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A Retrospective Analysis of Gender-Based Difference in Adherence to Influenza Vaccination during the 2018-2019 Season

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Abstract

Introduction: Improving flu vaccination rates in the general population is an important and effective strategy toward reducing morbidity, mortality, and the cost of seasonal influenza. In order to optimize immunization strategies, factors associated with decreased vaccination rates need to be explored. The literature suggests that there is a gender difference in the rate of influenza vaccination but is limited to population-based survey studies and also is inconsistent as to which gender has a higher rate of vaccination. The purpose of this study was to evaluate for a gender-based difference in the rate of influenza vaccination among patients who presented for an annual physical examination during the 2018 to 2019 influenza season.
Methods: In this multi-site, retrospective chart review, a total of 1193 patients (608 female and 585 male) who underwent an annual physical examination in April of 2019 were included. Baseline medical information was collected, as well as demographic characteristics and influenza vaccination status. The proportion of patients who underwent influenza vaccination was compared between males and females using multivariable logistic regression models; odds ratios (ORs) were estimated.
Results: The likelihood of influenza vaccination was significantly higher in females (62.8%) compared to males (53.2%) in both unadjusted analysis (OR = 1.49, $P < .001$) and in multivariable analysis adjusting for the potential confounding influences of clinic location, BMI, insurance type, and occupation (OR = 1.42, $P = .005$). Interestingly, a higher influenza vaccination rate for females compared to males was observed in patients age < 60 years (OR = 1.70, $P = .025$) and between ages 60 and 75 (OR = 1.66, $P = .009$), but not for patients older than 75 years (OR = 1.12, $P = .66$).
Conclusion: Our findings indicate that the rate of influenza vaccination is higher for females than for males who presented for an annual preventive physical exam and who are younger than 75 years old.

Keywords

influenza vaccination, preventive health, gender difference, influenza

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Background

The Centers for Disease Control and Prevention (CDC) estimates influenza affects 9.3 to 45 million people, causes 140 000 to 810 000 hospitalizations, and 12 000 to 61 000 deaths annually in the US.[1] The influenza virus has a tremendous impact on society and its economy, not only associated with direct medical costs but also with substantial indirect losses due to decreased work productivity. Although estimates vary widely from year to year, it is estimated that the virus has a total annual economic burden on the US healthcare system of 6.3 to 25.3 billion dollars.[2]

The most effective strategy to reduce morbidity, mortality, and the socioeconomic burden associated with influenza is to improve overall flu vaccination rates among men and women, especially in the elderly and other high-risk

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groups.[3] Since 2010, the CDC's Advisory Committee on Immunization Practices (ACIP) has recommended annual influenza vaccination of all persons aged ≥6 months who do not have contraindications, with special focus on those who are at increased risk for severe illness or complications.[4]

The effectiveness of the flu vaccine to prevent disease varies from year to year, and depends on several individual factors such as age and comorbidities, and how closely the vaccine matches the circulating strains of the seasonal influenza virus.[3] While determining the effectiveness of the flu vaccine may be challenging, most studies support the concept that it benefits public health.[5] For example, it is estimated that during the six influenza seasons between 2010 and 2011 through 2015 to 2016, vaccination in the United States prevented 1.6 to 6.7 million illnesses, 790 000 to 3.1 million outpatient medical visits, 39 000 to 87 000 hospitalizations, and 3000 to 10 000 respiratory and circulatory deaths each year.[5]

In order to devise effective strategies to promote adherence to influenza vaccine recommendations, barriers against vaccination need to be understood. There is evidence in the literature that a gender discrepancy exists in influenza vaccination rates; however, findings are inconsistent regarding the specific gender.[6-8]

Previous research in the US has not been consistent regarding which gender predicts a higher rate of influenza vaccination, though results most often point to a higher rate in females which supports the findings of our study. In 2018, an analysis of the US population using data from the Behavioral Risk Factor Surveillence System indicated that female gender was associated with a higher likelihood of vaccination.[7] Data from the National Health Interview Survey published by the CDC showed a consistently higher rate of vaccination for females than males from 2000-2018 with an overall rate for females of 48.9% and 42.7% for males in 2018.[9] A 2008 study evaluating difference in utilization of preventive care services in the US found female gender to have a higher likelihood of influenza vaccination.[10] In contrast, a cross-sectional study of 48 424 individuals aged 65 and older enrolled in the Department of Veterans Affairs (VA) healthcare system eligible for immunization during the fiscal years 2001 to 2003, found that women had significantly lower odds of influenza immunization.[8]

