An Exploration into the Current Obstacles in Pediatric Medicine that Impede Access to Essential Medical Devices and Medications

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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An Overview of Pediatric Medicine

The pediatric population faces unprecedented challenges in medicine. In the United States, pediatric medicine includes all those aged 0 to 18 (Espinoza, 2021). Despite representing approximately one quarter of the total population, less than 10% of all health care funding is available for pediatric needs (Espinoza, 2021). In addition, there is a distinct lack of medical innovation in the field with dire consequences. Children are not simply little adults, so adult medications or devices cannot always be scaled down with the same effects. Pediatric patients have different needs that must be acknowledged and addressed; however, current treatment options fail to do this. For example, certain diseases have no medical device options available and clinicians must modify adult devices to fit their needs (J. S. Sutherell et al., 2010). Approved devices have efficacy and safety data available, however, these modified devices are typically for other purposes and thus there is an inherent risk when using the device in a new manner (J. S. Sutherell et al., 2010). This paper explores the research question: why does the field of pediatric medicine struggle to access the medical devices and medications necessary for treatment?

These challenges will be investigated using Harrison's theory of iterative sociotechnical analysis (ISTA) with a particular focus on exploring the unintended consequences of the current actions taken and the inaction being taken in pediatric medicine. In addition, the Social Construction of Technology (SCOT) will be utilized to illustrate how the adoption and dissemination of a technology is dependent on the advocacy of various stakeholders.

Methods

The following methods are utilized to answer the question: why does the field of pediatric medicine struggle to access the medical devices and medications necessary for

treatment? Since pediatrics is too broad to analyze all at once this paper focuses on only two case studies. The lack of devices to treat congenital heart defects (CHD) and limited treatment options for Crohn's disease. The analysis for both case studies is guided by key phrases such as pediatric-specific (devices or therapeutics), off-label usage, and unintended outcomes. To analyze CHD, data from FDA guidance reports on device development and approval, pediatric-specific programs, and legislative acts is compiled. It is then organized into a timeline to conduct a historical analysis of the impact of FDA actions on pediatric device development. For Crohn's, information regarding the manifestation, progression, and management of the disease in adult and pediatric populations is the basis for analysis. The data is from an extensive literature review on medication each population has access to, symptoms, treatment options, and general outcomes. The data is organized into a comparative timeline to illustrate the major differences. Additionally, interviews with cardiologists (see Appendix A for questions) and a nurse practitioner specializing in gastrointestinal (GI) medicine (see Appendix B for questions), are used to provide additional context to the two case studies. The interview data is an essential component of the STS analysis as it identifies the connection between the events on the timelines and the impact or influence from various social groups. Harrison's theory is used to understand how unintentional roadblocks in pediatric medicine may be unintentionally worsening outcomes, while SCOT explores the role various groups play in treating and managing the condition.

Why Pediatric Medicine Matters

Pediatrics differs from adult medicine in a multitude of ways. One of the predominant ones being that children are still developing, which impacts the necessary care. Research shows that illness manifests differently in the adult and child populations, which underlines the need for

pediatric specific medicines (Kelsen & Baldassano, 2008). An example is Inflammatory bowel disease (IBD). The frequency of cases in both populations has been rising as of late; however, it is more problematic in the pediatric population as children's physiology is still in development (Kelsen & Baldassano, 2008). Crohn's disease, a type of IBD, impacts a person's ability to absorb nutrients (Kelsen & Baldassano, 2008). In children, this can be detrimental as it can permanently stunt growth and delay puberty if it is not treated promptly (Kelsen & Baldassano, 2008). However, despite the need for better treatments, current research targets the adult population with most clinical trials being intended for adults (Kelsen & Baldassano, 2008). Pediatric gastroenterologists must overcome more regulations in order for pediatric patients to get access to therapeutics that were not designed with children in mind (Kelsen & Baldassano, 2008). The fact that therapeutics are less accessible to the pediatric population is problematic as children need intervention earlier on in order to prevent irreversible damage.

Another challenge in pediatric medicine is the fact that there is a diversity of illness, so there are more versions of the same condition throughout the population (Stern, 2018). An example is with CHD, a type of abnormality that affects the structure of the heart and its function (Stern, 2018). The treatment often requires surgery to repair the defect unless heart function is only minimally impacted (Stern, 2018). This reconstructive surgery often requires various medical devices as it is a major repair. However, there are few pediatric devices on the market, so clinicians are forced to adapt by altering adult devices to fit their purpose (Shoji & Shinoka, 2018). This technology is prone to infection, blood clotting, and calcification as they are often not designed for the different environment where they are placed in the body (e.g. a device designed for a certain pressure environment may not thrive in a different one) (Shoji & Shinoka, 2018). A secondary problem is that children grow and current devices are often metals that are

stagnant. Thus, the child must face the burden of multiple surgeries as they age in order to get the device replaced with a larger size.

