

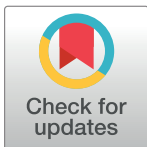
## RESEARCH ARTICLE

## High regional variation in prostate surgery for benign prostatic hyperplasia in Switzerland

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## Abstract

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**Citation:** Wertli MM, Zumbrunn B, Weber P, Haynes AG, Panczak R, Chiolerio A, et al. (2021) High regional variation in prostate surgery for benign prostatic hyperplasia in Switzerland. PLoS ONE 16(7): e0254143. <https://doi.org/10.1371/journal.pone.0254143>

**Editor:** Peter F.W.M. Rosier, University Medical Center Utrecht, NETHERLANDS

**Received:** February 16, 2021

**Accepted:** June 21, 2021

**Published:** July 22, 2021

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**Data Availability Statement:** The minimal anonymized dataset necessary to replicate your study findings is now available under the DOI [10.48350/156212](https://doi.org/10.48350/156212). Due to privacy laws in Switzerland, we are unable to share the data to reproduce tables with intervention or diagnostic codes and demographics. Requests for such data must be made to the SFSO: Swiss Federal Statistical Office (SFSO) Sektion Gesundheitsversorgung, Espace de l'Europe 10, CH-2010 Neuchâtel, Switzerland, Phone: +41 58 463 67 00, Email: [gesundheit@bfs.admin.ch](mailto:gesundheit@bfs.admin.ch).

## Background

Among various treatment options for benign prostatic hyperplasia (BPH), surgical therapy is the most invasive. As Switzerland has the highest transurethral prostatectomy rate among OECD countries, we assessed the regional variation in prostate surgery for BPH and explored potential determinants of variation.

## Methods

We conducted a population-based analysis using discharge data for men aged  $\geq 40$  years with transurethral or simple prostatectomy from all Swiss hospitals during 2013–2018. After excluding patients with genitourinary/prostate cancer, we derived hospital service areas (HSAs) by analyzing patient flows. We calculated age-standardized mean procedure rates and variation indices (extremal quotient [EQ] and systematic component of variation [SCV]). We estimated the reduction in variance across HSAs of prostatectomy rates in multilevel regression models, with incremental adjustment for age, regional cultural and socioeconomic factors, disease burden, density of urologists, and the time since urologists' graduation.

## Results

Overall, 44,253 prostatectomies (42,710 transurethral and 1543 simple) from 44 HSAs were analyzed. The mean age-standardized prostate surgery rate was 314 (range 166–500) per 100,000 men aged  $\geq 40$  years per year. The EQ was 3.01 and the SCV 5.53, indicating a high regional variation. In multivariate models, men aged 75–79 years had an 11.6-fold higher prostatectomy rate than those aged 50–54 years. French/Italian language areas had a 21% lower rate than Swiss German speaking areas. Socioeconomic factors, disease burden, and density of urologist/time since graduation were not associated with prostatectomy

**Funding:** This research project was supported by the National Research Program 74 of the Swiss National Foundation (Grant number SNF 407440\_167339), the Health Services Research funding program of the Gottfried and Julia Bangerter-Rhyner Foundation, and the Swiss Society of General Internal Medicine Foundation.

**Competing interests:** The authors declare no additional funding or competing interests such as consultancies, stock ownership or other payments other than the reported funding sources. Dr. Haynes is affiliated with CTU Bern, University of Bern, which has a staff policy of not accepting honoraria or consultancy fees. However, CTU Bern is involved in design, conduct, or analysis of clinical studies funded by not-for-profit and for-profit organizations. In particular, pharmaceutical and medical device companies provide direct funding to some of these studies. For an up-to-date list of CTU Bern's conflicts of interest see [http://www.ctu.unibe.ch/research/declaration\\_of\\_interest/index\\_eng.html](http://www.ctu.unibe.ch/research/declaration_of_interest/index_eng.html). This does not alter our adherence to PLOS ONE policies on sharing data and materials.

rates. After full adjustment, 80% of the variance in prostate surgery across HSAs remained unexplained.

## Conclusion

We found a remarkably high regional variation in prostate surgery rates for BPH within Switzerland.

## Background

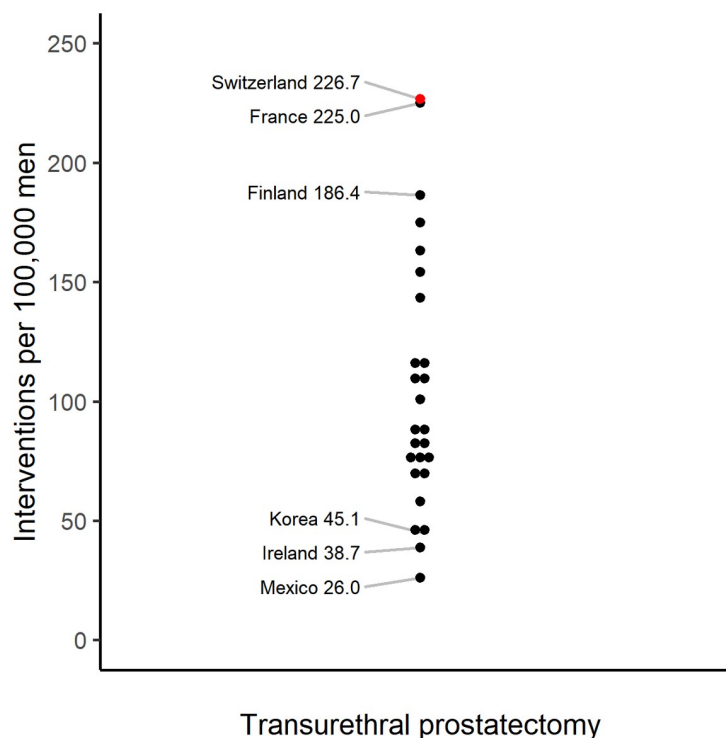
Benign prostatic hyperplasia (BPH) increases in frequency with age and may lead to prostatic obstruction, lower urinary tract symptoms (LUTS), and urinary retention [1, 2]. Almost 50% of men have at least moderate lower urinary tract symptoms in the eighth decade of life [2]. Transurethral resection of the prostate (TURP) and open simple prostatectomy were historically the standard treatments to remove prostatic obstruction [3]. These procedures require however hospitalization and carry a risk of bleeding, sexual dysfunction, urinary incontinence, and urethral stricture/bladder neck contracture [4, 5]. Over the last 30 years, a multitude of treatments for BPH, including drugs ( $\alpha$ -adrenergic antagonists, 5- $\alpha$  reductase inhibitors) and minimally invasive surgical techniques with the potential to reduce the need for hospitalization and complications [3, 6], were introduced into clinical practice [7]. Guidelines recommend conservative measures, including behavioral changes and drugs, as the first-line treatment for men with BPH who are bothered by their LUTS [8–10]. Surgery is recommended when patients have BPH-related complications (e.g., urinary retention, renal insufficiency, or recurrent urinary tract infections), or when patients fail to improve with conservative therapy or refuse drug treatment. However, only few studies directly compared the effectiveness, safety, patient satisfaction, and costs of drug vs. surgical treatment for symptomatic BPH and the optimal timing to switch from conservative to surgical treatment is not well defined [11, 12]. Limited evidence suggests that surgery may be more cost-effective in the long run and in patients with severe LUTS [13, 14]. In the USA and other countries, a decrease in surgery for BPH has been observed over time [15, 16].

