronically share the transfusion history of their patients" (Transfusion Antibody Exchange, n.d.). The research and planning for each of these initiatives, and others not included in this report, contribute to the collective knowledge base needed to develop, implement, and sustain a national RBCAX.

In this chapter, the elements of a successful exchange are synthesized to inform the development, implementation, and sustainment of a U.S. national RBCAX. Also outlined are unanswered questions and the next steps for planning a pilot exchange. Finally, several pilot options are recommended for consideration.

Elements of a Successful Exchange

The study of various health information registries and exchanges identified numerous obstacles to establishing a national exchange. Nonetheless, the findings indicate that with proper planning, this goal is achievable. We discuss the components and considerations for a successful exchange, including implementation plans, evaluation frameworks, stakeholder engagement and buy-in, system requirements, and interoperability considerations. Figure 4 synthesizes several key barriers to the progress of other HIEs and RBC registries and exchanges, as well as critical facilitators to the establishment and sustainment of existing systems.

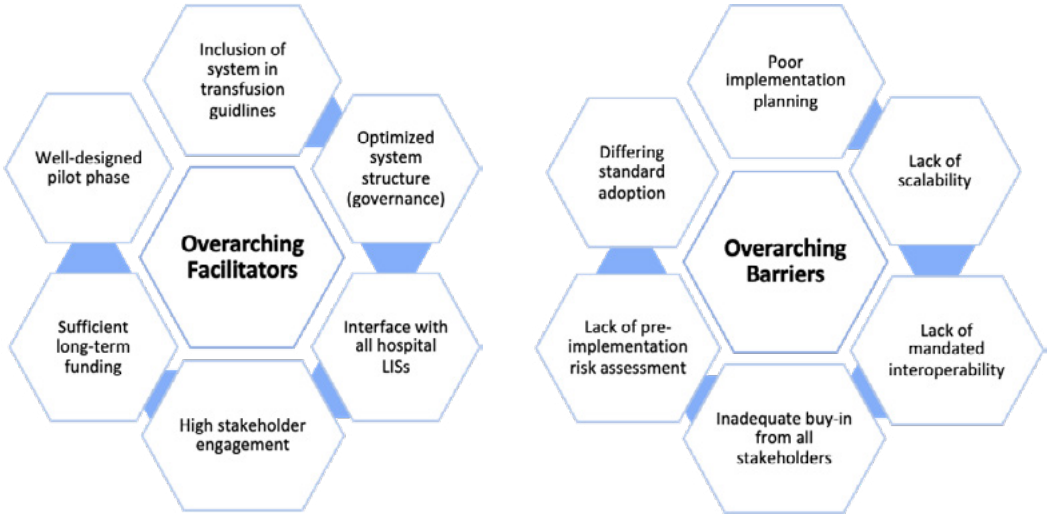

Figure 4. Overarching Barriers and Facilitators

A successful exchange requires a pre-defined, comprehensive implementation plan that is tested with a feasibility pilot. Case studies demonstrate that the absence of a well-designed implementation plan can result in unanticipated delays and significant additional costs. This plan must include a risk assessment that proactively addresses potential development, implementation, and sustainment barriers (Figure 4). It should also include pre-determined timelines and milestones (Chen & Chen, 2005; Mobey & Parker, 2022), as slowed implementation has been shown to increase project costs (European Commission, 2022a) and lower momentum and interest (Miller & Miller, 2007). The plan must include a comprehensive cost assessment (Mobey & Parker, 2022), which enables the subsequent identification of adequate funding from such sources as fees per blood unit, industry partnerships, and government program/agency funding. Moreover, during the pilot phase, it is essential to establish a carefully selected leadership and governance structure, including knowledgeable individuals who are accountable for oversight and for the development of implementation plans and evaluation. Having such leadership ensures smooth coordination and efficient decision-making throughout the pilot process.

A successful exchange requires a pre-defined comprehensive implementation plan that is tested with a feasibility pilot.

A well-structured evaluation framework is critical to an exchange implementation plan. The framework should include key criteria that enable assessment of the effectiveness, sustainability, and scalability of the data exchange system at a national level. Data required for evaluation should be identified during the system's development phase, and data collection should begin during the pilot phase and continue throughout implementation. In addition, the framework should guide the evaluation process, including successful data transfers as well as facility and clinician use. Other considerations, such as wider utility (patient outcomes, improvements in efficiencies, clinical and systems research, and impact on equity), should also be assessed. An efficient approach to monitoring system utility could involve recording data akin to TRIX hits. Any data collected for the purpose of evaluation should not be cumbersome or time-consuming for health care providers to input into the system and should be automated whenever possible.

Investing in stakeholder engagement and securing buy-in from all relevant parties are fundamental prerequisites for the success of a data exchange project; without this step, previous attempts have faltered, and some have failed.

Additionally, investing in stakeholder engagement and securing buy-in from all relevant parties are fundamental prerequisites for the success of a data exchange project; without this step, previous attempts have faltered. Research has shown that when the objectives of involved stakeholders do not align, it can lead to implementation issues, risks, and project failure (Klöcker, Bernnat, & Veit, 2015). Stakeholder engagement methods include word-of-mouth promotion, surveys of patient and doctor experiences (Moharra et al., 2015; epSOS, n.d.-c), dashboard communication (Bruthans & Jirakova, 2023), and stakeholder meetings and engagement in standard operating procedures (SOPs) and system development (Wisconsin Legislative Council, 2010; Canada Health Infoway, 2016). To ensure comprehensive stakeholder engagement, it is essential to consider all relevant parties throughout the entire project lifecycle including those providing funding, contributing to system development (subject matter experts), end users (clinicians, patients, and researchers), hospitals and blood bank leadership, IT technicians, and others. User training is a key aspect of engagement as it builds trust and fosters active participation. These investments not only encourage stakeholder buy-in, but they have also proven beneficial in identifying initial barriers to system development and areas for iterative system improvement (WISHIN, 2012b).

Several fundamental design requirements are essential to system development. An interface that seamlessly links the exchange with the users' information systems is required. A common hurdle that must be overcome is the difficulty in achieving interoperability between differing system. Efforts in this area should include consideration of technological proficiency across exchange participants, as varying levels of system proficiency have previously led to interoperability challenges. The system's data set must also be defined. The data set should be comprehensive

enough to offer maximum benefit to users while remaining manageable and easy to navigate. For maximum benefit, this may include all historical RBC patient antibodies.

It is beneficial to consult with potential users to identify the appropriate data fields and to weigh the limitations and benefits of each data type. For example, working group members involved in the development of this report suggested that it may be appropriate to include patient medication in the exchange. In addition to defining the data set, a clear process should be established to ensure data accuracy and validation, as accurate antibody identification is critical for the appropriate treatment of alloimmunized patients, especially for those with a complex antibody history. This step is also important for building clinicians' trust in the system, which influences their willingness to use it. The validation process should include the ability to dispute and correct antibody information in the registry when appropriate. System automation should also be considered, as it alleviates the burden on users; however, it should not interfere with users' confidence in the quality of the data.

An effective RBCAX must include a means for verifying patient identity. For example, the DoD identifies patients with an assigned DoD number, in addition to name and date of birth. The Netherlands uses citizen BSN (similar to a social security number) to identify patients; however, this method could limit system use to only patients who have been assigned such a number. This is a decision that should be made early in system development.

A national guideline that promotes system adoption should be considered for an exchange in the United States. After 5 years of TRIX register operation, the Dutch Institute for Healthcare Improvement (CBO) added a recommendation to its *Blood Transfusion Guideline* for the use of TRIX by hospital laboratories. This step was a critical element to the success of the register, ensuring widespread usage (van Gammeren et al., 2019).

Inclusion of system use in national guidelines promotes its adoption.

After 5 years of TRIX register operation, the Dutch Institute for Healthcare Improvement (CBO) added a recommendation to its Blood Transfusion Guideline for the use of TRIX by hospital laboratories. This step was a critical element to the success of the register, ensuring widespread usage.

van Gammeren et al., 2019

Finally, the varying applications and interpretations of data laws and regulations have presented significant interoperability hurdles in several of the presented case studies. A central coordinating body could aid in mitigating these challenges and reconciling discrepancies to enable seamless information exchange across state lines. The input of appropriate subject matter experts and regulatory governing bodies may provide the necessary guidance to a central coordinating body, and the mandated adoption of interoperability standards for system participant should be considered.

Unanswered Questions

Drawing from the insights gained through the presented case studies, several crucial questions remain unanswered:

- How can nationwide interoperability be established?
- What data should be included?
- What group(s)/agencies will be responsible for the governance structure?
- What procedures are needed to ensure and verify data accuracy, facilitating user confidence in the data from sources outside their own health system?

- What steps need to be taken to overcome user resistance and hesitancy to ensure participation in the exchange? How can cooperation among competing entities be achieved?
- How can government agencies and professional societies strategically promote the use of a national exchange through guidelines and recommendations?
- What steps are required to obtain patient consent and protect patient data?
- Has the long-term utility of the proposed system been explored to its fullest extent? For example, has it been designed for use in long-term research that will add to its benefit?

Next Steps

Figure 5 outlines the RBCAX Strategic Implementation Plan. Completion of this interim report represents the initial steps in Phase I. During the next stage of Phase I, the project team will address unanswered questions and build on the current findings to develop a pilot exchange. This work will be done in consultation with the established RBCAX Working Group and other subject matter experts, as needed, who will assist in resolving issues such as data systems requirements, clinical data inclusion, standardization, validation, and development of a pilot framework. Phase II will include refinement of the pilot model, RBCAX pilot launch, and continued management of the national exchange with the aim of sustainability and improvement.

