BioMedInformatics

Article

A Data-Driven Approach to Revolutionize Children's Vaccination with the Use of VR and a Novel Vaccination Protocol

Stavros Antonopoulos , Manolis Wallace * and Vassilis Poulopoulos

ΓABLAB—Knowledge and Uncertainty Research Laboratory, University of the Peloponnese, 221 00 Tripoli, Greece; paidiatros.antonopoulos@gmail.com (S.A.); vacilos@uop.gr (V.P.)
* Correspondence: wallace@uop.gr

Abstract: Background: This study aims to revolutionize traditional pediatric vaccination protocols by integrating virtual reality (VR) technology. The purpose is to minimize discomfort in children, ages 2–12, during vaccinations by immersing them in a specially designed VR short story that aligns with the various stages of the clinical vaccination process. In our approach, the child dons a headset during the vaccination procedure and engages with a virtual reality (VR) short story that is specifically designed to correspond with the stages of a typical vaccination process in a clinical setting. **Methods:** A two-phase clinical trial was conducted to evaluate the effectiveness of the VR intervention. The first phase included 242 children vaccinated without VR, serving as a control group, while the second phase involved 97 children who experienced VR during vaccination. Discomfort levels were measured using the VACS (VAccination disComfort Scale) tool. Statistical analyses were performed to compare discomfort levels based on age, phases of vaccination, and overall experience. **Results:** The findings revealed significant reductions in discomfort among children who experienced VR compared to those in the control group. The VR intervention demonstrated superiority across multiple dimensions, including age stratification and different stages of the vaccination process. **Conclusions:** The proposed VR framework significantly reduces vaccination-related discomfort in children. Its cost-effectiveness, utilizing standard or low-cost headsets like Cardboard devices, makes it a feasible and innovative solution for pediatric practices. This approach introduces a novel, child-centric enhancement to vaccination protocols, improving the overall experience for young patients.

Keywords: vaccination; protocol; VaccineHero; VACS; discomfort; crying

Academic Editor: José Machado

Received: 31 October 2024
Revised: 13 December 2024
Accepted: 19 December 2024
Published: 30 December 2024

Citation: Antonopoulos, S.; Wallace, M.; Poulopoulos, V. A Data-Driven Approach to Revolutionize Children's Vaccination with the Use of VR and a Novel Vaccination Protocol. *BioMedInformatics* **2025**, *5*, 2. https://doi.org/10.3390/biomedinformatics5010002

1. Introduction

It is well established that increased vaccine coverage has contributed to a significant reduction in diseases [1]. National childhood vaccination programs represent one of the most successful public health initiatives in history, leading to the eradication or control of numerous serious illnesses in the past [2]. However, vaccination coverage has begun to decline in recent years. For instance, global vaccination coverage dropped from 86% in 2019 to 81% in 2021 [3], putting both individuals and communities at risk. In at least six states in the U.S., vaccination coverage is below the threshold set by the CDC to prevent outbreaks [1]. In 2019, the World Health Organization listed vaccine hesitancy as one of the top 10 threats to global health [4].

Even the study of social media can reveal signs of parents' denial and hesitation towards classical vaccination. An analysis of public posts in English on Twitter over a

5-year period identified 155,363 posts expressing negative sentiment towards the 'measles' vaccine and vaccines in general. Grouping the references as follows, the rejection of 'anti-vaxxers', false beliefs and misinformation about the measles vaccine, negative emotional transfer due to COVID-19-related policies, and public reactions to recent measles outbreaks show correlations with all these events [5].

Adolescents born in 2008, who were due for routine vaccinations during the COVID-19 pandemic, experienced a notable decline in vaccination coverage compared to those born in 2007, who received their vaccines before the pandemic. By age 13, coverage for at least one dose of Tdap was 2.3 percentage points lower; for MenACWY, it was 2.6 percentage points lower; and for HPV, it was 3.2 percentage points lower. This trend persisted beyond age 13, with vaccination coverage among adolescents born in 2008 remaining consistently lower by ages 14 and 15 [6].

In Australia, vaccination coverage for the DTP booster dose was 93% in 2018 and remained at a similar level in 2023. For the HPV vaccine, coverage among 15-year-old girls was approximately 80% from 2015 to 2023, while coverage among boys increased from 68% to 75% during the same period [7].

Moreover, based on the statistics of the WHO, in India, routine immunization coverage dropped by 5%, while in Brazil, it fell by 7%. In Europe, vaccination rates varied, with some countries maintaining high coverage levels, while others, such as Romania, saw significant decreases.

In Greece, vaccination coverage with the booster dose for pertussis reached 96% in 2021, while the corresponding coverage for the influenza vaccine among the elderly in 2023 was 65% [8].

There are many factors that can contribute to reduced vaccine uptake, ranging from limited access to healthcare services to misinformation and concerns about potential side effects [9] as well as the nuances of legal regulations [10]. Moreover, since many people associate needles with discomfort or even fear, the vaccination process can be unpleasant for a large number of individuals.

Given that vaccination programs around the world generally cover individuals from birth until 18 years of age, with most vaccines administered in early childhood, it is mainly young children who face distress during vaccinations. Research in [11] found that needles and blood draws are the primary source of fear for children in medical procedures, emphasizing the need for gentler medical approaches involving needles, particularly for pediatric patients. Vaccination stands out as one of the most prominent medical procedures, as it is universally applied to all children (not just those with specific medical conditions) and involves multiple doses throughout childhood. In Greece, the standard vaccination schedule includes 27 needle-based vaccines from birth to age 12 [12].

Since this fear is especially common in toddlers [13], it is understandable that children often experience significant distress during needle-related procedures, including vaccinations [14]. Pediatricians from the American Academy of Pediatrics found that 75% of parents attempted to delay vaccinations due to concerns about their child's discomfort [15], with around 45% of children aged 4–6 exhibiting severe distress during vaccination [16]. Furthermore, 10% of the population completely avoids vaccinations due to needle phobia [17].

Efforts to track, measure, and reduce fear or discomfort during vaccinations could likely improve parent–child cooperation in this essential process. In our previous work, we developed the VACS tool to measure discomfort and tested a new vaccination process called VaccineHero to alleviate children's distress and enhance their overall experience.

In this study, we introduce a completely new protocol for the vaccination process using VR technology, relying on our prior work. We analyze the data from our study, dividing it according to the stages of a traditional vaccination procedure. We identify the factors that contribute to child distress at each stage and examine the impact of using VR technology—specifically designed for vaccinations—within the process. This integration, coupled with comprehensive data analysis, leads us to a revolutionary proposal to entirely overhaul the vaccination protocol for children and adolescents, with the primary goal of transforming an inherently unpleasant procedure into a more manageable experience.

2. Relevant Literature

Many efforts have been made in medicine to measure discomfort, pain, or a combination of both during vaccinations and other medical procedures performed on children and adolescents. As vaccination is the most common painful procedure among children, ref. [18] developed evidence-based guidelines to manage pain and stress during vaccination. Key recommendations include the following: (a) allowing breastfeeding during the injection or, if not possible, administering a glucose or sucrose solution beforehand; (b) using topical anesthetics in advance; (c) employing distraction techniques like storytelling, music, or electronic devices for children aged 2 to 19; and (d) adopting specific procedural strategies, such as avoiding the supine position, promoting skin-to-skin contact for infants, and ensuring quick vaccine administration in older children while they are supported by their parents [13]. Similar efforts from other researchers have highlighted the significance of addressing discomfort during vaccinations. We have to consider that [19] a notable association was identified between the fear of needles and vaccine non-compliance in both parents and children.

In one other study [20], the reaction of infants and toddlers aged 0–2 years was examined during vaccination, venipuncture, and nasopharyngeal swab collection. Parents answered a special questionnaire after the procedure, which was structured for the purposes of the study. The factors investigated were as follows: perceived levels of discomfort in their children, discomfort levels compared to the parents' expectations, and general opinions on participating in a vaccine trial. During vaccination, 70% of parents found their child's discomfort to be as expected, while 28% reported it was less than expected. Overall, the study showed that the procedures caused "no" or "little discomfort" compared to what parents expected.

Other researchers [21] used an agreement analysis between two researchers to assess pain during neonatal vaccination. The assessment was conducted using the NFCS (Neonatal Facial Coding System) pain scale, with one researcher evaluating pain in real time during vaccination and the other reviewing video footage afterward. The neonates were divided into two groups, one consisting of infants who breastfed during vaccination. This study demonstrated that breastfeeding is a non-pharmacological method that reduces pain in children. However, it also highlighted the issue of using scales for evaluation. In the NFCS, which is based on facial mimicry, understanding the extent to which breastfeeding affects access to the assessment is a key issue. The study proved that evaluating the clinical applicability of the scales we choose is important.

Even the position of the infant during vaccination has been studied [22], either sitting or lying down, using the Neonatal Infant Pain Scales (NIPS). In older children [23], the use of similar scales, such as the Faces Pain Scale-Revised (FPS-R), helped assess the importance of interventions (verbal suggestions for reducing the sensation of pain, focusing activities, and the use of ethyl chloride) for reducing pain during vaccination.

