# Modeling the Incidence of Uterine Fibroids among Women in the US

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#### Abstract

Heavy menstrual bleeding (HMB) and poor uterine receptivity and implantation, which results in infertility, are two of the most prevalent benign neoplasms of the uterus that impact millions of women in the United States and around the world. The primary aim of this study is to model the incidence of uterine fibroids among women in the US. The secondary data collected for this study on possible factors associated with Uterine fibroid was extracted from the US department of health from the period of December 2018 to December 2022. The multivariate logistic regression model was adopted which indicates that the incidence of Uterine Fibroids is significantly associated with health risk factors and socioeconomic factors like family history, age, and adult women. Meanwhile, Vitamin D Deficiency has an odd ratio of about 2.4 which is higher than the other risk factors considered in the study. Consequently, American adults' women must monitor their lifestyle, have their BMI, Vitamin D deficiency, and other risk factors for uterine fibroids diagnosed, and then make sure they are receiving adequate treatment to prevent the tendency to develop uterine fibroids, which in turn will lower infertility due to the incidence uterine fibroids.

Keywords: Uterine Fibroids, Logistic regression, odd ratio, Health and socioeconomic risk factors.

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#### 1. Introduction

The most prevalent benign neoplasm of the uterus is uterine fibroids (uterine leiomyomata) (Stewart, 2015). Fibroids are virtually exclusively found in women of reproductive age and become more common with ageing up until menopause, at which point ultrasound imaging is frequently no longer able to identify them. Age, black race, nulliparity, length of time since previous childbirth, and premenopausal status are the key risk variables that have been consistently established (Wise & Laughlin-Tommaso, 2016; Stewart et al., 2017). Even though they are benign, symptomatic fibroids are linked to a significant amount of morbidity, such as irregular bleeding that can result in anaemia, transfusions, emergency surgery, pain or pressure on the pelvic and abdominal organs, bladder pressure, and poor reproductive outcomes. The only effective treatment option for symptomatic women is still a hysterectomy, and fibroids are by far the most common reason for this procedure (Laughlin et al., 2010). In addition to these, BMI, vitamin D insufficiency, alcohol consumption, and endogenous and exogenous hormonal variables are risk factors for uterine fibroids (Pavone et al., 2018; Ali et al., 2019; Bariani et al., 2020). Although uterine fibroids are very common, there are currently no authorized effective pharmacotherapies, and surgery is still the only treatment option (Bulun, 2013). Uterine fibroids account for more than one-third of hysterectomies in the United States (Bonafede et al., 2018). Currently, current pharmaceutical treatments have a risk of recurrence after withdrawal as well as negative effects (Segars et al., 2014). Up to 25% of all women and up to 30% to 40% of women in the perimenopausal age range may have symptomatic uterine fibroids.

Heavy menstrual bleeding (HMB) and poor uterine receptivity and implantation, both of which are significant female reproductive problems impacting millions of women in the United States and around the world, are brought on by uterine fibroids. The degree of dysfunction appears to be correlated with the size and location of the UFs, and both illnesses are characterized by endometrial dysfunctions brought on by the presence of uterine fibroids. Our knowledge of how uterine fibroids impact endometrial function is seriously lacking. It is generally accepted that uterine fibroids cause the endometrial surface area to increase, increasing menstrual bleeding and altering the structure of uterine cells, which in turn affects gene expression and function. However, new research has shown that uterine fibroids actively affect both the surrounding endometrial function, notably HMB, infertility, and pregnancy problems, we conducted a literature review to highlight new and relevant insights into endometrial and uterine fibroids biology.

However, because many fibroids are asymptomatic, prevalence estimates change according to the casefinding techniques used (McCool & Durain, 2014). Despite their significant influence on public health, associated healthcare costs, and effects on the lives of many women, accurate incidence data are still scarce (Wise & Laughlin-Tommaso, 2016). Even fewer estimates and analyses of secular patterns through time are based on the population. We undertook this work to model the prevalence of uterine fibroids among US women aged 18 to 65 to close this knowledge gap.