Studies conducted in Europe also show inconsistency regarding which gender is more likely to undergo influenza vaccination. A French study of general practitioners published in 2013 found that male gender was a predictor of vaccination.[11] Endrich et al, collected data from national household surveys in eleven European countries during seven consecutive flu seasons (2001/2002 – 2007/2008) looking for associations between socioeconomic factors and immunization against influenza. They found that male gender was a positive predictor for influenza vaccination in France, Italy, the UK, Spain, the Czech Republic, Poland, and Portugal. However, this was not the case for Germany, Austria, Finland and Ireland.[12] Inconsistent results showing a gender difference in influenza vaccination rate both in the US and abroad likely point toward a significant sociocultural influence on gender-specific vaccination rates. A 2011 study from Norway found a positive association between the vaccination history of a co-resident/spouse and a person's likelihood of subsequent vaccination, further suggesting a strong sociocultural role toward vaccinate uptake behavior.[13]

The studies noted above were mainly based on surveys in the general population. Although these surveys are useful from a large-scale population health standpoint, the data may not be reflective of the population of patients who present for preventive health visits in primary care clinics across the country.

This study aimed to evaluate the presence of a gender-based difference in influenza vaccination rates in a population of patients who presented for an annual physical examination in the 2018 to 2019 influenza season.

Methods

Study subjects

This study was approved by the Institutional Review Board as # 19-000450. A total of 1193 consecutive patients (608 female and 585 male) were included in this retrospective study. The inclusion criteria were age ≥18 and undergoing a preventive primary care physical examination in April of 2019. Patients with a history of egg allergy, Guilian-Barre syndrome, or allergy to the influenza vaccine were excluded. Employees of our institution were also excluded as vaccination records are kept in the office of Employee and Occupational Health and were not available for our review. Data was abstracted retrospectively from medical charts by trained study staff. Information at the time of physical examination was collected regarding age, sex, race, ethnicity, clinic location, body mass index (BMI), type of insurance, Charlson comorbidity index, occupation, and influenza vaccination during the 2018 to 2019 influenza season.

Statistical analysis

Continuous variables were summarized with the sample median and range. Categorical variables were summarized with number and percentage of patients. Comparisons of characteristics between males and females were made using a Wilcoxon rank sum test (continuous variables) or Fisher's exact test (categorical variables). The proportion of patients who underwent influenza vaccination was compared between males and females using single-variable (i.e. unadjusted) and multivariable logistic regression models.

Table 1. Comparison of Patient Characteristics between Males and Females.

Variable	Female (N = 608)	Male (N = 585)	*P*-value
Age (years)	66.8 (19.3, 99.2)	66.3 (18.5, 101.5)	.17
Race			.59
White	550 (92.4%)	541 (94.3%)	
Black or African American	20 (3.4%)	13 (2.3%)	
Asian	13 (2.2%)	9 (1.6%)	
Other	12 (2.0%)	11 (1.9%)	
Ethnicity			.74
Not Hispanic or Latino	572 (96.6%)	553 (97.0%)	
Hispanic or Latino	20 (3.4%)	17 (3.0%)	
Clinic location			.20
Minnesota	315 (51.8%)	275 (47.0%)	
Florida	105 (17.3%)	103 (17.6%)	
Arizona	188 (30.9%)	207 (35.4%)	
BMI	26.7 (17.0, 56.6)	28.5 (18.2, 53.0)	<.001
Type of insurance			.010
Private	272 (44.7%)	309 (52.8%)	
Government	333 (54.8%)	271 (46.3%)	
Other	3 (0.5%)	5 (0.9%)	
Charlson Comorbidity Index Score	3.0 (0.0, 12.0)	3.0 (0.0, 17.0)	.93
Occupation			<.001
Healthcare-Nurse	8 (1.3%)	2 (0.3%)	
Healthcare-Physician	4 (0.7%)	5 (0.9%)	
Healthcare-Other	17 (2.8%)	6 (1.0%)	
Non-healthcare	173 (28.5%)	255 (43.7%)	
Retired	371 (61.1%)	307 (52.7%)	
Student or Unemployed	34 (5.6%)	8 (1.4%)	

The sample median (minimum, maximum) is given for continuous variables. *P*-values result from a Wilcoxon rank sum test (continuous variables) or Fisher's exact test (categorical variables). Information was unavailable regarding race (N = 24), ethnicity (N = 31), BMI (N = 1), and occupation (N = 3).