More recent researchers combined observational methods with objective biomarkers [24]. In children aged 5–11 years, they measured heart rate before and after vaccination, tracked biomarkers such as cortisol and IgA, and calculated pain using the Visual Analogue Scale (VAS) while presenting 0-1-3 magic tricks to the children. No differences were found among the three groups. Another scale, the Modified Behavioural Pain Scale, was used to examine the effect of a mother's singing on 2-month-old infants during vaccination [25]. Many scales are used in the literature to evaluate the overall condition of children during vaccination, and one of these was introduced by researchers as specifically for use in children aged 2–12 years [14].

Knowing that untreated pain in early life is recognized as a factor that contributes to the development of chronic pain in children and adults and that healthy neonates inevitably undergo painful procedures in the first hours of life due to the need for vitamin K administration and vaccines, efforts are being made to reduce pain and general discomfort in children.

One recent effort in this field, focusing on child vaccination, is the use of VR technology. Researchers have presented the first encouraging results of using VR with content specifically adapted for vaccination [26]. Significant efforts have also been made by other researchers [27], who used two groups of children in their study. One group used VR with four different themes of 2 min each, though it was not adapted to the vaccination process, while the other group was distracted by other means, such as parents talking. The Wong–Baker FACES pain scale was used by the children to measure pain, and the Children's Fear Scale was used to assess fear. Parents filled out the satisfaction procedure questionnaire of Gold and Maher, while information about the procedure and the child's heart rate was provided by the nurse. Children in the VR group reported significantly lower levels of perceived pain compared to those in the non-VR group. There was also a notable relationship between pain categories and the distraction techniques used. More children in the VR group claimed not to have felt any pain, while fewer reported experiencing the worst pain. Additionally, the perceived fear among children in the VR group was significantly lower, leading to higher parental satisfaction with the vaccination process. Conversely, parents in the non-VR group reported more instances of their children experiencing distress (anxiety or worry). More parents in the VR group felt that the vaccination process did not meet their expectations, yet many stated that the VR experience positively impacted their children's vaccination experience. Notably, among the three parents who gave the lowest scores, two did not use the VR headset, either due to the child's refusal or headset malfunction. A discrepancy in parental perceptions emerged regarding pain management, with worse evaluations reported for vaccinated girls compared to boys. Finally, younger children reported higher pain levels, and parents of younger children believed more efforts could have been taken to manage pain effectively.

Finally, Turkish researchers studied the reaction of 7-year-old children to vaccination using VR [28]. The Child and Parent Information Form and Children's Fear Scale (CFS) were the tools used for data collection. VR with a child-selected cartoon versus no intervention during vaccination were the factors studied. In terms of the Child Fear Scale (CFS), there were no significant differences in the pre-vaccination scores between the VR and non-VR groups. However, the post-vaccination scores revealed a notable difference, with the VR group performing significantly better. This group demonstrated a considerable decrease in CFS scores both before and after vaccination, whereas the non-VR group experienced an increase in their scores.

Regarding the Child Anxiety Scale (CAS-S), the pre-vaccination scores were comparable between the two groups, but the post-vaccination scores showed a significant advantage for the VR group. Additionally, the VR group experienced a significant reduction in CAS-S scores from pre- to post-vaccination, while the non-VR group exhibited an increase in their scores.

On the other hand [29], no differences were found in children's ratings of pain and distress. However, significant differences in favor of virtual reality (VR) were observed in the evaluations by parents and nursing staff. The VR intervention was regarded as more enjoyable than standard care. Subgroup analyses did not show any advantage of VR in children's assessments. However, parents and healthcare professionals rated VR as more effective for individuals who had not previously been exposed to it and for those with low to moderate levels of needle anxiety. No difference was identified between VR and standard care for those with prior VR exposure or high needle anxiety, though these findings may have been affected by the small sample size. In all subgroups, except those with prior VR experience, the VR intervention was considered more enjoyable than standard care.

Therefore, the analysis of the relevant literature highlights a gap in both the tools used to measure overall discomfort specifically during vaccination and in VR interventions with environments tailored to the stages of the vaccination process.

3. Materials and Methods

In our previous work (Wallace et al. [10]), we introduced VACS, a scale for measuring children's discomfort during vaccination. This is an observational process conducted by the physician administering the vaccination, who monitors the child from the moment they enter the office until they leave.

The recorded observations are made across four distinct stages:

- **Stage I—Entrance:** How the child behaves upon entering the examination area, with further parameters being *crying* and *hesitation*.
- **Stage II—Examination:** How the child behaves during the doctor's examination, leading up to the actual procedure, with parameters including *facial expressions*, *crying*, and *activity*.
- **Stage III—Procedure:** How the child behaves during the actual vaccination procedure, with parameters including *support,* cooperation*, and* crying.
- **Stage IV—Completion:** How the child behaves after the vaccination is completed, with parameters being *crying and* activity.

The four stages (entry, examination, procedure, and completion) do not all carry the same weight in terms of vaccination discomfort. The periods leading up to and including the vaccination tend to cause the most discomfort for children. This is reflected in the distribution of scores across the different VACS stages. The highest points are assigned to the observations during the examination and procedure stages, while the completion stage has the least significance.

- **Stage I—Entry:** 5 points, 20%;
- **Stage II—Examination:** 8 points, 32%;
- **Stage III—Procedure:** 8 points, 32%;
- **Stage IV—Completion:** 4 points, 16%.

For all examined parameters, the first category listed indicates no discomfort, meaning it does not contribute to the VACS score. The remaining categories are scored accordingly.

Subsequently, our previous work on using technology during the vaccination procedure for children has introduced the utilization of VR technology to reduce children's discomfort [22]. During the setup, the VaccineHero app (version 1) is loaded onto an Android phone, which is then placed into a child-sized VR headset. Clinics that receive children of varying ages may have multiple headsets of different sizes available. Upon arrival, the child wears the VR headset, ensuring that no time is wasted contemplating the vaccination procedure, preventing worry. The VR content begins, and the child takes on the role of the hero in an immersive 3D world where they encounter a magician.

Importantly, the doctor is not required to introduce the VR content, allowing them to focus on discussing with the parents and examining the child, as they would during a regular vaccination without VR. This minimizes any additional workload for medical staff. The VR content is designed to be simple and self-explanatory, ensuring that the child can follow along without needing guidance.

During the immersive experience, the magician touches the hero's left arm twice, synchronized with the doctor's touches—once for cleaning the area with cotton and alcohol, and the second time for administering the vaccine. This blurs the boundaries between the virtual and physical worlds, providing an "extended" rather than purely virtual reality experience. As a result, the vaccination is completed seamlessly, with the child remaining calm and unaware of the needle.

Once the vaccination and the VR story conclude, the headset is removed, and the child is free to go, having been both vaccinated and entertained! Notably, the 3D content is simultaneously displayed on an external monitor via the Miracast app, allowing the doctor to track the VR story's progress and perfectly time the vaccination with the magician's actions.

The goal of the entire process was to reduce children's discomfort during vaccination through the use of VaccineHero. This discomfort was measurable and was accurately recorded using the VACS scale.

3.1. Data Preparation

Our previous works describe in detail the method of data collection, still mentioning details about the procedures, as more incorporated data are essential. The vaccination procedures were performed by doctors from the private sector and two in public facilities (urban and peripheral health centers or pediatric departments in secondary hospitals) in Greece. All the doctors were trained on the usage of the VACS protocol to assure they understood the scale and how to answer each of the questions. Moreover, two of these doctors, one from the private and one from the public sector, were trained to use the VR environment and were provided with the appropriate technical support to set up the system and use it with ease. The data were collected for specific time periods without any exception on the visiting children to ensure representativeness of the population. The reporting of this study followed the CONSORT extension for non-randomized studies (CONSORT-NRS) to ensure transparency and reproducibility. Key methodological elements, including participant selection, intervention details, outcome measures, and statistical analysis, were described in accordance with these guidelines.

Participants were selected based on eligibility criteria [willingness to participate and ages between 2 and 12] and allocated to either the VR or non-VR group based on the clinic schedule. Outcome measures, such as distress scores and behavioral observations, were standardized using structured tools to minimize bias (VACS protocol). Statistical analyses were performed with appropriate corrections for sample size imbalance and other potential biases. More specifically, considering the sample size imbalance between groups, we applied a Welch's t-test to compare the results under varying assumptions.

The data were collected with the use of web forms and recorded to CSV files to be organized for further processing. After collection of data, they were examined and cleared to omit incomplete or malformed data. The data were furthermore examined to ensure that both files contain the same information organized in the same way to certify that there were absolute correspondences in the analysis by comparison.

While some simplistic analyses were performed using Excel (gender count, children count, age count, etc.), Python was used to analyze in depth the corresponding data.

