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Vaccine Schedule Type as a Predictor of Up-to-Date Status of Early Childhood Immunizations in the U.S.

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An abstract of
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Rollins School of Public Health of Emory University
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2017

Abstract

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By Allison L. Hargreaves

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Methods: We classified vaccination schedule adherence as routine, alternate, or other for the 15,059 2014 National Immunization Survey (NIS) 19-35-month-old participants with provider-verified data, and calculated the up-to-date status for participants using all ACIP-recommended immunizations. To determine schedule adherence, we accounted for vaccines received by 5 key time points. We then constructed logistic models using sociodemographic characteristics to predict alternate and other schedule adherence (versus routine schedule). Finally, we constructed a logistic model to estimate the association between schedule adherence and up-to-date status, while also accounting for key sociodemographic characteristics.

Results: Most children followed a routine schedule (63%), while 23% and 14% followed alternate and other schedules, respectively. Most children (68%) were up-to-date for all required immunizations. Alternate and other schedule adherence were strongly associated with not being up-to-date (ORs = 32.7 and 3.9 respectively). Factors including belonging to specific racial/ethnic groups, being below the poverty line, and having moved across state lines since birth were associated both with non-adherence to routine schedules and not being up-to-date.

Conclusion: Vaccination schedule in early childhood is strongly correlated with the likelihood that a child will be up-to-date for recommended immunizations. Understanding characteristics of families with early vaccine delays may be useful for future interventions targeting those at risk for non-adherence to routine immunization.

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Table of Contents

Chapter I: Background

History of Vaccination in the U.S.

The vaccination program in the United States is a major public health success story. Upon the founding of the country, the only available immunization was smallpox inoculation; nearly 250 years later, and over a dozen vaccine series are regularly recommended for all children (1, 2). The modern vaccine age began in the 1954 when the introduction of Jonas Salk's inactivated polio vaccine was accompanied by a 17-fold decrease in cases of paralytic polio by 1961 (3). Prior to the introduction of the first measles vaccine in 1963, 9 out of 10 children were expected to have had the measles by mid-adolescence; in the decades following its introduction, the annual number of measles cases in the US decreased from nearly half a million to tens of thousands (4). For children born between 1994 and 2013, it is estimated that over 300 million illnesses, 21 million hospitalizations, and 700,000 deaths will be avoided through their lives because of immunization (5). For the 2009 U.S. birth cohort alone, the vaccine schedule recommended to American children is estimated to prevent tens of thousands of premature deaths, tens of millions of cases of disease, and tens of billions of dollars in direct and societal costs saved (6). By the mid-2000's, there was a 99% or greater decrease in mortality due to vaccine-preventable diseases (VPDs) whose vaccines introduced to 1980 in the U.S. (diphtheria, measles, smallpox, polio), and 80% or greater reduction in several VPDs whose vaccines were introduced since 1980 (hepatitis A, acute Hepatitis B, varicella, and *Haemophilus influenzae* type B) (7).

Vaccine-Induced Immunity

Modern vaccination works through two mechanisms: individual and population level immunity. On an individual level, persons inoculated have an immune response that protects them from illness if they are exposed to an antigen. No vaccine is perfect: efficacy estimates range for the different diseases that vaccines prevent, and even between different formulations of vaccine. For instance, the inactivated poliovirus vaccine (IPV) is estimated to be 90% effective after 2 doses and 99% effective after 3 doses; the oral poliovirus vaccine (OPV), which protects against the same disease, is estimated to be 50% effective after 1 dose and 95% effective after 3 doses (8). The diphtheria, tetanus and acellular pertussis (DTaP) vaccine is also estimated to have a high efficacy: it prevents approximately 70-90% cases of disease for 5-10 years after a four-vaccine series is complete (8). Other recommended vaccines are less effective; for instance, the varicella vaccine is estimated to be 70-90% effective in general, although it has better estimated protection against severe disease (8). Some vaccines require multiple doses in order to achieve high levels of efficacy (e.g., MMR, DTaP, IPV) (2, 8).

Population-level immunity, or herd immunity, works through a different mechanism: if high numbers of individuals in a population are vaccinated, even those in the population who are not vaccinated are at a decreased risk of disease, due to decreased exposure to the antigen in the community. Different vaccines have different estimated thresholds of coverage necessary to attain population-level immunity, ranging from around 80-95% for common VPDs (9, 10). In any population, some individuals will be ineligible to receive vaccines, due to being younger than minimum age requirements or reduced immunity from conditions like cancer or HIV (2, 8, 11, 12). In the U.S., approximately 3% of the adult population is immunocompromised and has contraindications to certain vaccines (13). Others may be travelling from a country with limited vaccines available. Still others choose not to be vaccinated, relying on the herd immunity provided by others in their community (14). It is thus important for people who are eligible to be vaccinated, in order to maintain vaccination levels necessary for herd immunity.

Modern VPD Outbreaks in the U.S.

When an outbreak of a vaccine-preventable disease occurs, those ineligible for vaccination often suffer disproportionately. In an outbreak of pertussis in California in 2010, nearly 90% of cases were children too young to be fully vaccinated against DTaP (15). VPDs such as measles are known to be especially serious for patients with comorbidities (4). Children who are un- or undervaccinated against VPDs are at increased risk of disease, whether due to ineligibility or choice, and are more likely to be affected in outbreaks of diseases such as measles (16, 17), varicella (18), pertussis (19-21), mumps (22), and pneumococcal related disease (23). Research has demonstrated that cases of vaccine-preventable diseases cluster where large groups of individuals are unvaccinated, allowing for the possibility of outbreaks of VPDs in geographic locations and schools with low coverage rates (20, 24-28). Such communities exist in the U.S. and abroad, and have indeed been subject to outbreaks of VPDs (29, 30). Unvaccinated American residents are also subject to increased risk of exposure to diseases such as measles and Hepatitis A when travelling to and interacting with individuals from countries with lower coverage, allowing introduction of these diseases even though they are no longer endemic in the U.S. (31, 32).

