STABILITY OF JACKKNIFE VARIANCE ESTIMATES FOR PRESCRIPTION COUNT ESTIMATES OVER TIME INTERVALS

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Abstract

In order to obtain variance estimates for product specific point estimates of retail filled prescription (Rx) counts at the national, territory, and precriber level, a jackknife methodology is utilized. The sample data used for jackknife variance estimates are for over 3,000 products obtained from roughly 70 data suppliers representing approximately 35,000 retail pharmacies. Because variance estimates are required for multiple time intervals (weekly, monthly, and quarterly), 14 weeks of data will be used. These 14 weeks allow for the unique opportunity to test stability of the variance estimates among product specific Rx counts over the time period. The Rx counts for the products will have varying trends over the time period. The relationship of the size and trends of the Rx counts to the stability of variance estimates will be explored.

Keywords: Jackknife, survey methodology, variance estimation

1. Overview

IMS Health produces estimates of prescription (Rx) activity at national and subnational level on a weekly and monthly basis for thousands of pharmaceutical products. These estimates are derived from information obtained from a sample of pharmacies nationwide. Clients seek guidance on the uncertainty in the estimates due to the sample and estimation methodology.

Variances for product specific point estimates of national retail filled prescription (Rx) counts in the U.S. are estimated using a jackknife procedure. The variance estimates will be used in modeling generalized variance functions (GVFs), as discussed in Copeland, et al (2006). The GVFs in turn will be used by data users in calculating confidence intervals for the Rx count estimates. This paper explores the stability and variance of these jackknife variance estimates. Attributes of a product that could impact the stability or variance will also be considered.

2. Description of Data Source, Estimation Methodology

IMS obtains prescription information on a weekly basis from roughly over 35,000 retail pharmacies nationwide. This sample represents approximately 67% of retail pharmacies and 73% of retail prescription volume, and is geographically spread throughout the U.S. The reporting week is Saturday through Friday. Prescription information provided to IMS is that recorded within pharmacy software systems as part of regular prescription management conducted by pharmacies. Thus, there is an incentive for complete and accurate reporting by pharmacies.

The sample pharmacies are clustered by supplier. If a supplier is in sample then all pharmacies for that supplier are in sample; if supplier X has n pharmacies then all n pharmacies would either be in or out of sample. Pharmacies are geographically spread throughout the U.S. If a pharmacy is included in the sample then all Rx dispensed at that pharmacy are included in the sample. Each prescription contains various information about the Rx, such as date, NDC, quantity, price, prescriber, and method of payment (including cash, Medicaid, Medicare, or third-party). Approximately 50 million scripts are reported weekly.

The estimation methodology combines stratified ratio estimation with geo-spatial estimation. The approach estimates Rx activity within individual nonsample pharmacies, with weights applied to nearby sample pharmacies based upon the relative product volume and inversely proportional to the distance between sample pharmacies and the nonsample pharmacy. The methodology yields prescriber level estimated prescription volume at the product/form/strength level, which can be summed to any geographic level from zip code to national level. Estimates from the sample are reported on a weekly basis, 10 days following the week of interest.

3. Overview of Variance Estimation

In order to model the GVF, jackknife variance estimates were calculated for over 3,000 products. In order to create the jackknife replications, each of the 68 suppliers are treated as sampling units. For each replicate, a different supplier was removed from the sample and the estimation methodology was then used to create point estimates of Rx counts for the full population using the remaining sample. The jackknife variance was then calculated from these 68 replicates for all products for each of five weeks using the jackknife variance estimator (Wolter, 1985):

$$V_{J-K}\left(\hat{Y}\right) = \frac{(K-1)}{K}\sum_{k}\left(\hat{Y}_{(k)} - \hat{Y}_{(.)}\right)^2$$

where

$\hat{Y}_{(k)}$ = estimate obtained when the k[th] supplier is removed from the sample

K = number of replicates (=number of suppliers)

$$\hat{Y}_{(.)} = \frac{1}{K}\sum_{k}\hat{Y}_{(k)}$$

4. Overview of the Stability or Variance of the Jackknife Variance Estimation

The jackknife variance estimator itself is subject to variability. This variability can be expressed as a function of the fourth moment:

$$Var\left(\text{var}_{J-K}\left(\hat{Y}\right)\right) = n^2 o^4\left(\frac{(\beta-3)}{n} + \frac{2}{(n-1)}\right)$$

where

$$E\left(y_i - \frac{Y}{n}\right)^4 = \beta o^4$$

This formulation does not lend itself to calculation; therefore, two alternative formulations will be use to estimate the variance of the jackknife variance estimates.