Although transurethral prostatectomy rates decreased by 11% in Switzerland between 2008 and 2018, Switzerland had the highest procedure rates among Organization for Economic Co-operation and Development (OECD) countries during this period, with 227 interventions per 100,000 men in 2018 (Fig 1) [17]. However, whether prostatectomy rates are uniformly high across Swiss regions and which factors drive prostatectomy rates in Switzerland is largely unknown. The aim of this study was therefore to assess regional variations in prostatectomy rates using Swiss national data and to determine whether demographic, cultural, socioeconomic, health, and supply factors explain such variation.

## Methods

### Data sources

We conducted a population-based, small area variation analysis using routinely collected patient discharge data from all Swiss public and private acute care hospitals and census data for calendar years 2013–2018. The method has been described previously [18, 19]. Swiss hospitals are legally obligated to provide the Swiss Federal Statistical Office (SFSO) with an anonymized, standardized data set for each hospital discharge, which includes demographic



**Fig 1. Comparison of transurethral prostatectomy rates across OECD countries (incl. Costa Rica) in 2018.** Each dot represents the crude transurethral prostatectomy rate per 100,000 men in a given country. The red dot indicates Switzerland.

<https://doi.org/10.1371/journal.pone.0254143.g001>

information, procedure codes based on the Swiss Classification of Operations (CHOP; an adaptation of the U.S. ICD-9-CM volume 3 procedure classification), and diagnostic codes based on the International Classification of Diseases, 10<sup>th</sup> revision, German Modification (ICD-10-GM) [20]. Further, the area of patient residence and hospital location within one of 705 Swiss MedStat regions (administrative regions based on aggregated ZIP-codes) are recorded [21]. The Swiss Hospital Discharge Masterfile covers 100% of discharges and the SFSO reviews data integrity and completeness [22].

We used Swiss National Cohort data from 2014 to determine the main language (German, French, or Italian) [23] and data from the SFSO to determine the population density for each MedStat region. We abstracted measures of socioeconomic status (neighborhood information on rent, education, occupation, and crowding) using Swiss census data from 2012 to 2015 [24]. Finally, we obtained the number of urologists per MedStat region and their time since graduation from medical school for 2014 from the Swiss Medical Association. Because our study was based on anonymized administrative data only, it was exempted from ethics committee approval according to the Swiss Human Research Act.

### Derivation of Swiss Hospital Service Areas

Switzerland has compulsory basic health insurance coverage, with voluntary semiprivate and private insurance plans covering additional medical services. Although Swiss hospital care is primarily organized based on 26 geographic regions (cantons), patients may utilize hospital services outside their canton of residence and the use of cantons as a unit of observation may skew procedure rates. We therefore used a fully automated method to generate reproducible

general hospital service areas (HSAs) using all patient discharge data from the calendar years 2013–2016 (data that was available when the general HSAs were derived) [18]. Briefly, we identified 4,105,885 patient discharges aged  $\geq 18$  years from 155 Swiss public and private acute care hospitals during calendar years 2013–2016. Only patients living in Switzerland were considered. We analyzed the flows and assigned MedStat regions from which the highest proportion of residents was discharged to the same HSA (plurality rule). HSAs with less than 50% of the patients being treated within the same HSA or less than 10 discharges were merged with the neighboring HSA which received most discharges, yielding 63 general HSAs. We then identified patient discharges with specific CHOP codes for transurethral (CHOP 60.20–22, 60.29, 60.61.10, 60.95–97, 60.99.2) and simple supra-/or retropubic prostatectomy (CHOP 60.3, 60.4) from all Swiss acute care hospitals from 2013–2018. As prostatectomies are procedures that are not performed in every hospital, we further collapsed the general HSAs into intervention-specific HSAs by aggregating the 63 general HSAs into 44 intervention-specific HSAs, using the method described above. We then drew choropleth maps of the 44 final HSAs using Geographical Information System (GIS)-compatible vector files.

### Study population

Overall, we identified 57,976 discharges with specific codes for transurethral and simple prostatectomy. We excluded those with genitourinary cancer, including prostate cancer, ( $n = 13,625$ ), genitourinary injuries ( $n = 32$ ), congenital disease of the prostate ( $n = 2$ ), and men under 40 ( $n = 64$ ), leaving a final study sample of 44,253 patient discharges for prostate surgery. Of these, 42,710 underwent a transurethral and 1543 a simple prostatectomy. Those who underwent both types of procedures were assigned to the more invasive simple prostatectomy.

### Measures of variation

We calculated age-standardized prostatectomy rates per 100,000 men aged  $\geq 40$  years for each HSA using procedure counts and 2013–2018 census data for the adult Swiss population [25]. We used direct standardization with age bands 40 to 44, 45 to 49, 50 to 54, . . . , 75 to 79, 80+. To examine the variation in prostatectomy rates across Swiss HSAs, we determined the extremal quotient (EQ), which is the highest divided by the lowest procedure rate. While the EQ is an intuitive measure of variation, it is prone to distortion by extreme values [26]. We also calculated the coefficient of variation (CV), i.e., the ratio of the standard deviation of the procedure rates to the mean rate, and the systematic component of variation (SCV) [26, 27]. Although less intuitive than the EQ, the SCV represents the non-random part of the variation in procedure rates while reducing the effect of extreme values [26, 27]. The SCV is derived from a model that recognizes the differences in rates across areas and the random variation within each area's true rate. An SCV of 5.4–10 is considered indicative of high variation and an SCV of  $>10$  of very high variation [26, 28].