Multivariable models were adjusted by clinic location and also all characteristics that differed between males and females with a *P*-value <.05. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated. In secondary analysis, the aforementioned logistic regression analysis was also performed for the separate subgroups of patients of age <60 years, 60-75 years, and >75 years, where these age categories were defined by approximate sample tertiles. *P*-values less than .05 were considered as statistically significant and all statistical tests were two-sided. Statistical analyses were performed using SAS (version 9.4; SAS Institute, Inc., Cary, North Carolina).

Results

A comparison of patient characteristics between females and males is shown in Table 1. Compared to males, females had a significantly lower BMI (Median: 26.7 vs 28.5, *P* < .001). Type of insurance differed significantly between males and females (*P* = .010), where private insurance was less common in females (44.7% vs 52.8%). There was also a significant difference in occupation category between males and females (*P* < .001); a higher proportion of males had a non-healthcare occupation (43.7% vs 28.5%), whereas a higher proportion of females were retired (61.1% vs 52.7%). There were no other dramatic differences in patient characteristics between females and males (all *P* ≥ .17, Table 1).

The proportion of patients who underwent influenza vaccination is compared between females and males in Table 2. The likelihood of influenza vaccination was significantly higher in females (62.8%) compared to males (53.2%) in both unadjusted analysis (OR = 1.49, 95% CI: 1.18-1.88, *P* = .001) and in multivariable analysis adjusting for clinic location, BMI, type of insurance, and occupation (OR = 1.42, 95% CI: 1.11-1.82, *P* = .005). When performing age-stratified analysis, in multivariable analysis we observed a higher influenza vaccination rate for females compared to males for patients age <60 years (OR = 1.70, 95% CI: 1.07-2.69, *P* = .025) and between ages 60 and 75 (OR = 1.66, 95% CI: 1.14-2.44, *P* = .009), but not for patients older than 75 years (OR: 1.12, 95% CI: 0.68-1.84, *P* = .66).

Table 2. Comparison of Influenza Vaccination between Males and Females.

Patient group	No. (%) of patients who underwent influenza vaccination		Comparison of influenza vaccination between females and males (reference group)			
			Single-variable analysis		Multivariable analysis	
	Females	Males	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
All patients	382/608 (62.8%)	311/585 (53.2%)	1.49 (1.18, 1.88)	<.001	1.42 (1.11, 1.82)	.006
Age < 60 years	79/174 (45.4%)	62/178 (34.8%)	1.56 (1.01, 2.39)	.044	1.70 (1.07, 2.69)	.025
Age 60 to 75 years	182/264 (68.9%)	153/267 (57.3%)	1.66 (1.16, 2.36)	.006	1.66 (1.14, 2.44)	.009
Age > 75 years	121/170 (71.2%)	96/140 (68.6%)	1.16 (0.71, 1.88)	.56	1.12 (0.68, 1.84)	.66

Abbreviations: CI: confidence interval; OR: odds ratio.
ORs, 95% CIs, and *P*-values result from logistic regression models. ORs are interpreted as the multiplicative increase in the odds of influenza vaccination for females in comparison to males. Multivariable models were adjusted for clinic location, BMI, type of insurance, and occupation; occupation was not adjusted for in the age > 75 years subgroup due to the lack of variability in occupation in that patient group.

Discussion

Our multi-site, retrospective study found a higher rate of influenza vaccination in females compared with males aged ≤ 75 years of age. To our knowledge, this is the first US, multi-site study to evaluate for the existence of a gender gap in the rate of influenza vaccination in patients who present for an annual examination with a primary care physician.

