

Review Article

The MMR Vaccine and the Emergence of Disease

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Abstract

The relationship between MMR vaccine and ASD to this day has been a big problem in the public eye. The presumed causality of ASD from MMR vaccine has led to a big portion of parents worldwide to not vaccinate their children with the MMR vaccine. If there was a correlation between the MMR vaccine and ASD, then there should have been a rise in ASD cases the more children get vaccinated. To fully analyze the connection between ASD and the MMR vaccine, both case studies and qualitative studies were accessed. Qualitative studies provided information regarding the repercussions of under-vaccination over the years, while case studies were used to study any potential causal effects of the MMR vaccine and

ASD. Many studies and journals were accessed from PubMed and Medline Plus. Through all the accessed studies there has been no significant statistical correlation between MMR vaccine and autism. Health care professionals need to play a big role in educating parents about vaccines and the unproven claims of disease that the general public might think they cause.

Hypothesis: If there was a correlation between the MMR vaccine and ASD, then there should have been a rise in ASD cases the more children get vaccinated.

Keywords: MMR controversies; ASD; Controversies about vaccines; Autism

Introduction

Over the years, vaccinations have been surrounded by controversy especially concerning efficacy and side effects, which has led to a worldwide decrease in vaccinations. Media and unsubstantiated studies have caused mass hysteria, allowing the reemergence of many debilitating diseases in children. One of the most notorious controversies concerns the Measles Mumps Rubella (MMR) vaccine leading to Autism Spectrum Disease (ASD). This was initially proposed by a group of scientists in the 1990s, who published their work in the scientific journal the *Lancet*. They explain how the MMR vaccine causes inflammatory bowel disease, allowing Andrew Wakefield, a gastroenterologist at the time, to try to study and establish the link between the apparent inflammations caused by the MMR vaccine to Autism. His study mainly focused on the claim that the MMR vaccine caused inflammation of the small bowels, leading to the overproduction of unfolded proteins, which are then absorbed into the blood and stored in the central nervous system, causing ASD. Wakefield mainly developed this hypothesis based on previous researchers, Fudenberg and Gupta, who made this link with little systematic investigation [1].

Wakefield then developed research with 12 other researchers to study the link between the MMR vaccine and Autism. Their claim was based on 12 cases of children who exhibited symptoms of ASD after receiving the MMR vaccine. Although in the paper they claimed that there was no link between the vaccine and Autism, Wakefield then published a video with the paper claiming that there is a causal relationship between the MMR vaccine and Autism. Wakefield then attempted to patent the single antigen vaccine for measles in place of the trivalent MMR vaccine, as a solution to his claim regarding the MMR vaccine and its causal relationship with Autism. This was perceived as Wakefield seizing the opportunity for potential financial return by promoting his research and views [2].

The MMR vaccine is administered to children in most developed

countries in two doses, one between 12 to 15 months of age and the second one between 5 to 6 years; this provides coverage to 95% of serotypes of the trivalent vaccine [3]. The development of mistrust and fear with regards to the MMR vaccine has led to panicked parents delaying the vaccination of their kids, or completely opting out from vaccination, both in Britain and the United States. In 2011, Great Britain's vaccination rate for the first and second dose of MMR vaccine was 84% and 77% respectively, which is significantly short of the 95% which is required for minimum population immunity. This missing fraction resulted in a pool of unimmunized individuals susceptible to the debilitating effects of the measles virus [4]. In the following years, there was an alarming rise in rates of new cases of measles, mumps and rubella. Over a similar timeline, 12 years since Wakefield's claim, research has exhausted the possibility that there is any link between the MMR vaccine and Autism. In 2004, Dr. Richard Horton, editor of the *Lancet*, wrote that Wakefield should have mentioned that his research was funded by attorneys involved in a lawsuit against vaccine manufacturers, as this is a clear conflict of interest. Dr. Horton then publicly went on the record to say that Wakefield's views and claims were flawed and had no strong basis [1].

Wakefield's paper was retracted from the *Lancet* in 2010, which was followed by Britain's general medical council banning Wakefield from practicing medicine.