3.2. Data Description

The procedures of the VACS protocol were applied to vaccinations without using VR and using VR. The total number of vaccinations with both procedures were 412. The children vaccinated without the use of VR were 304, while the children that used VR were 108. The procedure of vaccination using the VACS scale was under investigation for a longer time, giving us the ability to collect a larger number of responses. Our initial work on VACS included a limited number of children, leading us to first analysis of how the larger number of data would “normalize” the results on the “traditional” vaccination. This will be analyzed. In parallel, within the time available, a number of children were vaccinated using the VR procedure. A primal analysis indicated that the results of the VR procedure were recording scores in the VACS scale with very low variance, indicating that were representative compared to the larger number of children, including a much higher number of children, as their variance in scores was higher, and thus, a larger number of children was essential to represent each differentiated behavior.

As we focused on specific age groups (2–12) to extract results about the application of both the VACS protocol and the protocol with the use of VR, we isolated a total of 339 children, 242 of them without using VR and 97 with the use of VR in the vaccination procedure. The gender distribution was 120 boys and 122 girls in the non-VR procedure and 62 boys and 35 girls in the VR procedure.

Considering the non-VR group of children, the mean age of the participants was 7.76 years old, ranging from 2 years 0 months 4 days to 12 years 6 months 25 days. One hundred twenty of the participants were boys (49.6%), and one hundred twenty-two were girls (50.4%). One hundred seventy-five (72.3%) of the children had completed their recommended vaccination schedule, while sixty-seven (27.7%) had skipped one or more of the vaccines recommended for their age group.

For the VR group of children, the mean age of the participants was 7.98 years old, ranging from 2 years 1 month to 12 years 4 months. Sixty-two of the participants were boys (63.9%), and thirty-five were girls (36.1%). Seventy-one (73.2%) of the children had completed their recommended vaccination schedule, while twenty-six (26.8%) had skipped one or more of the vaccines recommended for their age group.

The following table analyzes the data of both procedures according to gender, age group, and a combination of both [Tables 1 and 2].

Table 1. An analysis of gender per age group in the non-VR group of children.

Age Group	Boys	Girls
2–4	44	41
5–7	25	34
8–12	51	47
Total	120	122

Table 2. An analysis of gender per age group in the VR group of children.

Age Group	Boys	Girls
2–4	22	14
5–7	22	10
8–12	18	11
Total	62	35

The primitive analysis of data led to the assumption that the set of data collected was adequate and representative to further perform analysis on both procedures while being able to combine information from both sets of data to examine the efficiency of the alternative protocol that utilized the help of VR during the procedure.

4. Results

At first, we analyze the SCORE for both procedures to examine if any differentiations are recorded between them.

The mean SCORE in the VR group is calculated as 3.14, while the mean SCORE in the non-VR group is calculated as 7.28, indicating a large difference in the scale of 25 (SCORE can vary from 0 to 25) [Table 3]. The minimum score in both cases is 0, while the maximum score in VR group is 15 while in the non-VR group is 24.

Table 3. Analysis of SCORE per method.

Method	Mean	CI (95%)	*p*-Value
non-VR	7.28	6.44–8.06	<0.01
VR	3.14	2.49–3.79	<0.01

The following table presents additional score metrics.

The confidence intervale is the range within which the mean score lies with 95% confidence. The *p*-value is calculated between the two groups in order to perform a check for statistical significance. Both the values of the CI indicate that the mean score is differentiated and calculated with a high accuracy, and the *p*-value measuring lower than 0.01 indicates a high statistical difference between the mean scores.

Figure 1 presents the score distribution between VR and non-VR group, while Figure 2 depicts the density of the SCORE in each case. The first diagram has a list of all possible scores in each group and the frequency with which this score is recorded in the total number of children. The next figure includes the density of each score presentation. The density is representing the number of children having that score. The diagram is a combination of the score distribution and the density. The scope is to locate whether the score is concentrated around a value. In our case, it is obvious that the VR group is concentrated around smaller values.

Stage I – Entrance

Hesitation	No (0)		Yes (3)
Crying	No crying (0)	Light moaning (1)	Loud crying (2)

Stage II – Examination

Facial expressions	Relaxed (0)	Grimaces (1)	Sustained grimace (2)
Crying	No crying (0)	Light moaning (1)	Loud crying (2)
Activity	Relaxed (0)	Extensive (2)	Defensive/fetal (4)

Stage III – Procedure

Support	Relaxed (0)	Whining (1)		Inconsolable (2)
Cooperation	Alone (0)	Parent (1)	Parent and staff (3)	Staff (4)
Crying	No crying (0)	Light moaning (1)		Loud crying (2)

Stage IV – Completion

Crying	No crying (0)	Light moaning (1)	Loud crying (2)
Activity	Relaxed (0)	Extensive (1)	Defensive/fetal (2)

Figure 1. SCORE per parameter.

As we can observe, the VR group's scores are more concentrated around the lower values, indicating fewer issues during the vaccination process, while the non-VR group's scores are more spread out and include higher values, indicating a more challenging vaccination process for some children.

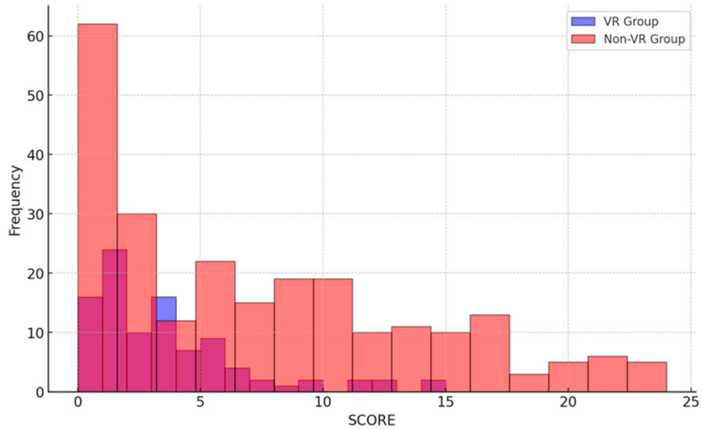

Figure 2. SCORE distribution for VR and non-VR groups.

We furthermore examine the mean SCORE for the different age groups to observe if there are any differences.

The analysis of the mean scores across age groups highlights evident differences between the VR and non-VR groups during the vaccination process [Table 4]. In the 2–4 age group, children in the VR group had a mean score of 3.44, whereas the non-VR group had a significantly higher mean score of 9.32, indicating more challenges in the non-VR group. Similarly, in the 5–7 age group, the mean score for the VR group was 3.94, compared to 7.88 in the non-VR group, again showing a smoother process with VR assistance. Lastly, in the 8–12 age group, the VR group's mean score was 1.90, while the non-VR group had a mean score of 5.14. These results suggest that the use of VR consistently led to lower scores, indicating a less stressful vaccination experience for children across all age groups.

Table 4. Analysis of SCORE per method per age.

Method	Age Group	Mean	CI (95%)
non-VR	2–4	9.32	8.59–10.04
non-VR	5–7	7.88	7.16–8.59
non-VR	8–12	5.14	4.44–5.83
VR	2–4	3.44	2.82–4.05
VR	5–7	3.94	3.3–4.57
VR	8–12	1.9	1.31–2.48

The difference per age group as depicted in the next table [Table 5] indicates that the higher the age, the smaller the difference. Still, in terms of percentage, in age groups 2–4 and 8–12, the difference is large, while the age group 5–7 is lowered just in half.

Table 5. Mean SCORE difference per age group.

Age Group	Non-VR	VR	Difference	Difference (%)
2–4	9.32	3.44	5.88	~92
5–7	7.88	3.94	3.94	~66
8–12	5.14	1.9	3.24	~92

After assuming from the data analysis that the VR procedure's SCORE is relatively lower, we further process the data to understand the reason of this difference. At first, we perform a per-stage analysis on the non-VR group to understand which is the score distribution across stages. Figure 3 presents the contribution of each stage to the final SCORE. The contribution is measured as the total of scores of each stage divided to the total

SCORE recorded. The analysis of the score contributions across different stages reveals that Stage 3 has the most significant impact on the final score, contributing a total of 498 points. This stage includes variables such as supportability, collaboration, and crying, which seem to play a critical role in determining the overall experience during vaccination.

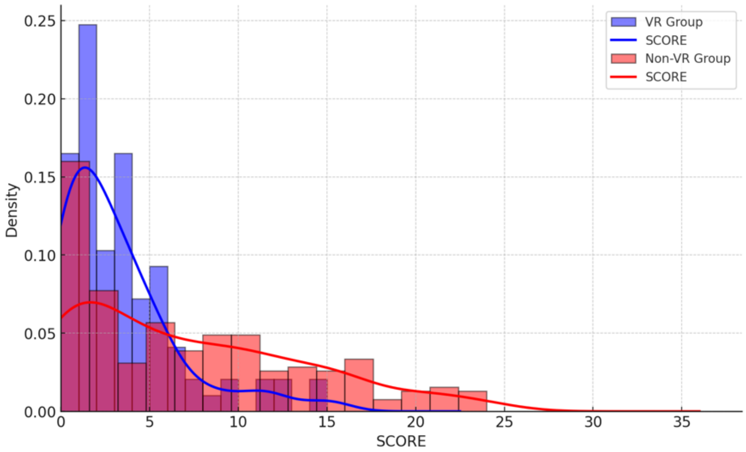

Figure 3. SCORE Distribution with Density Curves for VR and non-VR groups.

