

Attitudes toward Rubella and Varicella Vaccination during Preconception Care

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ABSTRACT

Introduction. Studies of anti-vaccine attitudes in the perinatal time period previously have not paid special attention to the MMR and varicella vaccines. Because both contain live attenuated virus, a contraindication during pregnancy, it is important to assess barriers to vaccination clinically during preconception to avoid the known fetal morbidity associated with congenital rubella or varicella infection.

Methods. The primary outcome of this study was to determine prevalence of patients with nonimmune status for rubella and varicella in the setting of advanced reproductive care. Secondary outcomes of interest included further understanding nonimmune reproductive-aged women's attitudes toward MMR and varicella vaccination during preconception. Patient records with laboratory orders for rubella or varicella immunoglobulin titers, placed at the KU Advanced Reproductive Care clinic between January 2017 and June 2020, were reviewed (n = 2,217). A cross-sectional survey was administered to patients with a laboratory reported negative titer result.

Results. Prevalence of nonimmunity to either rubella or varicella represented 6.0% (n = 134) and 3.8% (n = 85) of records, respectively; nineteen records (0.6%) demonstrated nonimmunity to both. The women who did not receive recommended vaccines following a non-immune titer result (n = 19) most commonly cited their rationale was to not delay fertility treatment further (n = 8), a requirement when receiving live attenuated virus vaccines.

Conclusions. The prevalence of nonimmune persons in the study population fell within the range recognized to be sufficient for herd immunity. The majority of survey respondents indicated that CDC recommended vaccinations were of high personal importance, with strong congruence of thought among those who answered in favor of vaccines when posed with several true or false statements about personal beliefs and vaccine efficacy. The risk/benefit analysis of postponing fertility treatment to achieve adequate levels of immunity should be a focused discussion when establishing fertility treatment goals with patients in the setting of advanced reproductive care.

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INTRODUCTION

Many components of prenatal care are endorsed by the literature of several physician organizations, one of which is routine screening for communicable disease.¹⁻⁴ The recommended tests for communicable disease screening are to be performed at the initial prenatal care

visit and include documentation of immunity to rubella and varicella, serum tests for human immunodeficiency virus, syphilis, hepatitis B virus (HBV), and endocervix or vaginal swab for chlamydia. Hepatitis C virus (HCV) historically has been included as a selective testing option and remains as such according to guidelines from Society for Maternal-Fetal Medicine; however, the U.S. Centers for Disease Control and Prevention (CDC) recently revised its position and now suggests all pregnant women be screened for HCV except where prevalence of infection is less than 0.01%.^{5,6} Importantly, screening is conducted because non-immune pregnant women and their fetuses who are exposed to these diseases experience higher morbidity than nonpregnant women.⁷

Of this panel, three diseases are preventable by vaccine: rubella, varicella, and HBV. An in-depth review of literature revealed that while there were several studies specifically regarding anti-influenza vaccine attitudes in women of childbearing age and pregnant women, measles, mumps, and rubella (MMR) and varicella largely have been ignored.^{8,9} Both MMR and varicella vaccines contain live virus, thus are contraindicated during pregnancy, so the window of opportunity requires anticipating pregnancy, if at all possible, through preconception counseling.¹⁰ Recommendations for non-immune pregnant women are to avoid exposure until postpartum, when live vaccines are no longer contraindicated. With increasing rates of nonimmunity due to anti-vaccine attitudes,¹¹ primarily held by parents for their young children, avoiding exposure may be a challenge in geographic locations where population disease burden is high.

As defined by The American Society of Reproductive Medicine, "The goal of prepregnancy care is to reduce the risk of adverse health effects for the woman, fetus, and neonate by working with the woman to... address modifiable risk factors".⁴ Control of existing health conditions, limiting teratogen exposure, nutritional status, and treating or preventing infections are a few examples of risk factors that are considered modifiable, thus should be discussed during preconception counseling.

Preconception counseling around vaccines within the setting of an infertility clinic is a unique, understudied population. Since the timing of conception theoretically is controlled with treatment, providers have the opportunity to prevent the morbidity known to be associated with exposure to rubella and varicella. The primary outcome of this study was to assess the prevalence of nonimmunity within the patient population seeking fertility assistance. Secondary outcomes of interest included further understanding non-immune, reproductive aged women's attitudes toward MMR and varicella vaccination during the preconception timeline and assess how these attitudes may impact fertility treatment goals.