Vaccine Schedules

In the U.S., the Advisory Committee on Immunization Practicices (ACIP), run by the Centers for Disease Control and Prevention (CDC), publishes recommended vaccine schedules annually for childhood, adolescent, and adult vaccinations (2). Included in the schedules are recommended ages for routine, early, and catch-up immunization, and variations of the schedule for specific vaccines with multiple brands available on the market. Currently, children following the ACIP-recommended schedule will be protected from 15 VPDs with up to 25 shots by 19 months of age (2). Recent additions to the recommended schedule include rotavirus vaccine, which was added back to the schedule in 2010 after an earlier vaccine was associated with rare but serious side effects (33, 34).

Coverage among all vaccines recommended for children is not equal. According to estimates published by ACIP, coverage ranged from approximately 57.5% coverage for the second Hepatitis A vaccine dose to 94.7% for the third dose of DTaP in 2014 (35). Some other vaccines also had relatively low coverage estimates for full series, including rotavirus (72%) and Hib (82%) (35). Historical trends in coverage have been observed: for instance, MMR coverage dipped after Andrew Wakefield's subsequently retracted article was published, alleging a link between the vaccine and autism in both the UK and the U.S. (36, 37). While coverage of Hepatitis B has met the Healthy People 2020 goal (as did several other vaccine series) of over 90% coverage for 3 doses of vaccine, only 72% of children received the first dose within 3 days of birth, when it is scheduled (35). Experts agree that initiating vaccination as soon as it is recommended is important for protecting against VPDs (38-40). One recent analysis of U.S. data collected in 2012 found that children 19-35 months of age were undervaccinated for an average of 282 days for the 4:3:1:3:3:1:4 vaccine series (4+ DTaP vaccines, 3+ IPV, 1+ MMR, 3 or 4 Hib, 3+ HepB, 1+ varicella, 4+ PCV), and 43% of children were undervaccinated for a total of 7 or more months (41). Spacing of vaccinations is also important for their effectiveness; one analysis of early childhood vaccinations in the U.S. from data collected in 2005 estimated that 6% of children received at least one dose of vaccine that was given at an invalid age, and 2.5% of children received vaccines too closely together to be valid (38).

Adherence to Recommended Vaccination Schedules

Historically, certain groups of children have had lower adherence to vaccine recommendations. These groups included those of minority racial and ethnic backgrounds, children of lower socio-economic status, and children living in certain geographic locations such as inner cities (42-47). Additional barriers included cost of vaccinations (which may not be covered by insurance) and access to vaccination facilities (48). Recent literature from several years of data suggests that children receiving vaccines exclusively from military providers are less likely to be up-to-date than other children for recommended immunizations (49).

In 1994, the United States enacted the Vaccines for Children (VFC) program, aimed at reducing vaccination coverage disparities due to access. Under it, children who are eligible for Medicaid, are un- and under-insured, or are American Indian or Alaska Natives are eligible for federally purchased vaccines (50). VFC has been a largely successful program, with great reductions in disparities associated with MMR and DTaP vaccination (51). The cost to completely vaccinate one child has dramatically risen with the addition of new immunizations, contributing to undervaccination of children who are underinsured (52). However, recent literature predicts that immunization coverage will increase modestly with the coverage required by the Affordable Care Act (53, 54). A recent paper hypothesized that working parents might face logistic barriers in vaccinating their children; however, researchers found no association between parent's employment status and timely vaccination (47). Should these provisions hold in the future, it stands to reason that remaining disparities will continue to decrease.

Parental Choice and the Provider's Role in Vaccination Schedule Adherence

Literature has demonstrated the importance of provider interactions and recommendations on vaccination of children. Vaccine providers who engage with patients and have conversations about why vaccines are important or why children are recommended to have receive vaccines at certain ages are more likely to have vaccines allowed (55-63). Despite the well-documented evidence supporting direct recommendations, some providers hesitate to do so, due to feeling unprepared for potentially challenging conversations or concern over decreasing patient satisfaction (56, 64).

Some providers refuse to care for patients who are unvaccinated or have delayed vaccinations, in order to protect patients too young to be vaccinated from unnecessary exposure to VPDs in waiting rooms; still, others engage allow un- or undervaccinated children in their practices under the reasoning that some vaccination is better than none, and providing even delayed vaccinations is important for boosting immunity in patients over time (62-64). Recent literature demonstrates that most physicians are asked about delaying vaccination, and that modern parents are using information from a wide variety of sources (not just public health recommendations) to influence their vaccination decisions (63-70). Information received from online sources, media, family, and friends are important – at least to some individuals – in making vaccination decisions for children (65).

The wide variety of information sources that parents are using to make vaccination decisions have an important impact on that decision, and on their level of confidence in vaccines (71).

Scales assessing vaccine confidence and hesitance often include items on non-scientific sources of vaccination information, in addition to scientific and governing bodies, and desire to adhere to social norms in making vaccination decisions for children (58, 72-76). One oft-cited concern is that vaccines, or specific ingredients included in them, can cause adverse outcomes in children; parents and physicians alike report that concern over potential side effects are a major reason for vaccine hesitancy and cause for delaying or refusing a vaccine (63, 67). Another concern is that there are too many vaccines on the early childhood immunization schedule now; parents may be concerned for their children's comfort and safety when several injections are in one visit (63, 77-79). Research suggests that while strategies such as vaccine education and school requirements exist for encouraging high coverage levels and vaccine confidence, further research is necessary to flesh out specific strategies that will be consistently effective at promoting vaccine uptake (80).

The desire to be involved in their children's medical decisions and construction of the vaccination schedule, the preponderance of vaccine concerns in social circles, and the concern over the safety and comfort of children receiving multiple vaccines has made the opportunity ripe for alternate and delayed schedules. One estimate is that only 61% of US parents neither delayed nor refused vaccinations; another using 2012 data estimated that only 26% of American children received all doses of six early childhood vaccine series on time; a third study using 2003 data showed that only about a third of American 24-month-old children were not undervaccinated, or undervaccinated for less than 1 month of their lives (41, 81, 82). While some of these children with delayed vaccinations and alternate schedules may ultimately become up-to-date for all vaccinations, delayed vaccination places children at excess risk of VPDs and contributes to the spread of disease in outbreaks (39, 82, 83). Moreover, children following delayed and otherwise modified vaccination schedules may be less likely to ever be fully vaccinated (68, 81, 82, 84).

Direction of Analysis

Given the negative ramifications of undervaccination in populations with circulating VPDs, efforts should be made to both identify children at risk of following alternate schedules, and to clearly describe the association between routine vs. alternate schedule adherence and up-to-date vaccination status of children in the U.S. Understanding who is likely to be undervaccinated, delay vaccination, or space out vaccination will provide insight to researchers and providers for creating and implementing specific interventions to increase schedule adherence and coverage levels.

