


# Identifying Parents Who Are Amenable to Pro-Vaccination Conversations

Global Pediatric Health  
Volume 2: 1–7  
© The Author(s) 2015  
DOI: 10.1177/2333794X15616332  
gph.sagepub.com  


Emily K. Brunson, MPH, PhD<sup>1</sup>

## Abstract

While health care providers are often cited as parents' most trusted source for information and advice about vaccination, parents differ in their level of receptiveness to pro-vaccination conversations. The purpose of this research was to identify points in individual parents' decision-making processes when parents are particularly open to receiving information and advice from their children's health care providers. Interview data were collected from 20 mothers and 5 couples. Analysis of these data suggested 3 primary circumstances when parents were particularly open to receiving information and advice: during parents' initial decision-making, as parents continued to assess vaccination options, and during particular circumstances that prompted parents to reconsider previously made vaccination choices. These results provide a mechanism for providers to identify parents who may be particularly receptive to pro-vaccination conversations. By prioritizing conversations with parents at one of these points, health care providers' efforts at promoting vaccination may be more effective.

## Keywords

immunization, communication, decision-making, general pediatrics, vaccination

## Introduction

Research on a wide variety of pro-vaccination interventions has provided mixed results. While some interventions appear to improve parents' knowledge and intent to vaccinate,<sup>1–9</sup> others do not.<sup>3,4,7,8,10–14</sup> Possible reasons for this differential success are the content of the intervention materials or the modes in which the interventions are delivered. While these 2 reasons are well explored in the literature, another possibility exists—timing—and specifically when in parents' decision-making processes interventions are administered.

Three previous studies on this subject have suggested that the timing of interventions does,<sup>15</sup> does not,<sup>16</sup> and may<sup>17</sup> influence an intervention's effectiveness. However, all of these studies made the critical assumption that the timing of parents' vaccination decision-making is homogenous, in other words that all parents are at the same decision-making stage before their pregnancies, during their pregnancies, and following their children's births. This assumption is incorrect. Other research has shown that when parents assess vaccination and make their vaccination decisions varies.<sup>18,19</sup>

The purpose of this article is not to add to this literature by examining the timing of parents' vaccination

decision-making generally. Instead it is meant to provide a means for clinicians and others to identify points in individual parents' decision-making processes when those parents are particularly open to receiving information and advice.

This is an important issue for clinicians to consider. Previous research has shown that once opinions are formed, attempts to change those opinions are generally ineffective and that they may even backfire by causing subjects to become more entrenched in their beliefs.<sup>20–24</sup> In relation to clinicians, this implies that pro-vaccination discussions with parents who have already made their vaccination choices and are not currently considering changing them may have little effect. If, however, clinicians can identify parents who are still making their vaccination decisions or who are in the process of reconsidering previous vaccination choices, pro-vaccination discussions may have more influence.

<sup>1</sup>Texas State University, San Marcos, TX, USA

## Corresponding Author:

Emily K. Brunson, Department of Anthropology, Texas State University, 601 University Dr, San Marcos, TX 78666, USA.  
Email: ebrunson@txstate.edu



## Methods

This qualitative study was conducted in the context of a larger grounded theory project about how parents make decisions about their children's vaccinations. The research took place in King County, Washington, a large, diverse county in western Washington State, historically known for lower than average vaccination rates.<sup>25</sup> All protocols of this study were approved by the University of Washington institutional review board.

Data reported in this article were collected through a combination of unstructured and semistructured interviews with parents. An interview guide was developed by the author based on a review of the literature and preliminary discussions with health care providers, parents, and other anthropologists. As the study progressed, questions in the guide were modified to clarify research questions, to include research topics identified in previous interviews, and to reflect the overarching goals of the larger project. Topics covered in the interviews that are of particular relevance to the data reported in this article included the processes parents went through to make their vaccination decisions, the factors that influenced those decisions, and, when applicable, how parents' decisions had changed over time and why these changes occurred.

Participation in the interviews was limited to US-born parents who had at least one child who was 18 months of age or younger. These inclusion criteria were chosen to ensure a comparable sample with regard to parents' cultural backgrounds and the ages of at least some of their children. Data collection continued until theoretical saturation was reached with regard to the larger grounded theory project.