### Determinants of variation

Differences in illness incidences and socioeconomic factors are possible and legitimate causes of variation [26]. We therefore explored four regional domains that could influence prostate surgery rates: demographics (age), cultural (language region) and socioeconomic factors (median density of male population, Swiss neighborhood index of socioeconomic position [SSEP], insurance status, and Swiss citizenship), disease burden of the male population, and supply factors (density of urologists per 10,000 men and their average time since graduation). The language spoken by the majority of people living in an HSA was used to classify each HSA

as either Swiss German or French/Italian language region as a proxy for culture. We used population density as a proxy for the level of urbanization a resident lives in. The socioeconomic status of each HSA was measured using the mean SSEP of residents of a given HSA [24]. The SSEP consists of four domains (median rent per m<sup>2</sup>, proportion of households led by a person with no/low education, proportion headed by a person in manual/unskilled occupation, and mean crowding, all on the neighborhood level). The SSEP varies between 0 (lowest) and 100 (highest) and correlates well with mortality [29]. The percentage of discharges with semiprivate/private vs. general health insurance and Swiss vs. foreign citizenship was used as an additional measure of the socioeconomic status of each HSA. As a proxy for the population burden of disease, we calculated age-standardized incidence rates of hip fractures, cancers of the colon or lung treated surgically, acute myocardial infarctions, or strokes for men in each HSA, as differences in these disease rates are likely to reflect true regional differences in burden of disease rather than differences in coding intensity or supply factors [30, 31]. The density of urologists and their average time since graduation were used as proxies for health services availability and physician training, respectively.

To explore determinants of prostate surgery rates in Switzerland, we used progressively adjusted multilevel Poisson regression with a log link to model the procedure rates in each HSA. Age was used in the bands 40 to 44, 45 to 49, . . . , 75 to 79, 80+ and adjustment was performed on an HSA level. Model 1 included only the calendar year of the procedure. Model 2 was additionally adjusted for demographics (age). Model 3 was additionally adjusted for HSA-level language and socioeconomic factors (male population density, SSEP, insurance status, and Swiss citizenship). Model 4 was further adjusted for HSA-level male population burden of disease. Model 5 was additionally adjusted for the density of urologists per HSA and their average time since graduation. HSA was included as a random intercept in all models. All covariates were selected *a priori*. We depicted the variation in HSA rates as average predicted prostate surgery rates per 100,000 men aged  $\geq 40$  years per HSA derived from the multilevel regression models. Where rates are shown in maps, categories for the rates were chosen to be about equal in width.

We expressed the impact of determinants on prostatectomy rates as incidence rate ratios (IRRs), defined as the prostatectomy rate in the defined category (e.g., French/Italian language region) relative to the estimated prostate surgery rate in the reference category (e.g., German language region). We also determined the percentage reduction in procedure variation across the 44 HSAs by examining the variance of the random intercept. We considered the residual, unexplained variation of the fully adjusted model a proxy for unwarranted variation, i.e. the variation that cannot be attributed to potential patient need [26, 32–34]. Statistical analyses were performed using Stata version 16.1 (StataCorp, College Station, TX, USA) and R statistical software version 3.6.1 [35].

## Results

### Characteristics of Swiss HSAs and the study population

Of 44 HSAs, 29 were located in the Swiss German and 15 in the French/Italian-speaking part of Switzerland. The median male adult population per HSA was 39,543 persons (interquartile range [IQR] 22,430–91,959), with a median population density of 125 men per km<sup>2</sup> (IQR 48–203), and a mean SSEP of 54 points (IQR 51–59). The average proportion of residents with semi-private/private insurance and Swiss nationality per HSA was 21% (IQR 17–28) and 82% (IQR 78–86), respectively. The median burden of disease was 0.59 (IQR 0.53–0.65) comorbidities per 1000 men. The median density of urologists was 8.2 (IQR 6.0–12.0) per 10,000 men (S1 Fig), with a median average time since graduation of 23 years (IQR 20–26).

The majority of the 44,253 patients discharged after a prostatectomy were 65 years or older (72%), had general health insurance (65%), and were Swiss nationals (88%) (Table 1). Almost all patients had undergone transurethral prostate surgery (97%).

### Variation in procedure rates across Swiss HSAs

The mean age-standardized prostate surgery rate was 314 (range 166–500) per 100,000 men  $\geq 40$  years of age per year (Fig 2). Detailed age-standardized prostate surgery rates for each HSA are shown in the S1 Table. The EQ was 3.01, the CV 0.25, and the SCV 5.53, indicating a high variation (Table 2). We could discern no clear time trends in the variation among HSAs between 2013 and 2018.

After full adjustment for procedure year, age, language region, socioeconomic factors, burden of disease, and urologist density/time since graduation, the average predicted prostate surgery rates per HSA varied between 182 and 500 per 100,000 men  $\geq 40$  years of age (Fig 3), of which four were above 436 per 100,000 (HSA number 19, 21, 38, and 41, located in different parts of Switzerland) and seven were below 244 per 100,000 (HSA number 2, 6, 10, 16, 23, 26, 36, also spread across the country). After full adjustment, 80% of the variance in prostate surgery rates amongst HSAs remained unexplained.

### Determinants of variation in procedure rates

Procedure rates decreased by 3% per year (IRR 0.97; 95% CI 0.96–0.97; Table 3). Age was the most powerful predictor of procedure variation across HSAs. Compared to men aged 50–54 years, men aged 75–79 years had an 11.6-fold higher prostate surgery rate (IRR 11.57; 95% CI 10.97–12.21). French/Italian language areas showed a 21% lower prostatectomy rate (IRR 0.79; 95% CI 0.66–0.94) than Swiss German-speaking areas. None of the other predictors were statistically significantly associated with prostatectomy rates.