Chapter II: Manuscript

Abstract

Objectives: To estimate the ability of sociodemographic factors to predict the proportion of American children adhering to the Advisory Council on Immunization Practices (ACIP) recommended vaccination schedule or utilizing alternate schedules, and to estimate the effect of both schedule adherence and sociodemographics on vaccination coverage for all ACIP-recommended early childhood immunizations.

Methods: We classified vaccination schedule adherence as routine, alternate, or other for the 15,059 2014 National Immunization Survey (NIS) 19-35-month-old participants with provider-verified data, and calculated the up-to-date status for participants using all ACIP-recommended immunizations. To determine schedule adherence, we accounted for vaccines received by 5 key time points. We then constructed logistic models using sociodemographic characteristics to predict alternate and other schedule adherence (versus routine schedule). Finally, we constructed a logistic model to estimate the association between schedule adherence and up-to-date status, while also accounting for key sociodemographic characteristics.

Results: Most children followed a routine schedule (63%), while 23% and 14% followed alternate and other schedules, respectively. Most children (68%) were up-to-date for all required immunizations. Alternate and other schedule adherence were strongly associated with not being up-to-date (ORs = 32.7 and 3.9 respectively). Factors including belonging to specific racial/ethnic groups, being below the poverty line, and having moved across state lines since birth were associated both with non-adherence to routine schedules and not being up-to-date.

Conclusion: Vaccination schedule in early childhood is strongly correlated with the likelihood that a child will be up-to-date for recommended immunizations. Understanding characteristics of families with early vaccine delays may be useful for future interventions targeting those at risk for non-adherence to routine immunization.

Introduction

Vaccination programs in the United States are a major public health success story. For children born between 1994 and 2013, it is estimated that over 300 million illnesses, 21 million hospitalizations, and 700,000 deaths will be avoided through their lives because of immunization (5). The U.S. Centers for Disease Control and Prevention's (CDC) Advisory Council on Immunization Practices (ACIP) recommends a childhood immunization schedule to prevent fifteen potentially serious illnesses (2). CDC annually assesses vaccination rates through the National Immunization Survey (NIS). While NIS-reported coverage is generally high, (e.g., 57.5% coverage for the second Hepatitis A vaccine dose to 94.7% for the third dose of diphtheria, tetanus, and acellular pertussis vaccine (DTaP) in 2014), vaccine-preventable diseases still occur in the US, with outbreaks noted among under and un-vaccinated populations (8, 15-20, 22, 35).

Concerns about the need for, and safety and effectiveness of vaccines has led to decreases in vaccine confidence (85-88). Recent publications have identified parental desire to be involved with the crafting of their children's vaccination schedule, with concern both with vaccinations in general and with number of vaccinations given at each visit; additionally, demographic and socioeconomic characteristics are associated with differences in vaccine uptake (61, 63, 65, 66, 77, 89, 90).

Most research on vaccine coverage focuses on the up-to-date status variables as reported by CDC (35, 41, 47, 49, 83, 84, 91). However, these variables do not account for at least two vaccines in the recommended childhood schedule - Hepatitis A and rotavirus, (33, 34). Additionally, analyses focusing on up-to-date status at specific time points (e.g. by 19-35 months of age) may miss early delays in vaccination, when children may have an excess of person-time at risk of disease. This is potentially important, as participants may be up-to-date as of the time period or age under investigation, but still be at increased risk of vaccine-preventable diseases during earlier ages (38, 41, 82). Prior studies that have assessed early variation in schedule adherence have often utilized data from limited geographies (83, 84, 92).

Understanding the associations between sociodemographics, vaccine schedule type, and up-to-date vaccination status will provide insight into the current state of immunization recommendation adherence in the U.S. This analysis attempts to harmonize the above considerations. First, we investigate the ability of socio-demographic characteristics to predict adherence to vaccination schedules. Second, we assess the association between schedule type and the same socio-demographic characteristics with up-to-date status for the full immunization schedule recommended by ACIP.

Methods

Data Source

We utilized the 2014 NIS for this analysis. NIS methodology has been previously described (93). Briefly, NIS is an annual telephone survey that collects vaccine information from a geographically representative sample of U.S. children aged 19-35 months. Participants are recruited via cell phone and landline random digit dialing, and permission is sought to verify children's vaccinations through their healthcare provider(s). This analysis was restricted to the 15,059 children living in the 50 states and Washington, D.C. with provider-verified vaccination data.

Exposure and Outcome Variables

We classified vaccination schedule adherence as either routine (following the ACIP-recommended schedule), alternate, or other (not fitting to either a routine or alternate schedule). Alternate schedules were further categorized as restrictive, selective, or both restrictive and selective. Definitions of each schedule type were modified from those described by Nadeau et al. with expansion to include vaccinations given through 19 months (Table 1) (92). We excluded vaccinations delivered prior to earliest valid dates, as described in Glanz et al.'s white paper on vaccine safety (94).

We first assessed if children were following a routine schedule by assessing adherence to the ACIP schedule at five timepoints, using the number of vaccines and the child's age in days at vaccination for each group of early childhood vaccinations (Table 2). For this analysis, we considered vaccine formulation where possible to evaluate completeness of rotavirus and *Haemophilus influenzae* type B (Hib) vaccinations, where these vaccines were not received at 6 months of age. Children who were coded as routine on at least four of the five vaccination time points (with an expected six vaccination days) were considered as adhering to a routine vaccination schedule overall.

Children not classified as routine were then assessed to determine if they were following an alternate schedule. Children with at least six vaccination visits with three or fewer immunizations at each visit were coded as following a restrictive schedule, while children who did not receive any doses of at least one vaccine type were coded as restrictive; children could be both restrictive and selective concomitantly. Children who were not following routine, restrictive, or selective schedules were coded as following an "other" schedule type (Table 1).

We assessed participants' up-to-date status as of the survey date if they received the following vaccines: at least four doses of DTaP, three doses of poliovirus vaccine, one dose of measles, mumps, and rubella vaccine (MMR), three or four doses of Hib, one dose of hepatitis A vaccine (children over 24 months of age required 2 doses), three doses of hepatitis B vaccine, one dose of varicella vaccine, four doses of pneumococcal conjugate vaccine (PCV), and two or three doses of rotavirus vaccines.