Following Stage 3, Stage 1 (hesitation and crying) and Stage 4 (crying and activity) also show notable contributions with 392 and 371 points, respectively. Stage 2 (facial expressions, crying, and activity) contributes the least, with 326 points.

This suggests that managing a child's crying, supportability, and collaboration during Stage 3 could potentially lead to a smoother vaccination process, as it seems to heavily influence the score.

Performing the same analysis for all the age groups, we record the findings depicted in Figure 4. The analysis first identifies each child of each group by subtracting the date of vaccination with the date of birth. After this, each child is assigned to an age group. For each age group, we summarize the points of each stage, and we divide it by the total points of the group [Figure 5].

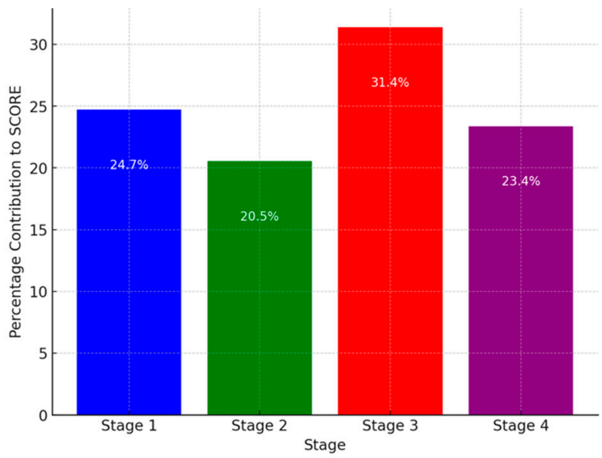

Figure 4. Stage-wise contribution to final SCORE in non-VR group.

The findings indicate that younger children, aged 2–4, struggle more with supportability and collaboration during the vaccination process, as Stage 3 plays the most significant role in SCORE forming. Stage 1 (hesitation and crying) also contributes significantly, indicating early emotional responses like crying and hesitation. In the 5–7 age group, Stage 3 remains the dominant factor, but its contribution is slightly reduced compared to the

2–4 group. Stage 4 (crying and activity) becomes more relevant, accounting for a higher percentage of the total score. This suggests that as children age, their physical reactions (such as defensive positioning) during the final stages of the procedure become more pronounced. For the 8–12 age group, Stage 1 (hesitation and crying) plays the most important role, accounting for the largest contribution to the final score. This suggests that older children may experience more hesitation or emotional responses at the beginning of the vaccination process, which impacts their overall experience more than later stages.

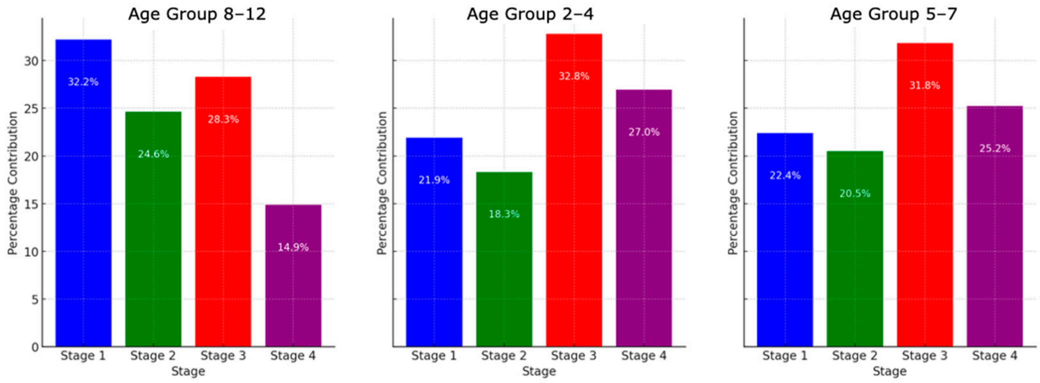

Figure 5. Stage-wise contribution to final SCORE in non-VR group by age group.

As crying is a common variable in each stage, we furthermore analyze how the variable of crying is progressing across the stages. The diagram presents the contribution of the crying variable per stage. For the calculation of the diagram, we sum the values of all recorded crying for each stage [Figure 6].

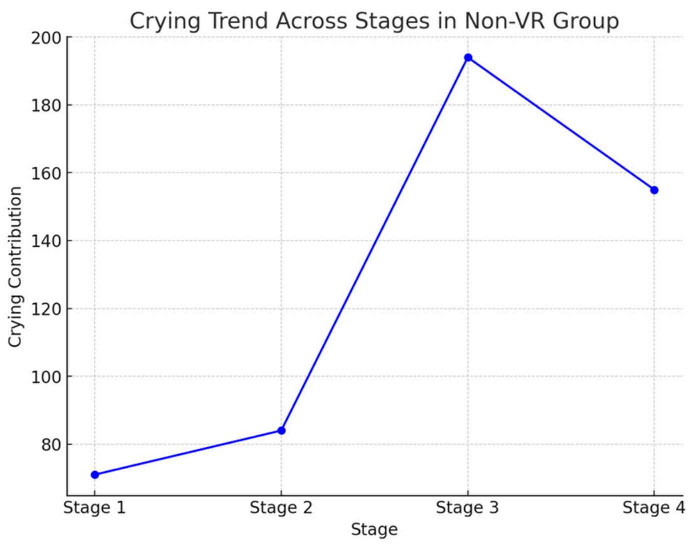

Figure 6. Analyzing crying variable contribution per stage.

We furthermore analyze the crying variable across the different age groups, which reveals a similar trend across all groups. Specifically, in age group 2–4, crying steadily increases through the stages, peaking in Stage 3 (crying, supportability, and collaboration). The emotional and physical demands of this stage seem to cause the most distress for younger children, and the crying continues into Stage 4, though slightly less. In age group 5–7, crying rises more sharply in Stage 3 compared to the previous stages, with Stage 4 seeing a significant decline. This suggests that children in this age group experience higher emotional reactions during Stage 3 but recover somewhat by Stage 4. In age group 8–12, crying is less prominent overall. The trend shows a sharp increase in

Stage 3, but the overall crying contribution is much lower compared to younger age groups, indicating that older children handle the vaccination process with less emotional distress.

To investigate which are the main factors that affect the final score, we perform a Pearson's correlation to the variables against the SCORE. The correlation analysis of the non-VR group reveals several important relationships between the variables and the final SCORE. Stage 2 activity shows the highest correlation with the final score (0.82), suggesting that children's physical activity during this stage (whether relaxed, extended, or defensive) has a major impact on their overall vaccination experience. Following this, Stage 3 supportability has a strong correlation (0.81), indicating that the level of emotional and physical support during Stage 3 (whether the child is relaxed, crying, or inconsolable) is a crucial factor in the process. Additionally, Stage 3 collaboration (whether the child is alone, supported by parents, or staff) also plays a key role with a strong correlation (0.74), reinforcing the importance of external support during this stage. Early emotional responses, such as Stage 1 hesitation and crying, are correlated with the final score (0.76 and 0.75, respectively), emphasizing that children's initial reactions play a critical role in shaping the outcome of the procedure. Similarly, Stage 2 crying and Stage 3 crying both show high correlations with the final score (0.78 and 0.75), further highlighting the importance of emotional response.

Overall, the analysis underscores that both physical reactions (activity) and emotional or social support (crying, supportability, and collaboration) are key determinants of the overall vaccination experience in the non-VR group.

The analysis of the application of the VACS protocol to child vaccinations can lead us with a data-driven approach on the procedure that needs more attention to smoothen the procedure of vaccination. We have already proposed the use of VR during the vaccination process, still, in this study, we present the experimental results of VR-VACS application on 93 children, and we compare the results to the aforementioned analysis from the non-VR procedure. The already-analyzed procedure reveals the factors of the "traditional process" that are the most important for generating anxiety in children, so we will examine if the VR process can possibly handle all these problems.

From a primitive analysis, it is obvious that the VR process records much lower scores overall, in all age groups and all genders. Therefore, we will proceed with an in-depth analysis and step-by-step comparison to locate the factors that alternate the children's behavior and produce a smoother process.

First, we will analyze the factors that contribute most to the score of the VR to compare it with the non-VR. The percentage contribution is calculated by summing all the scores per stage, divide it by the total score, and then reform it into a percentage [Figure 7].

The combined graph illustrates the stage-wise contribution to the final score across three age groups (2–4, 5–7, 8–12), revealing important trends in how children respond to vaccinations at different stages of the procedure.

For Stage 1 (hesitation, crying), younger children in the 2–4 age group show the lowest contribution (~13%) compared to older age groups. As children grow, the contribution of Stage 1 increases, with the 5–7 age group showing about 20% and the 8–12 age group reaching around 25%. This suggests that hesitation and emotional responses become more significant as children age, particularly in older children.

In Stage 2 (facial expressions, crying, activity), a similar pattern emerges. For the youngest group (2–4), the contribution is about 13%, increasing to around 18% for the 5–7 age group and 20% for the 8–12 age group. This indicates that facial expressions, crying, and activity during the vaccination process play a greater role in older children's reactions to vaccination.

