MINI-REVIEW

Considerations for addressing anti-vaccination campaigns: How did we get here and what can we do about it?

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INTRODUCTION

A course on vaccine development asked students to write a blog addressing general anti-vaccination strategies and their significance today, in the context of the resistance seen against novel SARS-CoV-2 mRNA vaccines. This perspective explores how and why these efforts are successful at reducing vaccine uptake and why, for the most part, efforts to combat the movement have been unsuccessful. This summary of the collective view of the class provides recommendations for combating current and future campaigns of misinformation. It is hoped that this perspective will serve as a call to action for clinical pharmacologists and translational scientists to do their part to educate the lay community and promote the science in an open and transparent manner to ensure that current and future vaccines fulfill their potential.

Anti-vaccination history and the modern anti-vaccination thought leader

Widespread vaccination began in the early 1800s with Dr. Edward Jenner’s demonstration that cowpox could protect against smallpox. Briefly, vaccination laws (anti-vax) messaging. While similar concerns against vaccination have been cited throughout time, the current accessibility and widespread adoption of social media makes gives today’s anti-vax influencers significantly more power than their predecessors. As such, misinformation and anti-vax messaging spread almost as quickly as the coronavirus itself, in the modern age of smartphones and tablets.
were passed as early as in the 19th century in the UK. Opposition to vaccination has existed as long as vaccination itself. Even the pre-vaccination practice of variolation came under criticism. Anti-vaccination leagues, such as the Leicester Anti-Vaccination League, were formed and numerous anti-vaccination tracts, books, and journals appeared in the 1870s and 1880s. Anti-vaccination groups also emerged in Europe and North America in the 19th century. The anti-vax movement succeeded in repealing compulsory vaccine laws in multiple states in the US. Since then, public health authorities and anti-vax constituents have been in constant conflict, battling vaccination in the courts, including the famous Jacobson vs. Massachusetts case of 1905 (in which the US Supreme Court upheld the constitutionality of compulsory vaccination) and instigating riots, such as the famous Montreal vaccination riot of 1885 and Milwaukee riot of 1894, both against smallpox. Table 1 provides a brief chronology of the major milestones that define historical anti-vaccination sentiments.

Current anti-vaccination sentiment is a continuation of longstanding and passionate opinions of a segment of the population that mistrusts the safety and efficacy of vaccines in addition to the people who develop, distribute, and recommend them. Figure 1 shows a timeline of anti-vaccination sentiment than spans the last four centuries. A more extensive historical account can be found in the past work of Dube. Anti-vaccine “thought leaders” have written books or produced movies that characterize vaccines as dangerous and unsafe. Some have downplayed the severity of infectious diseases. Others run groups dependent on donations from individuals who support their ideas. Financial incentives also motivate some. Some “thought leaders” rely on advertising revenue and product sales from sites where they share articles on the “dangers” of vaccines.

The current landscape also includes people who could be classified as influencers (individuals who have the power to affect the decisions of others because of their authority, knowledge, position, or relationship with their audience). Some influencers use modern technology (e.g., social media and podcasts, etc.) to spread anti-vax messaging. To this end, the European Union has accused Russia in both official reports and through sources like The Guardian newspaper of “state-sponsored disinformation campaigns,” meant to decrease trust in western-made vaccines, while promoting their own vaccine, Sputnik V. Such accusations have included claims that the Russian states hired western-based influencers who work through Instagram, YouTube, TikTok, and Reddit to spread misinformation. These instances were among multiple others that lend support to the theory that anti-vaccination influences enjoy financial benefit that extends beyond traditional donations, product sales, or advertising revenue.

Anti-vaccination strategies, memes, and research data – not new

Not surprisingly, much of the dialogue created by the anti-vax community is not based in science. One of the early and continued vehicles for communication of anti-vaccination sentiment is the political cartoon. One of

| Date     | Group responsible                                                                 | Actions/sentiment                                                                                                                                 |
|----------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| 1720s    | Boston, US Physicians (led by Dr. Williams Douglass and James Franklin)           | Following a smallpox outbreak and engagement of variolation as a potential treatment, The New England Courant, a newspaper devoted to countering variolation, was launched (perhaps one of the first reported instances of tabloid journalism) – set the stage for the continued use of mass media to amplify anti-vaccination sentiment. Concerns about variolation as “Eastern medicine” and violating religious law. |
| 1860s    | The National Anti-Vaccination League and the Anti-Compulsory Vaccination League formed | Demonstrations and rallies led to the development of a commission designed to study vaccination. In 1896 the commission ruled that vaccination protected against smallpox but suggested removing penalties for failure to vaccinate. The Vaccination Act of 1898 removed penalties and included a “conscientious objector” clause, so that parents who did not believe in vaccination’s safety or efficacy could obtain an exemption certificate. |
| 1885     | Leicester, UK Anti-vaccination members (citizens)                                 | The Leicester Demonstration March of 1885 was one of the most notorious anti-vaccination demonstrations. Between 80,000 and 100,000 anti-vaccinators led an elaborate march, complete with banners, a child’s coffin, and an effigy of Edward Jenner. |
| 1970s    | Country-specific and varied                                                        | Lack of confidence in vaccines due to alleged links between pertussis vaccine and encephalopathy along with MMR (measles, mumps, and rubella) and autism in the UK, polio and infertility in Nigeria, and human papillomavirus (HPV) vaccine and complex regional pain syndrome in Japan. |
the first occasions of such a political cartoon appeared in the British weekly satire magazine, *Punch*, in 1898. In the cartoon, the Grim Reaper happily holds the 1898 Vaccination Act, while a serpent on his left uncoils, ready to strike in the implied near future. While the magazine endorsed compulsory vaccination, it also lamented the political shortcomings of the struggle between individual liberty and social good, thus setting the stage for an ongoing debate on vaccination that continued well after the Victorians.