Although there is a clear need for more innovation in the pediatric space, not enough is being done to meet the needs. There is limited profit for companies to invest in pediatrics devices (Fischer et al., 2019). The pediatric population is smaller than the adult population and there are more variations of the same conditions, so companies face a low investment return on any new technology (Stern, 2018). Thus, there is less motivation to put money into research, development, and manufacturing. The FDA has programs like the humanitarian device exemption to help pediatric devices get to market, but even current regulatory processes are not enough to combat the problem (Fischer et al., 2019).

Using ISTA and SCOT to Explore Pediatric Needs

Harrison's theory of ISTA is focused on understanding the complexity of interaction between technology and the existing socio-technical systems in order to properly understand user needs and adapt technology as necessary (Harrison et al., 2007). Harrison's theory has been used to explore the unintended consequences of medical technology, specifically healthcare information technology (HIT) (Harrison et al., 2007). While this technology exists within the pediatric space it is not a pediatric innovation as it was not designed specifically for pediatric needs. HITs are the electronic record systems used in healthcare (Harrison et al., 2007). They were implemented to create a more patient-centered and safe environment (Harrison et al., 2007). However, despite its positive intentions it had undesirable consequences upon implementation because it made incorrect assumptions about the existing workflows in place (Harrison et al., 2007).

This idea of unintended consequences will be explored in the context of pediatrics. Physician's use off-label devices in order to meet the needs of their patients; however, these devices were approved based on testing and marketing for the adult population (Shoji & Shinoka, 2018). The lack of options has led to physicians having to find other technologies that have a meaningful impact even when the risks are higher. Despite the theory highlighting the potential downsides of technological integration in medicine, Harrison underscores an integration failure is an opportunity to learn and improved upon a technology rather than reject it (Harrison et al., 2007). This is a central message for understanding and addressing the current challenges in pediatric medicine.

SCOT is a theory developed by Pinch & Bijker. This theory explores the idea that technological development is influenced by social groups and their present needs (Pinch & Bijker, 1984). The pediatric population is unique as they cannot properly advocate for their own needs, so, other social groups like physicians must become involved in promoting change. SCOT has been previously investigated in relation to medicine. The lens of interpretative flexibility (a subset of SCOT) has been used to explore how high-risk technology can succeed despite the risks (Ulucanlar et al., 2013). One example is the case of a bioengineered trachea (a compassionate care case for a young child), the framing of the technology as a last-resort by the media and physicians convinced healthcare agencies to allow for the technology to be used (Gardner et al., 2017). Despite the fact that the technology was far from ready for regular use, it was framed in such a way that even if it failed it would still help future research as it could become a low-risk technology eventually (Gardner et al., 2017). This illustrates how the adoption of a technology can be influenced by stakeholders. That message is one that is necessary to promote change in the pediatric space.

Both ISTA and SCOT are used to analyze challenges in medicine as shown in the previous examples. However, the theories have yet to be used to understand pediatric-specific challenges. This is significant as the pediatric population is unique. They are inherently vulnerable as the population is still developing and unable to easily advocate for their own needs. Thus, other stakeholder groups, like parents and clinicians, play a central role in making medical decisions. SCOT is a framework that investigates the role of social groups in the adoption of technology, while ITSA outlines how to learn from technological integration failures. Analyzing pediatric challenges with these two theories creates an opportunity to understand why technological integration is failing, who might be involved, and what actions can be taken to learn from these failures. Thus, creating an outline for how to overcome the challenges in pediatrics.

Results and Discussion

Congenital Heart Defects Case Study

Congenital heart defects (CHD) can have varying degrees of severity. They can be mild or severe enough that cardiac structures are poorly formed or missing entirely (CDC, 2019). CHD are the most common type of birth defect in the US and affect nearly 1%, or 40,000, births per year (CDC, 2019). About 1 in 4 babies born with a heart defect will have a critical CHD, which is when surgery is required in the first year of life (CDC, 2019). Diagnosis is possible before birth with a fetal echocardiogram, upon birth if the baby has breathing issues, or later in life (CDC, 2019). Treatment depends entirely on the severity of the defect. More severe cases usually have multiple malformations and require immediate intervention while children with

milder cases may be able to compensate for the defect for several years. Treatment requires a personalized approach as every presentation is different.