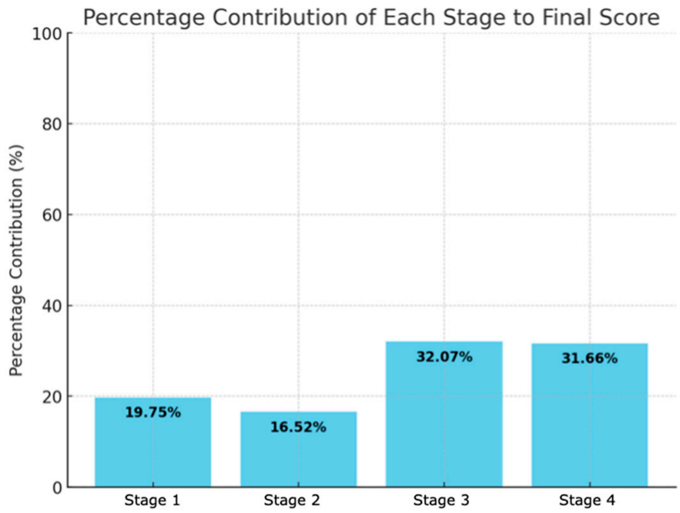

Figure 7. SCORE percentage contribution for non-VR groups.

Stage 3 (supportability, collaboration, crying) shows a distinct pattern. In the 2–4 age group, this stage has the highest contribution (~39%), underscoring the importance of support and collaboration—such as the presence of parents—in managing distress in younger children. The contribution of Stage 3 decreases as children age, dropping to about 34% for the 5–7 age group and further to around 29% for the 8–12 age group. This suggests that older children may rely less on external support and collaboration during the vaccination process.

For Stage 4 (activity, crying), the contribution is substantial across all age groups, with the highest in the 2–4 age group (~34%), followed by a slight decline in the 5–7 age group (28%) and the 8–12 age group (26%). This reflects that younger children exhibit more physical distress—such as defensive postures or crying—during the vaccination, while older children show a gradual decrease in these physical reactions.

Considering that the distribution of the variable score for each stage is 20%, 32%, 32%, and 16%, a first analysis of the result reveals a relatively lower contribution of Stage 2 (~16%) and a much higher contribution of Stage 4 (32%). From the variable score distribution, this should be quite opposite, but the explanation is clear for the VR group. At the end of Stage 1, the children are wearing the VR mask, which is uncovered at Stage 4. This early result is already indicative of the procedure.

Overall, Stage 3 (supportability, collaboration, crying) is the most important factor for younger children (ages 2–4), contributing nearly 40% to the overall score. This emphasizes the role of parental presence and support in managing anxiety and discomfort in younger children. As children grow older, Stage 1 (hesitation, crying) and Stage 2 (facial expressions, activity) become more noticeable factors, indicating that older children tend to show more emotional resistance and hesitation during the vaccination process.

Finally, physical activity and crying (Stage 4) remain important factors across all age groups but tend to decrease slightly with age, highlighting that younger children are more likely to react physically to the vaccination procedure.

In summary, the analysis suggests that strategies for managing vaccination distress need to focus on support and collaboration for younger children, while for older children, managing emotional responses and hesitation becomes more crucial for a smooth vaccination experience.

Trying to compare the data with the findings of the non-VR dataset, we observe the following.

In both the VR and non-VR groups, Stage 1 (hesitation, crying) becomes more significant as children grow older. However, in the VR group, Stage 1 shows a slightly lower contribution for the youngest children (2–4) compared to the non-VR group, where hesitation and crying have a larger impact on the overall score. This indicates that the VR setup may reduce early-stage emotional responses like hesitation in younger children. In the older age groups (5–7, 8–12), the differences between VR and non-VR are smaller, but Stage 1 contributes more to the non-VR group, especially for older children. In both groups, Stage 2 (facial expressions, crying, activity) increases in importance as the children grow older, but the VR group shows slightly lower contributions from Stage 2 across all age groups. The VR setup seems to help children maintain calmer facial expressions and reduce activity-related distress during the procedure. This is particularly noticeable in the 5–7 age group, where Stage 2 contributes less to the VR group compared to non-VR. In the older age group (8–12), while Stage 2 remains a factor in both groups, the VR intervention seems to slightly lessen its impact. The most noticeable difference between the VR and non-VR groups is in Stage 3 (supportability, collaboration, crying). In the non-VR group, Stage 3 is a dominant factor for younger children (ages 2–4), contributing around 40%, while in the VR group, this stage also contributes significantly but is lower. The reduction in reliance on support and collaboration in the VR group suggests that the immersive environment provided by VR may help younger children manage distress without needing as much external support. As children age, Stage 3's contribution decreases in both groups, but it remains a more prominent factor in the non-VR group, implying that the VR setup helps children feel less stressed and feel like relying on external emotional support. Both the VR and non-VR groups show Stage 4 (activity, crying) as an important factor across all age groups. However, the contribution of Stage 4 is lower in the VR group, especially for the youngest children. In the non-VR group, younger children (2–4) show higher levels of physical activity and distress, whereas the VR environment appears to reduce these reactions, making Stage 4 less significant. This effect shrinks as children grow older, but even in the 8–12 age group, VR seems to lower physical reactions compared to the non-VR group.

The comparison of the percentage of crying (average/yes) between the VR and non-VR groups shows that the VR setup significantly reduces emotional distress during the early stages of the vaccination process [Figure 8]. In Stages 1 to 3, the VR group consistently shows a lower percentage of children crying compared to the non-VR group. This suggests that the immersive environment provided by VR helps to calm children, reduce hesitation, and manage their emotional responses, leading to a smoother vaccination experience. Particularly in Stage 3, which involves support and collaboration, the VR group shows a notable reduction in crying, indicating that children in the VR setup are less reliant on external emotional support.

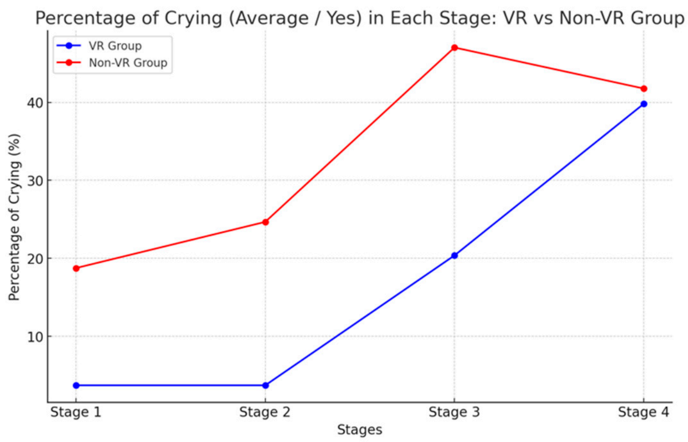

Figure 8. Crying in VR vs. non-VR groups.

However, by Stage 4, the percentage of children crying in the VR and non-VR groups becomes more similar, with the VR group even showing a slightly higher percentage of crying. This suggests that while VR is highly effective at managing emotional responses during the earlier stages, the final physical stage of the vaccination process triggers similar levels of emotional distress in both groups. The findings indicate that when children remove the VR mask from their face, they tend to react like the non-VR group children, having higher percentages of children reacting. This should be furthermore investigated during the VR procedure. This implies that we should investigate post-VR transition strategies to soothe the responses. Gradual de-escalation within the VR scenario (which currently ends quite abruptly) or calming activities by the supporting staff can be applied. It should also be noted that an examination of the cause of crying will be added in future research. It is not recorded if crying is related to the vaccination procedure or is caused by the termination of the VR experience. This implies that a new part of our research will focus on the causes of the high levels of crying in the post-VR stage.

Finally, we will check if factors like completed vaccination have affected the result. For children aged 2–12, the impact of the VR setup on the vaccination experience is clear when comparing both completed vs. non-completed vaccinations and the presence of a previous bad experience. We perform the same calculation as in the initial analysis, but this time, we select only children who are recorded to have a previous bad experience and the completed vaccination procedures.

When it comes to completed vaccinations, children in the VR group had an average score of 3.11, compared to 7.64 in the non-VR group. This results in a 4.53-point lower score in the VR group, reflecting a significantly smoother experience. In percentage terms, the VR group shows a 59.33% lower score compared to the non-VR group for completed vaccinations. For non-completed vaccinations, the VR group scored 4.00 on average, compared to 5.19 in the non-VR group, which results in a 1.19-point lower score in the VR group. The percentage difference is 23%, still showing an improvement, although less than for completed vaccinations.

Regarding the effect of a previous bad experience, the VR group's average score was 2.93 for those without a previous bad experience, while the non-VR group scored 6.56. This results in a 3.63-point lower score for the VR group, or 55.39% lower than the non-VR group. For those with a previous bad experience, the VR group scored 3.66 on average, compared to 10.50 in the non-VR group. This results in a 6.84-point lower score for the VR group, or 65.19% lower than the non-VR group, indicating a significant improvement in the vaccination experience for children with prior negative experiences when using VR.