Parents were recruited to participate in interviews through a variety of convenience methods, including flyers hung in local parks and community centers, emails sent to parenting listservs, and short presentations made to community groups. To ensure that a diverse sample was recruited, with regard to both parents' demographic characteristics and their vaccination decisions, targeted recruitment was conducted around King County. When more low-income and nonvaccinating parents were needed for the study, for example, recruitment efforts were intensified in areas where large proportions of low-income parents lived and areas where school data indicated that vaccine exemptions were particularly common.

Interviews were conducted in parents' homes or public venues, such as libraries and coffee shops, and lasted between 30 minutes and 2 hours. The author, an anthropologist, conducted every interview, which were also recorded and later transcribed verbatim. At the end of each interview, participants received \$20 as an incentive for their time.

Analysis of the interview data for this study proceeded in an inductive manner following the tenants of thematic analysis. After reading and rereading all the transcripts to ensure familiarity with the data, the author developed an initial code list by reviewing 5 randomly chosen transcripts and identifying data related to points in parents' decision-making when parents were either in the process of making their vaccination choices or reconsidering choices they had already made. This process resulted in an initial codebook that was used to begin thematic coding. As each subsequent interview was coded, the existing coding was reevaluated and, in an iterative fashion, new codes were created and existing codes were refined to reflect the emerging analysis. Codes were also organized into themes during this process. Once all interviews were evaluated in this manner, a final codebook inclusive of all codes and their corresponding themes was constructed. The author subsequently used this final codebook to reevaluate every interview. This process provided the author an opportunity to check that the coding, including the resulting themes, was an accurate representation of the interview data.

## Results

Interviews were conducted with 20 mothers and 5 couples. These parents were diverse with regard to their demographic characteristics and vaccination decisions (Table 1).

Analysis of the interview texts suggests that study parents' vaccination decisions could be influenced at 3 primary points: when parents were initially making vaccination decisions for their first child, when parents had not made set or final decisions and were actively in the process of assessing their options, and during particular events in children's lives when circumstances were influencing parents to reconsider previously made vaccination choices.

### *Initial Decision-Making*

All parents in this study described a decision-making process that occurred around the time of their first child's birth. The timing of this decision-making varied considerably among the parents, however. Some made their vaccination decisions years before they were married and became pregnant, others decided during their first pregnancy, and the rest made their decisions after the births of their first children.

How parents' decision-making took place varied as well. As described in an earlier article using a subset of the data used here,<sup>18</sup> some parents simply accepted social norms, others considered vaccination by relying on those

**Table 1.** Demographic Characteristics of Parents.

Parents' demographic characteristics <sup>a</sup> (n = 25)	
Age range (in years)	18-40 (28 median)
Percent first time parents	48
Percent white	80
Highest level of education (%)	
Less than high school	4
High school	8
Some college	20
At least a bachelor's degree	68
Household income (%)	
<\$25 000	16
\$25 000 to \$49 999	24
\$50 000 to \$74 999	16
\$75 000 to \$99 999	16
>\$100 000	28
Children's demographic characteristics	
Age range (in months)	1-18 (7 median)
Percent male	44
Vaccination status (%)	
Completely vaccinated	36
Partly vaccinated	40
Completely unvaccinated	24
Type of health insurance (%)	
Private	64
Medicare/Medicaid	24
No insurance	12

<sup>a</sup>When couples were interviewed, only data from the parent self-selected to be the parent most responsible for making the vaccination decisions is included in this table.

around them for information and advice, and the remainder actively investigated vaccination-related issues on their own by seeking information from government websites, books, and even the primary literature.

In spite of these differences, parents typically described this initial decision-making process as formative, and for many parents it represented the termination of their decision-making, as one mother explained:

When I was in my [Master of Public Health] program I became aware of the controversies [surrounding vaccination]. It caused me to become pretty informed and strongly opinionated that vaccinating kids on schedule was the right thing to do. I haven't looked back from that.

This sentiment was echoed by several parents with multiple children who explained that they did not reconsider their vaccination choices with the births of their subsequent children, as another mother with 4 children described: "I just did what I did before [with my older children]. I didn't have to figure it out again."