The analysis of CHD, beginning with the timeline on FDA actions along with additional context provided by interviews, found in the rest of this section illustrates how the challenges in access to pediatric-specific devices are caused by two main factors. The first is simply that there is not enough incentive for companies to invest in the creation of pediatric devices as they have minimal profit margins due to the population being so small. The second factor is that FDA regulations have been unintentionally acting as a barrier to pediatric devices going to market. Progressive actions have been slow and even then, they are not doing nearly enough. Although the regulations are intended to help, the rate of new innovations has not increased substantially even as the regulations changed. In fact, one study found that from 2011 to 2017 the rate of approval for pediatric medical devices remained relatively constant as only 10-20% of devices proceeding to market (Takahashi et al., 2021). Instead, off-label usage continues to be the standard to address CHD, although it has simply created a new problem as these devices have unintended consequences due to the lack of safety and performance data (J. Sutherell, 2011). Despite the challenges outlined in the analysis, there is still a clear path towards change. Stakeholder groups, like clinicians and parents, play a vital role in allowing the field to adapt to better help patients (D. Frank, personal communication, March 3, 2022).

The timeline of relevant FDA actions can be found in figure 1 below. The timeline begins in 1976 with the passing of the Medical Device Amendments, which created a division responsible for the regulation of all medical devices within the FDA (Center for Devices and Radiological Health, 2018). It then progresses until 2018 with the release of the Medical Device Safety Plan (Phoumyvong & Maltese, 2019).

Year	Event	Significance
1976	Medical Device Amendments	FDA division was created and helps regulate medical devices to assure their safety and effectiveness including establishing various pathways (Pre-market approval and 510(k)) for devices to get approval (Center for Devices and Radiological Health, 2018)
1983	Office of Orphan Product Development	New FDA office was established to ensure access to innovative, safe, and effective medical products for the treatment of orphan diseases and pediatric population diseases. Includes support for clinical trial research to develop new medical products (Takahashi et al., 2021).
1999	Pediatric Advisory Committee	A third-party committee that meets annually to advise and make recommendations to the FDA Commissioner regarding pediatric research, clinical trials, labeling, and adverse event reports (Takahashi et al., 2021).
2003	FDA Guidance: Developing Pediatric Medical Devices	FDA report on the current thinking on pediatric medical devices sent to all FDA staffs. Focus on the evaluation of the safety and efficacy of medical devices for the pediatric population (Takahashi et al., 2021).
2007	Pediatric Medical Device and Safety and Improvement Act (PMDSIA)	A new law creating incentives, mandates, FDA authority, and funding to help increase the availability of devices for the pediatric population while maintaining safety standards (Humes & Westover, 2020).
2008	Humanitarian Use Device Exemption (HDE)	A new approval pathway for devices particularly for treatment or diagnosis of a disease or condition that affects less than 8,000 individuals in the US per year (Humes & Westover, 2020).
2009	Pediatric Device Consortia (PDC) Grant Program	A non-profit consortia designed to stimulate projects that will promote pediatric device development (Takahashi et al., 2021).
2015	Expedited Access Pathway	Expedites the development and prioritizes the review of medical devices that provide a more effective treatment diagnosis of life-threatening or irreversibly debilitating conditions (Takahashi et al., 2021).
2016	21st Century Cures Act	Helps accelerate medical product development and bring innovations and to patients who need them faster (Office of the FDA Commissioner, 2020).
2017	FDA Guidance: The Potential of Additive Manufacturing (AM)	This FDA report advises on the advantage of using AM to create anatomically-matched devices and other structures that cannot be easily created with traditional manufacturing approaches. AM may introduce variability into the manufacturing process as it is not as highly controlled as traditional methods (Takahashi et al., 2021).
2017	Breakthrough Device Program	Established by the Century Cures Act to replace the Expedited Access Pathway Program. More specific regulatory measures for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases. Focus on more timely access to devices (Takahashi et al., 2021).
2018	Medical Device Safety Action Plan	Statement by FDA Commissioner outlining efforts to update the regulatory process for addressing unmet needs (Phoumyvong & Maltese, 2019).