### Discussion

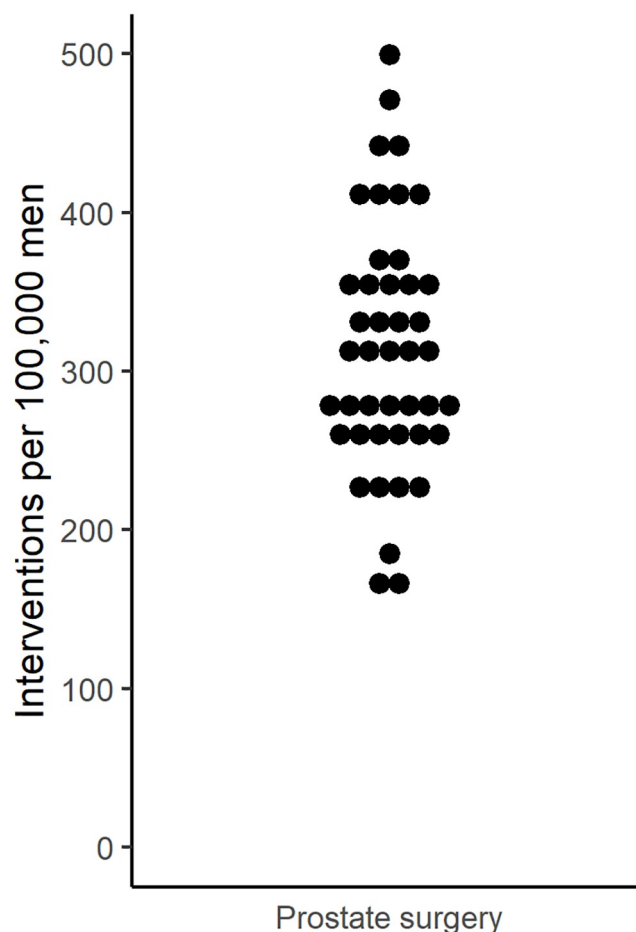
Our study demonstrates a rather high rate of prostate surgery for BPH in Switzerland and a high variation in prostate surgery among Swiss regions. This variation remained largely

**Table 1. Characteristics of 44,253 men aged  $\geq 40$  years with prostate surgery from 2013 to 2018.**

Characteristic	n (%)
Age, years	
40–49	607 (1)
50–59	5409 (12)
60–69	14,651 (33)
70–79	16,497 (37)
80+	7089 (16)
Insurance class	
General	28,891 (65)
(Semi-)private	15,362 (35)
Citizenship	
Swiss	39,142 (88)
Non-Swiss	5111 (12)
Procedure type	
Transurethral prostatectomy	42,710 (97)
Simple supra- or retropubic prostatectomy	1543 (3)

<https://doi.org/10.1371/journal.pone.0254143.t001>





**Fig 2. Variation in age-standardized prostate surgery rates across 44 Swiss Hospital Service Areas.** Each dot represents a Hospital Service Area.

<https://doi.org/10.1371/journal.pone.0254143.g002>

unexplained by procedure year, demographic, cultural and socioeconomic factors, disease burden, and the density of urologists.

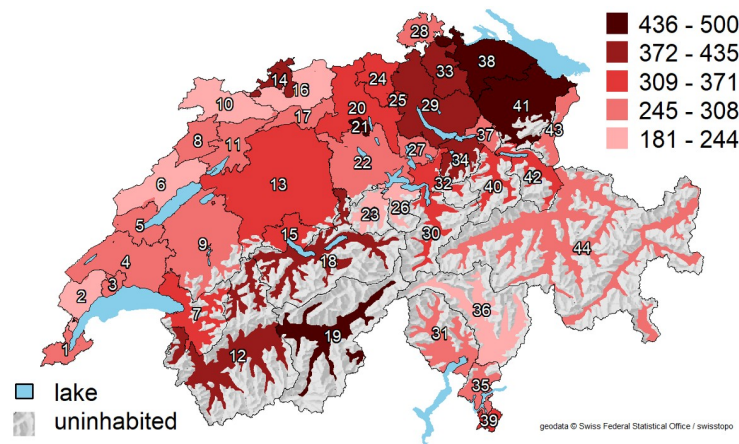
Transurethral prostatectomy rates and time trends differ greatly across OECD countries [17]. These between-country differences may reflect differences in a multitude of factors, including demographic composition, patient preferences, socioeconomic deprivation with limited access to care, physicians' clinical decisions, health service configuration and financing, and the availability of specialists [26]. Switzerland has one of the highest health care expenditure per capita across OECD countries [36], a number of doctors per capita above the OECD

**Table 2. Variation in prostate surgery rates across 44 Swiss Hospital Service Areas.**

	Overall	2013	2014	2015	2016	2017	2018
EQ	3.01	3.81	3.46	3.57	4.38	3.05	3.61
CV	0.25	0.28	0.34	0.30	0.28	0.24	0.29
SCV	5.53	5.87	8.72	6.62	6.04	4.09	6.29

Abbreviations: EQ, extremal quotient; CV, coefficient of variation; SCV, systematic component of variation.

<https://doi.org/10.1371/journal.pone.0254143.t002>



**Fig 3. Map of the average adjusted predictions of prostate surgery rates across 44 Swiss Hospital Service Areas.** Average predicted prostate surgery rates for each HSA are shown as red-scale categories per 100,000 men  $\geq 40$  years of age. Adjusted for procedure year, age, language region, density of male population, mean Swiss Neighborhood Index of Socioeconomic Position, insurance status, Swiss citizenship, disease burden of the male population, density of urologists, and urologists' time since graduation. Rate categories were chosen to be about equal in width. Shaded relief map reprinted from the Federal Office of Topography swisstopo, Switzerland <https://shop.swisstopo.admin.ch/en/products/maps/overview/relief> and shape files derived from postcode-level shape file used to create map of Switzerland, e.g., <https://www.geocat.admin.ch/> under a CC BY license, with permission from Alexandra Frank, original copyright 2006.

<https://doi.org/10.1371/journal.pone.0254143.g003>

average, and a high specialist-generalist ratio. Swiss residents also benefit from universal health care coverage and have timely access to care. These factors could contribute to the high prostatectomy rate in Switzerland compared to other countries.

The remarkably high variation of prostate surgery for BPH across geographically closely related Swiss regions, largely ( $>80\%$ ) was not associated with demographic, cultural, socioeconomic, health, and supply factors, is more difficult to interpret. As it is implausible that men from neighboring areas differ in terms of size/anatomy of their prostate or their preferences for outcomes associated with prostatectomy, the variation may be unwarranted and explained by Swiss urologists' differing practice styles.