Much of the strength in the use of cartoons to spread anti-vax messaging lies in the palatable nature of learning that pictures provide; unlike reading a scientific paper, a picture is more easily disseminated, thereby extending the reach of its influence. Furthermore, in the picture described above as well as its modern-day equivalent, “memes,” utilize humor to catch the reader’s attention. This stands in sharp contrast to charts, data, and graphs, which might alienate individuals based on their educational and socioeconomic status. Furthermore, imagery of needles used for vaccination gives a tangible enemy for the anti-vax community to unite over; in contrast, there is no such tangible “anti-vax enemy” in a similar context. Figure 2 provides a comparison between historical political cartoons of the past and modern-day memes to advance anti-vax messaging.

Who comprises the anti-vax audience?

A group often more susceptible to accepting the message of anti-vax influencers are parents, particularly those with undecided views on vaccines. The individuals with undecided views are considered “the vaccine hesitant,” distinct from anti-vax individuals who hold firm beliefs against vaccination. A recent study showed that most parents (76%) do not hold fixed views either for or against vaccination, even if they happen to vaccinate their children. Vaccinating parents may still be influenced to doubt childhood vaccination and delay or refuse vaccinations in the future. The sensitivity of parents to vaccination can be traced back to 1853 when the Vaccination Act was passed in the UK, which called for compulsory vaccination for all infants. The National Anti-Vaccination League was founded in London as an immediate response to the Vaccination Act. Parents are particularly sensitive to anti-vax messages because they may feel a sense of guilt when children experience side effects from the vaccine. The recent heart inflammation side effects in adolescents and young adults linked to the Pfizer COVID-19 vaccine provide a current context for this sentiment. Despite knowledge existing of how such side effects can be managed, the messaging persists. The reality is that some people tend to accept
risks associated with lack of action (e.g., not getting vaccinated) but do not accept risks associated with direct actions (e.g., getting vaccinated).

**Why have current strategies to fight anti-vax messaging not worked?**

Part of the reason that current strategies have not been particularly effective in curtailing the spread of the anti-vax message is that they do not address the root cause (false scientific credence being one of a multitude of underlying sentiments that drive the messaging). Some of the anti-vax influencers possess false scientific credence because they may have medical degrees or are currently employed at healthcare institutions. The influencers actively engage their following in a distinct niche, and this is key to their impact.

Preventing those with offensive or unacceptable views from contributing to public conversations, otherwise known as “deplatforming,” is an obvious solution that many health professionals have reached for. However, experience shows that while taking misinformation off social media is vital, it cannot be a standalone effort, and must be accompanied by efforts to address changing the views of individuals endorsing the information. Shutting down problematic user accounts can prevent the misinformation from reaching new audience, but it does not change the views of people who already endorse the misinformation. After these people relocate to a different
platform, the misinformation may become increasingly toxic, especially if an anti-vaxer were to claim that the government shut down his or her platform as part of a conspiracy. Closely linked to this issue are anti-government sentiments and the struggle between individual liberty and social good.

**New systemic strategies to combat anti-vaccination**

**Legal interventions**

Legal interventions might help combat the effects of anti-vaccination efforts, particularly the misinformation contained in some of the messaging. It is a fine line to walk between protecting civil liberties and enforcing laws meant to protect public health. The term “personal belief exemption” came into use in the 1990s, but the notion of granting exemption from compulsory vaccination based on secular convictions dates back to the late 19th century. The exemption has evolved through stages, with each prompted by new vaccines or vaccine laws. In each stage, the exemptions reflected political compromise in the lawmaking process and broader struggles over liberties and rights. California eliminated personal belief exemptions in 2015. California public health officials did not have the final say and their responses had been somewhat inconsistent and contradictory. In 2019, a new law required a centralized medical exemption review process by the State. In 2021, exemption forms were directly transmitted to the California Immunization Registry (CAIR). State Public Health Officers may revoke the medical exemption. If the State determines a physician is “contributing to a public health risk,” it will report the physician to California’s medical board. Certainly, there is tremendous heterogeneity across states, and controversy exists even at the Supreme Court level surrounding the constitutionality of federal mandates (January 2022, Occupational Safety and Health Administration [OSHA] Vaccine mandate ruling). As such, federal mandates, in particular, are most useful in public health emergencies, such as the current pandemic but still most avoid politicization at all costs.