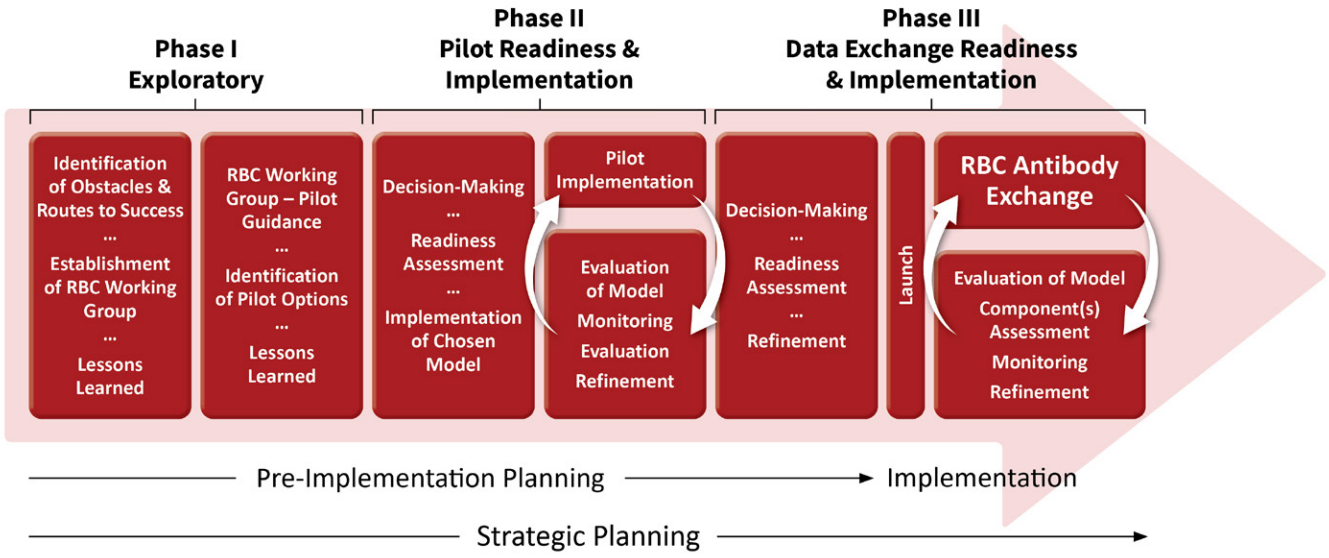

Figure 5. RBCAX Strategic Implementation Plan

Recommendation of Pilot Options

As part of phase II, a pilot exchange model should be developed to appraise the feasibility of establishing a nationwide RBCAX in the United States and to assess its practicability. This can be developed by drawing from the working group expertise and research findings. Three pilot options, summarized in Table 6, are proposed to answer the following questions toward the development of a national exchange.

DMV Area RBC Pilot Key Questions

1. Can an RBC antibody exchange system be constructed in a technically valid and reliable way across multiple hospitals in the DMV area?

2. Is this approach in part or fully generalizable for alignment and comparison to other regions and systems?
3. What lessons learned and information collected can be expanded to apply to larger regions?
4. How can the lessons learned be used to inform the development an RBCAX?

Mid-Atlantic RBC Pilot Key Questions

1. Can an RBCAX be constructed in a technically valid and reliable way using an existing multi-state data exchange system?
2. Can such a system be expanded to include additional states?
3. Is this approach in part or fully generalizable and compatible to expand to other regions and systems?
4. What lessons learned and information collected can be used to leverage the development of a national exchange?

Multi-Agency RBC Pilot Key Questions

1. Can an RBCAX be constructed in a technically valid and reliable way using an existing multi-state data exchange system and be subsequently linked successfully to an existing network?
2. Can such a test system serve as an early framework for the development of a national RBCAX?
3. How can the lessons learned and information collected be used to increase the successful development of a national RBCAX?

Table 6. RBCAX Pilot Options

	DMV RBC Antibody Exchange Pilot	Mid-Atlantic RBC Antibody Exchange Pilot	Multi-Agency RBC Antibody Exchange Pilot
GOAL	Test the feasibility of an RBC antibody exchange in an urban region	Test the feasibility of a multi-state RBC antibody exchange	Test the feasibility of a multi-state/multi-agency RBC antibody exchange with 2nd stage linkage to the FDA BEST exchange
GEOGRAPHIC REGION	Test hospitals within network in the DMV area	Network hospitals in DC, MD, WV (pilot to include VA exchange data)	Mid-Atlantic network hospitals with pilot linkage to the FDA BEST exchange network
PATIENT POPULATION	Transfused patients in the DMV-area receiving/seeking care in pilot hospitals	DC, MD, WV, VA transfused patients receiving/seeking care across the pilot region hospitals	Transfused patients in Mid-Atlantic region and BEST exchange network pilot transfused patients
UTILITY	Develop and test antibody exchange across pilot hospitals in the DMV	Demonstrate the success/failures of an antibody exchange in a multi-state, diverse population across multiple data exchanges	Demonstrate the success/failures of a multi-state antibody exchange linked across multiple data exchanges and with interoperability across multiple agencies
STAKEHOLDERS	DMV-area transfused patients, DMV member hospitals, existing health information exchange, health care providers, implementation SMEs, blood banks, laboratories	DC, MD, WV, VA transfused patients; area hospitals; existing health information exchanges; health care providers; implementation SMEs; blood banks; laboratories	Transfused patients in Mid-Atlantic region, BEST exchange pilot network, area hospitals, existing health information exchanges, health care providers, implementation SMEs, blood banks, laboratories, federal agencies

Table 6. RBCAX Pilot Options, continued

	DMV RBC Antibody Exchange Pilot	Mid-Atlantic RBC Antibody Exchange Pilot	Multi-Agency RBC Antibody Exchange Pilot
OPPORTUNITIES	• Racially and socioeconomically diverse urban population • Feasibility test of adding RBC data to an existing system • Generalizable to similar exchanges • Test of patient data portability across hospitals • Investigation of stakeholder engagement and process buy-in	• Urban-rural, racially diverse, socioeconomic disparate communities • Generalizable to a broader U.S. population • Insight into scalability across the U.S. population • Larger transfused patient population to measure health impact • Ability to test stakeholder buy-in in a complex geographical region • Increased scalability to inform future expansion and development	• Ability to test stakeholder buy-in in a larger geographic region and across multiple agencies • Demonstration of scalability at the national level • Largest transfused patient population to measure health impact • A more complete representation of the U.S. population • Representation of patients in the care of the Veterans Health Administration

The DMV area and Mid-Atlantic states were chosen because they are uniquely positioned as pilot sites. Combined, they represent racially and socioeconomically diverse urban and rural populations with nearly 45,000 people impacted by relevant diseases and conditions, including kidney disease requiring transfusions (61%) and SCD (23%) (Gill et al., 2013; Hoppe, 2013; Ibrahim et al., 2009; National Center for Health Statistics, n.d.-b; NORD, n.d.; Park et al., 2022; Small et al., 2017; U.S. Census Bureau, n.d.; Wood & McQuilten, 2020; Zakieh & Siddiqui, 2017). Depending on the scale, a pilot in this region could serve up to 90 hospitals and their patients (U.S. Census Bureau, 2020). The third option would be the multi-agency pilot with subsequent incorporation of FDA Biologics Effectiveness and Safety (BEST) exchange, which includes Cedars-Sinai Health system (CA), the MemorialCare Health System (CA), the South Broward Hospital District DBA Healthcare System (FL), The Metrohealth System (OH), and the Veterans Health Administration, serving 43 states, the District of Columbia, and Puerto Rico. This third option would significantly expand the reach of the pilot and enable testing across multiple states, exchanges, and federal agencies.

CHAPTER 5: CONCLUSION

This report presents a comprehensive review of several case studies that provide valuable insights for the development of a national RBCAX. Themes discovered in the case studies allowed identification and discussion of factors critical to successful planning and establishment of such an exchange. Additionally, potential pilot feasibility options are included in this report to inform the development of an RBCAX during the next project phase.

There is substantial support for a national RBCAX in the United States. In June 2020, the AABB submitted comments to HHS that advocated for the establishment of a national RBC antigen typing patient database and noted that such a resource would improve patient outcomes by expediting access to compatible units of blood for individuals with special transfusion requirements (Association for the Advancement of Blood & Biotherapies, 2022). Since that time, AABB has been working with the American Society for Clinical Pathology, the American Society of Hematology, America's Blood Centers, the American Red Cross, and others to identify opportunities to drive progress. In a recent survey about registry development submitted by members of the AABB Transfusion Medicine Subsection Coordinating Committee, 97% of respondents said they were in favor of a nationwide red blood cell antibody registry (Association for the Advancement of Blood and Biotherapies, 2022).

Further work is necessary to advance the development of an exchange pilot, and this report serves as a foundation of knowledge to move forward in this process.

APPENDICES

Appendix A: Acronyms and Abbreviations

AABB: Association for the Advancement of Blood & Biotherapies

ASH: American Society of Hematology

BEST: Biologics Effectiveness and Safety

BSN: Netherlands Citizen Service Number

CAD: Canadian Dollar

CBC: Community Blood Center

CBO: Dutch Institute for Healthcare Improvement

CBP: Personal Data Protection Board

CDC: Centers for Disease Control and Prevention

CEF: Connecting Europe Facility

CEO: Chief Executive Officer

CHCF: California Health Care Foundation

CTR: Central Transfusion Registry

DHTR: Delayed hemolytic transfusion reaction

DMV: District of Columbia, Maryland, Virginia

DoD: Department of Defense

DPA: Dutch Data Protection Authority

EC: European Commission

eHDSI: European Union eHealth Digital Service Infrastructure

EHDS: The European Health Data Space

EHR: Electronic health records

eHMSEG: eHealth DSI EU Countries Expert Group

eHN: eHealth Network

eHOMB: eHealth Operational Management Board

eIDAS: Electronic Identification, Authentication and Trust Services

EMR: Electronic medical record

EpSOS: Smart Open Service for European Patients

EU: European Union

FDA: Food and Drug Administration

FMH: Fetomaternal hemorrhage

HCL: Dutch web-based technology service that can be used in hospitals involved with data exchange

HHS: Health and Human Services

HIE: Health information exchange

HIPAA: Health Insurance Portability and Accountability Act

IHS: Indian Health Services

Infoway: Canada Health Infoway

IRL: Immunohematology Reference Laboratory

IT: Information technology

JASeHN: Joint Action to Support the eHealth Network

KPI: Key performance indicator

LIS: Lab information system

MSSS: Ministry of Health and Social Services

NCPeH: National Contact Point for eHealth

NIH: National Institutes of Health

NYBC: New York Blood Center

OIDP: Office of Infectious Disease and HIV/AIDS Policy

OMH: Office of Minority Health

ONC: Office of the National Coordinator for Health Information Technology

P4P: Pay-for-performance

PBCO: Provincial Coordinating Office

PIPEDA: Personal Information Protection and Electronic Documents Act

PPH: Postpartum hemorrhage

RBC: Red blood cell

RBCAX: Red Blood Cell Antibody Patient Data Exchange

RITM: Integrated Multimedia Telecommunications Network

RLA: Rose Li & Associates

RSSS: Health and Social Services Network

Santa Barbara Project: Santa Barbara County Care Data Exchange

SCD: Sickle cell disease

SIIATH: Integrated Information System on Transfusion Activities and Hemovigilance

SIIATH-GS: Integrated Information System on Transfusion Activities and Hemovigilance—*Blood Management*

SIIATH-ST: Integrated Information System on Transfusion Activities and Hemovigilance—*Transfusion Summary*

SME: Subject Matter Experts

SOP: Strategic and Operational Plan

TRIP: Transfusion and Transplantation Reactions in Patients

TRIX: The Transfusion Register of Irregular Antibodies and Cross (X)-match

TSO: Transfusion Safety Officer

VA: Veterans Affairs

VWD: Von Willebrand disease

WIRED for Health: Wisconsin Relay of Electronic Data for Health

Wisconsin DHS: Wisconsin Department of Health Services

WISHIN: Wisconsin Statewide Health Information Network

Appendix B: Glossary

Anemia

A condition that develops when there are low levels of healthy red blood cells, which leads to less-than-optimal oxygen flow throughout the body.