Wakefield's study was then further scrutinized and while it claimed that 8 out of the 12 children showed either Autism-like symptoms or gastrointestinal inflammation days after the vaccine, in actuality, only 2 patients displayed those symptoms. A further revelation determined that 2 of the children previously had developmental delays before the vaccine was administered. This shed light on the fact that Wakefield completely falsified the information about his study.

The MMR vaccine component was not the only component that was attacked as a cause for developmental delays. The

thimerosal component in the vaccine, which is a mercury-based preservative/antibacterial, also received numerous claims as a cause of the neurodevelopmental delays. In the 1990s, lawmakers, environmentalists and public health workers became concerned about mercury consumption, specifically in fish, and its harm on the human body. In 1999, the FDA requested to measure and reports the level of mercury in all products and the amounts of thimerosal exceeded the FDA recommendation.

The mercury in fish appears in the form of Methyl mercury which is not readily metabolized or excreted from the body, and as such, is able to cause harmful neurologic effects at high doses. However, thimerosal is in the form of Ethyl mercury, for which there was little research about any side effects. The FDA was faced with a dilemma, should they put the same regulation on Ethyl mercury as Methyl mercury, or not? This led to the rise of several studies about Ethylmercury and its effects on the human body. Although many studies found evidence to reject the hypothesis that there is a link between Ethylmercury and neurodevelopmental delays, thimerosal has currently been removed from all vaccines with the exception of some Influenza virus vaccines [5].

Multiple studies have been conducted to extensively research any link between the MMR vaccine and autism worldwide, including cohort studies, case series, and case-control studies. In the United States, a retrospective cohort study was conducted to report the occurrence of ASD in individuals who received the MMR vaccine with older siblings who do and do not have ASD [3]. The reason for this study was the reluctance of parents of children with Autism to vaccinate their younger, undiagnosed, children because the parents assumed that all their children have a higher predisposition for ASD. These portions of parents blamed the incidence of their children's autism to the MMR vaccine. These lower vaccination rates threaten public health as the low individual and herd immunity of measles results in new incidences of the disease each year. This coincided with a Canadian study of 98 younger siblings who were unvaccinated because of their older siblings having Autism; there was no statistical significance between vaccinated and unvaccinated children in correlation with Autism.

For cohort studies to show any correlation of the MMR vaccine and Autism in a healthy individual there needed to be exclusion criteria to certain syndromes and conditions which can predispose the individual to a later onset of Autism, which can be misinterpreted in the results [6]. A cohort study of nearly 700 000 individuals was conducted where they excluded individuals with Autistic risk factors with the intention for more concise results. Conditions that were excluded included patients with Tuberos Sclerosis, Fragile X Syndrome, Down syndrome, Angelman Syndrome, DiGeorge Syndrome, Neurofibromatosis, Prader-Willi Syndrome, and congenital Rubella Syndrome.

Autism Spectrum Disorder is defined behaviorally as a central nervous system development disorder, characterized by impairment in social engagement and communication, which is paired by repetitive behavior and interests. Currently, the ASD category includes "classic" Autism or autistic disorder, Asperger syndrome, Rett Syndrome and otherwise unspecified "atypical" Autism; classic Autism is the most severe. The etiology of Autism has not been identified yet, despite a rise in Autism cases over the years. In the 1980s, prevalence of Autism was 1:2000 in U.S children, versus recent surveys showing the ratio to be 1:110 U.S

children. However, this could be attributed to better screening in the current day, an actual increase in the incidences or a combination of both [7]. Although ASD is widely understood to have both genetic and environmental causes, the precise mechanism of both is still not fully understood. The current understanding of environmental risks includes paternal age, teratogenic substances, prenatal risk, medications, smoking, alcohol, nutrition, toxic exposure as well as the role of psychosocial factors. Maternal use of certain medications like selective Serotonin reuptake inhibitors, and valproate play a role in increasing the vulnerability of offspring with ASD. Maternal age, diabetes, enhanced steroidogenic activity, and immune activation play a role as well. Some factors do play a role in preventative measures from ASD, including adequate levels of folic acid and fatty acid intake. The specificity of many environmental risks remains unidentified, and the control of multiple confounding effects has been limited. Epidemiological studies show that there is no correlation of vaccines posing vulnerability towards an ASD diagnosis [8].