## 2. Literature review

This section shall examine the related literature works that is associated with uterine fibroids. This section is therefore summarized into two which includes the origin of Uterine Fibroids as well as the endometrial dysfunction caused by Uterine Fibroids: Heavy Menstrual Bleeding and Poor Receptivity and Implantation Leading to Infertility.

## **2.1 Origin of Uterine fibroids**

Uterine fibroids, also known as UFs, are a type of monoclonal tumor (Holdsworth-Carson et al., 2014), and there is growing evidence to suggest that they originate from a single myometrial stem cell (MMSC) (Mas et al., 2012; Yin et al., 2015). MMSCs make up a relatively insignificant component of the overall cell population and are distinguished from most other cells by the fact that they express surface markers (Mas et al., 2015). MMSCS can acquire mutations or engage in abnormal cellular reprogramming through epigenetic pathways due to their plasticity, which exists throughout both the creation of tissues and their maintenance. As a consequence of this, normal MMSCs have the potential to transform into tumour-initiating stem cells (TICs), which can kickstart the formation of UF. Somatic mutations present in exons 1 and 2 of the MED12 gene, which encodes a subunit of the mediator complex, a co-activator involved in the transcription of nearly all RNA polymerase II-dependent genes, are the most common genetic drivers associated with the development of UFs. This is because the MED12 gene encodes a subunit of the mediator complex (Makinen et al., 2011). A proportionally smaller fraction of Uterine Fibroids is thought to arise from genetic alterations leading to the overexpression of highmobility group AT-hook 2 (HMGA2, 20%) (Mehine et al., 2016), biallelic inactivation of fumarate hydratase (FH, 2%), and disruption of the COL4A6 locus (3%). This is in addition to MED12 mutations, which account for approximately 70 per cent of uterine fibroids.

# 2.2 Endometrial Dysfunction Caused by Uterine Fibroids: Heavy Menstrual Bleeding (HMB) and Poor Receptivity and Implantation Leading to Infertility

The development of non-invasive therapeutic methods has been constrained by the information gap that exists between uterine fibroids and HMB. The most frequent abnormal uterine bleeding in women with uterine fibroids is HMB, which frequently coexists with dysmenorrhea (ACOG Practice Bulletin, 2008; Zimmermann et al., 2012). HMB is the leading cause of hysterectomy and is associated with frequent trips to the ER (Côté et al., 2003). Additionally, women with UF-associated HMB are more likely to experience melancholy, emotional distress, anxiety, marital conflict, and decreased intellectual and professional productivity, all of which hurt their quality of life (Marsh et al., 2014). Angiogenesis, vasodilation, vasoconstriction, coagulation, and inflammation are a few of the many interrelated mechanisms that contribute to menstrual bleeding. Bulky submucosal and intramural UFs are thought to be the main culprits in affecting the myometrium's regular menstrual contractions. Myometrial contractions in normal menstrual cycles aid in the discharge of uterine menstrual products and lessen the loss of blood from endometrial arteries; however, in people with UFs, these contractions are aberrant, which causes severe and protracted menstrual bleeding (Bulun, 2013). The two main menstrual vasoconstrictors are prostaglandin F2 (PGF) and endothelin-1 (ET1). Myometrial contraction and mitogenesis are triggered by the potent vasoconstrictor ET1 (Maybin and Critchley, 2015). It is predominantly expressed in the endometrium, where it affects blood flow and spiral arteriole vasoconstriction. Endothelin type A receptor (ETAR) and endothelin type B receptor are the receptors that ET1 binds to function (ETBR). Contrary to normal endometrium, women with UFs exhibit higher endometrial expression of ETAR and reduced endometrial expression of ETBR. The imbalance in the expressions of ETAR and ETBR in women with UFs may affect ET1 signalling, resulting in incorrect vasoconstriction, aberrant uterine contractions, and excessive and extended menstrual blood flow. Everyone agrees that endometrial stromal venous spaces are more dilated in women with UFs and HMB than in those without UFs. One of the potential processes underlying HMB may be abnormal vasoconstriction (Farrer-Brown et al., 1971). Healthy endometrium expresses the vasoconstrictor PGF2 receptors, which regulate uterine contractions. Higher endometrial PGF2 levels in UF-affected women lead to aberrant uterine contractions that may exacerbate HMB (Pekonen et al., 1994; Miura et al., 2006).