## Ongoing Assessment

Not all parents in this study, however, ended their decision-making when they made their initial vaccination decisions. Some parents continued to assess issues related to vaccination and to make decisions about what (if any) vaccines to receive and when to receive them for months or years after the births of their first children, and in some cases after the births of subsequent children as well, as one mother with 3 children described:

Some of the decisions we haven't fully made yet. Umm, let's say we would lean toward yes for most, but no to things like chicken pox and flu unless we gather information over the next months or years to change our mind about that.

At the same time, the particular aspects of parents' choices that were under consideration varied considerably. Some parents were concerned about specific vaccines, others had questions about vaccination generally, some were concerned about additives like thimerosal or aluminum, and others about the number of vaccines given at one time. Having health care providers who listened and provided direction that applied to parents' specific concerns was important, as another mother explained:

[The doctor] sent us home with information trying to debunk the myth of linking autism with vaccination, but that wasn't my worry at all. It made me mad. I guess the doctor thought "Oh they must be concerned about autism, she must just be scared," but that wasn't it at all.

Ultimately this mother decided to change health care providers because she felt this doctor was unable or unwilling to listen to her specific concerns.

## Particular Windows of Opportunity

*Away From Complete, On-Time Vaccination.* Some parents also described particular circumstances that made them reconsider their decisions both for and against vaccination. For parents transitioning from complete, on-time vaccination, they described changes in perception that arose internally; changes in perception that were prompted by outside forces like friends, family, and the Internet; and circumstances that were not related to vaccination intent, but that had a direct impact on parents' vaccination-related behavior.

The 3 internal changes in perception described by parents in this study all related to changes in parents' perceptions of risk. Some parents described their children becoming ill, unrelated to vaccination, as a reason

they reconsidered, and in some cases changed their vaccination behavior. One mother who was completely vaccinating before her infant son contracted RSV described her situation thus:

Even if it doesn't make sense because he's perfectly healthy now, I view him as a little bit more fragile because of that experience. . . . He was just so sick that it made me think that maybe his immune system wasn't super strong and that we needed to be a little more cautious with him.

Due to this perception of her child being "fragile" the mother had begun delaying her son's vaccinations and particularly vaccinations for diseases she felt he was unlikely to contract.

Similar sentiments were found among parents whose children had bad reactions, either real or perceived, to vaccines, as another mother described: "So when he got his [hib] shot he had a pretty significant localized reaction to the vaccination. And that freaked me out . . . so we had to revisit the whole vaccinating according to the schedule thing."

Finally, while other parents did not perceive their children were either fragile or had been harmed by vaccines, changes to the vaccination schedule that occurred in between the births of 2 or more of their children caused them to question the vaccination policy. In some cases this questioning led parents to change their vaccination choices, as another mother whose 2 oldest children were completely vaccinated on time but her youngest was now being partially vaccinated on a delayed schedule described:

It seems like every time I have a child and they go to the doctor's office "Oh they can get 5 today! And they can get 6!" And I guess I just reached the third child and I finally started looking into it. I started getting concerned about the volume, just the number of shots babies were getting at very young ages.

Like changes in perception that arose internally, changes in perception that arose through outside sources also involved changes to study parents' perceptions of risk. Multiple parents noted that once they became aware of others' concerns or others' decisions and the reasoning behind them, this caused them to reevaluate their own vaccination choices, as one mother described:

I was talking to my friend in Canada. She had a baby 2 weeks later than mine. Apparently they have a different schedule. The vaccines are given much later. And then I learned that in Europe it's even later and their babies aren't dying. So I started to realize maybe there was another agenda to having babies vaccinated so soon in the US and then I started hearing about babies getting sick and the link to autism.

Additionally, through interactions with others as well as information provided by sources like magazines, books, and the Internet, other parents came to realize that options other than vaccinating completely and on time existed. While their vaccination decisions up until that time had been based entirely on existing pro-vaccination social norms, knowledge of other options changed some parents' perceptions of vaccination, as another mother explained: "So when I started to realize that I could delay them, I just kinda . . . took it easy and decided to do that."

Not all changes to children's vaccination outcomes, however, were related to changes in parents' concerns. Financial events like unemployment led some parents to question their ability to obtain vaccination for their children. As one mother described: "My husband has been worried about getting laid off, and it has actually been one of our biggest worries, how we'll finish her vaccines. If he gets laid off I'm not sure what we'll do." While programs exist in many areas to help parents in situations like this, some parents are unaware of them and as a result their children can become un- or undervaccinated.