METHODS

A cross-sectional survey was performed to assess prevalence of fertility clinic patients who were non-immune to rubella and varicella. The population of interest was identified through a report of all patients with a venipuncture order placed at the University of Kansas Center for Advanced Reproductive Medicine between January 2017 and June 2020 and was narrowed by laboratory draw orders that included rubella and varicella antibody titers. Using the electronic medical record, the

titer data were collected for the patients previously identified to have a laboratory order for rubella and varicella titer. The laboratory-reported qualitative value for each titer was used to determine each patient's status: immune, equivalent, or non-immune. To meet inclusion criteria, patients had to have a laboratory-reported qualitative value of non-immune for either rubella or varicella serology titers.

Patients within the equivalency range for IgG were considered to have positive immunity since the University of Kansas Center for Advanced Reproductive Care did not recommend further vaccinating patients within the equivalency range routinely; therefore, they would not have been advised to receive a vaccine and would not meet inclusion criteria for this study. Patients with unknown titer results for both rubella and varicella were excluded from analysis.

The survey was comprised of 27 questions and took an estimated 10 minutes to complete. Questions were posed in a variety of formats, including true/false, prepared answer multiple choice, and optional free-text response fields. Survey respondents supplied basic demographic information (gender, ethnicity, race, education, age, and annual household income as a function of federal poverty limits) followed by answering 15 questions about self-reported general attitudes toward vaccines, self-reported incidence of follow-up, recency of vaccine counseling, and knowledge of CDC vaccination recommendations.

In 2017, Reavis et al.¹² conducted a cross-sectional survey assessing parental attitudes toward MMR vaccination for children under 18, using a 5-point Likert scale to measure average support for or denial of statements regarding the vaccine. Similarly, conclusions in this study were drawn by making the assumption that personal affirmation of a statement is a surrogate marker for belief in effectiveness of the vaccine but hold no statistical significance. Respondents' attitudes toward the protective effects of vaccination were analyzed further by relationship to the respondent. This was measured using the following questions, with the relationship association in parentheses: personal feelings about the importance of receiving the influenza vaccine during pregnancy (Flu-self/fetus), plans to follow CDC recommended vaccination schedules for their children (CDC-children), and belief in the ability of the varicella vaccine to protect others who are immunocompromised (Varicella-others).

True knowledge regarding the vaccines of interest was measured by percent correctly answered questions based upon CDC "what everyone should know" criteria for the MMR and chickenpox (varicella) vaccines.^{13,14} This percentage was compared to self-reported confidence in knowledge of each vaccine, rated as a sliding scale between 0 and 100. In an attempt to control for the influence of recency bias on true knowledge, respondents were asked to provide the time frame in which they were last counseled on the MMR or varicella vaccines.

Study data were collected and managed using REDCap[®] electronic data capture tools hosted at University of Kansas Health System. Patients received an explanatory email with an informed consent form and a self-administered survey. In an attempt to maximize the response rate, reminder emails were sent twice after which the study team made one phone call per non-respondent.

Data were summarized using frequencies and percentages for categorical data and mean and standard deviations for continuous data.

Basic descriptive statistics were calculated for demographic data, and all quantitative variables regarding vaccine beliefs, history, and knowledge. Answers from open-ended questions were grouped into common themes, with consideration for similarity and pervasiveness, and analyzed qualitatively. This study was approved by the Human Subjects Committee at the University of Kansas School of Medicine.

RESULTS

A total of 2,217 records were identified to have lab orders for rubella and varicella titers with 89.3% (n = 1,979) of patients' demonstrating immunity to both. Non-immune status to rubella and varicella represented 6.0% (n = 134) and 3.8% (n = 85) of records, respectively. Non-immune status to both rubella and varicella was nominal (0.6%, n = 19) and had no underlying factors identified that would delineate this group from the larger study population.