Sociodemographic variables were considered as potential predictors, including respondent-identified race/ethnicity, poverty status (as defined by the U.S. Census for the previous year), number of vaccine providers, provider facility type, child's rank in the family, maternal education level, census region, child's receipt of Women, Infants and Children (WIC) benefits, child having moved across state lines since birth, insurance type, and the child's ever-uninsured status. We collapsed levels of several variables to ensure sufficient sample size; recoded levels of sociodemographic variables can be seen in Table 3.

Additionally, we created variables to (a) identify children who had any vaccination initiated later than recommended, (b) compute the total number of vaccination visits, and (c) calculate the average number of vaccinations per visit.

Univariate and Bivariate Analyses

We computed univariate frequencies of each schedule type, up-to-date status, and any lateness of vaccine receipt. Bivariate associations were assessed (a) between both the main exposure and predictors with up-to-date status and (b) between sociodemographic predictors and schedule type. We compared average number of vaccination days and average number of vaccinations per vaccination day by schedule type and up-to-date status. Based on previous research associations between the race/ethnicity categories were stratified by poverty status, and the percent up-to-date at each level was observed (44, 45).

Logistic Models

We assessed two independent logistic regression models, for outcomes of up-to-date vaccination status and vaccine schedule type. Due to the large number of missing values, insurance variables were excluded from the regression models.

The first model used polytomous logistic regression to identify important predictors of alternate or other schedules versus routine schedule type. All predictors, as well as the interaction between race/ethnicity and poverty status, were included in this model to understand sociodemographic characteristic associations with schedule type; there was no elimination-based model building conducted.

The second logistic model assessed the association between schedule type and up-to-date vaccination status. We considered all sociodemographic predictors and interaction between race/ethnicity and poverty status for inclusion in the initial model. We selected the model using the backwards change in estimate approach in order to control for confounding between predictors and ensure a parsimonious model.

All associations were tested using alpha of 0.05. Analyses were performed using SAS version 9.4 (The SAS Institute, Cary NC) using complex survey procedures with survey weighting provided with the publicly available NIS dataset (95). The Emory Institutional Review Board determined this secondary analysis to be exempt from the review process (Appendix B).

Results

Schedule Adherence

Most participants (63%) followed a routine schedule as recommended by the ACIP; nearly a quarter (23%) followed an alternate schedule and about 15% followed some other schedule (Table 3). Compared to children following routine schedules, children following alternate schedules were more likely to have moved across state lines, not be firstborn, live in the Northeast (versus the South), and be non-Hispanic black or multi-race below the poverty level (versus non-Hispanic white children above poverty). Compared to children following routine schedules, children following other schedules were more likely to have received WIC benefits, belong to any racial/ethnic group living below poverty, have moved across state lines since birth, and have received vaccinations from public facilities only (versus private providers). Although not included in the model, most children who initiated vaccination late for at least one time point followed alternate and other schedules.

Up-to-Date Status

Approximately 58% of the participants were up-to-date for recommended vaccinations as of the time their parents responded to the NIS (Table 4). Schedule type was strongly associated with up-to-date status; all children following selective schedules were not up-to-date by definition. Children following alternate schedules (compared to routine schedules) were 33 times more likely to not be up-to-date; children following other schedules were approximately four times more likely to be not up-to-date compared to children following routine schedules. Hispanic children above and below the poverty level were 40% less likely to be not up-to-date than white children above poverty; other combinations of race/ethnicity and poverty status were not significantly associated with up-to-date status. Not being up-to-date was more common among children who had initiated vaccination late on at least one time point, had ever moved across state lines since birth, had lower levels of maternal education, and had ever not had insurance. Approximately 2/3 of children who were not up-to-date had initiated vaccination late on at least one time point. On average, up-to-date participants following alternate schedules had approximately three more vaccination visits and received one fewer vaccine per visit than did up-to-date children following routine or other schedules (Table 5). Generally, up-to-date and not up-to-date participants received similar numbers of vaccines per visit, although not up-to-date participants had fewer visits.

Discussion

Over 60% of children in this study followed a routine vaccination schedule, and these children were much more likely to be up-to-date for required immunizations than children following alternate or other schedules. Our up-to-date classification was more strict than those calculated by the NIS, due to our inclusion of Hepatitis A and rotavirus vaccines in the up-to-date variable. This led to our lower estimate of up-to-date children (58%, compared to 71% reported up-to-date for the combined series reported in the NIS) (35). The vaccine schedule classification structure we used allows for flexibility of circumstances due to chance and access issues (e.g., if a physician's office lacked a particular vaccine and it was received on a different day than other age-appropriate immunizations, or the child lacked health coverage for a short period of time and vaccination was delayed) that might hinder a family attempting to adhere to the recommended schedule.

We found that the effect of schedule type is strongly associated with up-to-date vaccination status. While additional variables (maternal education, race/ethnicity group) were also significantly associated with the odds of being up-to-date vaccination, these effects were relatively small compared to that of schedule type, highlighting the importance of ensuring routine schedule adherence. There were few consistencies in demographic variables associated with schedule type, indicating that factors other than sociodemographics are more important in determining vaccination schedule.

Role of Vaccination Schedule

Our findings are in line with research showing increasing trends in shot-limiting as reported by American doctors over recent decades and the important role that physician recommendations, vaccine confidence, and perceived risks of vaccination play in the decision if and when to vaccinate children (55, 66, 68, 71). A review by Maman et al. discussed concern over number of shots per visit as a reason for reduced vaccination coverage in the U.S. and other developed nations (77).

The New York State-based study that informed our schedule classifications found that approximately one quarter of children born in the state between 2009 and 2011 followed an alternate schedule, roughly similar to the proportion we observed in our study (92). However, that study only classified approximately 5% of participants as following an unknown schedule, while our analysis estimated a proportion that was nearly three times higher. One potential reason for this increase in other/unknown schedules is the increased number of vaccinations and time included for participants in our study: the New York State study only included vaccinations through 9 months of age (92). This study, assessing older children, expected at least two additional vaccination days for children who were following fully routine schedules, thus providing additional opportunities for deviation from known schedules.