In summary, the VR setup has a notably positive effect on the vaccination experience for children aged 2–12, with the most significant improvements seen for completed vaccinations and children with prior bad experiences. In order to spread this analysis to other variables as well in order to check if the VR procedure can possibly help overcome the problems of the "traditional procedure", we measure the variables with the higher impact in the final score for the non-VR dataset. To perform this analysis, we create a summary of the values recorded for each of the variables, and we normalize it on the scale of each, as they have a differentiated scale [Figure 9].

The top variables contributing to the final score in the non-VR group highlight the factors that most influence the vaccination experience. Stage 1 hesitation contributes the most, indicating that emotional resistance and hesitation at the start of the procedure significantly impact the overall outcome. Following hesitation, Stage 2 activity and Stage 4 activity also play a major role, reflecting that children's physical reactions, such as movement or defensive postures, add to the difficulty of the procedure. Stage 3 collaboration also shows a high contribution, underscoring the importance of external support, such as the presence of parents or personnel, in managing the child's distress. Finally, Stage 3 crying is another key contributor, highlighting emotional distress during the middle of the procedure as a major factor in increasing the overall score. These findings suggest that the non-VR setup sees greater emotional and physical responses throughout the vaccination process.

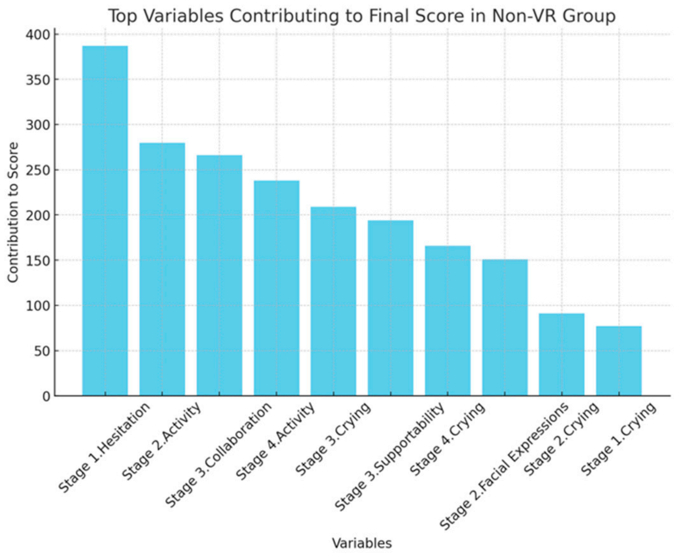

Figure 9. The contribution to SCORE of the parameters for the VR procedure.

We proceed with a comparison of how these variables contributed to the average score for both cases [Figure 10].

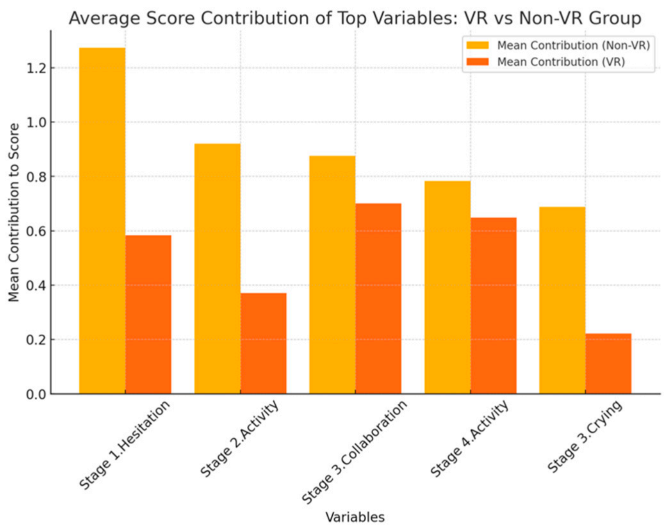

Figure 10. The average SCORE contribution of each variable to the final SCORE.

The comparison of the average score contribution of top variables between the VR and non-VR groups highlights key differences in how children respond to the vaccination process in each environment. Stage 1 hesitation contributes significantly more in the non-VR group (1.27) than in the VR group (0.58), suggesting that emotional resistance at the start of the procedure is much higher in the non-VR group. The VR setup appears to ease this initial emotional response, helping children feel more at ease from the beginning. Similarly, Stage 2 activity and Stage 4 activity also contribute more to the total score in the non-VR group, reflecting greater physical reactions during the procedure, such as movement or defensive postures. The VR environment reduces these physical responses, particularly in Stage 2, where the difference is most pronounced.

Stage 3 collaboration shows a smaller yet notable difference, with children in the non-VR group relying more on external support, such as parents or personnel, to manage their distress. The VR group, by contrast, shows lower dependence on external support, suggesting that the immersive environment provides emotional stability. The most striking difference is observed in Stage 3 crying, where the non-VR group has a much higher average score (0.69) compared to the VR group (0.22), indicating a significant reduction in emotional distress in the VR group. Overall, the VR setup consistently shows lower average contributions for these variables, demonstrating its effectiveness in reducing both emotional and physical reactions, leading to a smoother and less distressing vaccination experience for children.

Moreover, in this case, variables like acceptance of the procedure and willingness to repeat are recorded, so we will analyze if the procedure is accepted by children and/or parents.

Among the children participating in the procedure, 79.63% indicated a willingness to undergo vaccination with VR again, reflecting a high level of acceptability. The remaining 20.37% did not express interest in repeating the VR experience. In terms of VR experience feedback, most children found the experience either "Very nice" (40.74%) or "Nice" (38.89%). Only a small percentage described the experience as "Uninteresting" (11.11%) or "Scary" (9.26%). Using Pearson's correlation coefficient, we observed a mild negative correlation (−0.27) between the acceptability of VR for vaccination and the procedural score [Figure 11]. This suggests that children who found the VR experience more acceptable tended to have lower (better) scores, indicating that the VR experience helped reduce negative responses during the procedure. This finding highlights the need for flexibility in the design of VR interventions. In the current research study, we were able to work with a single scenario, understanding the possibility of children not feeling familiar with what they were presented. For that the reason, the respective parameter was recorded. Incorporating customizable VR settings, where children can select themes or environments that match their preferences, could address this variability. In addition, offering alternative distraction methods (e.g., music or storytelling) for children who are reluctant to use VR ensures that no child is excluded from anxiety-reducing interventions.

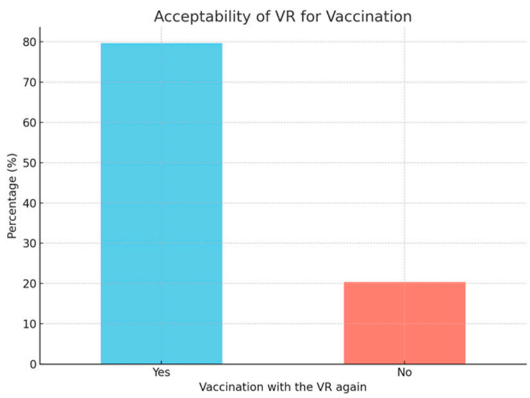

Figure 11. Acceptability of VR.

Interestingly parents' reaction towards the vaccination procedures have also changed among the two procedures. A first observation that is worth mentioning is related to the acceptance rate of the "traditional" procedure. Parents consider the vaccination procedure smooth and acceptable (90% and 10%, respectively) regardless of the final score. This indicates that parents believe that it is either smooth or acceptable that their children are undergoing a very stressful procedure, and none of them considered the procedure as being "bad". On the other hand, in the case of VR vaccinations, the procedure that recorded much lower levels of stress is equally considered to be accepted (similar rates), with some parents expressing their concerns about the procedure. In total, the parents have been accustomed to their children being under stress, and they are aware of novel procedures, especially when technological means are part of the procedure.

5. Discussion

The comparative analysis of the VACS protocol applied to VR and non-VR vaccination procedures in children provides a nuanced understanding of how immersive technology influences emotional and physical responses during what is typically a stressful experience. The findings suggest significant implications for enhancing pediatric vaccination practices, emphasizing the importance of emotional well-being in medical environments.

5.1. Emotional Responses Across Stages

5.1.1. Stage 1: Hesitation and Crying

The data indicate that emotional resistance at the beginning of the vaccination process is markedly lower in the VR group. Specifically, the contribution of Stage 1 (hesitation, crying) to the overall score is significantly diminished in the VR group (0.58) compared to the non-VR group (1.27). This reduction suggests that the VR setup is effective in mitigating initial anxiety. The immersive nature of VR likely distracts children from the impending procedure, reducing their hesitation and crying. This observation aligns with the existing literature that emphasizes the role of distraction techniques in reducing anxiety during medical procedures. The efficacy of VR in easing initial emotional responses could be attributed to its ability to engage children in a fantastical experience, thereby diverting their attention away from the stress of vaccination.

5.1.2. Stage 2: Activity and Facial Expressions

As children progress to Stage 2 (facial expressions, crying, activity), we observe an increase in the contribution to the overall score as children age, but a lower impact within the VR group across all ages. In traditional settings, physical reactions such as defensive postures and crying contribute significantly to distress, particularly for younger children. The VR environment appears to create a buffer that helps maintain calmer facial expressions and reduce active distress. The data show a marked difference in the average contributions from Stage 2 in the VR group, particularly for the 5–7 age group, where physical activity and emotional responses are less pronounced. This suggests that the VR intervention effectively modulates physical responses, allowing children to remain more composed. Such findings support theories that propose the efficacy of VR in reducing the perception of pain and anxiety through immersive engagement.