Antigen

An antigen is a substance or molecule that triggers an immune response in the body. Antigens come from various sources, including pathogens like bacteria and viruses, as well as non-infectious substances like pollen, toxins, or transplanted tissues. Antigens on the surface of red blood cells determine blood type and play a crucial role in blood transfusions. For example, blood group A has A antigens and blood group B has B antigens. If incompatible blood is transfused, the body will detect the foreign or "non-self" antigens and launch a potentially dangerous immune response. O negative is considered a desirable "universal blood type" because it has no antigens and does not trigger an immune response when transfused, regardless of recipient blood type.

Antibody

When the body detects foreign or incompatible antigens, it produces specialized proteins called antibodies that bind to the antigens to neutralize them or mark them for destruction by other immune cells. In blood and transfusion medicine, antibodies are important to consider because the body naturally possesses antibodies against foreign blood types. Blood type A has anti-B antibodies, blood type B has anti-A antibodies, and blood type O has anti-A and anti-B antibodies. Other types of blood antibodies may be formed in the body after an incompatible blood transfusion.

Alloantibody

Alloantibodies are a type of antibody that appear following exposure to incompatible red blood cell antigens. They may develop after a blood transfusion or organ transplantation.

Allogeneic transplantation

Allogeneic transplantation is a process where an organ or tissue is obtained from a donor (not the patient) and is transferred to a recipient. The donor is matched with the recipient and may be related or unrelated to them.

Alloimmunization

Alloimmunization describes the recipient's immune response following exposure to red blood cell antigens of an incompatible donor.

Blood typing

Blood typing is a test that determines an individual's genetic blood group. It requires drawing a blood sample.

Chelation therapy

Chelation therapy is a practice utilized after excess metals, such as iron, become built up in the body. This therapy is commonly used to prevent iron overload in transfusion patients.

Chelator

Small molecules that bind to metals, such as iron, in the blood. Chelators defuse the metals and help your body remove the compounds.

Cross-matching

Cross-matching is a test that helps eliminate the possibility of an antigenic transfusion reaction. The test looks specifically for any pre-existing antibodies the patient may have against donor blood. Tests can either be run in a laboratory or be analyzed by machine.

Delayed hemolytic transfusion reaction

Delayed hemolytic transfusion reaction (DHTR) occurs days to weeks following a blood transfusion. It can be characterized by mild anemia and/or hyperbilirubinemia and is a serious complication that can occur after blood transfusion. When transfused blood antibodies are not correctly matched with the recipient, the body mounts an immune attack against the transfused blood.

Evanescence

Evanescence is the decrease or disappearance of antibodies over time, making them difficult to detect during screening prior to transfusion or transplantation. Tracking a patient's antibodies through an exchange can alert providers of the potential presence of undetectable antibodies that could interfere with safe transfusion.

Fetomaternal hemorrhage

Fetomaternal hemorrhages (FMH) occur when fetal blood leaks across the placenta into the maternal blood circulation. This complication may occur due to trauma experienced during pregnancy. The foreign blood exchange between the mother and fetus leads to an immune attack and places the fetus at risk of severe morbidity and mortality.

Gene therapy

Gene therapy is the transplantation of healthy genes into patient cells that contain defective genetics. This process induces therapeutic effects that can effectively correct genetic disorders.

Genomics

A branch of molecular biology that studies the structure, function, and evolution of the complete set of genetic material in an organism.

Hemoglobinopathy

Hemoglobinopathy is a general term used to describe all inherited medical conditions that are due to abnormal or underproduced hemoglobin protein structures.

Hemolytic reaction

A hemolytic reaction is a serious, potentially fatal blood transfusion complication. It occurs when incompatible red blood cells are destroyed by the patient's body at a rapid rate following a transfusion.

Hemovigilance

Hemovigilance is the set of surveillance procedures that may be put in place to govern the entire blood transfusion chain, from the donation and processing of blood and its components to the transfusion of patients.

Hemophilia

Hemophilia is a medical condition that hinders the body's capability to produce blood clotting proteins. This causes severe bleeding even in the case of minor injuries such as cuts and scrapes.

Iron overload

Iron overload occurs when the body excessively stores iron in the liver, heart, and endocrine glands, which over time leads to organ damage and other health issues. Individuals that receive chronic transfusions are at high risk of these complications due to the constant influx of new red blood cells, which leads to higher-than-normal iron levels in the body.

Leukoreduction (leukocyte-reduced)

Leukoreduction is a common blood filtering procedure used to prevent adverse transfusion effects. In this process, leukocytes (white blood cells) are removed from the whole blood via a filtration system.

Obstetrics

A branch of medicine concerning childbirth and the care of women giving birth.

Packed red blood cells

Packed red blood cells (PRBCs) are a concentrated preparation of red blood cells which can be obtained from whole blood by removing its plasma. PRBCs are often only transfused into clinically symptomatic anemia patients.

Red blood cell exchange apheresis

Red blood cell exchange apheresis is a therapy that involves utilizing a Plasma Collection Machine to remove patient red blood cells and replace them with healthy donor cells.

Serology

A branch of study concerning the response of the immune system to pathogens or substances introduced in the blood and body. Serology professionals may perform diagnostic examination of blood serum.

Sickle cell disease

Sickle cell disease (SCD) is an inherited blood disorder that affects hemoglobin, leading to a “sickle” C-shaped malformation of cells. This hinders the ability of red blood cells to carry oxygen throughout the body and may lead to vessel and artery blockage due to the rigid, deformed red blood cells.

Sickle Cell Trait

Sickle cell trait (SCT) is not a disease but a condition in which an individual carries one copy of the sickle cell gene mutation and can pass that on (two copies required for disease).

Stakeholder

Groups or individuals with an interest or investment in an organization or system and its success.

Thalassemia

Thalassemia is an inherited blood disorder that occurs due to genetic mutations in the hemoglobin gene. The mutation in hemoglobin impairs the maturing of red blood cells and affects the blood cell structure, leading to cell death. The body’s continual struggle to rapidly produce more red blood cells eventually causes bone and spleen complications, and the constant loss of red blood cells leads to anemia.

Washed red blood cells

Donated whole blood is processed to remove its blood plasma proteins, white blood cells, and platelets. Red blood cell washing is done to further prevent any adverse effects that may occur due to transfusion.

Von Willebrand disease

An inherited blood disorder characterized by low levels of clotting proteins in the blood. It may lead to recurrent and prolonged nosebleeds, bleeding from the gums, increased menstrual flow, and excessive bleeding from a cut.

Appendix C: Question Bank

Case Study Interview Question Bank

The purpose of this question bank is to provide interviewers with a guide of questions for representatives of eHealth Exchanges, registry stakeholders, and other SMEs related to a national red blood cell antibody patient data exchange.

1. Background

- Thank you for meeting with me today. My name is _____, and my company, Rose Li & Associates, has been contracted by HHS to conduct this interview.
  - If it's okay with you, I'd like to audio-record our conversation. The recordings will be used to confirm our notes and allow us to revisit this conversation. For example, additional project staff may need to hear the tapes at a later date. The information that you provide during this interview will be used to inform our larger project.
- The purpose of these interviews is to collect information and learn from individuals and organizations involved in eHealth data exchanges as we prepare a report on national and international health data exchanges. This is being done to investigate the feasibility of a national red blood cell antibody patient data exchange, with the goal of developing a pilot of such an exchange.
- As you know, we've asked for your input because of your expertise/experience in _____, and we'd like to hear more.

2. Introduction

- Tell me a bit of basic information about your role in the _____ exchange.

3. Outcome Measures

- What methods were/are used to measure and report the outcomes associated with this exchange/registry?
  - *Follow-up: Describe the specific outcomes that are reported.*
  - *Follow-up: Who are the outcome measures reported to?*
  - *Follow-up: Have you used any frameworks to assess the exchange/registry?*

4. Technical and Data Aspects to the Exchange

- What technical challenges have emerged and how have they been addressed?
  - For example: data harmonization or standardization, data quality, data privacy, interoperability
- What technical processes have been particularly successful and why?
- How has your exchange achieved interoperability between the facilities included?
- What processes have been implemented to ensure data privacy?
- What processes have been implemented to ensure data quality?

- What data is included in the exchange?
  - *Follow-up: How was this determined?*
- How have patient inclusion/exclusion criteria been determined?
- Were any barriers encountered regarding compliance to data/privacy laws and regulation?
- Who owns the data that is included in the exchange/register?

5. Exchange Cost and Funding Mechanisms

- Broadly, what types of costs have been involved in this exchange?
  - *Follow-up: What were the initial costs of implementing this exchange?*
  - *Follow-up: What are the current annual costs of maintaining and housing the exchange?*
- Who is responsible for the costs involved in this exchange?
  - *Follow-up: Has funding for this exchange proven to be adequate?*
- How has the cost-effectiveness of this data exchange/registry been measured? What measurements have been used?

6. Benefits and Drawbacks

- What are the perceived benefits of this exchange/registry?
  - *Follow-up: What benefits have occurred specific to your organization and the health professionals utilizing this tool?*
  - *Follow-up: What benefits have occurred for the patients who use this exchange/registry?*
- What have been the drawbacks, if any, to using this exchange/registry?