We additionally observed associations between following other schedules and movement between, states, and lacking insurance at some point in a child's life. This may indicate that some other schedule followers were attempting to adhere to a routine schedule, but due to external circumstances, fell behind on the appointments required to maintain a routine schedule. Further research should be done to investigate these associations and provide support for future public health interventions that could support vaccine schedule adherence and, ultimately, higher levels of children who are up-to-date for immunizations.

Role of Sociodemographic Characteristics

One meaningful difference in the population of undervaccinated children illustrated in this study is the difference in the role poverty among different races and ethnicities. In this study, children above the poverty level were more likely to both follow routine schedules and be up-to-date than those below the poverty level, but these observed effects were diminished among Hispanic children. Moreover, Hispanic children living below the poverty level were roughly as likely to be up-to-date as any non-Hispanic child living above the poverty level. Our observations of the difference in schedule adherence among different racial and ethnic groups echo those found in other studies of HPV and early childhood vaccines wherein Hispanic groups are more likely to follow recommended schedules than other groups (45, 84, 96). These findings support an argument made by Kawachi that race and class should not be assessed independently of each other with regard to health disparities (44).

Overall, barriers facing historically disenfranchised groups have decreased in recent years, in part due to benefits from the Vaccines for Children program, from which low income Hispanic children experienced a greater increase in immunization coverage than any other group (5, 51, 97). In a study using 2008 NIS data with an added module investigating factors relating to socioeconomic status, there were no detected issues relating to parental employment that impacted vaccine coverage, although researchers had hypothesized that parents with strict work schedules would face access issues relating to timely vaccination (47). Health policies impacting vaccination coverage have a proven track record: states with Medicaid pay for performance programs have seemingly higher rates of routine schedule adherence, with higher up-to-date coverage rates as of 24 months, although overall up-to-date coverage for children up to 35 months is similar between states with and without pay for performance programs (91).

However, this study demonstrates that some disparities still persist. Decreasing levels of maternal education were associated with proportional decreases in the likelihood of full vaccination in this study, as were those who had ever received WIC benefits (although this was not a statistically significant finding). Our findings echo those from other NIS analyses, which also found associations between up-to-date status with maternal education, firstborn status, race/ethnicity, mobility, insurance status, and geographical region of residence (47, 96).

Recent analyses using vaccination dates have suggested that while overall coverage may be good at key time points in early childhood, many children may be subject to vaccine delay for periods of days or months, and that timely vaccination status may change many times throughout childhood (41, 82, 83). The differential distribution of late vaccine initiation between schedule types and up-to-date status we observed suggests that late vaccination may be an important flag for concern among health care providers of children at risk of not receiving early childhood vaccinations as recommended.

Strengths and Limitations

This study has several limitations. First, we are unable to examine the reasons behind vaccine schedule adherence and non-adherence, and so misclassification of the schedule variable is possible. For instance, vaccines may have given either early or late due to travel, illness, or limited vaccine availability, even if the parents were attempting to adhere to a routine schedule. Additionally, child ages at NIS ranged from 19-35 months, so older children had a longer period of time to become up-to-date; however, up-to-date status was similar among children over 19 months of age (Appendix A, Table 6). Finally, results of this study's up-to-date variable should not be directly compared to other literature, as many studies and reports using NIS data do not include rotavirus and Hepatitis A vaccines; we additionally considered sufficient timing between doses and minimum age at vaccination as described in Glanz et al.'s white paper on childhood vaccination in constructing our up-to-date variables (94). However, we feel that the inclusion of these vaccines is an asset to this study, as they provide more accurate measurement of up-to-date status and also more comprehensively demonstrate parental acceptance of and confidence in the recommended vaccine schedule. The steps we took to ensure appropriate age and spacing of vaccination, in addition to the use of provider-verified vaccination data only, limit misclassification of vaccination status and are a considerable strength of this study. The use of the NIS's geographic weighting allows us to provide a snapshot of early childhood vaccination which is generalizable to the total U.S.

Conclusion

While most children in the U.S. adhere to a routine schedule and are up-to-date for early childhood immunizations, coverage is differential among different racial and ethnic groups with regard to poverty status. Additional factors, such as maternal education, geographic mobility, insurance coverage, and late vaccine initiation are also associated with schedule type and up-to-date status. Schedule type is strongly associated with ultimate vaccine coverage status, and so future policies should focus on better identifying those at risk of following alternate or other schedules, and create interventions to ensure that routine schedules to ensure that ultimately greater numbers of U.S. children are up-to-date for all recommended immunizations.

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Tables

Table 1. Early childhood vaccine schedule classification.

Schedule Type		**Description**
Routine		Received all age appropriate vaccines as of 19 months of age on at least 4 separate occasions, with no more than 6 vaccine visits
Alternate		
	Restrictive only	Had at least 6 visits with ≤ 3 fewer vaccines at each visit
	Selective only	Omitted at least 1 vaccine (e.g., the child did not receive a single dose by 580 days of age)
	Restrictive and Selective	Did not receive > 3 age appropriate routine vaccines at each visit and omitted at least 1 vaccine
Other		Did not follow a routine or alternate schedule

Table 2. Classification structure for early childhood vaccination routine schedule type, at each vaccination time point. At least 4 of the 5 time points must be coded as routine for the participant to be considered as following a routine schedule overall.

Time Point	**Birth**	**2 Months**	**4 Months**	**6 Months**	**12-19 Months**
Age (days)	0-30	38-92	66-153	94-214	361-580
Days required since previous vaccination	__________________	__________________	24	24	__________________
Vaccines scheduled	Hepatitis B	DTaP Hib PCV Polio Rotavirus	DTaP Hib PCV Polio Rotavirus	Hepatitis B[a] DTaP Hib[b] PCV Polio[a] Rotavirus[b]	Hepatitis B[a] DTaP Hib[b] PCV Polio[a] MMR Varicella Hepatitis A
# Vaccines required to be routine	1	5	5	4 (Hep B, DTaP, PCV, Polio)	• ≥5 • 4 if 6 months is routine • ≥3 for visit 1 and ≥3 for visit 2 (if at least visit 1 or visit 2 is ≥ 4)
# Vaccination visits expected	1	1	1	1	1 or 2

a. Vaccine should be received between 94-580 days of age to be on time

b. Vaccine may not be needed, depending on brand.