In the 1980 and 1990s, Wennberg and colleagues found a similarly high variation in overall prostatectomy rates for various indications within different health care systems (SCV 5.0–9.3) [27] and TURP for BPH in the USA (SCV 5.2) [37]. They identified two clinical sources of unwarranted variation in prostatectomy for BPH [38]: (1) lack of information concerning the risks/benefits of the procedure, and (2) failure to base decisions on patient preferences for outcomes, as patients with similar LUTS report considerable difference in the degree to which they are bothered [39].

Several decades later, the high regional variation in prostatectomy for BPH persists in Switzerland and other countries [40, 41]. Over the last three decades, there was a proliferation of pharmacological and minimally invasive surgical treatments for BPH [3]. Although the European Urology Association and the American Urological Association publish regularly updated BPH guidelines since the early 2000s [42, 43], this apparently has not led to consolidation of practice into a single best practice [12]. Both guidelines recommend conservative management as the initial treatment for uncomplicated BPH and underline the importance of discussing the risks and benefits of various treatment options. However, guideline adherence is highly variable among urologists and may be due to the limited evidence on best evaluative practices and a lack of comparative effectiveness studies to help guide the multiple existing treatment choices



**Table 3. Determinants of variance in the incidence rates of prostate surgery across 44 Swiss Hospital Service Areas.**

Determinants		Model 1*	Model 2†	Model 3‡	Model 4#	Model 5&
		Incidence rate ratio (95% confidence interval)§				
Procedure year (per year)		0.99 (0.98–0.99)	0.97 (0.97–0.98)	0.97 (0.96–0.98)	0.97 (0.96–0.97)	0.97 (0.96–0.97)
Age category (years)	40–44		0.07 (0.06–0.09)	0.07 (0.06–0.09)	0.07 (0.06–0.09)	0.07 (0.06–0.09)
	45–49		0.31 (0.28–0.34)	0.31 (0.28–0.34)	0.31 (0.28–0.34)	0.31 (0.28–0.34)
	50–54		Reference	Reference	Reference	Reference
	55–59		2.67 (2.52–2.83)	2.67 (2.52–2.83)	2.67 (2.52–2.83)	2.67 (2.52–2.83)
	60–64		5.28 (5.00–5.57)	5.28 (5.00–5.57)	5.28 (5.00–5.57)	5.28 (5.00–5.57)
	65–69		8.28 (7.86–8.73)	8.28 (7.86–8.73)	8.28 (7.86–8.73)	8.28 (7.86–8.73)
	70–74		10.75 (10.20–11.33)	10.75 (10.20–11.33)	10.75 (10.20–11.33)	10.75 (10.20–11.33)
	75–79		11.57 (10.97–12.21)	11.57 (10.97–12.21)	11.57 (10.97–12.21)	11.57 (10.97–12.21)
Language region	80+		9.26 (8.77–9.77)	9.26 (8.77–9.77)	9.26 (8.77–9.77)	9.26 (8.77–9.77)
	Swiss German			Reference	Reference	Reference
	French/Italian			0.79 (0.68–0.93)	0.79 (0.67–0.93)	0.79 (0.66–0.94)
Density of male population (per 100/km <sup>2</sup> )				1.02 (0.95–1.09)	1.02 (0.96–1.09)	1.02 (0.96–1.10)
Mean SSEP (per 1 unit increase)				1.01 (0.99–1.03)	1.01 (1.00–1.03)	1.01 (0.99–1.03)
(Semi-)private insurance (per 10% increase)				0.88 (0.78–1.00)	0.88 (0.78–1.01)	0.89 (0.78–1.01)
Swiss citizenship (per 10% increase)				0.93 (0.85–1.01)	0.92 (0.84–1.01)	0.93 (0.85–1.01)
Burden of disease (per comorbidity/1000 men)					1.06 (0.97–1.16)	1.06 (0.97–1.16)
Density of urologists (per urologist/10,000 men)**						1.00 (0.98–1.01)
Average time since graduation (per 5 years)						1.00 (0.93–1.07)
Remaining variance from Model 1 (%)II			102.1	79.9	80.9	80.0

Abbreviations: SSEP, Swiss Neighborhood Index of socioeconomic position.

\*Model 1: adjusted for procedure year.

†Model 2: additional adjustment for age.

‡Model 3: additional adjustment for cultural and socioeconomic factors (language region, density of men, SSEP, insurance status, and Swiss citizenship).

#Model 4: additional adjustment for population burden of disease.

&Model 5: additional adjustment for density of urologists and their average time since urologists' graduation.

§Prostate surgery rate in the defined category relative to the reference category. For instance, the incidence rate ratio of 0.79 indicates a 21% lower prostate surgery rate in French/Italian-speaking than in Swiss German speaking language areas.

Burden of disease is defined as the sum of age-standardized incidence rates for the following comorbidities: hip fracture, colon or lung cancer treated surgically, acute myocardial infarction, and stroke. The incidence rate ratio is the increase (decrease) in procedure rates when the regional burden of disease increases by 1 comorbidity per 1000 men.

\*\*The incidence rate ratio is the increase (decrease) in procedure rates when the regional density of urologists increases by 1 urologist per 10,000 men.

II Expresses the variance around the mean prostate surgery rate.

<https://doi.org/10.1371/journal.pone.0254143.t003>

and the optimal timing for prostate surgery in BPH [11, 12, 44–47]. The same can be said about primary care physicians who are highly variable in their referral thresholds to urologists [48]. According to an international survey, urologists have discrepant attitudes to counselling patients on side effects related to BPH/LUTS treatments, and most urologists do not discuss alternative treatments with patients based on the risk of different outcomes [49].

Evidence suggests that adherence to guideline-recommended evaluative care work-up for BPH translates into lower prostate surgery rates. In an analysis of Medicare beneficiaries with

BPH, a high guideline compliance was associated with a 91% decrease in the adjusted odds of receiving prostate surgery [50]. Shared decision-making programs/decision aids for symptomatic BPH result in increased patient knowledge about their condition and a higher satisfaction with treatment choice but do not necessarily result in lower rates of prostate surgery [51–54]. While there is no published evidence about differing guideline adherence and shared decision-making processes among Swiss urologists, such differences could at least partially be responsible for the observed regional procedure variation in our study.

