

# The economics of counterfeit Avastin: a geospatial and statistical analysis of demographic correlates to FDA warning letters

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## ABSTRACT

**Purpose** In 2012, the Food and Drug Administration (FDA) sent warning notices to clinics and medical practitioners that may have purchased or administered counterfeit versions of the angiogenesis cancer drug Avastin Genentech, South San Francisco, California, USA. The purpose of this study was to explore potential differences in demographic, economic, and healthcare coverage characteristics between areas that received these counterfeit warning notices and those that did not receive notices. The aims of this study are to improve future counterfeit drug surveillance and better assess potential risk factors associated with counterfeit cancer drugs.

**Methods** Addresses for warning notices sent to healthcare practitioners were obtained from the FDA and then geocoded using ARCGIS. Variables chosen for statistical and geospatial analyses were then identified and assessed based on their potential association with Avastin access and affordability. These variables included demographic and economic factors (percent below the poverty line, percent uninsured, and median household income) and healthcare coverage data (percent Medicare enrollees) available from the US Center for Medicare and Medicaid Services. All variables were analyzed at the US county level.

**Results** Our analysis uncovered 401 distinct US counties where the FDA sent at least one counterfeit Avastin warning notice. A hot spot analysis of notices and variables was carried out using ARCGIS software to identify and visualize risk features with high and low values of clustering. In a multiple logistic regression model reassessing visually observed geospatial associations, the receipt of a notice was not significantly associated with percent uninsured ( $p = 0.3121$ ), but was significantly associated with percent Medicare enrollees (OR = 0.874 per 10% increase;  $p = 0.0121$ ), individuals below federal poverty line (OR = 2.990 per 10% increase;  $p < 0.0001$ ), and median household income (OR = 2.698 per \$10 000 increase;  $p < 0.0001$ ).

**Conclusions** Our study found that county-level economic and demographic factors are potentially associated with counterfeit Avastin warning receipt after controlling for the total number of people residing in each county. These geographic associations indicate that individuals in counties where patients have greater ability to afford more expensive treatment, and consequently where providers can seek higher reimbursement, may have been at higher risk to counterfeit Avastin exposure. These findings can help inform future efforts to improve drug safety surveillance and more proactively identify patients at the highest risk for counterfeit cancer drugs. Copyright © 2015 John Wiley & Sons, Ltd.

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## INTRODUCTION

### Background

The US Food and Drug Administration's (FDA) recent 2012 detection of counterfeit versions of the popular anti-cancer medication Avastin (International Nonproprietary Name *bevacizumab*) in US medical clinics raises several serious patient safety and public health concerns.<sup>1,2</sup> Many of these concerns focus on

pharmaceutical security and the need to institute mechanisms to prevent reoccurrences of counterfeit medications from penetrating into the US drug supply chain and subsequently harming patients.<sup>3–6</sup> However, developing solutions to address this failure in drug safety would also benefit from a better understanding of the economic aspects of Avastin access and how these factors may be associated with unique demographic characteristics of areas and populations in the USA that may have been exposed to counterfeit Avastin.<sup>7,8</sup> This requires that several distinct issues be considered,

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including the financing of oncology drugs in the US healthcare system, treatment modalities of Avastin, cost and reimbursement of Avastin, and demographic characteristics of patient populations likely to need this expensive form of cancer treatment.

From 2012 to 2013, warning notices from the FDA were sent to several healthcare providers who were suspected of having ordered and possibly administered counterfeit versions of Avastin that contained no active pharmaceutical ingredient thus rendering them completely ineffective.<sup>9</sup> Based on a review of criminal prosecutions pursued by the US Department of Justice that followed, court documents reveal a clear and predominant motive for criminals involved in counterfeit Avastin sourcing: lower cost. In fact, counterfeit versions of Avastin marketed by those prosecuted were offered at significantly lower prices than authentic versions. Hence, the opportunity for unscrupulous distributors, clinics, staff, and physicians to all profit from distributing, purchasing, and billing for counterfeit Avastin is likely the primary motivation for those implicated and has led to criminal restitution penalties in the millions of dollars.<sup>9,10</sup> Therefore, examining demographic and economic characteristics that can impact the price, accessibility, and affordability of Avastin is necessary to better understand what populations may have been at the highest risk for this economically driven form of pharmaceutical crime.