7. Patients and Medical Professionals

- How are patients informed about this exchange/registry and its benefits?
- How has this exchange/registry served underserved/marginalized communities?
  - *Follow up: Were underserved/marginalized communities considered in the design of the exchange?*
  - *Follow-up: What recommendations do you have for including underserved/marginalized communities in an exchange?*
- Do patients have access to their data stored in this exchange/registry?
  - *Follow-up: Are there any barriers to patient access to this exchange/registry? (For example, lack of health insurance)*
- How is patient consent obtained?
  - *Follow-up: What is the procedure in a scenario where a patient revokes their consent?*
- How were medical professionals educated about this exchange/registry during its implementation?
  - *Follow-up: Is there accessible ongoing education related to the use of the registry?*

8. Stakeholder Engagement and Buy-in

- Which stakeholders participated in the development of the exchange/registry?
  - *Follow-up: Which stakeholders engage in the current operation of the exchange/registry?*
- How was engagement achieved with relevant entities and stakeholders?
  - *Follow-up: For which entities was engagement a challenge? How were these challenges overcome?*
- Were any hospitals hesitant to join this exchange/registry?
  - *Follow-up: What were the reasons for this hesitancy?*
  - *Follow-up: What steps were taken to overcome this?*

9. Decision and Implementation Process

- What were the biggest obstacles in the first stages of implementation?
- How are outcomes measured and assessed and at what point in the process are they measured and assessed?
- Have any barriers been encountered regarding compliance to data/privacy laws and regulation?
- Please briefly describe the testing/pilot phase prior to launching the exchange/register.
  - *Follow-up: What barriers occurred during this phase? How were they overcome?*

10. Other Considerations

- Are there any other factors that affected this exchange/registry and its function or implementation?
- Is there any other information you would like to provide before the conclusion of this interview?

11. Closing Remarks

- Thank you for your time and participation in this interview. We will be contacting you with any follow-up questions, as necessary.

Appendix D: RBCAX Working Group Presentations

Table 7. RBCAX Working Group Presentations

Presenter	Organization	Presentation Title
Barbee Whitaker & Hussein Ezzeldin	FDA	BEST RBC Alloantibodies Exchange Proof-of-Concept
George Hauser	Transfusion Antibody Exchange	Alloantibody Exchange Discussion
Shay Jones	Kansas City Registry	Community Blood Center's Antibody Registry
Margaret A. Keller	The American Red Cross	American Rare Donor Program and American Red Cross Immunohematology Reference Laboratory Perspective
Eric Gehrie	The American Red Cross	American Red Cross Direct Patient Care – Focusing on Sickle Cell Disease Unmet Medical Need
Amanda Brandow & Ashima Singh	Sickle Cell Disease Epic Registry	Electronic Health Record Registry for Sickle Cell Disease
Sickle Cell Disease Patient Representative	Patient Representative	Sickle Cell Disease Patient Experiences
Navdeep Singh	Thalassemia Patient Representative	Patient Representative Q&A Session
Adriaan van Gammeren & Charles Veldhoven	The TRIX Register	TRIX: A Transfusion Registrar of Irregular Antibodies and Crossmatch (X) Problems in the Netherlands
David Feldman	Department of Veterans Affairs	Complex RBC Antibody VA Cases
Michelle Parker	Department of Defense	Enterprise Sharing of Antibody Information

Appendix E: TRIX Register Patient Profile

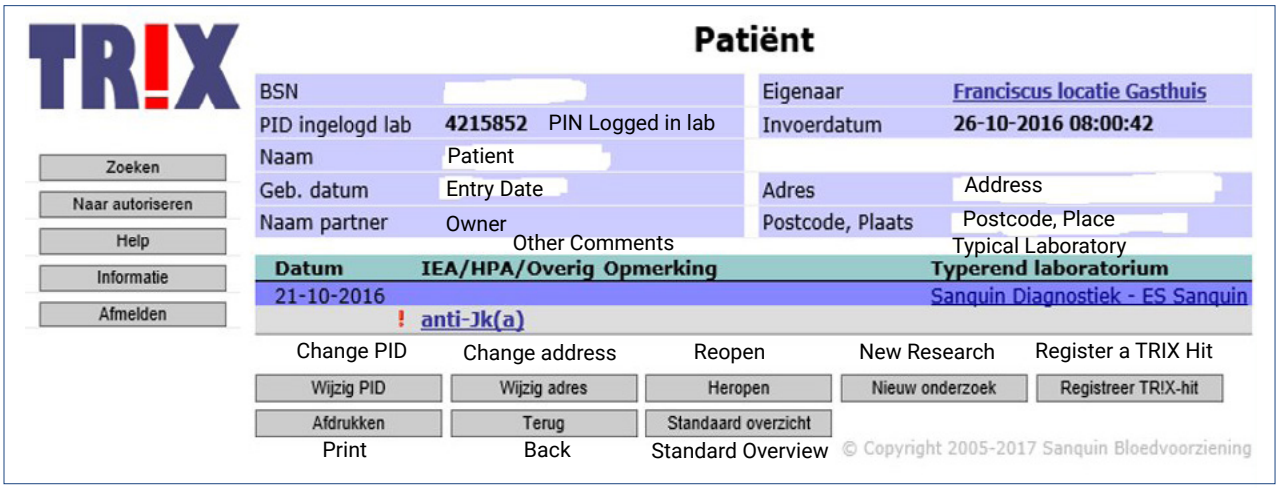

Figure 6. TRIX Register Patient Profile

Appendix F: References

Adesina, O. O., Brunson, A., Fisch, S. C., Yu, B., Mahajan, A., Willen, S. M., Keegan, T. H. M., & Wun, T. (2023). Pregnancy outcomes in women with sickle cell disease in California. *American Journal of Hematology*, *98*(3), 440–448. https://doi.org/10.1002/ajh.26818

Almoaber, B., & Amyot, D. (2020). Barriers to successful health information exchange systems in Canada and the USA: A systematic review. In I. R. Management Association (Ed.), *Virtual and Mobile Healthcare* (pp. 328–350). IGI Global. https://doi.org/10.4018/978-1-5225-9863-3.ch015

Arksey, H., & O'Malley, L. (2005). Scoping studies: Towards a methodological framework. *International Journal of Social Research Methodology*, *8*(1), 19–32. https://doi.org/10.1080/1364557032000119616

Association for the Advancement of Blood and Biotherapies. (2022). *Nationwide antibody registry could help further reduce risk of adverse events among patients receiving blood transfusions*. Retrieved August 1, 2023, from https://www.aabb.org/news-resources/news/article/2022/03/02/nationwide-antibody-registry-could-help-further-reduce-risk-of-adverse-events-among-patients-receiving-blood-transfusions

Baird, D. C., Batten, S. H., & Sparks, S. K. (2022). Alpha- and beta-thalassemia: rapid evidence review. *American Family Physician*, *105*(3), 272–280.

BC Provincial Blood Coordinating Office (2020, June 23). Central Transfusion Registry – Data elements. https://pbco.ca/images/Data/CTRC002F_CTR_Data_Elements_12.pdf

BC Provincial Blood Coordinating Office. (2021). Central Transfusion Registry. https://pbco.ca/index.php/data/central-transfusion-registry

Bell Browne Molnar & Delicate Consulting Inc. (2021). *2021 Independent performance evaluation, Canada Health Infoway*. Canada Health Infoway. https://www.infoway-inforoute.ca/en/component/edocman/4000-march-2021-independent-performance-evaluation-full-report/view-document?Itemid=101

Betts, M., Flight, P. A., Paramore, L. C., Tian, L., Milenković, D., & Sheth, S. (2020). Systematic literature review of the burden of disease and treatment for transfusion-dependent β-thalassemia. *Clinical Therapeutics*, *42*(2), 322-337.e2. https://doi.org/10.1016/j.clinthera.2019.12.003

Brailer, D. J., Augustinos, N., Evans, L. M., & Karp, S. (2003). *Moving toward electronic health information exchange: Interim report on the Santa Barbara County Data Exchange*. Prepared for: California HealthCare Foundation. https://www.chcf.org/wp-content/uploads/2017/12/PDF-SBCCDEInterimReport.pdf

Boston Children's Hospital (n.d.). *Thalassemia*. Retrieved March 28, 2023, from https://www.childrenshospital.org/conditions/thalassemia

Brennan-Cook, J., Bonnabeau, E., Aponte, R., Augustin, C., & Tanabe, P. (2018). Barriers to care for persons with sickle cell disease: The case manager's opportunity to improve patient outcomes. *Professional Case Management*, *23*(4), 213–219. https://doi.org/10.1097/NCM.0000000000000260

Bruthans, J., & Jiráková, K. (2023). The current state and usage of European Electronic Cross-Border Health Services (eHDSI). *Journal of medical systems*, *47*(1), 21. https://doi.org/10.1007/s10916-023-01920-9

Buckeridge, D. (2021). *An evidence-informed vision for a public health data system in Canada*. Public Health Agency of Canada Office of the Chief Public Health Officer. https://nccph.s3.amazonaws.com/uploads/2022/06/OCPHO_Report_David_Buckeridge_NCCMT_EN.pdf

Canada Health Infoway. (2012a). *Benefits evaluation indicators technical report*. https://www.infoway-inforoute.ca/en/component/edocman/resources/reports/450-benefits-evaluation-indicators-technical-report-version-2-0

Canada Health Infoway. (2012b). *Stakeholder engagement planning template*. https://www.infoway-inforoute.ca/en/component/edocman/stakeholder-engagement/resources-and-tools/790-stakeholder-engagement-planning-template

Canada Health Infoway. (2015, January). *Core electronic health record for Saskatchewan complete*. https://www.infoway-inforoute.ca/en/news-events-blog/news/2015-news-releases/core-electronic-health-record-for-saskatchewan-complete

Canada Health Infoway. (2016). *Digital health blueprint: Enabling coordinated & collaborative health care*. https://www.infoway-inforoute.ca/en/component/edocman/2944-digital-health-blueprint-enabling-coordinated-collaborative-health-care/view-document?Itemid=0

Canada Health Infoway. (2018). *Connected health information in Canada: A benefits evaluation study*. https://www.infoway-inforoute.ca/en/component/edocman/resources/reports/benefits-evaluation/3510-connected-health-information-in-canada-a-benefits-evaluation-study-document