As the prevalence of BPH increases with age [1, 2], it is not surprising that age was the most important predictor of prostate surgery in our analysis. French/Italian speaking areas had a 21% lower prostate surgery rate than Swiss German language regions, possibly due to more conservative physician practice styles or patient preferences for less invasive treatments. We previously have observed lower rates of other preference-sensitive surgical interventions in the French/Italian speaking parts of Switzerland, including vertebroplasty, hysterectomy and joint replacement [19, 55, 56]. We found no association between semi-/private insurance and prostatectomy rates, arguing against the suspicion that a semi-/private insurance (which results in higher physician fees) may fuel overtreatment in Switzerland. Similarly, we found no association between the density of urologists and procedure rates. Several high-volume areas (e.g., HSA 11, 18) had a relatively low density of urologists, indicating that procedure variation may be due to local urologists' attitudes and not their number.

Our study has several potential limitations. First, we did not have clinical data and could not verify the exact indication for prostate surgery and whether it was adherent to guideline recommendations for treating BPH. Second, we had no information about regionally differing physician or patient attitudes towards prostate surgery for BPH. Third, our analysis was limited to inpatient procedures and did not include prostate surgery done in the outpatient setting. However, this is not a major limitation, as >98% of transurethral prostatectomies in Switzerland are done on an inpatient basis [17]. Fourth, Swiss coding practices did not allow a regional comparison of different surgical techniques over time, including the uptake of minimally invasive methods, such as water vapor thermal therapy, prostatic urethral lift, and robot-assisted and laparoscopic simple prostatectomy [3]. Fifth, adjustment for ecological variables on a population level (i.e., age, language, SSEP, insurance, citizenship, and burden of disease) includes a risk of ecological fallacy by drawing conclusions about the behavior of individuals based on population level parameters [57]. Finally, our results describe associations and cannot infer causality.

In conclusion, we found a remarkably high regional variation in prostate surgery rates for BPH within Switzerland. The larger part of the variation was not associated with procedure year, age, cultural and socioeconomic factors, disease burden, and the density of urologists/time since graduation.

## Supporting information

**S1 Fig. Density of urologists (number per 10,000 men) across 44 Swiss Hospital Service Areas.** Shaded relief map reprinted from the Federal Office of Topography swisstopo, Switzerland <https://shop.swisstopo.admin.ch/en/products/maps/overview/relief> and shape files derived from postcode-level shape file used to create map of Switzerland, e.g., <https://www.geocat.admin.ch/>) under a CC BY license, with permission from Alexandra Frank, original copyright 2006.  
(TIF)

**S1 Table. Age-standardized prostate surgery rates per year for 44 Hospital Service Areas.**  
Abbreviation: HSA, Hospital Service Area.  
(DOCX)

## Acknowledgments

We thank Claudia Berlin for providing an updated version of the SSEP.

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## References

1. Berry SJ, Coffey DS, Walsh PC, Ewing LL. The development of human benign prostatic hyperplasia with age. *J Urol.* 1984; 132:474–9. [https://doi.org/10.1016/s0022-5347\(17\)49698-4](https://doi.org/10.1016/s0022-5347(17)49698-4) PMID: 6206240
2. Wei JT, Calhoun E, Jacobsen SJ. Urologic diseases in America project: benign prostatic hyperplasia. *J Urol.* 2005; 173:1256–61. <https://doi.org/10.1097/01.ju.0000155709.37840.fe> PMID: 15758764
3. Dornbier R, Pahouja G, Branch J, McVary KT. The New American Urological Association Benign Prostatic Hyperplasia Clinical Guidelines: 2019 Update. *Curr Urol Rep.* 2020; 21:32. <https://doi.org/10.1007/s11934-020-00985-0> PMID: 32607874
4. Emberton M, Neal DE, Black N, Fordham M, Harrison M, McBrien MP, et al. The effect of prostatectomy on symptom severity and quality of life. *Br J Urol.* 1996; 77:233–47. <https://doi.org/10.1046/j.1464-410x.1996.88213.x> PMID: 8800892
5. Welk B, Reid J, Ordon M, Razvi H, Campbell J. Population-based assessment of re-treatment and healthcare utilisation after photoselective vaporisation of the prostate or electrosurgical transurethral resection of the prostate. *BJU Int.* 2019; 124:1047–54. <https://doi.org/10.1111/bju.14891> PMID: 31389161
6. Huang SW, Tsai CY, Tseng CS, Shih MC, Yeh YC, Chien KL, et al. Comparative efficacy and safety of new surgical treatments for benign prostatic hyperplasia: systematic review and network meta-analysis. *BMJ.* 2019; 367:l5919. <https://doi.org/10.1136/bmj.l5919> PMID: 31727627