Fig.1. Timeline of Relevant Regulatory Actions that have Impacted the Development of Pediatric Medical Devices (Stiglitz, 2022)

There are several trends on the timeline that are important to highlight as they illustrate how the FDA is an obstacle to innovation. The first trend is the 31-year time difference between the first five events. The PMDSIA was supposed to be monumental for the time because it prioritized getting devices to market. It was the first-time general funding was provided to companies to incentivize them to invest in pediatric devices (Takahashi et al., 2021). Prior to the act, there was little innovation in the space because there was no market potential. Companies need enough patients for a product to be profitable, as well as a willingness to spend money to get FDA licensing approval (Hwang et al., 2014). There is a severely limited profit in pediatric devices because of the variability and the small population (Hwang et al., 2014). Medical devices require a lot of support as before production the company must invest in building a prototype, manufacture for clinical usage, and animal testing (Phoumyvong & Maltese, 2019). The American Academy of Pediatrics (AAP) recognized the need for incentivization and urged the FDA to pass the PMDSIA (Jenco, 2018). The advocacy by the AAP is an example of the SCOT, as it illustrates how the actions of relevant social groups influence change. The clinicians recognized they needed help getting access to the technologies that would help their patients and advocated to the group in control to do something drastic that would address the problem. However, it is important to concede that despite the passing of the act, there was a minimal uptick in the production of new devices. The passing of the PMDSIA was simply the first positive step towards change within the field.

Another obstacle is the current regulatory pathways. As noted on the timeline, there are three separate actions that directly impact the speed of the regulatory process: the HDE, the Expediated Access Pathway, and the Breakthrough Device Pathway. All these illustrate how the FDA is attempting to balance the necessity for safety while also increasing the efficiency of the

approval process. However, part of safety testing requires proof of success within a human (Phoumyvong & Maltese, 2019). High risk devices are typically not approved for pediatric usage because they are tested on people aged 18-21 (an available population) and there is limited regulation on if this data can be extrapolated to a younger group (Phoumyvong & Maltese, 2019). The expedited pathways illustrate how the FDA is attempting to make the adoption and dissemination of pediatric devices easier, thereby acting as an advocate under SCOT. However, there are some unintended consequences with these pathways. In particular, the inability to get high-risk devices approved because of the current requirements for proof-of-concept. These devices could be life-changing, but without a way to properly test them under the current guidelines they cannot be approved. As a result, physicians must turn to devices that are not ideal.

Some adult devices are approved for use in children. However, attempting to fit larger devices into the smaller structures of the heart can have consequences as they damage the internal structures when introduced into the vascular system (M. Hainstock, personal communication, March 2, 2022). Interviews with both clinicians revealed the common approach to the lack of technology is off-label usage. Off-label usage is the process of using a licensed medical product differently than it is approved for (Shoji & Shinoka, 2018). This type of usage is acceptable by FDA guidelines because once a license is issued, the FDA has a limited role in overseeing the devices ongoing usage outside of a significant reporting of adverse events (J. Sutherell, 2011). Through the lens of the SCOT, this off-label device usage is a clear example of how a social group, pediatric clinicians, have given new meaning to an existing technology and influenced its adoption in society. They have influenced its purpose such that it is now acting in its initial capacity and as something new. Without this adaption by clinicians, this technology

would never have become a treatment option in pediatric medicine. However, off-label usage does have consequences. As Harrison's theory underscores, implementation of a technology is not without its faults. In this case, off-label devices lack safety and efficacy data, which increases their risk (Shoji & Shinoka, 2018). These products were designed and licensed under the assumption that they would be safe for usage. However, when used in pediatrics those assumptions become false. These products now have questionable risk-profiles simply because some device is better than no device. For a population where the focus is on minimizing risk, off-label usage is a more daring approach than having access to properly regulated devices.

The role of parents throughout the treatment process is also essential to consider. They are one of the key stakeholder groups whose actions should be analyzed under the SCOT. Children are an inherently vulnerable population because they cannot advocate for their needs in the same way an adult can. CHD generally effects very young children who are not capable of making decisions on their care. Parents play an essential part in deciding how to best care for their children and what can be done to meet their needs. They also must ensure to create a relationship with the clinician. Clinicians have the medical knowledge of the situation, but the parent is the caregiver of the child and deserves an opportunity to make informed decisions whenever possible (D. Frank, personal communication, March 3, 2022). Fear is an initial response, so the care team is responsible for fostering an openness and taking the time to explain and make parents feel comfortable (D. Frank, personal communication, March 3, 2022). This example of collaboration illustrates how the collaboration between social groups is an essential component of pediatric medicine. Addressing and overcoming any challenges requires all the stakeholder groups to be actively involved. Pediatric medicine is a team effort.