First an empirical variance estimate will be considered. The empirical variance estimate is calculated as the variance of the five weeks of jackknife variance estimate. The formula is seen below. The relative variance is used to account for changes in Rx volume from week to week.

$$V_E\left(\text{RelVar}_{J-K}\left(\hat{Y}\right)\right) = \frac{1}{W}\sum_{W}\left(\text{RelVar}_{J-K,w}\left(\hat{Y}\right) - \frac{\sum_{W}\text{RelVar}_{J-K,w}\left(\hat{Y}\right)}{W}\right)^2$$

where

$\text{RelVar}_{J-K,w}\left(\hat{Y}\right)$ = JK variance estimate for week w

W = number of weeks (=5)

The formulation is a simulated variance estimate derived as a bootstrap variance estimate of the jackknife variance estimate for each week. To calculate the bootstrap variance estimate, 1,000 different samples of size 68 were selected with replacement from the 68 jackknife variance replicates. The simulated variance estimated is then calculated using the bootstrap variance estimator (Efron, 1979).

$$V_B\left(\text{var}_{J-K}\left(\hat{Y}\right)\right) = \frac{1}{B}\sum_{B}\left(\left(\frac{(K-1)}{K}\sum_{k}\left(\hat{Y}_{(k)} - \hat{Y}_{(.)}\right)^2\right)_b - V_{J-K}\left(\hat{Y}\right)_{(.)}\right)^2$$

where

$$V_{J-K}\left(\hat{Y}\right)_{(.)} = \frac{1}{B}\sum_{B}\left(\frac{(K-1)}{K}\sum_{k}\left(\hat{Y}_{(k)} - \hat{Y}_{(.)}\right)^2\right)_b$$

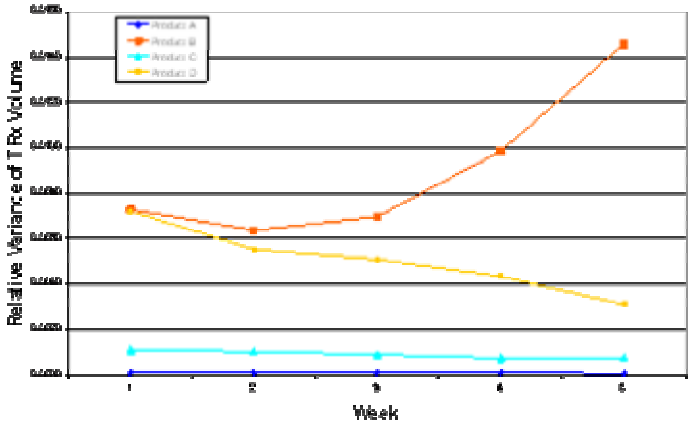
B = number of bootstrap samples (=1,000)

Average coefficient of variations (CVs) across the five weeks of bootstrap variance estimates for the jackknife variance estimates were used to evaluate the magnitude of the jackknife variance estimates.

5. Empirical National Level Stability

For 92% of the products the national variance estimates were stable over the five weeks. This was assessed using an ordinary least square linear model of Relative Variance $=B_0 + B_1(\text{week})$. If $B_1 \neq 0$ then the product's variance was considered to be unstable across the five weeks. Figure 1 illustrates the weekly profiles for four products' relative variances.

Figure 1: Stability of Relative Variance over 5 Weeks for 4 Select Products



To determine whether this instability is related to any specific attribute of the product, the CV over the five weeks of data is considered. The mean CV over all products is 42% and the median CV is 36%. These results suggest that there is a relatively large variability associated with the jackknife variance estimates. The distribution is skewed to the right, with some products having much larger CVs that influence the mean.

Attributes of the product that were considered are brand status, specialty status, sample coverage, and Rx volume. The distributions of the CV's associated with the empirical variance estimates for these attributes are seen in Table 1. These results suggest the variance estimates for branded products and products with large Rx volume tend to have smaller relative variances.

Table 1: Coefficient of Variation for the Simulated Variance, by Product Attributes

	N	Mean	StD	Q1	Median	Q3
All	3262	42.0%	26.9%	23.3%	36.0%	53.7%
Generic	2207	46.1%	28.1%	28.6%	39.5%	59.0%
Brand	1055	33.4%	21.7%	17.5%	28.5%	43.0%
Non-Specialty	3117	42.0%	27.0%	23.2%	36.0%	53.8%
Specialty	145	42.1%	23.2%	28.3%	37.6%	50.3%
Coverage						
>=75%	2066	41.1%	26.6%	22.3%	35.6%	53.2%
(75%,50%]	1175	43.6%	27.4%	24.5%	38.9%	54.3%
<50%	21	36.5%	20.2%	25.5%	29.3%	39.2%
TRx Volume						
>=1m	72	34.1%	27.1%	16.9%	25.9%	38.9%
(1m,10k]	385	29.8%	21.0%	14.7%	24.6%	38.6%
(10k,1k]	962	49.4%	33.9%	23.4%	39.3%	69.4%
(1k,500]	1843	41.0%	22.2%	25.6%	36.9%	51.3%

6. Simulated National Level Stability

The simulated variance is used to estimate the magnitude of the variance of the variance. The magnitude is expressed as the CV of the bootstrap estimate. The mean of this CV over all products is 50% and the median is 48%. The simulated variances are larger then the empirical variance estimates. They also have a normal distribution, with a relatively close mean and median. Figure 2 graphs simulated variance for each week for the same four products as were displayed in Figure 1.