Canada Health Infoway. (2019). *Implementation of the immunization module in Quebec: Benefits evaluation report*. https://www.infoway-inforoute.ca/en/component/edocman/3791-implementation-of-the-immunization-module-in-quebec-benefits-evaluation-report/view-document

Canada Health Infoway. (2021). *Personal health information privacy and access across Canada*. https://www.infoway-inforoute.ca/en/component/edocman/3950-personal-health-information-privacy-and-access-across-canada-infographic/view-document?Itemid=101

Canada Health Infoway. (2022a). *Canadian interoperability landscape study: Executive summary*. https://www.infoway-inforoute.ca/en/component/edocman/6407-canadian-interoperability-landscape-study-executive-summary/view-document?Itemid=101

Canada Health Infoway. (2022b). *First pan-Canadian projectathon*. https://www.infoway-inforoute.ca/en/component/edocman/6376-first-pan-canadian-projectathon/view-document

Canada Health Infoway. (2022c). *PrescribeIT policy and priorities table*. https://www.prescribeit.ca/component/edocman/other/260-prescribeit-policy-and-priorities-table-executive-summary

Canada Health Infoway. (2023). *A path forward for data sharing in Canada: A white paper*. https://www.infoway-inforoute.ca/en/component/edocman/resources/reports/privacy/6428-a-path-forward-for-data-sharing-in-canada-a-white-paper

Canada Health Infoway. (n.d.-a). *Our history: Working towards a more connected and collaborative health system*. https://www.infoway-inforoute.ca/en/about-us/our-history

Canada Health Infoway. (n.d.-b). *Vendor certification services*. https://www.infoway-inforoute.ca/en/about-us/our-partners/vendor-certification-services

Castillo, E. G., & Harris, C. (2021). Directing research toward health equity: A health equity research impact assessment. *Journal of General Internal Medicine*, *36*(9), 2808. https://doi.org/10.1007/S11606-021-06789-3

Centers for Disease Control and Prevention [CDC]. (2022, May 2). Data & statistics on sickle cell disease. https://www.cdc.gov/ncbddd/sicklecell/data.html

CDC. (n.d). *What is thalassemia?*. https://www.cdc.gov/ncbddd/thalassemia/facts.html

Chapin, J., Cohen, A. R., Neufeld, E. J., Vichinsky, E., Giardina, P. J., Boudreaux, J., Le, B. C., Kenney, K., Trimble, S., & Thompson, A. A. (2022). An update on the US adult thalassaemia population: A report from the CDC thalassaemia treatment centres. *British Journal of Haematology*, *196*(2), 380–389. https://doi.org/10.1111/bjh.17920

Chen, H. T., & Chen, H. T. (2005). Practical program evaluation: Assessing and improving planning, implementation, and effectiveness. Sage. https://doi.org/10.4135/9781412985444

Community Blood Center. (2018). Community blood center and New York blood center merge as one organization. [News release]. https://www.savealifenow.org/2018/04/01/community-blood-center-and-new-york-blood-center-merge-as-one-organization/

Community Blood Center. (n.d.) Community Blood Center. Retrieved March 17, 2023, from https://savealifenow.org/

Coppolino, L., D'Antonio, S., Romano, L., & Staffa, M. (2017). KONFIDO project: A secure infrastructure increasing interoperability on a systemic level among eHealth services across Europe. *2017 IEEE International Conference on Internet of Things (IThings) and IEEE Green Computing and Communications (GreenCom) and IEEE Cyber, Physical and Social Computing (CPSCom) and IEEE Smart Data (SmartData)*, 342–347. https://doi.org/10.1109/iThings-GreenCom-CPSCom-SmartData.2017.57

Coyne, E., Jirakova, K. (2022, April). MyHealth@EU MS updates. [PowerPoint slides]. https://ue.esante.gouv.fr/sites/default/files/2022-04/5%20-%20eHMSEG.pdf

Daudt, H. M. L., Van Mossel, C., & Scott, S. J. (2013). Enhancing the scoping study methodology: A large, inter-professional team's experience with Arksey and O'Malley's framework. *BMC Medical Research Methodology*, *13*(1), 1–9. https://doi.org/10.1186/1471-2288-13-48

Delaney, M., Dinwiddie, S., Nester, T. N., & AuBuchon, J. A. (2013). The immunohematologic and patient safety benefits of a centralized transfusion database. *Transfusion*, *53*(4), 771–776. https://doi.org/10.1111/j.1537-2995.2012.03789.x

Digitalhealth. (2009, February 25). epSOS makes strong start. *https://www.digitalhealth.net/2009/02/epsos-makes-strong-start/*

Doyle, J. (2005). Executive Order #129: Relating to the Governor's eHealth Care Quality and Patient Safety Board. https://docs.legis.wisconsin.gov/code/executive_orders/2003_jim_doyle/2005-129.pdf

Doyle, J. (2009). *Executive Order # 303 Relating to the Governor's WIRED for Health board*. https://wishin.org/wp-content/uploads/2022/10/SOP-Appendices-FINAL.pdf

epSOS. (2014). Smart open services for European patients: Open eHealth initiative for a European large scale pilot of patient summary and electronic prescriptions, recommendations D2.2.7. https://web.archive.org/web/20150814132648/http://www.epsos.eu/uploads/tx_epsosfileshare/D2.2.7_Recommendations_v1.5.pdf

epSOS. (n.d.-a). epSOS results & outlook. https://web.archive.org/web/20150327001819/http:/www.epsos.eu/home/epsos-results-outlook.html

epSOS. (n.d.-b). Industry team. https://web.archive.org/web/20130516083746/http:/www.epsos.eu/home/project-members-beneficiaries/industry-team.html

epSOS. (n.d.-c). Participating nations. https://web.archive.org/web/20130516084835/http://www.epsos.eu/home/project-members-beneficiaries/participating-nations.html

Ernst & Young LLP. (2020). Review of connect care, Alberta netcare and MyHealth records. https://open.alberta.ca/dataset/1394ebca-9869-40d6-b5af-3c6870557f21/resource/d9558cbb-220e-4b28-a05e-3d9773d4d9ac/download/health-review-of-connect-care-alberta-netcare-myhealth-records-2020-03.pdf

European Commission. (2014). *Cross-border health project epSOS: What has it achieved?* https://digital-strategy.ec.europa.eu/en/news/cross-border-health-project-epsos-what-has-it-achieved

European Commission. (2020, November 17). Periodic reporting for period 2 – KONFIDO (KONDIFO – secure and trusted paradigm for interoperable eHealth services). https://cordis.europa.eu/project/id/727528/reporting

European Commission. (2021). Study on eHealth, interoperability of health data and artificial intelligence for health and care in the European Union. Lot 2: Artificial intelligence for health and care in the EU. https://www.digitalhealthnews.eu/images/stories/pdf/artificial_intelligence_in_healthcare-final_country_factsheets.pdf

European Commission. (2022a). Commission staff working document impact assessment report accompanying the document proposal for a regulation of the European parliament and of the council on the European Health Data Space. https://pink.pharmaintelligence.informa.com/-/media/supporting-documents/pink-sheet/2022/05/impact-assessment.pdf

European Commission. (2022b). eHealth network guideline on the electronic exchange of health data under cross-border directive 2011/24/EU. https://health.ec.europa.eu/system/files/2022-06/ehealth_health-data_electronic-exchange_general-guidelines_en.pdf

European Commission. (n.d.-a). European health data space. *https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en*

European Commission. (n.d.-b). Electronic cross-border health services. https://health.ec.europa.eu/ehealth-digital-health-and-care/electronic-cross-border-health-services_en#which-services-are-available-in-which-countries

European Court of Auditors. (2019). Special report EU actions for cross-border healthcare: Significant ambitions but improved management required. https://www.eca.europa.eu/Lists/ECADocuments/SR19_07/SR_HEALTH_CARE_EN.pdf

Expert Advisory Group. (2021). Pan-Canadian health data strategy: Building Canada's health data foundation (No. 2). https://www.canada.ca/content/dam/phac-aspc/documents/corporate/mandate/about-agency/external-advisory-bodies/list/pan-canadian-health-data-strategy-reports-summaries/expert-advisory-group-report-02-building-canada-health-data-foundation/expert-advisory-group-report-02-building-canada-health-data-foundation.pdf

Farkas, A. (2022). Interoperability specifications for patient summaries: Release review. https://infocentral.infoway-inforoute.ca/en/resources/docs/3988-release-review-interoperability-specifications-20220920/view-document

Fried, B. M. (2007). What killed the Santa Barbara county care data exchange? California Healthline. https://californiahealthline.org/news/what-killed-the-santa-barbara-county-care-data-exchange

Gadsden, N. L. and V. L. (2016). Health inequities, social determinants, and intersectionality. *NAM Perspectives*. https://doi.org/10.31478/201612a

Gagnon, J. (2022). *Implementation of Electronic Medical Records in Primary Care: Case Study of Quebec Health Policy* [Doctoral]. McGill University.

García-Roa, M., del Carmen Vicente-Ayuso, M., Bobes, A. M., Pedraza, A. C., González-Fernández, A., Martín, M. P., Sáez, I., Seghatchian, J., & Gutiérrez, L. (2017). Red blood cell storage time and transfusion: current practice, concerns and future perspectives. *Blood Transfusion*, *15*(3), 222–231. https://doi.org/10.2450/2017.0345-16

Georgia Health Policy Center. (2015, February 18). Georgia State University receives $2.7 million federal grant to improve blood transfusion outcomes. https://ghpc.gsu.edu/2015/02/18/georgia-state-university-receives-2-7-million-federal-grant-improve-blood-transfusion-outcomes/

Gevers J. K. (2001). Evaluatie van de Wet op de Geneeskundige Behandelingsovereenkomst (WGBO) [Evaluation of the Dutch Medical Treatment Act (WGBO)]. *Nederlands tijdschrift voor geneeskunde*, *145*(11), 509–512.