The reasons for the gender difference in the rate of influenza vaccination are not clear. Overall, the male population in our study had a higher BMI, was more likely to carry private insurance, less likely to be retired, and less likely to work in a health-care related field. However, a multivariable analysis adjusting for these factors still found a higher rate of influenza vaccination in the female population. The literature describes several general barriers to vaccination but not one specifically associated with gender. These barriers include factors such as a perceived low risk of disease, concerns about safety of the vaccine, and perceived low utility of vaccination.[14] A qualitative study by the CDC using data collected from 2000 to 2013 found that overestimation of effectiveness of non-vaccine measures and limited understanding of vaccination recommendations were recurrent themes that represented additional barriers toward vaccination,[15] Furthermore, there are likely influences on vaccination rate between genders based on culture, age, and sex-based differences in biological response to vaccination.

Advancing age has been shown to be strongly associated with increasing influenza vaccine uptake.[15] CDC survey data shows that the gender difference toward influenza vaccination diminishes with age as the overall vaccine rate improves.[6] For example, early results from data published by the National Health Interview Survey for 2018 show a vaccination rate for females of 39.2% compared to 29.2% in males in the 18-49 age range group. In the ≥65 age group, females had a 70.0% vaccination rate compared to 67.2% for males.[9] Our results are similar and suggest that as patients age, health-conscious behavior increases for both genders, leading toward improved vaccination rates. By age 75, the gender difference in influenza vaccination was no longer apparent in our study population. This finding is likely a result of the overall high rate of influenza vaccination at age ≥ 75. It is likely that with age, males match females in motivation for health-promoting behaviors.

There are also sex-based differences in immune response to vaccination, which may impact vaccination rates. Females are reported to develop higher innate, humoral, and cellular immune responses to vaccines, be more prone to autoimmune diseases, and have a higher rate of adverse reactions to vaccination compared with males.[16] Despite the higher adverse reaction rate, females have a higher rate of vaccine uptake. A review of the differences in sex-based biology and influenza vaccination strategies published in 2014 proposed that vaccine design should be matched to an individual's biologic sex.[17] Our study suggests that approaches to enhance vaccination rates may need to be matched to an individual's gender in the age group ≤ 75. Focusing on enhancing vaccination strategies in the 19 to 64 age group has previously been recommended in the literature due to the lower overall vaccination rate in this population.[18]

The limitations of our study include its retrospective design, which introduces biases into the data collection. Additionally, unmeasured confounding variables that are unaccounted for (such as socioeconomic factors and psychiatric comorbidities) may have contributed to our findings. Further, selection bias is important to consider. BMI for both males (28.5) and females (27.0) found in this study was lower than the median BMI in the US of 29.1 reported by National Health and Nutrition Examination Survey (NHANES).[19] This is likely a reflection of a highly motivated, health-conscious group included in this study. It is also important to consider that this study included only patients with health insurance. Health insurance is associated with increased seasonal influenza vaccine uptake.[19]

This effect was observed with the addition of influenza vaccination coverage for Medicare recipients in 1993. There was a subsequent increase in the rate of influenza vaccine uptake among those age $\geq$ 65 from around 30% in 1988 to the current rate in Medicare recipients of 67.5%.[6,19] Furthermore, our study population included patients who presented for an annual preventive health visit, which likely selects a population sample with a higher degree of health-promoting behavior than the population that is captured with national surveys.

Conclusions

In a population of patients who presented for a preventive care annual examination there was a higher rate of influenza vaccination in females compared with males in the age group $\leq$ 75. Occupation, BMI, insurance type, and clinic location did not account for the observed difference in vaccination rate. Increasing age was associated with a higher overall influenza vaccination rate. These finding are important to consider when developing strategies within primary care clinics to enhance influenza vaccination rates. Further studies are needed to determine the reason for this gender difference toward influenza vaccination.

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Authors' contributions

AA contributed with manuscript preparation and data collection. FS contributed with manuscript preparation, protocol design, and data collection supervision. DH contributed with manuscript preparation. AM, JD, and JG contributed with data abstraction. MH contributed with statistical analysis, manuscript preparation, and protocol design. DEB contributed with statistical analysis and manuscript preparation. TS contributed with protocol design and study concept. JRV contributed with manuscript preparation, protocol design, and data collection supervision.