There was a small discrepancy between the number of non-immune patients (n = 238) and number of surveys administered (n = 244). Surveys were administered to 238 non-immune patients with a valid/current email address or phone number on file. Some non-immune patients were identified by providers on the same day as their lab titer resulted and subsequently were administered a survey without being included in the REDCap[®] report totals. In addition, a select few patients represented two survey invitations since they provided a valid email address after the initial survey link was sent. There were 73 completed surveys, making the response rate per all administered surveys equal to 29.9%.

Self-reported demographics are shown in Figure 1 and Table 1. The minimum and maximum participant ages were 21 and 43 years, respectively, and the average age was 31.8 years. Eight of the 73 survey respondents did not provide age data.

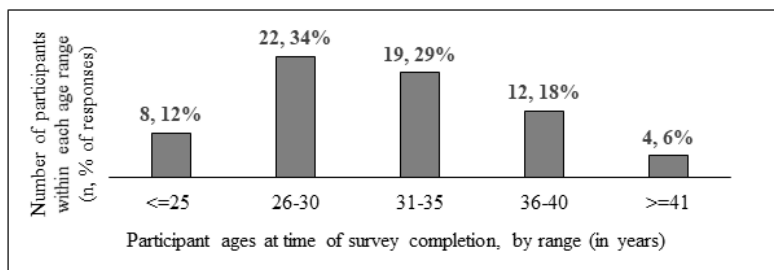


Figure 1. Survey participant age in years at time of survey completion. Ages are presented by number that fell within each age range, and the percentage each range represents of all respondents who provided a value for this metric (n = 65).

Table 1. Survey participant demographics including race, ethnicity, highest level of education, and annual income by household (n = 73).

Race	Number of responses n (% of total)
White	62 (84.9%)
Black or African American	6 (8.2%)
Asian	3 (4.1%)
More than one	2 (2.7%)
Ethnicity	
Hispanic or Latino	3 (4.1%)
Not Hispanic or Latino	70 (95.9%)
Highest level of education	
High school or equivalent	4 (5.5%)
Post-secondary non-degree award	2 (2.7%)
Some college, no degree	7 (9.6%)
Associate degree	7 (9.6%)
Bachelor's degree	26 (35.6%)
Master's degree	22 (30.1%)
Doctoral or professional degree	5 (6.8%)
Annual income by household	
< \$16,910	1 (1.4%)
\$16,911 - \$33,820	3 (4.1%)
\$33,821 - \$50,730	5 (6.8%)
\$50,731 - \$67,640	9 (12.3%)
\$67,641 - \$84,550	6 (8.2%)
\$84,551 - \$101,460	16 (21.9%)
\$101,461 - \$118,370	5 (6.8%)
> \$118,370	28 (38.4%)

Of respondents, 73.6% elected to receive recommended vaccines (n = 54). The highest selected rationale as to why they elected to receive the recommended vaccinations was that “It was recommended by my provider” (n = 50). Several respondents also selected, “I understand the potential severity of rubella and/or varicella symptoms” (n = 35).

The desire not to postpone attempts to conceive was the most selected option among the 19 participants that opted not to receive the recommended vaccines (n = 8, Table 2). “Other” open-ended rationale included the following comments: “I’ve just been lazy. I need to do it”, “I was not offered vaccine”, “I was immune”, “Already pregnant when notified of titer results...would have gotten vaccination and delayed attempts to conceive”.

Participants’ answers to questions regarding vaccine attitudes, as they related to CDC-children and Varicella-others, indicated that they placed an overall high importance on recommended vaccinations. Sixty-seven (91.7%) of respondents anticipated following CDC guidelines for childhood vaccines for current and future children and acknowledged the statement, “Healthy people who get vaccinated against varicella

can protect immunocompromised people from being exposed to the disease” as true. Participants were less likely to recognize the protective effects of vaccines in relationship to Flu-self/fetus, with 56 (76.7%) indicating that they personally felt it was important to receive the flu vaccine during pregnancy. Respondents provided rationale as to why the flu vaccine was not important during pregnancy included, “never received flu vaccine prior in life” and “rarely effective at predicting what viruses to protect against in upcoming flu season”.

Table 2. Participant prepared multiple choice survey results regarding why they did or did not elect to receive the recommended vaccines, and the timeframe in which they last spoke with their health care provider about these vaccines.