*Toward Complete, On-Time Vaccination.* Circumstances that caused study parents to transition to complete, on-time vaccination, or at least more complete vaccination than before, also related to parents' perceptions of risk. In relation to this, travel to foreign countries, children becoming older and thus more robust, having a child enter child care or school, and having a disease outbreak in a local community were all factors that parents suggested would lead them to reconsider decisions to not vaccinate completely and/or on time, as 4 different parents described: "There aren't any vaccines we would get for him, unless we go to a Third World country, which we might. Then we would need to protect him against anything specific to that area." "I'll revisit it with him when he gets older . . . his body will be bigger, his immune system will be stronger then." "If I was thinking about putting her in daycare . . . there's more [disease] exposure there . . . that might bump me into the vaccinating category," and "No one in [local community] is immunized for chicken pox. If an outbreak happens I'll get him the vaccine but for right now I'm going to wait until he's older for that one." While each of these parents was, at the time of their interviews, set in their decisions to not completely vaccinate or vaccinate on time, in other words they were not in the process of ongoing assessment, they acknowledged that the particular circumstances described above would prompt them to reassess their vaccinating behavior in the future.

Changes to the risks for others was also something that some study parents suggested could sway their



vaccination decisions. While some parents cited herd immunity as a factor in their decision-making, the specific circumstance of having a new baby was the impetus that caused some parents to change their vaccination decisions for their older children, as one mother explained:

[Older brother] was a premie, and so we knew there was a really good chance [infant] would be born prematurely too. So it occurred to us, wait a sec, we probably want the older boys, who are in school now, and at Sunday school and other things, vaccinated from the things they could actually be exposed to so they don't bring them home to the baby.

## Discussion

Vaccine uptake is a critical public health concern in the United States today. Growing numbers of parents across the country are opting to delay vaccination, partially vaccinate, or completely forgo vaccination for their children.<sup>26-30</sup> While a variety of responses to this phenomenon exist, research has repeatedly shown that health care providers, and particularly pediatricians, are an important resource for maintaining and improving vaccination rates.<sup>31-33</sup> By discussing vaccination and related issues with parents, health care providers have the ability to influence parents' vaccination decision-making and ultimately their vaccination choices.

To efficiently engage with parents and their myriad concerns, however, health care providers must be able to tailor their discussions to account for parents' specific hesitancies and life circumstances as well as the timing of parents' vaccination decision-making. To aid in these efforts, this research identified 3 primary circumstances when parents are particularly open to receiving information and advice from their children's health care providers: during parents' initial decision-making, as parents are continuing to assess vaccination options, and at particular points in time when circumstances are influencing parents to reconsider previously made vaccination choices.

As previously described, the initial decision-making process that takes place in relation to the births of first children was formative for many parents in this study. Once their initial vaccination decisions were made, many parents stuck with those decisions even through the births of subsequent children. For this reason, health care providers' influence is likely to be especially strong with first-time parents of very young children. Thus, health care providers should prioritize their pro-vaccination interactions with first-time parents either during their pregnancies, as the providers are interviewed by prospective parents for example, or in the office visits

that occur shortly after first children's births. If everything is equal, for example, this finding suggests that a health care provider's time would be better spent discussing vaccination with a first-time parent of a newborn than a parent of a 12-month-old or a parent with 2 or more children.

While many parents in this study made decisions and then stuck with them, some parents continued to assess vaccination for months or even years after the births of their children. In relation to the broader literature, this finding suggests that health care providers may be able to influence parents experiencing this ongoing assessment, but to do so they must engage parents to determine their specific concerns and questions.

Finally, this research suggests that there are particular events that may cause parents to reconsider previously made decisions. In broader discussions with delaying, partially vaccinating, or nonvaccinating parents, health care providers should pay particular attention to plans for international travel; children becoming older, for example, transitioning from infants to toddlers or toddlers to children; children entering child care or school; and subsequent births in the family, and discuss vaccination related to these issues accordingly. Health care providers should also make these parents aware of any local disease outbreaks and discuss how vaccination can offer protection to their children as well as the wider community.