5.1.3. Stage 3: Supportability and Collaboration

Stage 3 (supportability, collaboration, crying) exhibits a complex interaction between emotional support and the VR environment. In the non-VR group, reliance on external support—such as parental presence—remains critical for younger children, contributing approximately 39% to the overall score. However, in the VR group, this reliance diminishes, with the contribution dropping to 34%. This reduction suggests that the immersive nature of VR provides an internal mechanism of emotional support, possibly through the engaging nature of the virtual experience. Children in the VR setup may feel more empowered and less dependent on parental support due to the sense of agency afforded by the VR experience. This finding is crucial, as it implies that VR not only serves as a distraction but also enhances children's ability to self-regulate their emotional states during stressful situations.

5.1.4. Stage 4: Physical Distress

In Stage 4 (activity, crying), the contribution to the overall score remains substantial across both groups, with the VR group exhibiting a decrease in physical distress responses. Interestingly, the data show that younger children in the non-VR group have higher levels of crying and defensive activity, suggesting that the traditional method provokes greater physical reactions. However, the percentage of crying in the VR group approaches that of the non-VR group in Stage 4, indicating that while VR effectively mitigates distress during earlier stages, the final physical aspects of the vaccination still elicit a significant emotional response. This could indicate that once children are removed from the immersive experience, they revert to more typical responses to stress, suggesting the need for additional strategies to support children during this final stage of the vaccination process.

5.2. Parental Perspectives

Parents' perceptions of both procedures offer a critical lens through which to evaluate the effectiveness of the VR intervention. In the traditional setting, parents overwhelmingly view the vaccination experience as acceptable (90% acceptance rate), indicating a normalization of stress in medical contexts. This acceptance may reflect a learned helplessness, where parents have come to expect distress during vaccinations. In contrast, while the VR procedure receives a similar acceptance rate, it is notable that some parents express concerns regarding the use of technology in medical settings. This hesitation points to a need for comprehensive education for parents about the benefits of VR in reducing children's anxiety, which may enhance the overall acceptance and uptake of such innovations in pediatric healthcare.

5.3. Willingness to Repeat and Acceptance

The high willingness among children (79.63%) to undergo vaccinations with VR again underscores the positive reception of the technology. Feedback categorized as "Very nice" or "Nice" by most children indicates that the VR experience is generally viewed favorably. Moreover, the mild negative correlation (-0.27) between the acceptability of the VR experience and procedural scores suggests that children who find VR more acceptable tend to have lower scores, indicating better experiences. This correlation reinforces the notion that a favorable perception of the VR intervention is associated with reduced emotional distress, supporting the potential of VR to foster positive associations with medical procedures.

5.3.1. Possible Risks

Throughout the study, risks associated with the use of VR technology in younger age groups were neither analyzed nor evaluated. However, no symptoms potentially associated with such use were observed. The children and adolescents studied engaged in very limited use of the VR application, specifically less than 2 min in total. Moreover, the application was used only once and not repeatedly or daily, which would have increased the exposure time for the children. This limited exposure was not considered likely to cause side effects related to developmental, physical, psychosocial, or cognitive issues. As a result, no symptoms such as nausea, sleep and vision disturbances, attention disorders, addiction, anxiety, emotional effects, or social isolation were observed. It is important to note, however, that these aspects were not actively studied in this phase of the research.

5.3.2. Implications for Future Research

While the findings are promising, they also highlight areas for further exploration. For instance, the increase in crying rates in Stage 4 within the VR group raises questions about the transition from the VR experience back to the reality of the vaccination. Future research should investigate how the withdrawal from the VR environment affects emotional regulation and whether strategies can be implemented to ease this transition, such as gradual re-exposure to reality or incorporating calming techniques post-VR.

Moreover, exploring the long-term impact of VR experiences on children's attitudes towards healthcare procedures could yield valuable insights. Understanding whether positive experiences translate to a more favorable outlook on future medical interventions is critical for improving compliance with vaccinations and other necessary medical treatments.

6. Limitations and Future Directions

While this study highlights the benefits of using virtual reality (VR) to improve the pediatric vaccination experience, several limitations and areas for future exploration remain. One key limitation is the challenge of transitioning out of the immersive VR environment. While VR effectively reduces physical distress, emotional responses during the final stage of vaccination remain significant, suggesting that children may experience lingering anxiety when shifting back to reality. Addressing this challenge requires the development of post-VR strategies, such as calming activities or guided relaxation, to support children during this critical stage.

Age-related variability in VR effectiveness also emerged as an important consideration. The findings suggest that while younger children (ages 2–7) benefit significantly from VR, its impact is less pronounced in older children (ages 8–12). This highlights the need for age-specific adaptations to VR content, such as gamified elements for older children or simpler interactive experiences for younger ones. Tailored interventions could enhance engagement and ensure that VR remains impactful across different age groups.

Parental acceptance is another critical factor for the successful adoption of VR in healthcare settings, as in any kind of technological adoption in "traditional" procedures. Some parents expressed hesitation about using technology during medical procedures, underscoring the importance of parental education. Providing evidence-based materials and workshops could help address concerns and build trust in the benefits of VR for reducing children's anxiety. The VACS protocol is a means of evidence concerning children's anxiety levels. Similarly, while most children responded positively to VR, a small percentage found it uninteresting or scary, suggesting that customizable VR settings may be necessary to accommodate individual preferences and ensure inclusivity.

Technical and logistical challenges are also barriers to widespread adoption. Issues such as occasional equipment malfunctions, reluctance to wear VR headsets, and the time required for the setup in busy clinics can limit adoption. Streamlining workflows, preloading VR programs, and training staff to effectively manage technical issues could mitigate these challenges. In addition, while the affordability of VR has improved, initial investment and maintenance costs remain significant, particularly in resource-limited settings. Exploring low-cost solutions, such as smartphone-based VR systems, and conducting cost–benefit analyses could help justify a broader adoption of the technology.

Naturally, we must consider that the VACS scale is an observational tool and, as such, includes the subjectivity of the observer/pediatrician completing it. Values including the presence or absence of crying, hesitation to enter a medical office, and parental assistance in holding the child during vaccination are objective. However, aspects such as the intensity of crying and the posture adopted by the children (defensive or relaxed) are left to the pediatrician's judgment to characterize. The training of pediatricians prior to scoring can standardize discrepancies, but it certainly cannot eliminate them entirely. Moreover, another approach could furthermore enhance the procedure through dual observer validation, recording the same parameters not only by a single person but also by the supporting medical staff.

Furthermore, another part of the procedure that requires detailed research is the post-VR crying levels, as they seem to raise unexpectedly. This could lead to alterations of the VACS protocol so that more stages are included to investigate the reasons for increased or unexpected results.

Finally, this study focuses primarily on the immediate outcomes of VR-assisted vaccination, and the long-term impact on children's healthcare attitudes remain unexplored. Understanding whether positive VR experiences translate into improved cooperation and reduced anxiety in subsequent medical procedures will be crucial for assessing the sustainability of its benefits. Future research should also investigate how combining VR with traditional anxiety-reduction techniques, such as storytelling, could enhance outcomes. By addressing these limitations and exploring these directions, VR can be further optimized as a valuable tool for improving pediatric healthcare experiences.

7. Conclusions

In this manuscript, we have presented an extensive data analysis on information collected from vaccination procedures using the traditional method and a method where children were using VR. The scope of the procedure was to measure children's reactions and record factors related to children's stress levels during the process. We incorporated the results from our work published in [10], which is a novel protocol for recording stress levels during the vaccination procedure, and the experimental results from [22], which introduces a protocol for vaccination using VR technology. From the results, it is obvious that the VACS protocol helps us identify the levels of stress, and the VR process can help at lowering these levels significantly. In total, the results are adequate to propose the new protocol as a novel health procedure that led us to a data-driven approach that can become the paradigm shift for children's vaccination.

Author Contributions: Conceptualization, S.A., M.W. and V.P.; methodology, S.A. and V.P.; validation, V.P.; formal analysis, S.A. and V.P.; investigation, S.A. and M.W.; resources, S.A., M.W. and V.P.; data curation, V.P.; writing—original draft preparation, S.A., M.W. and V.P.; writing—review and editing, S.A., M.W. and V.P.; visualization, V.P.; supervision, V.P. All authors have read and agreed to the published version of the manuscript.