Similar to the empirical variance estimates, the average CV's for the Bootstrap variance estimates is considered, relative to the same attributes: brand status, specialty status, sample coverage, and Rx volume. Table 2 shows the CV distribution over these product attributes. These results suggest the variance estimates for products with large Rx volume tend to have smaller relative variances, while brand products do not tend to have smaller relative variances, as was the case for the empirical variance estimates.

Figure 2: Stability of CV over 5 Weeks for 4 Select Products

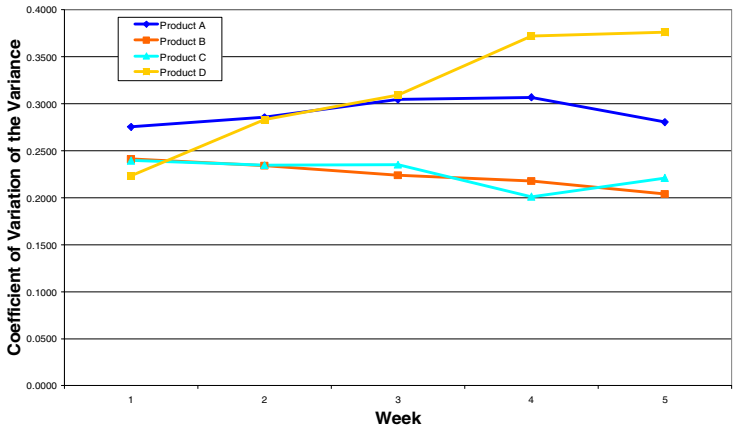


Table 2: Coefficient of Variation for the Bootstrap Variance Estimates, by Product Estimates

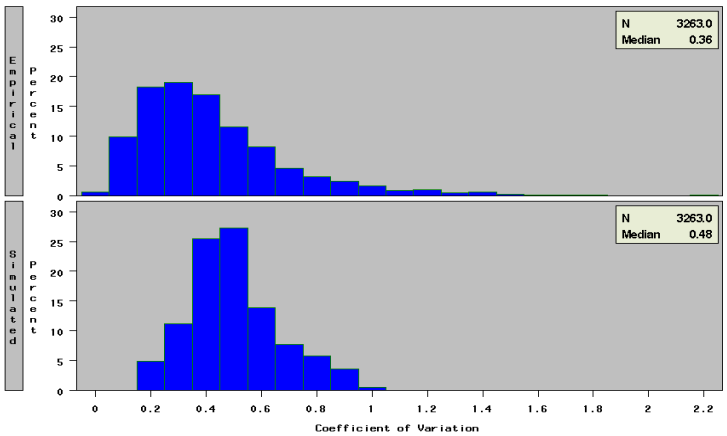
	N	Mean	StD	Q1	Median	Q3
All	3262	50.1%	16.3%	39.3%	47.6%	58.5%
Generic	2207	50.0%	16.2%	39.5%	47.8%	58.0%
Brand	1055	50.4%	16.5%	38.6%	47.0%	60.2%
Non-Specialty	3117	50.2%	16.4%	39.2%	47.6%	58.6%
Specialty	145	49.3%	13.8%	40.3%	47.5%	57.4%
Coverage						
>=75%	2066	50.2%	17.1%	38.7%	47.8%	60.1%
(75%,50%]	1175	49.9%	14.7%	40.0%	47.4%	57.0%
<50%	21	53.5%	20.0%	38.0%	45.9%	62.8%
TRx Volume						
>=1m	72	38.7%	18.2%	25.2%	32.9%	49.7%
(1m,10k]	385	42.0%	18.2%	27.1%	38.5%	51.7%
(10k,1k]	962	49.7%	15.2%	40.0%	47.2%	56.7%
(1k,500]	1843	52.5%	15.6%	41.6%	49.2%	60.8%

7. Summary

This research showed that for most products the jackknife variance estimates are stable over the observed weeks, and that products with higher Rx volume tend to have smaller relative variance associated with their jackknife variance estimates. The branded products also had a smaller empirical variance associated with their jackknife variance estimates, although this did not hold true for the simulated variances.

The simulated variances estimates detected a somewhat higher magnitude of variance then the empirical variance estimates. This may be due to the limited number of samples used in the empirical variance estimates. But even with the difference in magnitude the empirical variance is a good proxy for the simulated variance estimates. The histograms of the distributions comparing the estimated and simulated variances are in Figure 3. The increased spread of the empirical variance estimates as well as the higher magnitude of the simulated variance estimates is evident in the histograms.

Figure 3: Distribution of the Empirical and Simulated Variance Estimates



GVF models for the variance of the Rx count estimates will be developed, thus providing stability that would not be present from individual point estimates of the variance of the Rx count estimates. See Copeland, et al (2006), for a discussion of the derivation of the GVFs for the variance of the Rx count estimates.

8. Future Research

The first next steps for this research are to rerun the analysis when more weeks of empirical data are available. This may help to understand the difference in magnitude between the empirical and simulated variance estimate results. Another research avenue is to further investigate the relationship between Rx volume and the magnitude of the variance estimates. Finally another next step is to explore these results using sub-national variance estimates.

References

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