In their interactions with vaccinating parents, health care providers should also be aware of children becoming ill unrelated to vaccination, children having real or perceived reactions to vaccines, and to family financial troubles as these may cause changes to children's vaccination outcomes. This research also suggests that health care providers should be aware of parents' concerns about changes to the vaccination schedule and new knowledge about alternative schedules and/or the possibility of nonvaccination so that they can provide relevant assurances and information, including information about other resources, to these parents.

The findings of this research should be interpreted in light of a few limitations. Qualitative research is inherently ungeneralizable. As such, the results of this study may not be representative of parents in King County or parents nationally. Likewise, limiting the study to US-born parents means that the experiences of immigrant groups are not represented in this research. Finally, because of the qualitative nature of the research, including the small sample size, it is possible that some points of intervention were not identified in this study. Future research, including a national survey, would go far in addressing these limitations and in expanding the understanding of what intervention points exist and how common they are in different areas of the country.

## Conclusion

As previous research has suggested, influencing parents' vaccination choices is a complex endeavor. There is no one-size-fits-all approach with regard to content, mode of delivery, or timing. As such, health care providers must be willing and able to tailor their pro-vaccination conversations to the needs of individual parents. This can be an overwhelming process, particularly for very busy clinicians who have numerous commitments and time constraints. To aid in health care providers' efforts to promote vaccine uptake, this research has identified points in individual parents' vaccination decision-making processes when parents are particularly open to receiving information and advice. By prioritizing conversations with parents at one of these points, health care providers' efforts at promoting vaccination may become more effective.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was supported by the James Fellowship, Department of Anthropology, University of Washington.

## References

- Klein NP, Kissner J, Aguirre, et al. Differential maternal responses to a newly developed vaccine information pamphlet. *Vaccine*. 2009;28:323-328.
- Cox DS, Cox AD, Sturm L, Zimet G. Behavioral interventions to increase HOV vaccination acceptability among mothers of young girls. *Health Psychol*. 2010;29:29-39.
- Gillespie L, Hicks CW, Santana M, et al. The acceptability of human papillomavirus vaccine among parents and guardians of newborn to 10-year-old children. *J Pediatr Adolesc Gynecol*. 2011;24:66-70.
- Kepka D, Coronado GD, Rodriguez HP, Thompson B. Evaluation of a radionovela to promote HPV vaccine awareness and knowledge among Hispanic parents. *J Community Health*. 2011;36:957-965.
- Lachuga J, Swain GR, Weinhardt LS. Impact of framing on intentions to vaccinate daughters against HPV: a cross-sectional perspective. *Ann Behav Med*. 2011;42:221-226.
- Sales JM, Painter JE, Pazol K, et al. Rural parents' vaccination-related attitudes and intention to vaccinate middle and high school children against influenza following educational influenza vaccination intervention. *Hum Vaccine*. 2011;7:1146-1152.
- Cates JR, Ortiz R, Shafer A, Romocki LS, Coyne-Beasley T. Designing messages to motivate parents to get their preteenage sons vaccinated against human papillomavirus. *Perspect Sex Reprod Health*. 2012;44:39-47.
- Williams SE, Rothman RL, Offit PA, Schaffnew W, Sullivan M, Edwards KM. A randomized trial to increase acceptance of childhood vaccines by vaccine-hesitant parents: a pilot study. *Acad Pediatr*. 2013;13:475-480.
- Shourie S, Jackson C, Cheater FM, et al. A cluster randomized controlled trial of a web based decision aid to support parents' decisions about their child's Measles Mumps and Rubella (MMR) vaccination. *Vaccine*. 2013;31:6003-6010.
- Kennedy A, Glasser J, Covello V, Gust D. Development of vaccine risk communication messages using risk comparisons and mathematical modeling. *J Health Commun*. 2008;13:793-807.
- Gust DA, Kennedy A, Weber D, Evans G, Kong Y, Salmon D. Parents questioning immunization: evaluation of an intervention. *Am J Health Behav*. 2009;33:287-298.
- Fahy A, Desmond DM. Irish mothers' intentions to have daughters receive the HPV vaccine. *Ir J Med Sci*. 2010;279:427-430.
- Jackson C, Cheater FM, Harrison W, et al. Randomised cluster trial to support informed parental decision-making for the MMR vaccine. *BMC Public Health*. 2011;11:475.
- Kennedy A, Sapsis KF, Stokley S, Curtis CR, Gust D. Parental attitudes toward human papillomavirus vaccination: evaluation of an educational intervention, 2008. *J Health Commun*. 2011;16:300-313.
- Le Menach A, Boxall N, Amirthalingam G, Maddock L, Balasegaram S, Mindlin M. Increased measles-mumps-rubella (MMR) vaccine uptake in the context of a targeted immunization campaign during a measles outbreak in a vaccine-reluctant community in England. *Vaccine*. 2014;32:1147-1152.
- Vannice KS, Salmon DA, Shui I, et al. Attitudes and beliefs of parents concerned about the timing of vaccines: impact of timing of immunization information. *Pediatrics*. 2011;127 (suppl 1):S120-S126.
- Saitoh A, Nagata S, Saitoh A, et al. Perinatal immunization information improves immunization rates and knowledge: a randomized controlled trial. *Prev Med*. 2013;56:398-405.
- Brunson EK. How parents make decisions about their children's vaccinations. *Vaccine*. 2013;31:5466-5470.
- Glanz JM, Wagner NM, Narwaney KJ, et al. A mixed methods study of parental vaccine decision making and parent-provider trust. *Acad Pediatr*. 2013;13:481-488.
- Nyhan B, Reifler J. When corrections fail: the persistence of political misperceptions. *Polit Behav*. 2010;32:303-330.
- Nyhan B, Reifler J. Misinformation and fact-checking: research findings from social science (New America Foundation Media Policy Initiative Research paper). [http://www.dartmouth.edu/~nyhan/Misinformation\\_and\\_Fact-checking.pdf](http://www.dartmouth.edu/~nyhan/Misinformation_and_Fact-checking.pdf). Published February 2012. Accessed June 1, 2015.
- Lewandowsky S, Ecker UKH, Seifert CM, Schwarz N, Cook J. Misinformation and its correction: continued