# 3. Data and Methodology

### 3.1 Data

This study will adopt a quantitative survey research design with a secondary data on possible factors associated extracted fibroid department of health with Uterine which was from the US (https://www.health.ny.gov/community/adults/women/uterine\_fibroids/) from a period of December 2018 to December 2022 and was used for the analysis of the study. The period was determined based on the availability of the dataset.

# 3.2 Methodology

The method of data analysis employed for this study are summary statistics (percentage, mean and standard deviation) and multiple logistic regression model.

# **3.3 Model specification**

The model can specify functionally as:

Patient has a Uterine fibroid = f (Number of Adult women, Daily Alcohol consumption, Family history, BMI, Vitamin D deficiency, Age).

Multiple regression model will be employed because the dependent variable is a binary response (Yes = 1, No = 0) with more than one independent variable.

The multiple regression model adopted for this study can be adequately specified as:

Iny = Log (P/1-P) =  $\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \beta_5 x_5 + \beta_6 x_6 + U$ 

Where  $\beta_1$  to  $\beta_6$  are the coefficient estimates of the factors that are associated with the uterine fibroids, U is the stochastic random error and the other components of the model are described below:

Iny: Patient has a Uterine fibroid (1 = Yes, 0 = No)

x1: Number of Adult women between age 18 to 65 examined daily (in 000')

x<sub>2</sub>: Daily Alcohol consumption (in percentage)

 $x_3$ : Family history (1 = those that with Uterine fibroids, 0 = there is no one with Uterine fibroids)

x<sub>4</sub>: Body mass index (BMI) measured in kg/m<sup>2</sup>

x<sub>5</sub>: Vitamin D deficiency measured in nmol/L.

x<sub>6</sub>: Age (in years)

The odd ratio =  $\text{Exp}(B) = e^B$  which will help us determine the major one/ most critical out of the six factors that is associated with the incidence of Uterine fibroid.

### 3.4 Goodness of fit diagnostic for Logistic regression

Hosmer & Lemeshow test is a diagnostic test for goodness of fit for logistic regression model using Chi-square statistic.

Hypothesis for goodness of fit

H<sub>0</sub>: The fit is good

H<sub>a</sub>: The fit is not good

Decision rule: Reject the null hypothesis if P-value is less than the significant level and do not reject if otherwise. The generally acceptable significant level in practice are 1% and 5% respectively (Adebanjo et al, 2022).

### 4. Result and discussion

This section presents the results of the analysis and discussion of the crucial findings of this study. Table 1: Summary statistics

	Ν	Mean	Std. Deviation
Adult Women	760	120.97	32.023
Alcohol Intake	760	69.12	19.446
BMI	760	31.999	7.8997
Vitamin D Deficiency	760	0.473	0.332
Age (18-65)	760	33.21	11.741
Patient has a Uterine fibroid	%		
Yes	35		
No	65		
Family history	%		
Those diagnosed	49.3		
Those that are not affected by family history	50.7		

Source: Author's computation using Stata Software

Table 1 shows that the average number of Adult women between ages 18 to 65 examined daily for Uterine Fibroids is about 121 thousand with a variability of about 32 thousand during the period under review. The Alcohol intake on average is about 69% with a variability of about 19%. The average body mass index (BMI) is about 21% with a variability of about 16%. The average body mass index (BMI) is about 22% with a variability of about 16%. The average body mass index (BMI) is about 32% with a variability of about 8%. The average vitamin D deficiency is about 0.5 nanomoles per litre with a variability of about 0.3 nanomoles per litre while the average age of the women of age 18-65 under study is about 33 years with a variability of about 12 years. More so, about 35% of the adults in the US are diagnosed with Uterine Fibroids while about 65% do not have Uterine Fibroids. Additionally, about 49% of the patient were traced to family history while about 51% was not.