The complication of being under-vaccinated, especially with measles, can give rise to many dangerous sequelae. Measles can give rise to debilitating diseases like pneumonia and encephalitis, or even cause death. In the 1990s, measles was almost eradicated in America. Comparatively, there have been 704 new cases in 2019 alone. Under-vaccination in other countries also pose a threat against America eradicating measles, especially in visiting individuals or incoming immigrants. Additionally, unvaccinated individuals who travel from America and acquire the disease abroad, come back to under vaccinated communities, causing a spread of disease. 13 outbreaks this year in close-knit communities gave rise to new cases of measles, accounting for 88% of the new cases. 71% of individual cases were not vaccinated and 11% were vaccinated with only one dose of the MMR vaccine. The latter expresses the importance of parents giving both doses of the MMR vaccine to their children, to ensure they are covered over a wider range of the serotypes of measles. While there are no cases of encephalitis or death reported by the CDC as of April 26, 2019, 66 patients were hospitalized and 24 had pneumonia as a result of this new spread of disease. Up to 44 cases were imported from other countries including 34 that originated in the United States. Source countries included Philippines, Ukraine, Israel, Thailand, Vietnam and Germany. Before this year, the highest ever recorded cases of measles were in 2014 accounting for 667 cases [9].

Methods

This research encompasses both medical and controversial aspects of the MMR vaccine, as such; there is a wide range of studies and journals that can be included to account for both aspects. PubMed, Medline Plus and Web of Science research databases were all accessed. It is important to review all literature to determine support or rejection of the hypothesis. The nature of this subject matter requires the use of case studies to properly discuss the controversies and history surrounding the anti-vaccination movement, their claims and the medical aspects. Small sample size studies were excluded as the results may be broad, contain outliers and would likely not be significant, as was the case in Wayfield's study. The keywords used to obtain the articles for this research were controversies about MMR vaccine, Autism and MMR vaccine and causes of Autism. They key word "controversy" were

added in each search to focus on this aspect and find more sources pertaining to the topic. The accessed studies were all limited by a time frame and are no older than 10 years, ranging from 2009 till the present for more recent and accurate studies. Older cases were also accessed for discussion of the history but were not used to discuss the results for this paper. Abstracts were first scrutinized to catch any duplicated studies, and then the remaining studies were read in more detail to determine if they met the inclusion criteria. Studies were selected based on the inclusion and exclusion criteria and if the information was deemed relevant to this paper. The quality of the study was assessed to make sure it was peer reviewed and had a large sample size, to ensure the validity of the study. The articles utilized are in Table 1 of the appendix.

Inclusion Criteria

Case studies or examples of any link between Autism and MMR vaccine, studies included were also required to discuss the apparent pathophysiological change caused by the MMR vaccine and how that could lead to Autism.

Exclusion Criteria

Review studies, literature reviews, EPI review, and Meta-analysis.

Results

Each of these studies covers the Autism controversy in different countries. One of the most relevant studies is a nationwide cohort study in Denmark, conducted with 657 461 children of Danish born mothers, from January 1, 1999 through December 31, 2010. All the individuals were assigned with an identification number, to track them demographically. This unique identifier is used in all other nations' registries, and allows for health-related information to be individually linked, including vaccination history and Autism diagnoses. The Danish childhood vaccination program is free of charge and is voluntary, with the first vaccine offered at 15 months, and the second one at four years of age. The MMR vaccine from the Danish childhood vaccination program was thimerosal free during the study period. Any diagnosis of Autism was made after the first year of life, specifically after the first dose of the MMR vaccine. While gathering information, there was an exclusion of 5775 children who would have been outliers to the study conducted. Examples of the reasons they were excluded: emigration, early death, or an exclusionary diagnosis (Neurofibromatosis, Tuberous Sclerosis, Down syndrome, Prader Willi syndrome, etc.) The adjusted hazard risk was then determined for each child, based on a few criteria of history of autism in the family, low birth weight and history of smoking in mothers. Comparing the Autism rate in vaccinated children with unvaccinated children yielded a fully adjusted hazard risk of 0.93 (95% confidence interval. 0.83 to 1.02). The test of homogeneity of adjusted hazard risk score in the age interval one to three, three to five, five to seven, seven to 10, and more than 10 years of age yielded a p-value of 0.138 [6].