Gheorghiu, B., & Hagens, S. (2016). Measuring interoperable EHR adoption and maturity: A Canadian example. *BMC Medical Informatics and Decision Making*, *16*, 8. https://doi.org/10.1186/s12911-016-0247-x

Gill K. S., Muntner P., Lafayette R. A., Petersen J., Fink J. C., Gilbertson D. T., & Bradbury B. D. (2013) Red blood cell transfusion use in patients with chronic kidney disease. *Nephrology Dialysis Transplantation*, *28*(6), 1504–1515. https://doi.org/10.1093/ndt/gfs580

Goree, J. H., & Jackson, J. (2022). Do racial and ethnic disparities lead to the undertreatment of pain? Are there solutions? *Current Opinion in Anaesthesiology*, *35*(3), 273–277. https://doi.org/10.1097/ACO.0000000000001139

Harm, S. K., Yazer, M. H., Monis, G. F., Triulzi, D. J., Aubuchon, J. P., & Delaney, M. (2014). A centralized recipient database enhances the serologic safety of RBC transfusions for patients with sickle cell disease. *American Journal of Clinical Pathology*, *141*(2), 256–261. https://doi.org/10.1309/AJCP47QAAXTOZEKJ

Harvey, S. A., Lim, E., Gandhi, K. R., Miyamura, J., & Nakagawa, K. (2017). Racial-ethnic disparities in postpartum hemorrhage in Native Hawaiians, Pacific Islanders, and Asians. *Hawai'i Journal of Medicine & Public Health*, *76*(5), 128–132. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5418537/

Haywood, C., Lanzkron, S., Bediako, S., Strouse, J. J., Haythornthwaite, J., Carroll, C. P., Diener-West, M., Onojobi, G., & Beach, M. C. (2014). Perceived discrimination, patient trust, and adherence to medical recommendations among persons with sickle cell disease. *Journal of General Internal Medicine*, *29*(12), 1657–1662. https://doi.org/10.1007/s11606-014-2986-7

Haywood, C., Tanabe, P., Naik, R., Beach, M. C., & Lanzkron, S. (2013). The impact of race and disease on sickle cell patient wait times in the emergency department. *The American Journal of Emergency Medicine*, *31*(4), 651–656. https://doi.org/10.1016/j.ajem.2012.11.005

HealthIT.Gov. (2019, April 29). State health information exchange | HealthIT.gov. https://www.healthit.gov/topic/onc-hitech-programs/state-health-information-exchange

Heck, J. L., Jones, E. J., Bohn, D., McCage, S., Parker, J. G., Parker, M., Pierce, S. L., & Campbell, J. (2021). Maternal mortality among American Indian/Alaska Native women: A scoping review. [Review]. *Journal of Women*, *30*(2), 220–229. https://doi.org/10.1089/jwh.2020.8890

Hendrickson, J. E. (2020). Red blood cell alloimmunization and sickle cell disease: a narrative review on antibody induction. *Annals of Blood*, *5*, 33. https://doi.org/10.21037/aob-2020-scd-01

Hiratsuka, V. Y., Hahn, M. J., Woodbury, R. B., Hull, S. C., Wilson, D. R., Bonham, V. L., Dillard, D. A., Avey, J. P., Beckel-Mitchener, A. C., Blome, J., Claw, K., Ferucci, E. D., Gachupin, F. C., Ghazarian, A., Hindorff, L., Jooma, S., Trinidad, S. B., Troyer, J., & Walajahi, H. (2020). Alaska Native genomic research: Perspectives from Alaska Native leaders, federal staff, and biomedical researchers. [Review]. *Genetics in Medicine*, *22*(12), 1935–1943. https://doi.org/10.1038/s41436-020-0926-y

Hoppe C. C. (2013). Prenatal and newborn screening for hemoglobinopathies. *International Journal of Laboratory Hematology*, *35*(3), 297–305. https://doi.org/10.1111/ijlh.12076

Horgan, D., Hajduch, M., Vrana, M., Soderberg, J., Hughes, N., Omar, M. I., Lal, J. A., Kozaric, M., Cascini, F., Thaler, V., Solà-Morales, O., Romão, M., Destrebecq, F., & Sky Gross, E. (2022). European health data space-an opportunity now to grasp the future of data-driven healthcare. *Healthcare*, *10*(9), 1629. https://doi.org/10.3390/healthcare10091629

Ibrahim, H. N., Ishani, A., Guo, H., & Gilbertson, D. T. (2009). Blood transfusion use in non-dialysis-dependent chronic kidney disease patients aged 65 years and older. *Nephrology, Dialysis, Transplantation: Official Publication of The European Dialysis And Transplant Association - European Renal Association*, *24*(10), 3138–3143. https://doi.org/10.1093/ndt/gfp213

Jansen, G. (2007). Evidence based studies in clinical transfusion medicine. Journal of Blood Transfusion. https://www.researchgate.net/publication/264713490_Evidence_based_studies_in_clinical_transfusion_medicine

Jones, S. (2023, April 3). *Community Blood Center's Antibody Registry*. [Presentation] Red Blood Cell Alloantibody Exchange Working Group Meeting, Virtual.

Kallio, H., Candidate, P., Anna-Maija, P., Martin, J., & Mari, K. (2016). Systematic methodological review: Developing a framework for a qualitative semi-structured interview guide. *Journal of Advanced Nursing*. https://doi.org/10.1111/jan.13031

Kalra, A., & O'Reilly, S. (2022, November 15). *Connected care. A healthier Canada*. Infoway Partnership Conference. https://www.infoway-inforoute.ca/en/component/edocman/6415-connected-care-a-healthier-canada/view-document?Itemid=101

Kanter, J., Gibson, R., Lawrence, R. H., Smeltzer, M. P., Pugh, N. L., Glassberg, J., Masese, R. V., King, A. A., Calhoun, C., Hankins, J. S., & Treadwell, M. (2020). Perceptions of US adolescents and adults with sickle cell disease on their quality of care. *JAMA Network Open*, *3*(5), e206016. https://doi.org/10.1001/jamanetworkopen.2020.6016

Kavanagh, P. L., Fasipe, T. A., & Wun, T. (2022). Sickle cell disease: A review. *JAMA*, *328*(1), 57–68. https://doi.org/10.1001/jama.2022.10233

Klöcker, P. N., Bernnat, R., & Veit, D. J. (2015). Stakeholder behavior in national eHealth implementation programs. *Health Policy and Technology*, *4*(2), 113-120. https://doi.org/10.1016/j.hlpt.2015.02.010

Knerr, S., Wayman, D., & Bonham, V. L. (2011). Inclusion of racial and ethnic minorities in genetic research: Advance the spirit by changing the rules? *The Journal of Law, Medicine & Ethics: A Journal of the American Society of Law, Medicine & Ethics*, *39*(3), 502–512. https://doi.org/10.1111/j.1748-720X.2011.00617.x

Kruse, G., Lopez-Carmen, V. A., Jensen, A., Hardie, L., & Sequist, T. D. (2022). The Indian Health Service and American Indian/Alaska Native health outcomes. [Review]. *Annual Review of Public Health*, *1*, 559–576. https://doi.org/10.1146/annurev-publhealth-052620-103633

Laberge, M., Brundisini, F. K., Champagne, M., & Daniel, I. (2022). Hospital funding reforms in Canada: A narrative review of Ontario and Quebec strategies. *Health Research Policy and Systems*, *20*(1), 76. https://doi.org/10.1186/s12961-022-00879-2

Lal, A., Wong, T. E., Andrews, J., Balasa, V. V., Chung, J. H., Forester, C. M., Ikeda, A. K., Keel, S. B., Pagano, M. B., Puthenveetil, G., Shah, S. J., Yu, J. C., & Vichinsky, E. P. (2018). Transfusion practices and complications in thalassemia. *Transfusion*, *58*(12), 2826–2835. https://doi.org/10.1111/trf.14875

Lal, A., Wong, T., Keel, S., Pagano, M., Chung, J., Kamdar, A., Rao, L., Ikeda, A., Puthenveetil, G., Shah, S., Yu, J., & Vichinsky, E. (2021). The transfusion management of beta thalassemia in the United States. *Transfusion*, *61*(10), 3027–3039. https://doi.org/10.1111/trf.16640

Lauridsen, L., & Campbell-Lee, S. A. (2022). Doing more with less: Patient blood management meets sickle cell disease management. *Transfusion*, *62*(9), 1688–1692. https://doi.org/10.1111/trf.17073

Lawrence, R. H., Singleton, A., & Branscomb, J. (2020). Blood transfusion: Knowledge, perspectives, and experience of individuals with sickle cell disease. *Journal of Patient Experience*, *7*(6), 1109–1114. https://doi.org/10.1177/2374373520956744

Le, C. H. H. (2016). The prevalence of anemia and moderate-severe anemia in the US population (NHANES 2003-2012). *PLoS ONE*, *11*(11), e0166635. https://doi.org/10.1371/journal.pone.0166635

Lee, C., Ayers, S. L., & Kronenfeld, J. J. (2009). The association between perceived provider discrimination, health care utilization, and health status in racial and ethnic minorities. *Ethnicity & Disease*, *19*(3), 330–337.

Lee, L., Smith-Whitley, K., Banks, S., & Puckrein, G. (2019). Reducing health care disparities in sickle cell disease: A review. *Public Health Reports (Washington, D.C.: 1974)*, *134*(6), 599–607. https://doi.org/10.1177/0033354919881438

Liem, R. I., Gilgour, B., Pelligra, S. A., Mason, M., & Thompson, A. A. (2011). The impact of thalassemia on Southeast Asian and Asian Indian families in the United States: A qualitative study. *Ethnicity & Disease*, *21*(3), 361–369.

Linden, F. (2014, July 1). *Smart Open Services for European Patients – Open eHealth initiative for a European large-scale pilot of patient summary and electronic prescription*. Letter.