7. Kaplan SA. AUA Guidelines and Their Impact on the Management of BPH: An Update. *Rev Urol.* 2004; 6 Suppl 9:S46–52. PMID: [16985925](#)
8. Parsons JK, Dahm P, Kohler TS, Lerner LB, Wilt TJ. Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline Amendment 2020. *J Urol.* 2020; 204:799–804. <https://doi.org/10.1097/JU.0000000000001298> PMID: [32698710](#)
9. From the European Association of Urology web site. <https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Non-Neurogenic-Male-LUTS-incl.-BPO-2020.pdf>. Accessed December 20, 2020.
10. From the National Institute of Health and Care Excellence (NICE) web site. <https://www.nice.org.uk/guidance/cg97/resources/lower-urinary-tract-symptoms-in-men-management-pdf-975754394053>. Accessed December 20, 2020.
11. Stoddard MD, Cho A, Te AE, Chughtai B. A Systematic Review on the Timing of Surgical Intervention for Benign Prostatic Enlargement (BPE). *Curr Urol Rep.* 2020; 21:64. <https://doi.org/10.1007/s11934-020-01016-8> PMID: [33230722](#)
12. Strophe SA. Evidence-based guidelines in lower urinary tract symptoms secondary to benign prostatic hyperplasia and variation in care. *Curr Opin Urol.* 2018; 28:262–6. <https://doi.org/10.1097/MOU.0000000000000504> PMID: [29601306](#)
13. Hollingsworth JM, Wei JT. Economic impact of surgical intervention in the treatment of benign prostatic hyperplasia. *Rev Urol.* 2006; 8 Suppl 3:S9–S15. PMID: [17173101](#)
14. DeWitt-Foy ME, Gill BC, Ulchaker JC. Cost Comparison of Benign Prostatic Hyperplasia Treatment Options. *Curr Urol Rep.* 2019; 20:45. <https://doi.org/10.1007/s11934-019-0907-3> PMID: [31218458](#)
15. Malaeb BS, Yu X, McBean AM, Elliott SP. National trends in surgical therapy for benign prostatic hyperplasia in the United States (2000–2008). *Urology.* 2012; 79:1111–6. <https://doi.org/10.1016/j.urology.2011.11.084> PMID: [22546389](#)
16. Welliver C, Feinstein L, Ward JB, Fwu CW, Kirkali Z, Bavendam T, et al. Trends in Lower Urinary Tract Symptoms Associated with Benign Prostatic Hyperplasia, 2004 to 2013: the Urologic Diseases in America Project. *J Urol.* 2020; 203:171–8. <https://doi.org/10.1097/JU.000000000000499> PMID: [31430232](#)
17. From the OECD web site. <https://stats.oecd.org/index.aspx?queryid=30167>. Accessed December 20, 2020.
18. Haynes AG, Wertli MM, Aujesky D. Automated delineation of hospital service areas as a new tool for health care planning. *Health Serv Res.* 2020; 55:469–75. <https://doi.org/10.1111/1475-6773.13275> PMID: [32078171](#)
19. Stoller N, Wertli MM, Zaugg TM, Haynes AG, Chiolerio A, Rodondi N, et al. Regional variation of hysterectomy for benign uterine diseases in Switzerland. *PLoS One.* 2020; 15:e0233082. <https://doi.org/10.1371/journal.pone.0233082> PMID: [32407404](#)
20. From the Swiss Federal Statistical Office (SFSO) web site. <https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheitsnomenklaturen/medkk/instrumente-medizinische-kodierung.html>. Accessed December 20, 2020.
21. From the Swiss Federal Statistical Office web site. <https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheitsnomenklaturen/medsreg.html>. Accessed March 10, 2020.
22. From the Swiss Federal Statistical Office web site. <https://www.bfs.admin.ch/bfs/de/home/statistiken/wirtschaftliche-soziale-situation-bevoelkerung/gleichstellung-menschen-behinderungen/erwerbstaetigkeit/geschuetzte-arbeit.assetdetail.349863.html>. Accessed March 10, 2020.
23. Bopp M, Spoerri A, Zwahlen M, Gutzwiller F, Paccaud F, Braun-Fahrlander C, et al. Cohort Profile: the Swiss National Cohort—a longitudinal study of 6.8 million people. *Int J Epidemiol.* 2009; 38:379–84. <https://doi.org/10.1093/ije/dyn042> PMID: [18326512](#)
24. Panczak R, Galobardes B, Voorpostel M, Spoerri A, Zwahlen M, Egger M, et al. A Swiss neighbourhood index of socioeconomic position: development and association with mortality. *J Epidemiol Community Health.* 2012; 66:1129–36. <https://doi.org/10.1136/jech-2011-200699> PMID: [22717282](#)
25. Breslow NE, Day NE. Indirect standardization and multiplicative models for rates, with reference to the age adjustment of cancer incidence and relative frequency data. *J Chronic Dis.* 1975; 28:289–303. [https://doi.org/10.1016/0021-9681\(75\)90010-7](https://doi.org/10.1016/0021-9681(75)90010-7) PMID: [1141424](#)
26. From the King's Fund web site. [https://www.kingsfund.org.uk/sites/default/files/field/field\\_publication\\_file/Variations-in-health-care-good-bad-inexplicable-report-The-Kings-Fund-April-2011.pdf](https://www.kingsfund.org.uk/sites/default/files/field/field_publication_file/Variations-in-health-care-good-bad-inexplicable-report-The-Kings-Fund-April-2011.pdf). Accessed December 20, 2020.
27. McPherson K, Wennberg JE, Hovind OB, Clifford P. Small-area variations in the use of common surgical procedures: an international comparison of New England, England, and Norway. *N Engl J Med.* 1982; 307:1310–4. <https://doi.org/10.1056/NEJM198211183072104> PMID: [7133068](#)