A retrospective study was performed on a large sample size in the United States, where they use the Optum database, which contains the health information of 34 million individuals, both commercially insured and Medicare managed care individuals. The individual data was gathered nationwide (16% west, 20% Midwest, 26% south, and 27% Northeast). The New England Institutions review

board waived the need for informed consent and deemed the study exempt based on its use of existent data. The database included children from January 1, 2001 to December 31, 2007, who had continuous healthcare from birth until five years of age and also had siblings enrolled in healthcare for at least six months between the beginning and the end of the study. Siblings had to be seven months to 17 years older than their siblings to be included. A claims-based algorithm was used to establish ASD status in study children and their siblings. To be included in the study, two or more claims of Autistic disorders (including Asperger syndrome and Pervasive Developmental Disorder) based on ICD-9 were required on two or more separate dates. The ASD status was determined throughout the entire study enrollment time, for both study children and their siblings. Inclusion criteria included study children with an older sibling with an ASD diagnosis (based on two claims) or older siblings with no claims. Exclusion criteria included children with older siblings with a single ASD claim [3]. Since the recommended age for the MMR vaccines first dose is at the age of 12 to 15 months, and the second dose is at four to six years of age, relative risks were estimated to compare ASD status in children receiving one dose of MMR at in ages two through four years and two doses at age five, versus those who were not vaccinated at those ages. Separate relative risks were calculated for children with and without older siblings with an ASD diagnosis. Since no children were lost to follow-up during the study before reaching the age of five, an unadjusted relative risk was reported as cumulative incidence rate ratios, by the taking the ratio of the proportion of children with an ASD diagnosis in an exposed group to the proportion of children with an ASD diagnosis in the unvaccinated group at ages two through five years old (Table 2). Out of 95 727 children in the study, 1929 (2.02%) of individuals had an older sibling with ASD. Overall 994 were diagnosed with ASD on further follow-up. 134 (6.9%) children were diagnosed with ASD who also had an older sibling with ASD. Comparatively, 860 (0.9%) children were diagnosed with ASD and have no siblings with ASD. Children vaccinated with one or more dose with unaffected siblings (not diagnosed with ASD) were 78 549 (84%) at two years and 86 063 (92%) at age five. In contrast, children vaccinated with one or more dose of the MMR vaccine with older siblings suffering from ASD were lower (73% at age two [1409] and 86% [1660] at age five). However, research limitations that could have altered the administrative claims database include claims that generated profit, so claims that could have not affected the study but generated profit would have been over reported versus claims that could have affected the study, but generated no profit, would have been under reported. The MMR vaccination rate in this study was reported between 4% and 14%, which was lower than the National Immunization Survey, indicating that children that could have been marked as unvaccinated could have been vaccinated by schools or public health clinics that did not report it to the database. Additionally, the positive predictive value of the diagnosis of ASD determined by a claims-based algorithm was 87%, resulting in an underestimation to patients with ASD who did not receive health care during the study period. However, there was a series of quantitative bias analyses conducted to assess the potential effect on the measurement of the study which was believed to not strongly affect the findings of this study. The prevalence of ASD in the children included in this study was 1.04% compared to 1.5% prevalence in the general US population. Younger siblings had a 6.9% risk of getting ASD,

which is consistent with the published estimates from the range of 6.4% to 24.7%. Even though there was a modest number of older siblings with ASD (1929 children), the upper confidence interval never exceeded 1.50 which implies that any true, large effect was unlikely masked because of the statistical imprecision [3].