Linder, G. E., & Ipe, T. S. (2022). Pregnancy and postpartum transfusion. *Annals of Blood*, *7*(0), Article 0. https://doi.org/10.21037/aob-21-73

MAK-SYSTEM. (n.d.). Software. https://www.mak-system.com/software/

McClure, E., Ng, J., Vitzthum, K., & Rudd, R. (2016). A mismatch between patient education materials about sickle cell disease and the literacy level of their intended audience. *Preventing Chronic Disease*. 13. https://doi.org/10.5888/pcd13.150478

Migotsky, M., Beestrum, M., & Badawy, S. M. (2022). Recent advances in sickle-cell disease therapies: A review of Voxelotor, Crizanlizumab, and L-glutamine. *Pharmacy (Basel, Switzerland)*, *10*(5), 123. https://doi.org/10.3390/pharmacy10050123

Miller, R. H., & Miller, B. S. (2007). The Santa Barbara county care data exchange: what happened? *Health affairs (Project Hope)*, *26*(5), w568–w580. https://doi.org/10.1377/hlthaff.26.5.w568

Ministry of Health and Long-Term Care and eHealth Ontario. (2016). Electronic health records' implementation status. https://www.auditor.on.ca/en/content/annualreports/arreports/en16/v1_303en16.pdf

Mobey, A., & Parker, D. (2002). Risk evaluation and its importance to project implementation. *Work Study*, *51*(4), 202–208. https://doi.org/10.1108/00438020210430760

Moharra, M., Almazán, C., Decool, M., Nilsson, A. L., Allegretti, N., & Seven, M. (2015). Implementation of a cross-border health service: physician and pharmacists' opinions from the epSOS project. *Family Practice*, *32*(5), 564-567. https://doi.org/10.1093/fampra/cmv052

Nalin, M., Baroni, I., Faiella, G., Romano, M., Matrisciano, F., Gelenbe, E., Martinez, D. M., Dumortier, J., Natsiavas, P., Votis, K., Koutkias, V., Tzovaras, D., & Clemente, F. (2019). The European cross-border health data exchange roadmap: Case study in the Italian setting. *Journal of Biomedical Informatics*, *94*, 103183. https://doi.org/10.1016/j.jbi.2019.103183

Narayanan, D., Hogan, N. B., Schaser, K. A., Ruegsegger, P., & Rose, W. N. (2022). A case study in process improvement to minimize delays from obtaining blood for red cell exchange for a patient with sickle cell disease and multiple red blood cell alloantibodies. *Case Reports in Hematology*, *2022*, 1–4. https://doi.org/10.1155/2022/1562921

National Academies of Sciences, Engineering, and Medicine. (2020). Addressing sickle cell disease: A strategic plan and blueprint for action. Washington, DC: The National Academies Press. https://doi.org/10.17226/25632

National Center for Health Statistics. (n.d.-a). Anemia or iron deficiency fast statistics. Centers for Disease Control and Prevention. https://www.cdc.gov/nchs/fastats/anemia.htm

National Center for Health Statistics. (n.d.-b). Emergency department visits. Centers for Disease Control and Prevention. https://www.cdc.gov/nchs/fastats/emergency-department.htm

National Institutes of Health National Heart, Lung, and Blood Institute. (2022, March 24). Anemia—treatment and management. https://www.nhlbi.nih.gov/health/anemia/treatment

Newfoundland & Labrador Centre for Health Information. (2020). Annual business report. https://www.gov.nl.ca/hcs/files/Newfoundlandand-Labrador-Centre-for-Health-Information-Annual-Report-2019-2020.pdf

NORD. (n.d.) Rare disease database: Immune thrombocytopenia. https://rarediseases.org/rare-diseases/immune-thrombocytopenia/#:~:text=The%20incidence%20(how%20many%20people,time)%20is%209.5%20per%20100%2C000

NPAR. (n.d.). Home | NPAR - National Patient Antibody Registry. Retrieved June 16, 2023, from https://www.npar.com/

Office of the Auditor General of British Columbia. (2010). Electronic Health Record Implementation in British Columbia. https://www.bcauditor.com/sites/default/files/publications/2010/report_9/report/bcoag-electronic-health-records-ehr.pdf

Office of the Auditor General of Canada (2010). *Electronic health records in Canada: An overview of federal and provincial audit reports*. [Audit Report]. https://www.assembly.pe.ca/sites/www.assembly.pe.ca/files/overview-electronic-health-records-in-Canada.pdf

Office of the National Coordinator for Health Information Technology. (n.d.). Health information exchange strategic and operational plan profile. Retrieved March 26, 2023, from https://www.healthit.gov/sites/default/files/wi_state_hie_profile.pdf

Office of the Privacy Commissioner of Canada. (2018, January 9). PIPEDA in brief. https://www.priv.gc.ca/en/privacy-topics/privacy-laws-in-canada/the-personal-information-protection-and-electronic-documents-act-pipeda/pipeda_brief/

Park, H., Desai, R., Liu, X., Smith, S. M., Hincapie-Castillo, J., Henry, L., Goodin, A., Gopal, S., Pepine, C. J., & Mohandas, R. (2022). Medicare bundled payment policy on anemia care, major adverse cardiovascular events, and mortality among adults undergoing hemodialysis. *Clinical Journal of the American Society of Nephrology*, *17*(6), 851–860. https://doi.org/10.2215/CJN.14361121

Palojoki, S., Vakkuri, A., & Vuokko, R. (2021). The European cross-border health data exchange: Focus on clinically relevant data. *Studies in Health Technology and Informatics*, *281*, 442–446. https://doi.org/10.3233/SHTI210197

Patterson, S., Singleton, A., Branscomb, J., Nsonwu, V., & Spratling, R. (2022). Transfusion complications in thalassemia: Patient and perspectives. *Frontiers in Medicine*, *9*. https://www.frontiersin.org/articles/10.3389/fmed.2022.772886

Piha, T., Kaliola, M., Kesisoglou, I., Abboud, L., Cosgrove, S., Gutter, Z., Bencze, L., Csizmadia, I. (2022). Preliminary study on funding sources and costs of secondary use of health data in the EU. Towards the European Health Data Space. https://tehdas.eu/app/uploads/2022/04/tehdas-preliminary-study-on-funding-sources-and-costs-of-secondary-use-of-health-data-in-the-eu.pdf

Prabhakar, H. (2009). Sickle cell disease and Native Americans: Overview and long-term considerations for delivery of care. *The IHS Primary Care Provider*, *310*(11). https://www.ihs.gov/sites/provider/themes/responsive2017/display_objects/documents/2000_2009/PROV1109.pdf

ProPublica. (n.d.). Wisconsin statewide health information network inc - nonprofit explorer - ProPublica. Retrieved March 26, 2023, from https://projects.propublica.org/nonprofits/organizations/274344294

Punaglom, N., Kongvattananon, P., & Somprasert, C. (2019). Experience of parents caring for their children with thalassemia: Challenges and issues for integrative review. *The Bangkok Medical Journal*, *15*(1), Article 1. https://doi.org/10.31524/bkkmedj.2019.02.018

Quebec Management Standards and Practices. (2005). Financial management manual. https://g26.pub.msss.rtss.qc.ca/Formulaires/MGF/ConsMGF.aspx?enc=5UP13ChV7SM=

Quebec Ministry of Health and Social Services. (1999, December 1). Le système du sang au Québec – Rapport Gélineau - Publications du ministère de la Santé et des Services sociaux. https://publications.msss.gouv.qc.ca/msss/document-000417/?&txt=Le%20syst%C3%A8me%20du%20sang%20au%20Qu%C3%A9bec&msss_valpub&date=DESC

Quebec Ministry of Health and Social Services. (2017a). Comité de biovigilance - Biovigilance - Professionnels de la santé - MSSS. https://www.msss.gouv.qc.ca/professionnels/soins-et-services/biovigilance/comite-de-biovigilance/

Quebec Ministry of Health and Social Services. (2017b). Composition - Biovigilance - Professionnels de la santé - MSSS. https://www.msss.gouv.qc.ca/professionnels/soins-et-services/biovigilance/composition/

Quebec Ministry of Health and Social Services. (2017c). Fonctionnement - Biovigilance - Professionnels de la santé - MSSS. https://www.msss.gouv.qc.ca/professionnels/soins-et-services/biovigilance/fonctionnement/#siiath-sommaire-transfusionnel

Quebec Ministry of Health and Social Services. (2017d). Historique - Biovigilance - Professionnels de la santé - MSSS. https://www.msss.gouv.qc.ca/professionnels/soins-et-services/biovigilance/historique/

Quebec Ministry of Health and Social Services (2017e.). Système du sang du Québec - Biovigilance - Professionnels de la santé - MSSS. Retrieved August 3, 2023, from https://www.msss.gouv.qc.ca/professionnels/soins-et-services/biovigilance/systeme-du-sang-du-quebec/

Quebec Publications. (2013). Loi sur Héma-Québec et sur le Comité de biovigilance. https://www.legisquebec.gouv.qc.ca/fr/document/lc/H-1.1

Rangi, S. K., & Terry, S. F. (2014). Genetic testing and native peoples: The call for community-based participatory research. [Review]. *Genetic Testing & Molecular Biomarkers*, *18*(8), 531–532. https://doi.org/10.1089/gtmb.2014.1557

Regulation (EC) No 1882/2003 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. (2003). *Official Journal of the European Journal L284,* p. 1–53.

Regulation (EU) No 1316/2013 on establishing the Connecting Europe Facility. (2013). *Official Journal of the European Union L384*, p. 129–171.

Regulation (EU) No 910/2014 the electronic identification and trust services for electronic transactions in the internal market. (2014). *Official Journal of the European Union L257*, p. 73–114.

Robillard, P., Nawej, K. I., & Jochem, K. (2004). The Quebec hemovigilance system: description and results from the first two years. *Transfusion and Apheresis Science: Official Journal of the World Apheresis Association: Official Journal of the European Society for Haemapheresis*, *31*(2), 111–122. https://doi.org/10.1016/j.transci.2004.07.005

Rozenblum, R., Jang, Y., Zimlichman, E., Salzberg, C., Tamblyn, M., Buckeridge, D., Forster, A., Bates, D. W., & Tamblyn, R. (2011). A qualitative study of Canada's experience with the implementation of electronic health information technology. *CMAJ: Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne*, *183*(5), E281–288. https://doi.org/10.1503/cmaj.100856

Salzberg, C. A., Jang, Y., Rozenblum, R., Zimlichman, E., Tamblyn, R., & Bates, D. W. (2012). Policy initiatives for health information technology: A qualitative study of U.S. expectations and Canada's experience. *International Journal of Medical Informatics*, *81*(10), 713–722. https://doi.org/10.1016/j.ijmedinf.2012.07.007

Sanquin. (2011). Blood transfusion guideline. https://web.archive.org/web/20130718002720/http:/www.sanquin.nl/repository/documenten/en/prod-en-dienst/287294/blood-transfusion-guideline.pdf

Sanquin. (2017). TRIX procedures: methods of use. https://www.sanquin.org/binaries/content/assets/nl/producten-en-diensten/trix/trix-procedures-v1.4.pdf

Sanquin. (2021a). Frequently asked questions. https://www.sanquin.org/nl/producten-en-diensten/trix/trix-faq

Sanquin. (2021b). TRIX charges. https://www.sanquin.org/nl/producten-en-diensten/trix/kosten

Sanquin. (2021c). TRIX implementation. https://www.sanquin.org/nl/producten-en-diensten/trix/trix-implementatie

Sayani, F. A., & Kwiatkowski, J. L. (2015). Increasing prevalence of thalassemia in America: Implications for primary care. *Annals of Medicine*, *47*(7), 592–604. https://doi.org/10.3109/07853890.2015.1091942

Schmidt, K. (2016, November 18). Infoway announces enhanced certification services program for digital health solutions. [News Release]. Canada Health Infoway. https://www.infoway-inforoute.ca/en/news-events-blog/news/2016-news-releases/infoway-announces-enhanced-certification-services-program-for-digital-health-solutions

Schwickerath, V., Kowalski, M., & Menitove, J. E. (2010). Regional registry of patient alloantibodies: First-year experience. *Transfusion*, *50*(7), 1465–1470. https://doi.org/10.1111/j.1537-2995.2010.02629.x

Singh, N. (2023, June 12). *Q & A Session: Thalassemia Patient Representative Navdeep Singh.* Red Blood Cell Alloantibody Exchange Working Group Meeting, Virtual.