- influence and successful debiasing. *Psychol Sci Public Interest*. 2012;13:106-131.
23. Nyhan B, Reifler J, Richey S, Freed GL. Effective messages in vaccine promotion: a randomized trial. *Pediatrics*. 2014;133:e835-e842.
  24. Nyhan B, Reifler J. Does correcting myths about the flu vaccine work? An experimental evaluation of the effects of corrective information. *Vaccine*. 2015;33:459-464.
  25. Smith PH, Singleton JA. County-level trends in vaccination coverage among children aged 19-35 months, United States, 1995-2008. *MMWR Surveill Summ*. 2011;60(4):1-86.
  26. Omer SB, Enger KS, Moulton LH, Halsey NA, Stokley S, Salmon DA. Geographic clustering of nonmedical exemptions to school immunization requirements and associations with geographical clustering of pertussis. *Am J Epidemiol*. 2008;168:1389-1396.
  27. Parker FA, Redd SB, Gallagher K, et al. Measles in the United States during the postelimination era. *J Infect Dis*. 2010;202:1520-1528.
  28. Omer SB, Richards JL, Ward M, Bednarczyk RA. Vaccination policies and rates of exemption from immunization. *N Engl J Med*. 2012;367:1170-1171.
  29. Richards JL, Wagenaar BH, Otterloo JV, et al. Nonmedical exemptions to immunization requirements in California: a 16-year longitudinal analysis of trends and associated community factors. *Vaccine*. 2013;31:3009-3013.
  30. Elam-Evans LD, Yankey D, Singleton JA, Kolasa M. National, state, and selected local area vaccination coverage among children aged 19-35 months—United States, 2013. *MMWR Morb Mortal Wkly Rep*. 2014;63(34):741-748.
  31. Smith PJ, Kennedy AM, Wooten K, Gust DA, Pickering LK. Association between health care providers' influence on parents who have concerns about vaccine safety and vaccination coverage. *Pediatrics*. 2006;118:1287-1292.
  32. Freed GL, Clark SJ, Butchart AT, Singer DC, Davis MM. Sources and perceived credibility of vaccine-safety information for parents. *Pediatrics*. 2011;127(suppl 1):S107-S112.
  33. Gust DA, Darling N, Kennedy A, Schwartz B. Parents with doubts about vaccines: which vaccines and reasons why. *Pediatrics*. 2008;122:718-725.