28. McPherson K, Downing A, Buirski D. Systematic Variation in Surgical Procedures and Hospital Admission Rates: PHP Departmental Publication no. 23. London: London School of Hygiene and Tropical Medicine; 1996.
29. Moser A, Panczak R, Zwahlen M, Clough-Gorr KM, Spoerri A, Stuck AE, et al. What does your neighbourhood say about you? A study of life expectancy in 1.3 million Swiss neighbourhoods. *J Epidemiol Community Health*. 2014; 68:1125–32. <https://doi.org/10.1136/jech-2014-204352> PMID: 25124188
30. Fisher ES, Wennberg JE, Stukel TA, Skinner JS, Sharp SM, Freeman JL, et al. Associations among hospital capacity, utilization, and mortality of US Medicare beneficiaries, controlling for sociodemographic factors. *Health Serv Res*. 2000; 34:1351–62. PMID: 10654835
31. Wennberg JE, Freeman JL, Culp WJ. Are hospital services rationed in New Haven or over-utilised in Boston? *Lancet*. 1987; 1:1185–9. [https://doi.org/10.1016/S0140-6736\(87\)92152-0](https://doi.org/10.1016/S0140-6736(87)92152-0) PMID: 2883497
32. Anthony DL, Herndon MB, Gallagher PM, Barnato AE, Bynum JP, Gottlieb DJ, et al. How much do patients' preferences contribute to resource use? *Health Aff (Millwood)*. 2009; 28:864–73. <https://doi.org/10.1377/hlthaff.28.3.864> PMID: 19414899
33. Birkmeyer JD, Reames BN, McCulloch P, Carr AJ, Campbell WB, Wennberg JE. Understanding of regional variation in the use of surgery. *Lancet*. 2013; 382:1121–9. [https://doi.org/10.1016/S0140-6736\(13\)61215-5](https://doi.org/10.1016/S0140-6736(13)61215-5) PMID: 24075052
34. Wennberg JE. Time to tackle unwarranted variations in practice. *BMJ*. 2011; 342:d1513. <https://doi.org/10.1136/bmj.d1513> PMID: 21415111
35. R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <http://www.R-project.org/>.
36. From the OECD web site. <https://www.oecd.org/els/health-systems/Health-Policy-in-Switzerland-July-2017.pdf>. Accessed December 20, 2020.
37. Birkmeyer JD, Sharp SM, Finlayson SR, Fisher ES, Wennberg JE. Variation profiles of common surgical procedures. *Surgery*. 1998; 124:917–23. PMID: 9823407
38. Wennberg JE, Mulley AG Jr., Hanley D, Timothy RP, Fowler FJ Jr., Roos NP, et al. An assessment of prostatectomy for benign urinary tract obstruction. Geographic variations and the evaluation of medical care outcomes. *JAMA*. 1988; 259:3027–30. PMID: 2452906
39. Fowler FJ Jr., Wennberg JE, Timothy RP, Barry MJ, Mulley AG Jr., Hanley D. Symptom status and quality of life following prostatectomy. *JAMA*. 1988; 259:3018–22. PMID: 2452905
40. From the Dartmouth Institute web site. [https://www.dartmouthatlas.org/downloads/reports/Decision\\_making\\_report\\_022411.pdf](https://www.dartmouthatlas.org/downloads/reports/Decision_making_report_022411.pdf). Accessed December 20, 2020.
41. Sosnowski R, De Nunzio C, Ahyai S, Autorino R, Bachmann A, Briganti A, et al. Surgical management of benign prostatic obstruction: current practice patterns and attitudes in Europe. *Neurourol Urodyn*. 2015; 34:395–6. <https://doi.org/10.1002/nau.22727> PMID: 25620532
42. de la Rosette JJ, Alivizatos G, Madersbacher S, Perachino M, Thomas D, Desgrandchamps F, et al. EAU Guidelines on benign prostatic hyperplasia (BPH). *Eur Urol*. 2001; 40:256–63; discussion 64. <https://doi.org/10.1159/000049784> PMID: 11684840
43. AUA guideline on management of benign prostatic hyperplasia (2003). Chapter 1: Diagnosis and treatment recommendations. *J Urol*. 2003; 170:530–47. <https://doi.org/10.1097/01.ju.0000078083.38675.79> PMID: 12853821
44. Hood HM, Burgess PA, Holtgrewe HL, Fleming B, Mebust W, Connolly RP. Adherence to Agency for Health Care Policy and Research guidelines for benign prostatic hyperplasia. *J Urol*. 1997; 158:1417–21. PMID: 9302134
45. Auffenberg GB, Gonzalez CM, Wolf JS Jr., Clemens JQ, Meeks W, McVary KT. An observational analysis of provider adherence to AUA guidelines on the management of benign prostatic hyperplasia. *J Urol*. 2014; 192:1483–8. <https://doi.org/10.1016/j.juro.2014.06.016> PMID: 24931806
46. Rahman F, Putra IB, Mochtar CA, Rasyid N. Adherence of Indonesian urologists to practice guidelines for the management of benign prostatic hyperplasia. *Prostate Int*. 2019; 7:35–40. <https://doi.org/10.1016/j.prii.2018.01.003> PMID: 30937297
47. Stroe SA, Elliott SP, Saigal CS, Smith A, Wilt TJ, Wei JT, et al. Urologist compliance with AUA best practice guidelines for benign prostatic hyperplasia in Medicare population. *Urology*. 2011; 78:3–9. <https://doi.org/10.1016/j.urology.2010.12.087> PMID: 21601254
48. Collins MM, Barry MJ, Bin L, Roberts RG, Oesterling JE, Fowler FJ. Diagnosis and treatment of benign prostatic hyperplasia. Practice patterns of primary care physicians. *J Gen Intern Med*. 1997; 12:224–9. <https://doi.org/10.1046/j.1525-1497.1997.012004224.x> PMID: 9127226
49. Giona S, Ganguly I, Muir G. Urologists' attitudes to sexual complications of LUTS/BPH treatments. *World J Urol*. 2018; 36:1449–53. <https://doi.org/10.1007/s00345-018-2283-x> PMID: 29680951

50. Strobe SA, Wei JT, Smith A, Wilt TJ, Saigal CS, Elliott SP, et al. Evaluative care guideline compliance is associated with provision of benign prostatic hyperplasia surgery. *Urology*. 2012; 80:84–9. <https://doi.org/10.1016/j.urology.2012.03.011> PMID: 22608799
51. Barry MJ, Fowler FJ Jr., Mulley AG Jr., Henderson JV Jr., Wennberg JE. Patient reactions to a program designed to facilitate patient participation in treatment decisions for benign prostatic hyperplasia. *Med Care*. 1995; 33:771–82. <https://doi.org/10.1097/00005650-199508000-00003> PMID: 7543639
52. Barry MJ, Cherkin DC, Chang Y, Fowler FJ, Skates S. A randomized trial of a multimedia shared decision-making program for men facing a treatment decision for benign prostatic hyperplasia. *Disease Management and Clinical Outcomes*. 1997; 1:5–14.
53. Piercy GB, Deber R, Trachtenberg J, Ramsey EW, Norman RW, Goldenberg SL, et al. Impact of a shared decision-making program on patients with benign prostatic hyperplasia. *Urology*. 1999; 53:913–20. [https://doi.org/10.1016/s0090-4295\(99\)00051-5](https://doi.org/10.1016/s0090-4295(99)00051-5) PMID: 10223483
54. van der Wijden FC, de Angst IB, Lamers RED, Cuypers M, de Vries M, van Melick HHE, et al. Effectiveness of a web-based treatment decision aid for men with lower urinary tract symptoms due to benign prostatic hyperplasia. *BJU Int*. 2019; 124:124–33. <https://doi.org/10.1111/bju.14646> PMID: 30589205
55. Scheuter C, Wertli MM, Haynes AG, Panczak R, Chiolerio A, Perrier A, et al. Unwarranted regional variation in vertebroplasty and kyphoplasty in Switzerland: A population-based small area variation analysis. *PLoS One*. 2018; 13:e0208578. <https://doi.org/10.1371/journal.pone.0208578> PMID: 30532141
56. Wertli MM, Schlapbach JM, Haynes AG, Scheuter C, Jegerlehner SN, Panczak R, et al. Regional variation in hip and knee arthroplasty rates in Switzerland: A population-based small area analysis. *PLoS One*. 2020; 15:e0238287. <https://doi.org/10.1371/journal.pone.0238287> PMID: 32956363
57. Robinson WS. Ecological correlations and the behavior of individuals. *Int J Epidemiol*. 2009; 38:337–41. <https://doi.org/10.1093/ije/dyn357> PMID: 19179346