Small, C., Kramer, H. J., Griffin, K. A., Vellanki, K., Leehey, D. J., Bansal, V. K., & Markossian, T. W. (2017). Non-dialysis dependent chronic kidney disease is associated with high total and out-of-pocket healthcare expenditures. *BMC Nephrology*, *18*(1), 3. https://doi.org/10.1186/s12882-016-0432-2

Soucie, J. M., Miller, C. H., Dupervil, B., Le, B., & Buckner, T. W. (2020). Occurrence rates of haemophilia among males in the United States based on surveillance conducted in specialized haemophilia treatment centres. *Haemophilia: The Official Journal of the World Federation of Hemophilia*, *26*(3), 487–493. https://doi.org/10.1111/hae.13998

Staffa, M., Coppolino, L., Sgaglione, L., Gelenbe, E., Komnios, I., Grivas, E., ... & Castaldo, L. (2018). KONFIDO: An OpenNCP-based secure eHealth data exchange system. In *Security in Computer and Information Sciences: First International ISCIS Security Workshop 2018, Euro-CYBERSEC 2018, London, UK, February 26–27, 2018, Revised Selected Papers 1* (pp. 11–27). Springer International Publishing.

TECHNATION. (2021). Canadian national health interoperability standards. https://technationcanada.ca/wp-content/uploads/2021/11/TN-white-paper-health-interoperabilty-standards-final.pdf

TI MSSS (2016a). Extranet. Retrieved July 5, 2023, from https://www.ti.msss.gouv.qc.ca/extranet.aspx

TI MSSS (2016b). SIIATH – Gestion du sang. Retrieved July 5, 2023, from https://www.ti.msss.gouv.qc.ca/Familles-de-services/Actifs-informationnels/SIIATH-Gestion-du-sang.aspx

TI MSSS (2016c). SIIATH - Sommaire transfusionnel. Retrieved July 5, 2023, from https://www.ti.msss.gouv.qc.ca/Familles-de-services/Actifs-informationnels/SIIATH-Sommaire-transfusionnel.aspx

Transfusion Antibody Exchange Inc. (n.d.) Alloantibody exchange. Alloantibody. Retrieved August 14, 2023, from https://www.alloantibody.org/

Tormey, C. A., & Hendrickson, J. E. (2019). Transfusion-related red blood cell alloantibodies: Induction and consequences. *Blood*, *133*(17), 1821–1830. https://doi.org/10.1182/blood-2018-08-833962

TRIP Foundation. (2007). *TRIP report 2007: Hemovigilance*. https://www.tripnet.nl/en/publications/trip-reports/

TRIP Foundation. (2012). *TRIP report 2012: Hemovigilance.* https://www.tripnet.nl/en/publications/trip-reports/

TRIP Foundation. (2013). *TRIP report 2013: Hemovigilance.* https://www.tripnet.nl/en/publications/trip-reports/

TRIP Foundation. (2016). *TRIP report 2016: Hemovigilance.* https://www.tripnet.nl/en/publications/trip-reports/

UBC Centre for Blood Research. (2023, February 22). BC provincial blood coordinating office: Old dog, new tricks. [Video] CBR Seminars – Dr. Andre Shih. https://www.youtube.com/watch?v=oa4VoxLUInw

Unni, N., Peddinghaus, M., Tormey, C. A., & Stack, G. (2014). Record fragmentation due to transfusion at multiple health care facilities: a risk factor for delayed hemolytic transfusion reactions. *Transfusion*, *54*(1), 98–103. https://doi.org/10.1111/trf.12251

United Network for Organ Sharing. (2022). *2022 organ transplants again set annual records*. [Press Release]. https://unos.org/news/2022-organ-transplants-again-set-annual-records/

U.S. Census Bureau. (2020). Annual Business Survey: Statistics for Employer Firms by Industry, Sex, Ethnicity, Race, and Veteran Status for the U.S., States, and Metro Areas: 2020. AB2000CSA01. https://data.census.gov/table?q=hospital&g=0400000US11,24,51,54&tid=ABSCS2020.AB2000C

U.S. Census Bureau. (n.d.) QuickFacts: United States. https://www.census.gov/quickfacts/fact/table/US/LFE046221

Valle, J., Baker, J. R., Madrigal, D., Ferrerosa, J., & Paulukonis, S. (2022). Sickle cell disease among Latinx in California. *PLOS ONE*, *17*(10), e0276653. https://doi.org/10.1371/journal.pone.0276653

van Gammeren, A., Bos, A., Som, N., Veldhoven, C., Vossen, R., & Folman, C. (2019). A national transfusion register of irregular antibodies and cross (X)-match problems: TRIX, a 10-year analysis. *Transfusion, 59*(8), 2559–2566.

Veldhoven, C. (2016). TRIX manual. Sanquin. https://www.sanquin.org/binaries/content/assets/nl/producten-en-diensten/trix/handleiding.pdf

Williams, L. A., 3rd, Lorenz, R. G., Tahir, A., Pham, H. P., & Marques, M. B. (2016). High percentage of evanescent red cell antibodies in patients with sickle cell disease highlights need for a national antibody database. *Southern Medical Journal*, *109*(9), 588–591. https://doi.org/10.14423/SMJ.0000000000000528

Wisconsin Legislative Council. (2010). Act Memo: 2009 Wisconsin Act 274 [2009 Assembly Bill 779] Electronic health information exchange. https://docs.legis.wisconsin.gov/2009/related/lcactmemo/act274

Wisconsin Department of Health Services Office of The Secretary. (2010). Department of Health and Human Services Office of the Secretary of HHS Notice of Grant Award. https://web.archive.org/web/20150201202108/https://dhs.wisconsin.gov/sites/default/files/legacy/ehealth/WIREDforHealth/WIsNOA2.26.10.pdf

Wisconsin State Legislature. (2020, April 15). 2019 Assembly Bill 2038: 2019 Wisconsin Act 185. https://docs.legis.wisconsin.gov/2019/related/acts/185

WISHIN. (2012a). WIRED for health HIT: Wisconsin HIT strategic & operational plan - 2012 update. https://wishin.org/wp-content/uploads/2022/10/SOP-FINAL.pdf

WISHIN. (2012b). SOP – WISHIN. https://wishin.org/sop/

WISHIN. (2014). WISHIN pulse statement on privacy, security and HIPAA compliance. https://wishin.org/wp-content/uploads/2023/01/SEC-STM-07-14-Pulse-Statement-on-Privacy-Security-HIPAA.pdf

WISHIN. (2023). The window is closing on the first phase of the DHS HIE P4P program – WISHIN. https://wishin.org/the-window-is-closing-on-the-first-phase-of-the-dhs-hie-p4p-program/

WISHIN. (n.d.-a). *Our history – WISHIN*. https://wishin.org/our-history/

WISHIN. (n.d.-b). *Wisconsin privacy law fact sheet*. https://wishin.org/wp-content/uploads/2022/10/SEC-PLA-072014-Wisconsin-Privacy-Law-Fact-Sheet.pdf

WISHIN. (n.d.-c). Dashboard – WISHIN. https://wishin.org/dashboard/

WISHIN. (n.d.-d). Direct+ – WISHIN. https://wishin.org/direct-plus/

WISHIN. (n.d.-e). WISHIN – Wisconsin's premier interoperable health information technology. https://wishin.org/

WISHIN. (n.d.-f). Founders – WISHIN. https://wishin.org/founders/

WISHIN. (n.d.-g). Health information exchange: A guide to patient choice. https://wishin.org/wp-content/uploads/2023/05/WISHINPulse-OptOut.pdf

WISHIN. (n.d.-i). Participant map – WISHIN. https://wishin.org/participant-map/

WISHIN. (n.d.-j). Partners – WISHIN. https://wishin.org/partners/

Wood, E. M., & McQuilten Z. K. (2020). Outpatient transfusions for myelodysplastic syndromes. *Hematology ASH Education Program, 1*, 167–174. https://doi.org/10.1182/hematology.2020000103

Wylie, B. J., & D'Alton, M. E. (2010). Fetomaternal hemorrhage. *Obstetrics and Gynecology*, *115*(5), 1039–1051. https://doi.org/10.1097/AOG.0b013e3181da7929

Zakieh A., Siddiqui A. H. (2017). Emergency department utilization by haemophilia patients in United States. *Haemophilia*. *23*(3), e188-e193. https://doi.org/10.1111/hae.13187

Zimlichman, E., Rozenblum, R., Salzberg, C. A., Jang, Y., Tamblyn, M., Tamblyn, R., & Bates, D. W. (2012). Lessons from the Canadian national health information technology plan for the United States: Opinions of key Canadian experts. *Journal of the American Medical Informatics Association*, *19*(3), 453–459. https://doi.org/10.1136/amiajnl-2011-000127

Zinszer, K., Tamblyn, R., Bates, D. W., & Buckeridge, D. L. (2013). A qualitative study of health information technology in the Canadian public health system. *BMC Public Health*, *13*(1), 509. https://doi.org/10.1186/1471-2458-13-509