A Polish case-control study was conducted to determine if there is a link between ASD and the MMR vaccine. The age range included in this study was between two and 15 years old. All the Autism cases were diagnosed by a child psychiatrist and all recorded in general practitioners' files. All uncertain Autism diagnoses (i.e., if it was secondary to trauma or disease state) were excluded from the study. The parents of all the case individuals took a standardized questionnaire for family history, prenatal care and socioeconomic status. They were additionally asked about the onset of symptoms, as well as any suspicions that they had as to what could have caused the disease. The questionnaire did not contain content about the MMR vaccination, to avoid a bias in the parent's answers. In this study, cases of ASD were considered as vaccinated only if the vaccination took place before the onset of ASD symptoms. The controls were considered as vaccinated, if they were vaccinated before the expected average time of the onset of symptoms of ASD. A conditional logistic regression analysis was used to compare the association between the MMR vaccine and ASD between cases and controls. The odds ratios were calculated for vaccinated versus unvaccinated children in the single measles vaccine as well as the MMR vaccine, and also MMR vs single measles vaccine. Potential risks such as the mother's age, education, gestational time, medications taken during pregnancy, prenatal care, and Apgar score were all examined and other risks associated with autism, were all taken into multivariate models. The population taken into the study consisted of 96 cases, and 192 controls. The average age was 7.5 years. Sex of the children was 81.2% boys and 19.8% girls. Women who were 35 years old and above and delivered babies with ASD were 12.9% versus 7.2% in women who delivered babies without ASD. A gestational period of 38 weeks or less was also more common in cases than controls. Mothers of cases also significantly took more medication than mothers of controls. Case children also significantly suffered from some form of perinatal injury compared to controls. Despite insignificant results, a five-minute Apgar score of less than nine often occurred in cases more than controls. Those five factors were considered as partition confounders and included in multivariate analysis (Tables 3 and 4). The majority of the children were vaccinated by the age of 12 to 18 months (64% of cases and 76.6 of controls). In both groups, nine children were not vaccinated against measles. The MMR vaccine was used in 55% of vaccinated controls and 44.3% of vaccinated cases. The odds ratio was calculated between an Autism diagnosis and the status of vaccination, as well as the type of vaccine used. The logistic univariate regression model was utilized and it was determined that there was no positive association found between vaccination and Autism. All relative risks were below one and actually indicated that vaccinated children, especially with the MMR vaccine, have a smaller risk of Autism [10].

A study in Italy was conducted to explore reasons for vaccination hesitancy of parents since vaccinations are not mandatory and parents are the decision makers over their children's healthcare. This was conducted using a survey-based study in Sicily since there was a suboptimal vaccination rate there. The survey evaluated

their level of acceptance for vaccinations. The sample of parents that were included in the study had children of ages 13 to 14 years, as the vaccination calendar should be completed by that age. The survey was conducted from January to June 2017 in six lower secondary schools in the Sicilian city of Messina. Surveys were handed out to parents and collected back after 20 days. There were 1300 questionnaires handed out, and 1093 (84%) were returned. Each questionnaire had 11 items on it, including age and parents' education, personal opinions about vaccines, vaccines carried out on children, booster shots given, opinions and information from their physicians, reasons why they opposed vaccines and direct or indirect knowledge of people harmed by vaccines. The topics in the questionnaire were answered as favorable, indifferent or contrary. The vaccination correlated negatively with age and education ($P < 0.0001$). When parents were asked about specific vaccinations that they deem acceptable for their children, the research indicated good coverage percentage for the MMR and DTP vaccinations but poor coverage based on the international guidelines for pneumococcal, meningococcal, HPV and HiB vaccinations. The hesitancy of parents to vaccinate children was based on a lack of knowledge and a false perception of the benefits of vaccines, associated with false information on the internet as well as the anti-vaccination movement. Parents hesitancy for vaccination based on poor information accounted for 32.2% (95% CI: 18.7-45.7), fear of side effects 26.6% (95% CI: 12.6-40.6) and efficacy of vaccine 17.5% (95% CI: 2.6-32.4). When asked about information received regarding vaccination 58.5% (95% CI: 54.5-6.5) said they received information while 41.5% (95% CI: 36.8-46.2) said they did not receive any information. The information received from physician accounted for 52.8% (95% CI: 46.4-59.2), media and internet 13.3% (95% CI: 4.6-22), and school 10.2% (95% CI: 1.4-19). When asked about people hurt by vaccination 14.4% (95% CI: 8.8-20) answered they knew people directly, 30.5% (95% CI: 25.5-35.5) answered indirectly knowing people, while 55.1% (95% CI: 51-59.1) answered no. This is why physicians as educators are critical in raising awareness and teaching the importance of vaccines and adverse effects of the anti-vaccination movement. Surprisingly, in this study, younger parents and those with less education were more likely to fully comply with vaccinations for their children, while older parents with higher education were four times as likely to opt out some of the vaccinations based on fear of adverse effects [11].