Table 3. Bivariate proportions and multivariate predictors of vaccine schedule type, National Immunization Survey, 2014.

		Bivariate Analysis			Multivariate Analysis	
		Routine Schedule N (%)	Alternate Schedule N (%)	Other Schedule N (%)	Alternate vs Routine OR (95% CI)	Other vs Routine OR (95% CI)
	Overall (n = 14,893)	9,845 (62.8)	3,160 (22.7)	1,888 (14.5)	N/A	N/A
Race/Ethnicity*Poverty	Non-Hispanic white, above poverty (n = 7,151)	5,001 (69.0)	1,503 (21.3)	647 (9.7)	Referent	Referent
	Non-Hispanic white, below poverty (n = 1,259)	691 (52.7)	374 (31.6)	194 (15.6)	1.28 (0.85, 1.92)	**2.03 (1.25, 3.31)**
	Non-Hispanic black, above poverty (n = 682)	452 (65.6)	140 (20.5)	90 (14.0)	1.09 (0.76, 1.57)	1.23 (0.73, 2.05)
	Non-Hispanic black, below poverty (n = 638)	346 (48.8)	161 (30.2)	131 (20.9)	**2.04 (1.42, 2.93)**	**2.19 (1.41, 3.41)**
	Non-Hispanic multiple race/other, above poverty (n = 1,394)	936 (62.5)	272 (24.4)	186 (13.1)	1.30 (0.95, 1.77)	1.42 (0.97, 2.09)
	Non-Hispanic multiple race/other, below poverty (n = 549)	302 (52.6)	125 (25.5)	122 (21.8)	**1.50 (1.02, 2.21)**	**2.31 (1.45, 3.66)**
	Hispanic, above poverty (n = 1,397)	976 (71.7)	246 (16.4)	175 (11.9)	0.77 (0.57, 1.04)	0.97 (0.65, 1.46)
	Hispanic, below poverty (n = 1,331)	826 (55.4)	230 (20.7)	275 (23.9)	1.11 (0.77, 1.58)	**2.23 (1.50, 3.33)**
Maternal education	< 12 years (n = 1,630)	918 (57.2)	384 (24.5)	328 (18.4)	1.4 (1.0, 1.9)	1.0 (0.7, 1.50
	12 years (n = 2,660)	1,602 (57.8)	637 (24.0)	421 (18.2)	1.2 (0.9, 1.6)	1.2 (0.9, 1.7)
	> 12 years, non-college grad (n = 3,827)	2,466 (63.4)	817 (22.3)	544 (14.4)	1.1 (0.9, 1.4)	1.1 (0.8, 1.5)
	College graduate (n = 6,776)	4,859 (69.0)	1,322 (21.1)	595 (9.8)	Referent	Referent
Child ever received WIC benefits	Yes (n = 6,923)	4,247 (59.1)	1,467 (22.7)	1,209 (18.2)	0.87 (0.69, 1.10)	**1.38 (1.03, 1.84)**
	Not Yes[a] (n = 7,970)	5,598 (67.8)	1,693 (22.7)	679 (18.2)	Referent	Referent
Geographic mobility	Has moved across state lines since birth (n = 1,508)	816 (45.2)	445 (33.4)	247 (21.4)	**2.33 (1.76, 3.08)**	**2.48 (1.69, 3.63)**

		Bivariate Analysis			Multivariate Analysis	
		Routine Schedule	Alternate Schedule	Other Schedule	Alternate vs Routine	Other vs Routine
		N (%)	N (%)	N (%)	OR (95% CI)	OR (95% CI)
	Has not moved across state lines since birth (n = 13,385)	9,029 (64.7)	2,715 (21.5)	1,641 (13.7)	Referent	Referent
Child's rank in family	Firstborn (n = 9,295)	5,934 (60.9)	2,054 (23.6)	1,307 (15.4)	Referent	Referent
	Not Firstborn (n = 5,598)	3,911 (65.5)	1,106 (21.4)	581 (13.2)	**1.20 (1.02, 1.42)**	1.20 (0.95, 1.50)
Census region	South (n = 5,397)	3,649 (63.5)	1,037 (20.7)	711 (15.8)	Referent	Referent
	Northeast (n = 2,786)	1,765 (57.7)	709 (30.0)	312 (12.3)	**1.68 (1.39, 2.04)**	0.95 (0.73, 1.23)
	Midwest (n = 3,282)	2,214 (64.0)	675 (23.3)	393 (12.7)	1.06 (0.88, 1.29)	0.92 (0.72, 1.16)
	West (n = 3,428)	2,217 (63.8)	739 (20.7)	472 (15.5)	1.03 (0.80, 1.34)	0.99 (0.72, 1.36)
Vaccine provider facility type	All private facilities (n = 8,127)	5,653 (65.8)	1,573 (21.2)	901 (12.9)	Referent	Referent
	All hospital facilities (n = 2,235)	1,452 (59.2)	500 (26.6)	283 (14.3)	1.17 (0.95, 1.45)	1.05 (0.80, 1.39)
	All public/ military/ other/ unknown (n = 1,934)	1,097 (55.6)	460 (22.6)	377 (21.9)	1.12 (0.84, 1.48)	**1.51 (1.08, 2.12)**
	Mixed facility types (n = 2,450)	1,643 (64.4)	480 (21.5)	327 (14.1)	1.11 (0.82, 1.50)	0.85 (0.60, 1.21)
Number of vaccine providers	0 (n = 147)	0 (0.0)	147 (100.0)	0 (0.0)	N/A	
	1 (n = 11,775)	7,851 (63.1)	2,465 (22.6)	1,459 (14.3)	Referent	Referent
	2+ (n = 2,971)	1,994 (63.7)	548 (20.3)	429 (16.0)	0.79 (0.60, 1.03)	1.18 (0.85, 1.65)
Insurance						
Employer/Union plan	Yes (n = 8,321)	5,899 (67.7)	1,623 (21.3)	799 (11.0)	N/A	N/A
	Not Yes[a] (n = 6,376)	3,840 (58.5)	1,467 (23.6)	1,069 (17.9)	N/A	N/A
Medicaid/S-CHIP	Yes (n = 3,547)	2,187 (59.5)	738 (20.9)	622 (19.6)	N/A	N/A