From the following list, please select any that align with why you elected to receive the MMR (measles, mumps, rubella) and/or varicella (chickenpox) vaccines upon a negative immunity titer. (N = 54)	Number of responses n (% of total)
It was recommended by my provider	50 (92.6%)
Personal or religious beliefs	10 (18.5%)
I understand the potential severity of rubella and/or varicella symptoms	35 (64.8%)
Other	4 (7.4%)
Of the following, please select all that may be true as to why you did not elect to receive the MMR (measles, mumps, rubella) and/or varicella (chickenpox) vaccines. (N = 19)	Number of responses n (% of total)
I did not wish to postpone my attempts to conceive	8 (42.1%)
Personal or religious beliefs	-
I have already received the vaccination series once and did not want to proceed with receiving a second series	6 (31.6%)
I have already received the vaccination series twice and did not continue with a third series upon the recommendation from my provider	3 (15.8%)
Effectiveness has not been proven	-
These diseases have been eradicated	-
Preference for natural way of living	-
Fear of needles	-
Fear of adverse reactions	-
Too many vaccines given at once can compromise the immune system	-
Other	6 (31.6%)
Select the time frame in which you last recall speaking with a health care provider about either the MMR (measles, mumps, rubella) or varicella (chickenpox) vaccines. (N = 73)	Number of responses n (% of total)
< 6 months	34 (46.6%)
6 months - 1 year	17 (23.3%)
> 1 year	13 (17.8%)
I do not recall	9 (12.3%)

The time frame in which women reported they last spoke with their providers about MMR or varicella vaccines was evaluated in six-month intervals. Most survey participants reported having discussed the vaccines with their providers within the previous six months (n = 34, Table 2).

The study population's average self-reported confidence in knowledge of MMR and varicella CDC recommendations was 66.0% and 61.0%, while their calculated true knowledge of CDC recommendations for specific populations, scheduling, and effectiveness of MMR and varicella vaccines were 72.7% and 79.0%, respectively.

To analyze differences between thought and action, self-reported follow-up immunizations for rubella and/or varicella were compared with the vaccine attitudes (Flu-self/fetus, CDC-children, Varicella-others). Forty-four of the 54 women who elected to receive the necessary vaccine(s) after a negative titer result affirmed protective effects for Flu-self/fetus. Seven of the 19 women who did not elect to receive the necessary vaccine(s) after a negative titer result denied protective effects for Flu-self/fetus.

Higher rates of concordant thought were observed in those who acknowledged some protective effects compared to those who denied some or all of the above-mentioned questions. Fifty-four women affirmed protective effects for all Flu-self/fetus, CDC-children, and Varicella-others (96.4%, total n = 56), compared to five women who denied protective effects for both Flu-self/fetus and Varicella-others (29.4%, total n = 17), two of which also denied protective effects for CDC-children.

By percent, calculated true knowledge of vaccines was generally greater than self-reported confidence. Since participants were more likely to have discussed vaccines with their provider within the past six months to one year, recency may have influenced retention of knowledge about each vaccine (Table 2). All participants demonstrated a fairly high level of understanding regarding the vaccine specific CDC recommendations, with an average of 79% correct for varicella recommendations and 72.5% for MMR recommendations. Further analysis demonstrated that there was no difference in true knowledge or self-reported confidence between the individuals who were or were not open to further education regarding MMR and varicella vaccines (Table 3).

Table 3. Survey participant self-reported confidence in knowledge of MMR and varicella vaccines, broken down by openness to receiving further education on the topic.

	Indicated openness to further vaccine education	Average self-reported confidence in knowledge of CDC recommendations	Average answer accuracy regarding vaccine specific CDC recommendations
MMR	Yes, n = 52	66.4%	73.0%
	No, n = 21	66.2%	72.0%
Varicella	Yes, n = 52	61.3%	79.0%
	No, n = 21	61.0%	79.0%

DISCUSSION

At 6.0% prevalence of non-immunity to rubella, the study population was well within the 15% non-immune population threshold value accepted by the World Health Organization (WHO) to be protected

by herd immunity.¹⁵ Plans-Rubió¹⁶ suggested that the rubella R₀ requires a threshold of 83 - 94% prevalence of protected individuals to achieve herd immunity, notably much higher than that recognized by the WHO. The same analysis found that the varicella R₀ requires 86 - 91% prevalence of protected individuals for herd immunity. Based on these suggested thresholds, the 3.8% prevalence of non-immunity to varicella found in this study population is protected by herd immunity. Non-immunity rate within the study population would theoretically have decreased even further if the 73.6% (n = 54) survey respondents who reported receiving the recommended vaccines achieved adequate immunity; however, record of receiving the vaccine was not requested nor were any subsequent titers reviewed.