CHD has a diversity of presentation and as a result no single hospital is going to have enough experience to be an expert in every manifestation of the condition (D. Frank, personal communication, March 3, 2022). Being prepared to help requires having the necessary information available. National registries are an example of a technology that can help with organizing diseases, and keeping track of relevant studies (D. Frank, personal communication, March 3, 2022). This information sharing demonstrates how the actions of one group can help for the better. It ensures patients are receiving the best outcome possible. Additionally, sharing information at the clinician level is essential as well. Off-label usage is the standard and as a result clinicians are going to be developing new techniques and adapted devices to solve the problems they see. This practice supports the SCOT because it demonstrates how clinicians are essential in the dissemination of technology within the field. The sharing of information through conferences can allow a physician to share their techniques with others. This practice will lead to more physicians being trained and hospitals being prepared for any critical CHD cases that may arrive. Thus, more children are able to be treated.

Crohn's Case Study

Before analyzing the results, it is important to understand what exactly Crohn's disease is. Crohn's is a type of inflammatory bowel disease (IBD) characterized by chronic inflammation within the gastrointestinal (GI) tract (Roda et al., 2020). It is a disease where the immune system is constantly turned on and mistakenly targets itself (*Causes of Crohn's Disease*, 2022). This abnormal state can cause damage to the GI tract and requires intervention to quell the inflammation (*Causes of Crohn's Disease*, 2022). The condition is currently incurable and affects both men and women equally (*Causes of Crohn's Disease*, 2022). Patients will typically

go through periods of remission, where the disease is inactive, but it will eventually return. The current cause is not well understood, but evidence suggests genetics may be a risk factor as 5%-20% of IBD patients have a first-degree relative with the condition (*Causes of Crohn's Disease*, 2022). Environmental factors may also play a role as it is more common in urban areas of developed countries (*Causes of Crohn's Disease*, 2022). The disease can occur at any age, but is most prevalent in adolescents and those aged 15-35 (Ames & Soliman, 2021).

Despite 20-30% of all patients presenting with Crohn's before the age of 20, this age group faces unique obstacles compared to adults (Grossman & Cuffari, 2021). This investigation into the challenges of treating pediatric Crohn's disease, based on a comparative timeline between the adult and child populations and some additional context from an interview, reveals the four main obstacles. The first is that children can have different symptoms compared to adults, which can be a struggle to diagnose. Children are not necessarily able to verbally advocate for themselves and can in fact compensate for illness in some cases. Both of these factors can lead to delays in diagnosis. This leads into the second challenge, diagnosis is often made based on a stunted growth profile, which is far from ideal as this can be permanent. Additionally, there is a more restricted availability of therapeutic options and it can be a challenge to get access to non-approved ones for off-label usage. Finally, children face the unique challenge of transitioning care later in life (Grossman & Cuffari, 2021). However, just like in the previous case-study there are ways to overcome these challenges. The role of stakeholder groups, like parents and clinicians, can help overcome each of these challenges in a variety of ways.

The details for this case study were compiled into the timeline seen in figure 2 below**.** Due to the nature of the disease, it was not possible to track the year-by-year events in adults and

children. There is too much variability in IBD and this would require generalizing the condition, which could lead to biased data. The information was compiled into a timeline separated by four stages representing the common milestones of the disease progression in both populations. There is some variability in how long these stages may last for each patient, but each will occur.

	Adults	Pediatrics
Stage 1: Disease Manifestation Profile (Grossman & Cuffari, 2021)	*Age of onset:* - 18-35 *Physical Symptoms (GI):* - Diarrhea (with or without blood) - Abdominal pain + cramping - Weight loss + reduced appetite - Fever - Anemia - Intestinal damage *Physical Symptoms (other manifestations):* - Joint pain (arthritis) - Mouth ulcers	*Age of onset:* - Between 0-18 *Physical Symptoms (GI):* - Diarrhea (with or without blood) - Abdominal pain + cramping - Weight loss + reduced appetite - Fever - Anemia - Intestinal damage - Growth and development delays *Physical Symptoms (other manifestations):* - Joint pain (arthritis) - Erythema nodosum (skin tags) - Mouth ulcers Urinary problems
Stage 2: Diagnosis (*Diagnosing Crohn's Disease in Children*, 2022)	*Testing Available:* - Blood test - Stool Test Colonoscopy/Endoscopy	*Testing Available:* - Blood test - Stool test - Colonoscopy/Endoscopy - Bone density testing - Stunted Growth Profile
Stage 3: Initial Treatment Options (Konkel & Sassi, 2021)	*Mild Treatment:* - Amino salicylates - Antibiotics *Moderate to Severe Treatment:* - Corticosteroids - Immunomodulators - Biologics *Very Severe Treatment:* - Surgery	*Mild Treatment:* - Amino salicylates - Antibiotics - Nutrient Therapy *Moderate to Severe Treatment:* - Corticosteroids - Immunomodulators - Biologics *Very Severe Treatment:* - Surgery
Stage 4: Long-Term Management (Maintaining Remission) (J. Murray, personal communication, March 10, 2022)	*Outcomes:* - 50% will reach remission 5 years after diagnosis (Vann & Sassi, n.d.) *Treatment During Flare:* - Find another therapy to suppress inflammation	*Outcomes:* - Remission for up to 2 years before relapse (Lahad & Weiss, 2015) *Treatment During a Flare:* - Find another therapy to suppress inflammation