Table 2: Logistic regression model

Logistic regression				
	Number of observations $=$ 760			
Accuracy of the logistic regression classifier = $77.6\%$				
	LR $chi2(7) = 249.53$			
	Prob > chi2 = 0.0000			
Log likelihood = -369.34386	Pseudo R2 $= 0.2536$			
Patient has a Uterine fibroid (Yes or No)	Odds ratio	Standard error	Test Statistic	P-value
Adult Women	1.03	0.0035	9.62	0.000
Alcohol Intake	0.99	0.0051	-2.23	0.026
Family history	0.75	0.1442	-1.50	0.135
BMI	1.09	0.0153	6.16	0.000
Vitamin D Deficiency	2.39	0.7058	2.97	0.003
Age (18-65)	1.03	0.0085	3.80	0.000
Constant	0.00	0.0002	-11.66	0.000
Pearson or Hosmer-Lemeshow goodness of fit $(Prob > chi2) = 0.0162$				

Source: Author's computation using Stata Software

Table 2 shows the results of the estimated multivariate logistic regression. We can see that the overall model Prob > chi2 = 0.0000 which means that the model is statistically significant at a 1% significant level and this suggests that the incidence of Uterine Fibroids is significantly associated with health risk factors (Daily Alcohol consumption, BMI, Vitamin D deficiency) and socioeconomic factors like family history, age and adult women. Meanwhile, the accuracy of the logistic regression classifier is 77.6%. The model goodness of fit using Hosmer-Lemeshow shows that P>0.01, indicating that the fitted logistic regression model is a good fit for the data. Vitamin D Deficiency has an odd ratio of about 2.4 which is higher than the other risk factors considered under the review. This tells us that Vitamin D deficiency contributes majorly to the incidence of Uterine Fibroids, we can see that number of Adult women, family history, BMI, Vitamin D deficiency, and age are statistically significant at a 1% level. In comparison, daily Alcohol intake is statistically significant at a 5% level. This suggests that number of Adult women, daily Alcohol intake, BMI, Vitamin D deficiency, and Age contribute significantly to the incidence of Uterine Fibroids. This is very consistent with the works of Pavone et al. (2018), Ali et al. (2019), and Bariani et al. (2020).



Figure 3: Sensitivity and Specificity curve



Figure 4: ROC curve showing the area under the ROC curve.

Figures 3 and 4 demonstrate that the sensitivity is 58.27%, specificity is 88.06%, and the area under the ROC curve is 0.83, or almost 83%. The diagnostic test indicates that individuals who have not been diagnosed with uterine fibroids are more prevalent than those who have, with an accuracy rate of roughly 78%.

### 4.1 Discussion of findings

The discussion of notable findings from the result of the analysis of this study is discussed as follows.

According to Table 1, there were approximately 121 thousand adult women between the ages of 18 and 65 who were checked daily for uterine fibroids, with a range of roughly 32 thousand for the period under consideration. With a fluctuation of roughly 19%, the average alcohol consumption is around 69%. Body mass index (BMI) fluctuation ranges from roughly 16% to 21% on average. Body mass index (BMI) fluctuation is roughly 8%, with the average BMI being around 32%. The average age of the women in the study, ages 18 to 65, is about 33 years old with a variability of about 12 years, and their average vitamin D deficiency is around 0.5 nanomoles per litre with a variety of about 0.3 nanomoles per litre. Furthermore, 65% of adults in the US do not have uterine fibroids, compared to 35% of those who have them. Furthermore, 51% of the patients had no family history, compared to 49% who did.

Table 2 displays the estimated multivariate logistic regression findings. We can see that the overall model Prob > chi2 = 0.0000, which indicates that the model is statistically significant at a 1% significant level, suggests that the incidence of uterine fibroids is significantly correlated with socioeconomic factors like family history, age, and adult women, as well as health risk factors like daily alcohol consumption, BMI, and vitamin D deficiency. The logistic regression classifier's accuracy, meanwhile, is 77.6%. P>0.01 in the Hosmer-Lemeshow test for model goodness of fit indicates that the fitted logistic regression model is a good fit for the data. The odd ratio of vitamin D deficiency is roughly 2.4, which is greater than the odd ratios of the other risk variables taken into account throughout the evaluation. This demonstrates that, compared to other risk factors, vitamin D insufficiency is a considerable contributor to the development of uterine fibroids. In addition, we can see that the percentage of adult women, family history, BMI, vitamin D insufficiency, and age are statistically significant at a 1% level when examining the contributions of the risk variables linked to uterine fibroids. Daily alcohol consumption, in contrast, is statistically significant at a level of 5%. This suggests that the prevalence of uterine fibroids is greatly influenced by the number of adult women, daily alcohol consumption, BMI, vitamin D deficiency, and age. The works of Pavone et al. (2018), Ali et al. (2019), and Bariani et al. are all quite consistent with this (2020).