Those who did not continue to receive the recommended vaccinations most commonly cited their rationale as “not wishing to delay treatment”. The American Society for Reproductive Medicine and the American College of Obstetricians and Gynecologists committee opinions uphold that pregnancy is contraindicated for four weeks after vaccination with a live attenuated virus.^{17,18} In contrast, Keller-Stanislowski et al.¹⁹ conducted a review over the risks of disease compared to the risk of vaccinating during pregnancy and determined that the wait time prior to conception following MMR is “purely precautionary”. Further research regarding the necessity of a wait period prior to conception may be valuable for managing expectations in women who would forgo vaccination in this scenario.

Survey respondent demographics were not depictive of all women who seek preconception care. The study population was remarkable for being highly educated, wealthy, and non-Hispanic Whites. Fujimoto et al.²⁰ conducted a retrospective cohort study across several assisted reproduction technology (ART) centers and reported demographic findings similar to this study population in regard to age, racial, and ethnic distributions. This comparison supported external validity within the setting of ART, while validity to other preconception/prenatal care settings remains unknown without comparison to demographic data, although unlikely.

One respondent stated that they were a healthcare worker and required to have immunity to these diseases. The results of the study could have been clearer if occupation demographic data were collected to isolate for healthcare workers, a population expected to have increased knowledge about vaccines compared to the general public. Without controlling for this variable, it was possible that this data set represented a higher-than-average true knowledge, as well as higher confidence, than the general population. Level of education was collected but not quantified, therefore cannot be correlated with confidence. Some responses could be quantified, but to do so would compromise the validity of any positive or negative correlation.

CONCLUSIONS

The purpose of this study was to determine the prevalence of non-immunity within the patient population at the University of Kansas Center for Advanced Reproductive Medicine. Rubella and varicella

immunity titer results showed that this population falls well within the parameters recognized to be protected by herd immunity. Upon receipt of a non-immune titer result, most study participants continued to receive the recommended vaccination. The number of participants with negative and mixed attitudes of MMR, varicella, influenza, and general childhood vaccines was lower than the number who held positive attitudes and recognized the beneficial effects of vaccines. Additionally, many patients expressed they would feel open to further vaccine education from their provider. In light of the increased literature demonstrating maternal anti-vaccine attitudes, these results are reassuring for providers who wish to initiate such conversations with their patients.^{8,11,14}

Additional retrospective analyses need to be performed that evaluate the necessity of a 28-day wait time until treatment, following the administration of a live attenuated virus vaccine. Based on the attitudes presented in the results of this survey, the risk/benefit analysis of postponing fertility treatment to achieve adequate levels of immunity should be a focused discussion when establishing fertility treatment goals with patients in the setting of ART clinics.

Potential areas for further investigation include comparing prevalence of non-immunity within this study population to local immunity rates via state vaccine records, and how the two compare demographically to determine generalizability. Other ideas to be explored could include analysis of data from generalist obstetrics and gynecology or primary care offices to evaluate the number of patients screened for preventable disease prior to conception as compared to the first prenatal visit, screening results, and surveys to assess the rate of follow-up if results show non-immunity.