Funding: This study received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of University of the Peloponnese (VACS—protocol code 20836/14 September 2022, VaccineHero—protocol code 15884/2023).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The datasets presented in this article are not readily available because they are part of a study and include sensitive medical data that are available for analysis to the authors according to the approval by the Ethics Committee of University of the Peloponnese. Requests to access the datasets should be directed to V.P.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Vanderslott, S.; Dattani, S. Fiona Spooner and Max Roser (2013)—"Vaccinatio". Published Online at OurWorldInData.org. Available online: https://ourworldindata.org/vaccination (accessed on 14 December 2022).
2. Orenstein, W.A.; Ahmet, R. Simply put: Vaccination saves lives. *Proc. Natl. Acad. Sci. USA* **2017**, *114*, 4031–4033. [CrossRef] [PubMed]

3. Immunization Coverage. Available online: https://www.who.int/news-room/fact-sheets/detail/immunization-coverage (accessed on 2 November 2022).
4. World Health Organization. Ten Threats to Global Health in 2019. Available online: https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019 (accessed on 4 August 2023).
5. Ng, Q.X.; Teo, Y.Q.J.; Kiew, C.Y.; Lim, B.P.; Lim, Y.L.; Liew, T.M. Examining the Prevailing Negative Sentiments Surrounding Measles Vaccination: Unsupervised Deep Learning of Twitter Posts from 2017 to 2022. *Cyberpsychol. Behav. Soc. Netw.* **2023**, *26*, 621–630. [CrossRef]
6. Centers for Disease Control and Prevention (U.S.). *Supplementary Figure 2. National Vaccination Coverage Among Adolescents Aged 13–17 Years—National Immunization Survey-Teen, United States*; Centers for Disease Control and Prevention (U.S.): Atlanta, GA, USA, 2023; Volume 73.
7. Comparison of Immunization Coverage (Australia), World Health Organization. Available online: https://immunizationdata.who.int/compare?CODE=AUS&COMPARISON=type1__WIISE/MT_AD_COV_LONG+type2__WIISE/MT_AD_COV_LONG+option1__HPV_coverage+option2__DTP_PLUS_coverage&YEAR= (accessed on 1 November 2024).
8. Comparison of Immunization Coverage (Greece), World Health Organization. Available online: https://immunizationdata.who.int/global/wiise-detail-page/influenza-vaccination-coverage?CODE=GRC&ANTIGEN=&YEAR= (accessed on 1 November 2024).
9. Foschi, N.; Santoro, P.E.; Borrelli, I.; Gavi, F.; Amantea, C.; Russo, P.; Moscato, U. Urological Safety and COVID-19 Vaccinations. *Vaccines* **2022**, *10*, 1887. [CrossRef] [PubMed]
10. Beccia, F.; Rossi, M.F.; Amantea, C.; Villani, L.; Daniele, A.; Tumminello, A.; Aristei, L.; Santoro, P.E.; Borrelli, I.; Ricciardi, W.; et al. COVID-19 Vaccination and Medical Liability: An International Perspective in 18 Countries. *Vaccines* **2022**, *10*, 1275. [CrossRef]
11. Dalley, J.S.; Morrongiello, B.A.; McMurtry, C.M. Children's Perspectives on Outpatient Physician Visits: Capturing a Missing Voice in Patient-Centered Care. *Children* **2021**, *8*, 34. [CrossRef]
12. Immunization Coverage. Available online: https://www.moh.gov.gr/articles/health/dieythynsh-dhmosias-ygieinhs/emboliasmoi/ethniko-programma-emboliasmwn-epe-paidiwn-kai-efhbwn/12614-ethniko-programma-emboliasmwn-paidiwn-kai-efhbwn-2024-xronodiagramma-kai-systaseis (accessed on 25 July 2024).
13. Orenius, T.; LicPsych, S.H.; Mikola, K.; Ristolainen, L. Fear of Injections and Needle Phobia among Children and Adolescents: An Overview of Psychological, Behavioral, and Contextual Factors. *Sage Open Nurs.* **2018**, *4*, 2377960818759442. [CrossRef]
14. Wallace, M.; Antonopoulos, S.; Poulopoulos, V. VACS: VAccination disComfort Scale. *Clin. Pract.* **2022**, *12*, 1078–1091. [CrossRef] [PubMed]
15. Hough-Telford, C.; Kimberlin, D.W.; Aban, I.; Hitchcock, W.P.; Almquist, J.; Kratz, R.; O'Connor, K.G. Vaccine delays, refusals, and patient dismissals: A survey of pediatricians. *Pediatrics* **2016**, *138*, e20162127. [CrossRef]
16. Jacobson, R.M.; Swan, A.; Adegbenro, A.; Ludington, S.L.; Wollan, P.C.; Pol, G.A. Making vaccines more acceptable—Methods to prevent and minimize pain and other common adverse events associated with vaccines. *Vaccine* **2001**, *19*, 2418–2427. [CrossRef]
17. Taddio, A.; Appleton, M.; Bortolussi, R.; Chambers, C.; Dubey, V.; Halperin, S.; Hanrahan, A.; Ipp, M.; Lockett, D.; MacDonald, N.; et al. Reducing the pain of childhood vaccination: An evidence-based clinical practice guideline. *Coll. Emerg. Med. Team* **2010**, *182*, E843–E855.
18. García Sánchez, N.; Merino Moína, M.; García Vera, C.; Lacarta García, I.; Carbonell Muñoz, L.; Pina Marqués, B.; Álvarez García, F.J.; Arístegui Fernández, J. Relief of Pain and Distress during Immunizations. Synthesis of the Evidence: Recommendations of the Advisory Committee on Vaccines of the Spanish Association of Pediatrics. *Pediatr. Atención Prim.* **2015**, *17*, 317–327. [CrossRef]
19. Taddio, A.; Ipp, M.; Thivakaran, S.; Jamal, A.; Parikh, C.; Smart, S.; Sovran, J.; Stephens, D.; Katz, J. Survey of the Prevalence of Immunization Non-Compliance Due to Needle Fears in Children and Adults. *Vaccine* **2012**, *30*, 4807–4812. [CrossRef] [PubMed]
20. Westra, A.E.; Van Gils, E.J.M.; Aarts, F.; Rodenburg, G.D.; Veenhoven, R.H.; Hak, E.; Scharloo, M.; Sukhai, R.N.; Wit, J.M.; De Beaufort, I.; et al. Perceived Discomfort Levels in Healthy Children Participating in Vaccine Research. *J. Empir. Res. Hum. Res. Ethics* **2013**, *8*, 66–72. [CrossRef] [PubMed]
21. Jesus, A.M.M.D.; Carvalho, T.L.A.D.; Silveira, L.F.A.; Silva, R.R.; Alberice, R.M.C.; Marcatto, J.D.O. Analysis of Agreement in the Evaluation of Pain in Newborns during Hepatitis B Vaccination. *BrJP* **2024**, *7*, e20240037. [CrossRef]
22. Steny, M.; Kale, A. A comparative study to assess the pain in supine versus sitting position during intramuscular injection among infants from selected immunization clinics at sangli, miraj, kupwad corporation area. *Afr. J. Biol. Sci.* **2024**, *6*, 331–341.
23. Berberich, F.R.; Landman, Z. Reducing Immunization Discomfort in 4- to 6-Year-Old Children: A Randomized Clinical Trial. *Pediatrics* **2009**, *124*, e203–e209. [CrossRef]
24. Teichfischer, J.; Weber, R.; Kaiser, E.; Poryo, M.; Weise, J.J.; Nisius, A.; Meyer, S. SimSAARlabim Study—The Role Magic Tricks Play in Reducing Pain and Stress in Children. *Vaccine* **2024**, *42*, 2572–2577. [CrossRef]
25. Monaci, M.G.; Caruzzo, C.M.; Raso, R.; Spagnuolo, C.; Benedetti, M.C.; Grandjean, D.; Filippa, M. Maternal Singing Reduced Pain Indexes in 2-Month-Old Infants and Increased Proximity during Vaccinations. *Acta Paediatr.* **2024**, *113*, 1664–1671. [CrossRef] [PubMed]

26. Antonopoulos, S.; Rentoula, V.; Wallace, M.; Poulopoulos, V.; Lepouras, G. VaccineHero: An Extended Reality System That Reduces Toddlers' Discomfort during Vaccination. *Electronics* **2023**, *12*, 3851. [CrossRef]
27. Sánchez-López, M.I.; Lluesma-Vidal, M.; Ruiz-Zaldibar, C.; Tomás-Saura, I.; Martínez-Fleta, M.I.; Gutiérrez-Alonso, G.; García-Garcés, L. The Effect of Virtual Reality versus Standard-of-Care Treatment on Pain Perception during Paediatric Vaccination: A Randomised Controlled Trial. *J. Clin. Nurs.* 2024, *ahead of print*. [CrossRef] [PubMed]
28. Kırbaş, Z.Ö.; Kahriman, İ. Evaluating the Effect of the Use of Virtual Reality Headset in School Vaccinations on Children's Fear and Anxiety Levels: A Randomized Controlled Trial. *Int. J. Health Med. Res.* **2024**, *3*, 615–623. [CrossRef]
29. Ellerton, K.; Tharmarajah, H.; Puleio, D.; Medres, R.; Brown, L.; Ringelblum, D.; Vogel, K.; Dolphin, A.; McKellar, S.; Bridson, F.; et al. Virtual Reality for IMMunisation (VRIMM) Pain in Young Children. Results of a Randomised Controlled Trial in General Practice. *Aust. J. Gen. Pract.* **2023**, *52*, 704–710. [CrossRef] [PubMed]