Discussion

Based on the studies discussed, it was shown that there was no significant, causal link between the MMR vaccine and ASD. Additionally, other studies showed the hesitancy of parents to vaccinate, and the reasons behind that hesitancy. Importantly, these studies were gathered and discussed on a worldwide scale, to show how serious the controversies in vaccination have become and to explain the global aspects and opinions on the matter. The Danish nationwide cohort study is to discuss links between the MMR vaccination and ASD. Hviid et al. [6] found that there was no correlation between the MMR vaccines activating ASD in susceptible subgroups, in the case of environmental or familial risk using adjusted hazard risk ratio, or in clustered autism cases after receiving the MMR vaccine. The reason for using the adjusted hazard risk ratio is because normal observational studies would be unable to discern a link between the vaccination and

people who are “susceptible” to ASD in cases of environmental or familial risk, as well as hazards introduced during the critical prenatal developmental period in pregnancy. By accounting for these factors, the study serves to decrease the confounding effects surrounding ASD and the MMR vaccine. Additionally, unvaccinated individuals are usually not counted; however, this study assessed and accounted for these individuals. This added to the studies overall power by increasing the large sample size up to 6517 cases, leaving a much smaller margin for statistical errors. Health registries with mandatory reporting were utilized to decrease recall bias. A possible bias in this study was that they used the date that individuals were diagnosed with ASD, not the first onset of symptoms. However, children could have revealed symptoms before vaccination but were not diagnosed until after the vaccination was administered, which would have been a source for information bias, biasing the hazard risk ratio toward an effect. The onset of symptoms could have influenced the reason to not vaccinate or persistence of vaccination.

As a way of determining individuals with higher susceptibility to ASD, siblings with ASD were taken into account to calculate adjusted relative risk [3]. This used a specific pool of cases showing a narrower approach to susceptible individuals, unlike other studies. Like other studies they did not observe any increase in ASD brought by the administration of the MMR vaccine, specifically after both the first and second doses of the vaccine. This specific pool was important because of the refusal to vaccinate the second child based on the older sibling’s diagnosis of ASD. There was no significant difference between the relative risk of younger siblings in both groups (older siblings with ASD and without ASD). There was lower relative risk in younger children versus older children who had older siblings with ASD, however, this bias could be introduced based on parents of children with ASD not vaccinating their subsequent children, due to higher diagnosis rates of ASD at an older age, allowing parents to opt out of vaccination. Since the relative ratio was calculated for both the first and second dose of the MMR vaccine, this introduced another variable where a diagnosis between the two doses would influence the parents to give the second dose of the vaccine. This study conducted their observational study over the span of 11 years, using an administrative database which limited recall bias.

The case control study of lack of association between MMR vaccine and ASD [10] revealed that what was no significant association with increased risk of ASD in children who have had the MMR vaccination and similar findings were also uncovered in a separate analysis using the single antigen measles vaccine. There was an unexpected finding between the odds ratio associated with the MMR vaccine being lower than the single measles vaccine. This completely went against Wakefield’s claims that the single measles vaccine decreased the risk of ASD in children, as well as the claim that three doses of the MMR vaccine was too great of a burden on the child’s immune system. If anything, this served evidence that Wakefield’s claims were motivated by his intent to patent the single measles vaccine and benefit from his fraudulent research. This study had a unique take on the association of an increased risk of ASD and a measles containing vaccine, since they studied the risk of the single measles vaccine alone. At the time of the study, these findings were relevant to countries such as Poland, which had launched the trivalent MMR vaccine comparatively late on worldwide timescale. Even though there was a slightly