In addition to providing negative reinforcement for vaccination, legal interventions can be used to provide positive reinforcement as well. Governments, schools, and private businesses can provide incentives for vaccination and limit misinformation. Vaccinated individuals can be allowed to enter indoor venues, return to office, and be exempted from certain travel bans or the 14-day back-to-college quarantine periods.

**Misinformation harm reduction**

Another general approach would be to alter the current methods used to enact “misinformation harm reduction.” One such approach could be to for government, nonprofits, and other influential bodies to impose advertising boycotts against those social media platforms that refuse to curtail the spread of misinformation. The US/UK’s Center for Countering Digital Hate (CCDH), which aims to actively disrupt misinformation and hate speech online related to anti-vaccine rhetoric, and neo-Nazism, found strong public support for this idea. The work of the CCDH and other such groups is particularly timely, given the modern relationship between anti-vaccination opinions and extreme political polarization. In many countries, including the USA, the anti-vaccination stance has been utilized as a “cause” to recruit individuals to extreme political views; from that standpoint, misinformation harm reduction surrounding vaccines could also help decrease political polarization.

Pro-vaccination social media networks must continue to work together to spread factual scientific information for long-term benefit. In instances where pro-vaccine social media accounts are flooded by anti-vax groups, certain nonprofit services exist to counteract algorithmic attacks. ‘Shots around the World’ is an example of an online defense resource freely available to the public who are in favor of vaccination. Given the dependence of social media on advertising for sustained profits, such strategies would prove effective, especially when taken on by nongovernmental sources, reducing the grounds for accusation of overreach of governmental power.

**Utilizing healthcare workers more effectively**

Furthermore, the fight against anti-vax misinformation must utilize its frontline soldiers, namely healthcare workers (HCWs). Given that one of the few people that many individuals still trust on healthcare matters is their primary care physician or office nurse, HCWs have a pivotal role with respect to the public in imparting information and promoting vaccines. This is especially the case for newer vaccines such as the SARS-CoV-2 mRNA vaccine, which might have slow uptake in certain communities. Unfortunately, while physicians have high rates of COVID vaccination (~96%), only <50% of nurses, 55% of nursing house staff, and 20% of home health aides have been vaccinated against COVID-19. Strategies to improve vaccine uptake among HCWs and to enable HCWs to be more vocal on the reasons why they chose to be vaccinated might serve to combat anti-vax messaging.
Re-engaging the vaccine-hesitant and anti-vax individuals

Finally, the role of the anti-vax audience must be discussed and, in tandem is the inser with it, the role of physicians, psychologists, clinical pharmacologists, community leaders, and scientists in re-engaging the anti-vax audience in discussion. A technique known as “motivational interviewing” has been used by psychologists to elicit behavior change by helping clients to explore and resolve ambivalence. This technique has been applied to encourage childhood vaccination. A clinical cohort study found that motivational interviewing of postpartum women improved vaccine coverage of their infants. In this study, clinical research assistants performed motivational interviewing sessions, but any patient-facing HCW can apply the technique while initiating a conversation on vaccination. Instead of trying to force change upon individuals, helping them find their own intrinsic motivation to change would likely be more effective and long lasting. The motivational interviewing technique, for example, seeks to use directed and open-ended questions to motivate the interviewee to name their own inspirations and biases alike as opposed to dictating to them. This technique does not prosecute individuals for their beliefs and, in fact, may help keep vaccine-hesitant individuals engaged in discussion for longer, thereby decreasing their likelihood to close off the conversation (“shut down”) or fight back later.

As Clinical and Translational Science (CTS) is a journal for translational scientists and clinical pharmacologists, which represents a unique intersection of drug developers (e.g., industry), regulators (e.g., FDA), and academics (e.g., university-based scientists), this perspective article should represent a call to action to our community to emphasize the facts. Make data more accessible to lay people, shifting the dialogue towards reliance on science. Some participation in the social media exchange with pro-vaccination data and personal decision to have children, elderly parents, or other vulnerable loved ones vaccinated is likewise warranted to build trust with fearful parents across communities. This can perhaps be achieved through participation in the social media with pro-vaccination data. Several examples exist (e.g., [link to CDC website] and [link to CHOP website]) but these and others need to be more visibly promoted. It is also reasonable to re-engage members of the anti-vax community and seek collaboration with religious/community leaders who can help promote the benefits of vaccination to historically vaccine-hesitant populations. We believe that it is not constructive to “fight fire with fire” – reduce the use of alienating memes or other mockeries of the anti-vax proponents, as this serves to further disengage the target community. Targeted outreach sessions, either over social media or in person at local community health centers, primary care offices, or pharmacies, to discuss vaccination in detail would help. Likewise, ensuring inclusion of diverse sets of participants in vaccine trials, to assure minority communities of appropriate result extrapolation to their loved ones, is essential in addition to appropriate and objective communication of the results. In conclusion, as refusal of vaccination increases, a consistent and coordinated strategy must be established to treat the topic with the seriousness it deserves and to allow for current and future vaccines to fulfill their potential.

CONFLICT OF INTEREST
The authors declared no competing interests for this work.

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