	If all the therapies fail, patient will have to undergo surgery to have parts of GI system removed	- If all the therapies fail, patient will have to undergo surgery to have parts of GI system removed *Transition of Care:* - Ages 13+ begin to take ownership of personal care - Ages 18-22: prepare to transition to an adult GI practice

Fig.2. Timeline divided into four stages comparing the disease manifestation, diagnostic process, treatment options, and long-term management in the adult and pediatric populations (Stiglitz, 2022)

In Stage 1, there is one striking difference between the clinical presentation of Crohn's in both populations. Pediatric patients are more likely to have extraintestinal manifestations of the disease compared to adults (Ames & Soliman, 2021). One study found that in up to 30% of cases, pediatric patients had at least one extraintestinal manifestation of the disease like erythema nodosum and joint pain (Greuter et al., 2017). Additionally, pediatric patients under 10 years old are more likely to have more severe symptom manifestation (Ashton et al., 2017). This is most likely due to the fact that the disease can have a direct impact on growth, psychological wellbeing, and nutrition (Ashton et al., 2017). The inflammation from Crohn's causes the bowel to be unable to absorb nutrients properly, this means that the body does not have access to the resources it needs to properly grow and develop. Poor nutrient absorption generally manifests as stunted growth or even delayed puberty in kids (Ashton et al., 2017). The symptoms of Crohn's come and go and are sometimes even confused with a virus (Grossman & Cuffari, 2021). The inconsistency of symptoms can cause delays in treatment as patients await a diagnosis. Additionally, pain is subjective and can be challenging for kids to articulate to others. One way that children are able to non-verbally advocate for a diagnosis is through their stunted growth profile, which is not influenced by the variable symptom presentation (J. Murray, personal communication, March 10, 2022). Kids will find ways to advocate for themselves even if it is something non-traditional, it just requires listening to their struggles and being willing to look

further. Pediatric medicine requires other social groups, especially the parents and clinical team members, to be prepared to work together and listen to kids in the instances when they can. This proactiveness allows them to be better prepared to advocate for their child's needs.

The biggest challenge in treating Crohn's disease is the treatment process or more specifically access to the right medications (Stage 3 of the timeline). Treatment can be divided into two stages, attempting to get the inflammation under control initially and then keeping it under control (remission). Upon first glance, the same types of treatments can be used in both populations with varying degrees of success. However, pediatric patients do not have access to the same number of approved therapeutics. A recent report found that of 16 approved treatments on the market for treating IBD in adults, only 5 of those have been approved for pediatrics (Rosenthal & Irwin, 2021). The lack of approval poses a problem. Any use of the 11 unapproved medications would be classified as off-label usage, and it becomes a case-by-case approval process, which requires additional steps and time.

Health insurance is useful to have as it can help with the costs of medications, however for kids with chronic illness it poses a barrier in getting access to the right medication. Health insurance agencies want to minimize risk and as a result they often require convincing for approval of off-label drug usage. The patient's clinical team (physicians, nurses, etc.) often must step up to pitch their patient's case in order to get them access (J. Murray, personal communication, March 10, 2022). This pitch requires finding other case studies, research, data to craft a solid case and a back and forth with the provider representative to convince them and get the desired outcome (J. Murray, personal communication, March 10, 2022). Through the lens of SCOT, this situation shows how the insurance company is controlling the purpose of the drug by putting conditions on its access. They are preventing its adoption into the pediatric space.

However, the advocation and collaboration by the clinical team overcomes this. The actions of the clinical team illustrate how essential it is for other groups to advocate for pediatric care as it can be the difference between access to a life-changing drug and being denied. The adoption of a technology is not controlled solely by one group, which is why advocates are so important in pediatrics. These groups are able to overcome the barriers that other groups may be setting.