		Bivariate Analysis			Multivariate Analysis	
		Routine Schedule	Alternate Schedule	Other Schedule	Alternate vs Routine	Other vs Routine
		N (%)	N (%)	N (%)	OR (95% CI)	OR (95% CI)
	Not Yes[a] (n = 5,328)	3,760 (69.9)	971 (19.6)	487 (10.6)	N/A	N/A
Indian Health Service Military Health Care, Tricare, Champus, or Champ-VA	Yes (n = 876)	561 (60.8)	199 (22.1)	116 (13.8)	N/A	N/A
	Not Yes[a] (n = 13,737)	9,158 (63.1)	2,894 (22.5)	1,685 (14.5)	N/A	N/A
Other insurance	Yes (n = 991)	676 (64.1)	199 (22.1)	116 (13.8)	N/A	N/A
	Not Yes[a] (n = 13,658)	9,036 (62.9)	2,881 (22.5)	1,741 (14.6)	N/A	N/A
Any time no insurance?	Yes (n = 1,044)	578 (53.4)	300 (32.8)	166 (13.8)	N/A	N/A
	Not Yes[a] (n = 13,107)	8,893 (64.7)	2,589 (20.8)	1,625 (14.6)	N/A	N/A
Late initiation of vaccination on at least 1 time point	Yes (n = 3,706)	862 (21.0)	1,456 (40.2)	1,388 (38.8)	N/A	N/A
	No (n = 11,187)	8,983 (79.1)	1,704 (15.9)	500 (5.0)	N/A	N/A

a. Not yes includes no, don’t know, and refused to answer responses.

Table 4. Bivariate proportions and multivariate predictors of vaccination status, National Immunization Survey, 2014.

		Not Up-to-Date[b]	**Multivariate Regression**
		N (%)	OR (95% CI)
	Overall (n = 14,893)	6,054 (41.7)	
Schedule Type	Routine (n = 9,845)	2,240 (21.6)	Referent
	Alternate (n = 3,160)	2,875 (90.4)	**32.68 (24.97, 42.77)**
	Restrictive Only (n = 486)	201 (39.4)	N/A
	Selective Only (n = 2,158)	2,158 (100.0)	N/A
	Selective and Restrictive (n = 516)	516 (100.0)	N/A
	Other (n = 1,888)	939 (52.4)	**3.86 (3.11, 4.78)**
Race/Ethnicity*Poverty	Non-Hispanic white, above poverty (n = 7,151)	2,785 (39.6)	Referent
	Non-Hispanic white, below poverty (n = 1,259)	660 (54.2)	1.11 (0.75, 1.64)
	Non-Hispanic black, above poverty (n = 682)	284 (40.2)	0.86 (0.60, 1.21)
	Non-Hispanic black, below poverty (n = 638)	306 (50.9)	0.82 (0.57, 1.17)
	Non-Hispanic multiple race/other, above poverty (n = 1,394)	520 (39.6)	0.80 (0.58, 1.11)
	Non-Hispanic multiple race/other, below poverty (n = 549)	258 (53.3)	1.13 (0.78, 1.64)
	Hispanic, above poverty (n = 1,397)	517 (32.0)	**0.63 (0.47, 0.84)**
	Hispanic, below poverty (n = 1,331)	531 (41.0)	**0.63 (0.45, 0.88)**
Maternal education	< 12 years (n = 1,630)	770 (46.8)	**1.47 (1.07, 2.01)**
	12 years (n = 2,660)	1,207 (45.3)	**1.36 (1.04, 1.78)**
	> 12 years, non-college grad (n = 3,827)	1,644 (42.8)	**1.32 (1.04, 1.67)**
	College graduate (n = 6,776)	2,433 (34.6)	Referent
Child ever received WIC benefits	Yes (n = 6,923)	3,057 (44.5)	1.208 (0.97, 1.51)

		Not Up-to-Date[b] N (%)	Multivariate Regression OR (95% CI)
	Not Yes[a] (n = 7,970)	2,997 (37.9)	Referent
Geographic mobility	Has moved across state lines since birth (n = 1,508)	747 (52.4)	N/A
	Has not moved across state lines since birth (n = 13,385)	5,307 (40.5)	
Child's rank in family	Firstborn (n = 9,295)	2,056 (38.9)	N/A
	Not Firstborn (n = 5,598)	3,998 (43.6)	
Census region	South (n = 5,397)	2,205 (42.7)	N/A
	Northeast (n = 2,786)	1,087 (41.8)	
	Midwest (n = 3,282)	1,333 (42.4)	
	West (n = 3,428)	1,429 (39.6)	
Vaccine provider facility type	All private facilities (n = 8,127)	3,111 (40.0)	N/A
	All hospital facilities (n = 2,235)	925 (44.4)	
	All public/military/other/unknown (n = 1,934)	905 (46.4)	
	Mixed facility types (n = 2,450)	966 (38.6)	
Number of vaccine providers	0 (n = 147)	147 (100.0)	N/A
	1 (n = 11,775)	4,759 (42.2)	
	2+ (n = 2,971)	1,148 (37.5)	
Insurance			N/A
Employer/Union plan	Yes (n = 8,321)	3,043 (38.0)	
	Not Yes[a] (n = 6,376)	2,909 (44.9)	

		Not Up-to-Date[b]	Multivariate Regression
		N (%)	OR (95% CI)
Medicaid/S-CHIP	Yes (n = 3,547)	1,576 (43.8)	
	Not Yes[a] (n = 5,328)	1,912 (37.6)	
Indian Health Service Military Health Care, Tricare, Champus, or Champ-VA	Yes (n = 876)	386 (42.7)	
	Not Yes[a] (n = 13,737)	5,547 (41.5)	
Other insurance	Yes (n = 991)	389 (46.0)	
	Not Yes[a] (n = 13,658)	5,542 (41.3)	
Any time no insurance?	Yes (n = 1,044)	519 (49.9)	
	Not Yes[a] (n = 13,107)	5,095 (39.7)	
Late initiation of vaccination on at least 1 time point	Yes (n = 3,706)	2,385 (65.8)	N/A
	No (n = 11,187)	3,669 (32.3)	

a. Not yes includes no, don't know, and refused to answer responses.

b. Children who are up-to-date have received the following doses: ≥ 4 diptheria, tetanus, and acellular pertussis vaccine; ≥ 3 poliovirus vaccine; ≥ 1 measles-containing vaccine; ≥ 3 *Haemophilus influenzae* type B; ≥ 1 Hepatitis A vaccine (≥ 2 for children over 24 months of age); ≥ 3 Hepatitis B vaccine; ≥ 1 varicella-containing vaccine; ≥ 4 pneumoccocal conjugate vaccine; ≥ 2 rotavirus vaccine.