Besides, looking at Figures 3 and 4 reveal that the sensitivity is 58.27%, specificity is 88.06%, and the area under the ROC curve is 0.83, accounting for almost 83%. The diagnostic test indicates that those not diagnosed with Uterine Fibroids are more prevalent than those who have, with an accuracy rate of roughly 78%.

#### 5. Conclusion and policy implication.

Heavy menstrual bleeding (HMB) and poor uterine receptivity and implantation, both of which impact millions of women in the United States and around the world, are brought on by uterine fibroids.

The application of multivariate logistic regression yielded statistically significant results, which suggests that the incidence of uterine fibroids is significantly correlated with socioeconomic risk factors such as age, family history, and the presence of adult women as well as with health risk factors. The odd ratio for vitamin D deficiency is roughly 2.4, which is greater than the odd ratios for the other risk variables the study took into account. Therefore, to prevent the tendency to develop uterine fibroids, which in turn will lower infertility caused by the heavy menstrual bleeding and poor uterine receptivity brought on by uterine fibroids, American adult women must monitor their lifestyle, have their BMI, Vitamin D deficiency, and other risk factors for uterine fibroids diagnosed, and then make sure they are receiving adequate treatment.

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#### Appendix

. logistic PatienthasaUterinefibroid NoofWomen AlcholIntake Familyhistory BMI VitaminDDeficiency Age1865

Log likelihood = -367.29209	Э		Numi LR Proi Psei	ber of ob chi2(6) b > chi2 udo R2	s = 760 = 249.53 = 0.0000 = 0.2536	
PatienthasaUterinefibroid	Odds ratio	Std. err.	z	P> z	[95% conf.	interval]
NoofWomen	1.033511	.0035421	9.62	0.000	1.026592	1.040477
AlcholIntake	.9885968	.0050873	-2.23	0.026	.9786759	.9986183
Familyhistory	.749952	.1442174	-1.50	0.135	.5144528	1.093255
BMI	1.090705	.0153675	6.16	0.000	1.060997	1.121244
VitaminDDeficiency	2.398441	.7058484	2.97	0.003	1.347178	4.270052
Age1865	1.031754	.0084969	3.80	0.000	1.015234	1.048543
_cons	.0002947	.0002055	-11.66	0.000	.0000751	.0011562

Note: \_cons estimates baseline odds.

#### . estat classification

Logistic model for PatienthasaUterinefibroid

True					
Classified	D	~D	Total		
+ -	155 111	59 435	214 546		
Total	266	494	760		

Classified + if predicted Pr(D) >= .5 True D defined as PatienthasaUterinefibroid != 0

Sensitivity	Pr( +  D)	58.27%
Specificity	Pr( - ~D)	88.06%
Positive predictive value	Pr( D  +)	72.43%
Negative predictive value	Pr(~D  -)	79.67%
False + rate for true ~D	Pr( + ~D)	11.94%
False - rate for true D	Pr( -  D)	41.73%
False + rate for classified +	Pr(~D  +)	27.57%
False - rate for classified -	Pr( D  -)	20.33%
Correctly classified		77.63%

#### . estat gof

Goodness-of-fit test after logistic model Variable: PatienthasaUterinefibroid

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Number of observations = 760
Number of covariate patterns = 760
Pearson chi2(753) = 838.37
Prob > chi2 = 0.0162
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. lsens

. lroc

Logistic model for PatienthasaUterinefibroid

Number of observations = 760 Area under ROC curve = 0.8317

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