REFERENCES

- ¹ No authors listed. ACOG Committee Opinion No. 741: Maternal immunization. *Obstet Gynecol* 2018; 131(6):e214-e217. PMID: 29794683.
- ² Coonrod DV, Jack BW, Boggess KA, et al. The clinical content of preconception care: Immunizations as part of preconception care. *Am J Obstet Gynecol* 2008; 199(6 Suppl 2):S290-s295. PMID: 19081423.
- ³ Zolotor AJ, Carlough MC. Update on prenatal care. *Am Fam Physician* 2014; 89(3):199-208. PMID: 24506122.
- ⁴ American Society for Reproductive Medicine, American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice. Prepregnancy counseling: Committee Opinion No. 762. *Fertil Steril* 2019; 111(1):32-42. PMID: 30611411.
- ⁵ Society for Maternal-Fetal Medicine, Hughes BL, Page CM, Kuller JA. Hepatitis C in pregnancy: Screening, treatment, and management. *Am J Obstet Gynecol* 2017; 217(5):B2-B12. PMID: 28782502.
- ⁶ Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC recommendations for hepatitis C screening among adults—United States, 2020. *MMWR Recomm Rep* 2020; 69(2):1-17. PMID: 32271723.
- ⁷ Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. *N Engl J Med* 2014; 370(23):2211-2218. PMID: 24897084.
- ⁸ Danchin MH, Costa-Pinto J, Attwell K, et al. Vaccine decision-making begins in pregnancy: Correlation between vaccine concerns, intentions and maternal vaccination with subsequent childhood vaccine uptake. *Vaccine* 2018; 36(44):6473-6479. PMID: 28811050.
- ⁹ Scheminske M, Henninger M, Irving SA, et al. The association between influenza vaccination and other preventative health behaviors in a cohort of pregnant women. *Health Educ Behav* 2015; 42(3):402-408. PMID: 25504630.

- ¹⁰ Marin M, Marlow M, Moore KL, Patel M. Recommendation of the Advisory Committee on Immunization Practices for use of a third dose of mumps virus-Containing vaccine in persons at increased risk for mumps during an outbreak. *MMWR Morb Mortal Wkly Rep* 2018; 67(1):33-38. PMID: 29324728.
- ¹¹ Hussain A, Ali S, Ahmed M, Hussain S. The anti-vaccination movement: A regression in modern medicine. *Cureus* 2018; 10(7):e2919. PMID: 30186724.
- ¹² Reavis RD, Ebbs JB, Onunkwo AK, Sage LM. A self-affirmation exercise does not improve intentions to vaccinate among parents with negative vaccine attitudes (and may decrease intentions to vaccinate). *PLoS One* 2017; 12(7):e0181368. PMID: 28704520.
- ¹³ U.S. Centers for Disease Control and Prevention. Measles, Mumps, and Rubella (MMR) Vaccination: What Everyone Should Know. January 26, 2021. <https://www.cdc.gov/vaccines/vpd/mmr/public/index.html>. Accessed March 2, 2021.
- ¹⁴ U.S. Centers for Disease Control and Prevention. Chickenpox Vaccination: What Everyone Should Know. August 7, 2019. <https://www.cdc.gov/vaccines/vpd/varicella/public/index.html>. Accessed March 2, 2021.
- ¹⁵ World Health Organization. Manual for the Laboratory-based Surveillance of Measles, Rubella, and Congenital Rubella Syndrome. Immunization, Vaccines and Biologicals. Third Edition. June 2018. https://www.who.int/immunization/monitoring_surveillance/burden/laboratory/manual/en/.
- ¹⁶ Plans-Rubió P. Evaluation of the establishment of herd immunity in the population by means of serological surveys and vaccination coverage. *Hum Vaccin Immunother* 2012; 8(2):184-188. PMID: 22426372.
- ¹⁷ American College of Obstetricians and Gynecologists. Management of pregnant and reproductive aged women during a measles outbreak. April 2019. <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2019/04/management-of-pregnant-and-reproductive-aged-women-during-a-measles-outbreak>. Accessed August 9, 2020.
- ¹⁸ Practice Committee of the American Society for Reproductive Medicine. Current recommendations for vaccines for female infertility patients: A committee opinion. *Fertil Steril* 2018; 110(5):838-841. PMID: 30316421.
- ¹⁹ Keller-Stanislawski B, Englund JA, Kang G, et al. Safety of immunization during pregnancy: A review of the evidence of selected inactivated and live attenuated vaccines. *Vaccine* 2014; 32(52):7057-7064. PMID: 25285883.
- ²⁰ Fujimoto VY, Luke B, Brown MB, et al. Racial and ethnic disparities in assisted reproductive technology outcomes in the United States. *Fertil Steril* 2010; 93(2):382-390. PMID: 19081561.

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