Table 5. Average number of vaccination visits and vaccinations per visit among 2014 National Immunization Survey participants following routine, alternate, and other schedules, stratified by up-to-date status.

		Up-to-Date[a]				Not Up-to-Date			
		N	%	Average # visits	Average # vaccines per visit	N	%	Average # visits	Average # vaccines per visit
	Overall (n = 14,893)	8,839	58.3	7.36	3.47	6,054	41.7	5.99	3.46
Schedule Type	Routine (n = 9,845)	7,605	78.4	7.25	3.51	2,240	21.6	6.49	3.71
	Alternate (n = 3,160)	285	9.6	10.27	2.50	2,875	90.4	5.66	3.11
	Restrictive Only (n = 486)	285	60.6	10.27	2.50	201	39.4	9.04	2.67
	Selective Only (n = 2,158)	0	0.0	-------------	-------------	2,158	100.0	4.51	3.37
	Selective and Restrictive (n = 516)	0	0.0	-------------	-------------	516	100.0	8.87	2.36
	Other (n = 1,888)	949	47.6	7.25	3.50	939	52.4	5.96	3.91

a. Children who are up-to-date have received the following doses: ≥ 4 diptheria, tetanus, and acellular pertussis vaccine; ≥ 3 poliovirus vaccine; ≥ 1 measles-containing vaccine; ≥ 3 *Haemophilus influenzae* type B; ≥ 1 Hepatitis A vaccine (≥ 2 for children over 24 months of age); ≥ 3 Hepatitis B vaccine; ≥ 1 varicella-containing vaccine; ≥ 4 pneumoccocal conjugate vaccine; ≥ 2 rotavirus vaccine.

Chapter III: Public Health Implications

This study supports the push for routine vaccination schedule adherence over alternate schedules as a means for ensuring that American children become up-to-date for vaccinations. Following an alternate schedule, either by limiting the number of shots per visit or by excluding a series of shots altogether, is an important predictor of not being up-to-date for early childhood vaccinations. The variation in sociodemographic factors observed among followers of alternate and other schedules, and children's up-to-date status, may be helpful in preparing interventions to target children and families who might have a difficult time accessing complete vaccination. For instance, the high prevalence of non-routine schedule adherence and not being up-to-date among children who had moved across state lines, had received WIC benefits, and had ever been uninsured indicates that work should be done to ease the transfer of public health benefits as they move to a new home and change providers.

The final models in this study does not account for the contribution of insurance status and Vaccines for Children (VFC) eligibility in ensuring that children follow routine vaccination schedules, or are up-to-date. As the cost of vaccination should be covered by insurance and VFC, both may be meaningfully associated with vaccination status; research should be done to establish this assumed association empirically. The effects of both insurance and VFC have important implications within the realm of vaccine-related public policy, and their impact on schedule adherence and up-to-date status should be investigated.

This analysis assumed that routine schedule adherence would be a product of both vaccine access and confidence. However, due to the data available, we were not able to measure vaccine confidence and its impact on schedule type directly. Similarly, the variable measuring late vaccination was not included in the models in this study, although late vaccination was observed to be differential between individuals adhering to different schedule types and up-to-date status. It is possible, for instance, that high levels of late vaccination among children following other schedules may be a result more of access (rather than confidence) issues among children attempting to follow routine schedules. This should be potential association should be investigated directly. There may be nuanced differences between children following alternate or other schedules, and initiating vaccination late, as a result of parental confidence issues, as opposed to access issues. Additional analyses which measure both schedule type and parent confidence would help to tease apart these nuances and provide clearer direction for interventions aimed at increasing schedule adherence and overall vaccine coverage.

Appendix A

Table 6. Up-to-date vaccination status by child's age group, National Immunization Survey, 2014.

		Up-to-Date[a]		Not Up-to-Date	
		N	%	N	%
	Overall (n = 14,893)	8,839	58.3	6,084	41.7
Age of child	19 - 23 months (n = 4,407)	2,780	62.4	1,627	37.6
	24 - 29 months (n = 4,495)	2,430	53.8	2,065	46.2
	30-35 months (n = 5,991)	3,629	59.0	2,362	41.0

a. Children who are up-to-date have received the following doses: ≥ 4 diptheria, tetanus, and acellular pertussis vaccine; ≥ 3 poliovirus vaccine; ≥ 1 measles-containing vaccine; ≥ 3 *Haemophilus influenzae* type B; ≥ 1 Hepatitis A vaccine (≥ 2 for children over 24 months of age); ≥ 3 Hepatitis B vaccine; ≥ 1 varicella-containing vaccine; ≥ 4 pneumoccocal conjugate vaccine; ≥ 2 rotavirus vaccine.

Appendix B

EMORY UNIVERSITY | Institutional Review Board

July 26, 2016
Paula Frew, PhD MA MPH
School of Medicine
Infectious Diseases

RE: **Determination: No IRB Review Required eIRB#: IRB00090542**
Title: ***Transforming Vaccine Hesitancy into Confidence: Research to Address Parents' Vaccine Decision-Making and Inform Development of Novel Immunization Communication/ Education Strategies***
PI: Frew

Dear Dr. Frew:

Thank you for requesting a determination from our office about the above-referenced project. Based on our review of the materials you provided, we have determined that it does not require IRB review because it does not meet the definition of "research" with human subjects or "clinical investigation" as set forth in Emory policies and procedures and federal rules, if applicable. Specifically, in this project, you will collaborate with the National Vaccine Program Office under Goal 3 of the National Vaccine Plan. This project was designed to improve the health of Americans by better understanding the decision-making processes surrounding vaccines and vaccine programs. The goal is to improve current and future vaccine/immunization programs using data collected under this project.

Please note that this determination does not mean that you cannot publish the results. This determination could be affected by substantive changes in the study design, subject populations, or identifiability of data. If the project changes in any substantive way, please contact our office for clarification.

Thank you for consulting the IRB.

Sincerely,

Sam Roberts, CIP
Research Protocol Analyst, Sr.

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