Additionally, parents can both act as an advocate and a barrier towards care. Escalating therapies is daunting because as they become more serious the side effects become things like cancer (J. Murray, personal communication, March 10, 2022). Thus, it is essential for the two groups (parents and clinical team) to work together to form a relationship to address care. It is essential to have a conversation about what is right, which means the clinical team must be able to explain the medicine in an understandable manner while parents must continue to be an active participant in the disease management process. Collaboration is key in getting medications adopted in the pediatric space.

Another unintentional barrier is the two conflicting treatment philosophies by healthcare professionals. The first is the "top-down" approach where the severity of the disease is treated with equally aggressive methods (e.g. start in the moderate-to-severe category of medications for an equivalent presentation) (J. Murray, personal communication, March 10, 2022). These medications are generally injectable therapies that come with much more serious side effects and higher cost (Lahad & Weiss, 2015). The second is the "bottom-up" approach where clinicians begin with the lowest risk therapy and escalate as necessary (Ames & Soliman, 2021). The second approach has generally been the standard, although recent literature has indicated that it is better in the long-term to reach remission faster by beginning with more aggressive therapies. However, the challenge right now is that the first approach is still relatively new (within the last

5 years) and continually evolving. Large, research hospitals have an advantage as they are on the cutting edge of research and have begun a transition to the more aggressive treatment, but the research will take time to fully disseminate to physicians in smaller practices (J. Murray, personal communication, March 10, 2022). These two groups illustrate how even within clinicians there are sub-groups to be considered. Both of these sub-groups are influencing the technology pediatric patients are getting access to. Medications are disseminating into the pediatric population, which is the goal. However, they are having slightly different impacts.

The ITSA theory on unintentional consequences illustrates how from the current approach to the disease management is not ideal. Crohn's can permanently impact the growth of a child and it can cause permanent damage to the GI tract, so the stakes are much higher when trying to find treatment. Any unnecessary delays that cause the inflammation to continue (e.g., from going back and forth with health insurance) and increase the risks that someone will be dealing with permanent consequences before the age of 20. It is absolutely essential to reach remission early because kids have their whole lives ahead of them and having to get surgery (the most extreme treatment) because one could not access the correct treatment is unacceptable. An abundance of caution with medications can lead to unintended poorer outcomes as it causes delays in getting inflammation under control.

Pediatric patients also face a unique challenge in the long-term management of the disease. Crohn's is a chronic illness, so it requires management for life. Parents are the primary persons who manage pediatric care including picking up prescriptions, driving them to appointments, and making decisions on treatment (J. Murray, personal communication, March 10, 2022). However, at some point the child will become an adult who must take charge. A chronic illness is daunting as it requires learning to advocate for yourself. A teenager cannot

afford to slip up on their medication or forget to go the doctor because there is the potential of becoming very sick. So, if the people around them are not able to help set them up for a smooth transition, then things can progress towards a disaster quite fast. This is again an example of how essential various groups are in pediatric medicine.

Through the lens of the SCOT, the analysis for both case studies illustrate how impactful the role of different stakeholder groups are. These groups can create the challenges the prevent access to important devices and medications (e.g., FDA, health insurance, etc.), but at the same time other groups (e.g. parents, clinicians, etc.) can overcome these challenges. By promoting the adoption and dissemination of the things that matter. Moreover, there are also several instances where Harrison's theory of unintended consequences is clear as well. These actions by the different groups, and even inaction, can lead to unfavorable outcomes even when they are meant with the best intentions.

Limitations and Future Research

It is important to acknowledge that there are some limitations of this project. Interview data provided relevant information on the topic; however, it encompasses only a portion of the clinical population and only one hospital system. As noted by one of the interviewees, UVA hospital (and hospitals in general) are on the cutting edge of medical research and as a result the treatment reflects that. They are more likely to be treating with the newest data and this does not necessarily reflect in smaller practices. So, some challenges may not have been as pronounced from this research. Also, this was a very general overview of two cases within the pediatric population. It by no means encompasses all the challenges it faces and may in fact be missing certain things. Medicine is complicated and that is an inherent limitation. Analyzing two cases

studies in two fields was a way to illustrate this, but all the results cannot necessarily be generalized to pediatric medicine as a whole.

There are several directions for future research on the topic. One is analyzing how the challenges change based on where the clinical team is based (i.e., a smaller practice, a non-teaching hospital, or a research hospital). There may be a variability in the challenges each location would face and potentially an opportunity to investigate how to help overcome challenges that certain practices have that other do not face. Additionally, there is ample opportunity to analyze more in-depth the conditions that may potentially have easier access to innovations, like therapeutics or devices, and what factors allow for this. Alternatively, using the same research question with different case studies could reveal some interesting similarities and differences in challenges the field faces.