Declaration of Conflicting Interests

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References

1. Centers for Disease Control and Prevention NCfIaRD. Past seasons estimated influenza disease burden. https://www.cdc.gov/flu/about/burden/past-seasons.html. Published 2020. Accessed May 20, 2020.
2. Putri W, Muscatello DJ, Stockwell MS, Newall AT. Economic burden of seasonal influenza in the United States. *Vaccine*. 2018;36:3960-3966.
3. Nichol KL, Margolis KL, Wuorenma J, Von Sternberg T. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. *N Engl J Med*. 1994;331:778-784.
4. Fiore AE, Uyeki TM, Broder K, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Recomm Rep*. 2010;59:1-62.
5. Rolfes MA, Foppa IM, Garg S, et al. Annual estimates of the burden of seasonal influenza in the United States: a tool for strengthening influenza surveillance and preparedness. *Influenza Other Respir Viruses*. 2018;12:132-137.
6. Prevention. NCfHaSCfDCa.Table 68. Influenza vaccination among adults aged 18 and over by selected characteristics: United States, selected years 1989–2016. https://www.cdc.gov/nchs/data/hus/2017/068.pdf. Published 2017. Accessed May 21, 2020.
7. La EM, Trantham L, Kurosky SK, Odom D, Aris E, Hogea C. An analysis of factors associated with influenza, pneumoccocal, Tdap, and herpes zoster vaccine uptake in the US adult population and corresponding inter-state variability. *Hum Vaccin Immunother*. 2018;14:430-441.
8. Bean-Mayberry B, Yano EM, Mor MK, Bayliss NK, Xu X, Fine MJ. Does sex influence immunization status for influenza and pneumonia in older veterans? *J Am Geriatr Soc*. 2009;57:1427-1432.
9. NCHS NHIS, combined Sample Adult and Sample Child Core components. Figure 4.2. percentage of persons aged 6 months and over who received an influenza vaccination during the past 12 months, by age group and sex: United States, 2018. https://public.tableau.com/profile/nhis#!/vizhome/FIGURE4_2/Dashboard4_2. Accessed June 8, 2020.
10. Vaidya V, Partha G, Karmakar M. Gender differences in utilization of preventive care services in the United States. *J Womens Health (2002)*. 2012;21:140-145.
11. Pulcini C, Massin S, Launay O, Verger P. Factors associated with vaccination for hepatitis B, pertussis, seasonal and pandemic influenza among French general practitioners: a 2010 survey. *Vaccine*. 2013;31:3943-3949.
12. Endrich MM, Blank PR, Szucs TD. Influenza vaccination uptake and socioeconomic determinants in 11 European countries. *Vaccine*. 2009;27:4018-4024.
13. Mamelund SE, Riise Bergsaker MA. Vaccine history, gender and influenza vaccination in a household context. *Vaccine*. 2011;29:9441-9450.
14. Schmid P, Rauber D, Betsch C, Lidolt G, Denker ML. Barriers of Influenza Vaccination Intention and Behavior - A Systematic Review of Influenza Vaccine Hesitancy, 2005 - 2016. *PLoS One*. 2017;12:e0170550.

15. Yeung MP, Lam FL, Coker R. Factors associated with the uptake of seasonal influenza vaccination in adults: a systematic review. *J Public Health (Oxf)*. 2016;38:746-753.
16. Ruggieri A, Anticoli S, D'Ambrosio A, Giordani L, Viora M. The influence of sex and gender on immunity, infection and vaccination. *Ann Ist Super Sanita*. 2016;52:198-204.
17. Klein SL, Pekosz A. Sex-based biology and the rational design of influenza vaccination strategies. *J Infect Dis*. 2014; 209 Suppl 3:S114-119.
18. Nowak GJ, Cacciatore MA, Len-Rios ME. Understanding and increasing influenza vaccination acceptance: insights from a 2016 national survey of U.S. adults. *Int J Environ Res Public Health*. 2018;15:711.
19. (NCHS). CCNCfHS. National Health and Nutrition Examination Survey Data. *US Department of Health and Human Services, Centers for Disease Control and Prevention*. 2015-2016. https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Examination&CycleBeginYear=2015.