increased risk ratio in the single measles vaccine compared to the MMR vaccine, it was not statistically significant in its claim that it would have increased the risk of acquiring ASD in susceptible children. Like other studies, there might have been a lower risk of ASD among vaccinated children due to confounding factors. For example, children with symptoms of developmental delay or actual diagnoses of ASD might have influenced the decision of avoiding administration of the vaccine. The vaccination histories of the participants in this study were directly taken from the physician’s records, eliminating the potential of recall bias.

The study by Facciola [11] addressed causes of hesitancy towards vaccination. A couple of factors were presented in this study, one of which was the degree of education each individual had regarding vaccination hesitancy. An unexpected result arose where younger individuals with a lower level of education had a higher rate of vaccination than people with higher levels of education. This was in concordance with the data contained in international literature. Parents with higher level education were four times more likely to be concerned about the safety of vaccination than those with lower levels of education. These findings are likely related to the lack of knowledge about vaccines who paradoxically, know much more about the diseases requiring vaccination. Other factors that could influence vaccination rates in those individuals with higher level education, is that they assume their children will be safe and benefit from herd immunity. In this study, the vaccination hesitancy did not involve all vaccinations but the concept of not vaccinating children can come in any form. For example, parents who choose to vaccinate their kids with the MMR vaccine and other well-known vaccinations, but not vaccinate against Hepatitis B, human papilloma virus, while others may choose to not vaccinate their kids against any disease. Herd immunity is protective to a certain extent, but exploiting this could also be the result of epidemics of preventable diseases. When parents were asked about sources of information that would oppose vaccination, parents claimed the main source was physicians, followed by internet and lastly word of mouth from friends and relatives. Although the majority of physicians do support and encourage vaccinations, some physicians are hesitant towards vaccines. This can affect the vaccination rate as hesitancy from physicians can translate to total mistrust in vaccinations as perceived by certain patients. Moreover, friends and family who may have a doctor that is vaccine hesitant can also spread their perceived knowledge by word-of-mouth with the actual message getting lost in translation. Additionally, hesitancy towards the influenza vaccine from a physician can be misinterpreted as hesitancy towards all vaccines. The fact that there is such a prevalent fear of side effects from certain vaccines like the Hepatitis B vaccination causing Multiple Sclerosis or the MMR vaccination causing ASD, the latter still a current fear, demands a better form of education for patients and a more thorough review of scientific literature, as well as physician education workshops.

The spread of scientific news on social media is relevant because the internet allows for publications by both qualified and unqualified individuals. Publications are easily produced and most people do not check if sources are peer-reviewed or backed up by relevant health organization. In this day and age, Facebook, Instagram, and Twitter contain many posts of false claims in the form of a picture, where a people could easily mistake it as fact without further discussion with healthcare professionals. A study

in Denmark asked important questions such as, the influence and changes in media coverage have been an early indicator of reduced public trust in the MMR vaccine, and could a proactive information campaign reduce the distrust in vaccinations? They also ask what would be the cost of this campaign. However, something to explore further would be what is the cost of not introducing this campaign? The costs to the healthcare system would need to be weighed against the cost of educating parents [12].

A study was done where it was demonstrated that media against Anti-vaccination just mere mistrust in vaccine can have a potential in improving public health communication [13]. In the UK, they monitored the HPV media debates and created derived question that could support proactive communication and preparedness. They hired several full-time positions to combat anxiety of parents and generate questions to further promote health care. This method could generate new research into programs that could monitor information gathering, processing and information retrieval regarding vaccine topics, and be used to automate in forms where it can be accessible at low costs.

Mass hysteria by world leaders, social media, and other unsupported claims need to be countered on a global scale. The success of vaccination programs depends momentarily on health care professionals and it is necessary to improve their knowledge about vaccinations so they promote vaccination practices to their patients. This could be achieved by organizing workshops or information meetings between vaccination experts with pediatricians and family doctors to promote vaccination practices and increase vaccine coverage.

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