Conclusion

Pediatric patients face challenges in medicine, especially for conditions that are not considered common. In particular, access to medications and devices is limited by the current regulatory frameworks. In addition, children face a unique challenge in that they rely more on the people around them to help advocate for their care including parents, the clinical team, and even the FDA and insurance companies. All of whom can create unintentional roadblocks. Although unfortunate in their outcome, these roadblocks do stem from a place of good intentions as they are meant to ensure that any care received is not intentionally risky. There is no question that the pediatric population is a more vulnerable one, so caution is important. Thus, the answer to making changes is for the groups around them to be accountable for change. Pediatrics is not a

solo endeavor; it is a team effort. So, it is essential that everyone understands that the end goal is about doing what is best for the patient and putting their health first.

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Appendix A: Cardiologist Interview Questions

1. Please provide a general overview of your patient population.
2. How variable is the condition presentation (including structural and symptoms)?
3. With such a younger population, are you typically getting patients who have the condition before birth or are there some who present later? How much do you follow patients (continuum of care)?
4. In terms of treatment and management, are there any particular challenges you face within pediatrics due to them being so much younger and not able to advocate for themselves?
5. Are there ways you notice kids advocate for themselves (non-verbally)?
6. What is the role of families in advocating for care? What type of role do they play throughout the process? Is it more involved in the medicine or defer care? Are there instances where statistics on certain things may make people hesitant to proceed?
7. In particular for medical devices, what does the current market look like for children? Are there devices you can use that are specifically marketed to the pediatric population or do you find that off-label usage is the standard?
8. What would you say is the biggest problem with medical devices for pediatric patients?
9. Do you think the FDA is a barrier to getting devices to market or do you think it is more caused by being a smaller market commercially?
10. With the market being smaller, do you feel like there are times when it can take longer to find an alternative treatment? Are there ever delays in treatment just because something doesn't exist or does the adaptability sort of makeup for this?

11. Pediatric physicians are much more adaptable it seems when approaching any situation. Do you feel like the lack of devices impacts patient outcomes or has the field adapted and found ways to compensate for the smaller device market?
12. Working with a much smaller population and less access to technology, what does the situation look like between doctors? Is it more collaborative in some ways (communicating and sharing information? Is there an incentive to be more collaborative? How does this manifest itself?
13. How has the field changed as you have been a physician? Has device access improved at a pretty steady pace, is it slow, is there still a long way to go?
14. What do you believe is the biggest challenge to accessing pediatric-specific devices?
15. What is one change you believe can alleviate the problem?

Appendix B : GI Interview Questions

1. Please provide a general overview of your patient population.
2. How variable is the condition presentation (including structural and symptoms)? Do you know if this differs a lot from the adult presentation of the illness?
3. In terms of treatment and management, are there any particular challenges you face within pediatrics due to them being so much younger and not able to advocate for themselves?
4. Are there ways you notice kids advocate for themselves (non-verbally)?
5. What is the role of families in advocating for care? What type of role do they play throughout the process? Is it more involved in the medicine or defer care? Are there instances where statistics on certain things may make people hesitant to proceed?

6. In particular for medications, what does the current market look like for children? Is there a lot of off-label usage?
7. What would you say is the biggest problem with medications for pediatric patients?
8. Do you think the insurance companies are a barrier to getting access to certain medications? I believe I saw something where you have to go on an oral regime first before even getting access to IV injection medication? Can this be a problem where you delay the problem (even not managing symptoms?)? Is the FDA doing enough to get more access?
9. With the market being smaller for pediatric medications, do you feel like there are times when it can take longer to get access to the right medication? Do these delays ever cause problems or general frustration?
10. Pediatric medicine seems more adaptable in general. Would you agree this is also the case within GI?
11. Do you feel like the lack of medications impacts patient outcomes or has the field sort of adapted well enough that it has figured out ways to compensate?
12. Working with a much smaller population, what does the situation look like between doctors? Is it more collaborative in some ways (communicating and sharing information)? Is there an incentive to be more collaborative? How does this manifest itself? Is pediatrics more of a team effort (or is that medicine as a whole?)
13. How has this access changed as you have been working in the field? Has it improved at a pretty steady pace, is it slow, is there still a long way to go?
14. What do you believe is the biggest challenge to accessing more medications?
15. What is one change you believe can alleviate the problem and help?