In order to evaluate the potential relationship between counterfeit Avastin receipt and economic risk factors, we will first evaluate the specific financing and reimbursement mechanisms for Avastin, thereby informing us about variables that should be geospatially and statistically assessed. Using these identified economic and demographic variables, we will then conduct geospatial and statistical analyses in order to identify associated patterns among areas that received an FDA warning notice versus those that did not receive a notice. After these assessments are made to determine any potential significant relationships between counterfeit Avastin warning notice distribution and demographic/economic characteristics, areas with high-risk attributes can be identified and more closely monitored in post-market surveillance activities. Further, more robust surveillance and detection can be initiated in the event of a future counterfeit cancer drug incident to allow for more effective protection of cancer patients.

### *Economics of Avastin*

Avastin is an expensive medication in an injectable class of anti-cancer drugs called angiogenesis

inhibitors, which is used in combination with chemotherapy.<sup>11,12</sup> When malignant tumors grow, so do their demand for oxygen and nutrients. To facilitate this increased demand, they release higher quantities of a protein called vascular endothelial growth factor, which stimulates the growth of new blood vessels.<sup>13</sup> Avastin works by binding to this protein and consequently inhibiting or delaying tumor growth. In 2004, when Avastin was originally approved by the FDA for the treatment of colorectal cancer, it became the first commercially available angiogenesis inhibitor.<sup>14</sup> Avastin later became approved in the USA for treatment of glioblastoma, breast cancer (approval later withdrawn), cervical cancer, kidney cancer, and lung cancer.<sup>15</sup>

Treatment with Avastin varies by type of cancer. Typical dosages range from 5 to 15 mg/kg every 2–3 weeks.<sup>16</sup> For example, treatment of glioblastoma requires an injection of 10 mg/kg every 2 weeks. For a 70-kg person, 1 year of Avastin treatment is equivalent to 18 200 mg. Providers often order Avastin in 400 mg (16 ml) vials.<sup>17</sup> Although there is variation, a reasonable estimate would be approximately \$2300 for the price of each 400 mg vial in the USA.<sup>18</sup> Therefore, the price for a provider to acquire 1 year's worth of Avastin treatment for a 70-kg person can be estimated at around \$104 000.

The cancers usually treated with Avastin disproportionately affect the elderly.<sup>19,20</sup> In the USA, this population almost always receives health insurance coverage from the federal government through the Medicare program, which is generally open to individuals aged 65 years and older. As Avastin would typically be given as part of outpatient care, it would usually be billed to Medicare Part B.<sup>21</sup> While Medicare Advantage (also known as Medicare+Choice or Medicare Part C) plans can complicate reimbursement coverage, Medicare Part B works by reimbursing a Medicare-approved amount (also known as the "assignment" or the "allowance"), 80% of which is paid by the Center for Medicare and Medicaid Services (CMS) with the remaining 20% being paid as coinsurance by the beneficiary/patient.<sup>22</sup> While the enrollee can buy additional private "Medigap" insurance to cover this price gap, 2007 data show that only 17% of those with Medicare had bought this additional insurance.<sup>23</sup> In situations where a patient is unable to pay his or her share of the cost for Avastin, providers may consider this unreimbursed care (also known as "charity care") at their discretion.<sup>24</sup> In this situation, the provider is likely to lose money, as 80% of the Medicare-approved amount is likely less than the price that the provider paid to source the drug.

While Medicare is probably the most important source of reimbursement for Avastin treatment in the USA, it is worthwhile to note that the Medicaid program (state-managed program for families and individuals with low incomes) may also cover Avastin treatment in certain states, although with certain limitations. North Carolina, for example, stopped covering Avastin treatment in 2012 for breast carcinoma.<sup>25</sup> For those states that do reimburse Avastin, each state has its own policy, with some following Medicare Part B's policy. Because Medicaid is predominantly the health insurance for those below the poverty line, it is easy to imagine scenarios where beneficiaries would be unable to meet a coinsurance payment.

For those who are neither poor nor elderly, a large proportion of those that receive health insurance do so through their employer and employer-based private insurance programs.<sup>26</sup> The number of individual health insurance plans in the USA is virtually innumerable, with each plan having its own policy for reimbursement of Avastin, although many may also follow reimbursement guidelines set forth by Medicare. Although deductibles and premiums may be markedly higher than those for Medicare, private health insurance plans may come with certain policies that allow for more comprehensive coverage, such as maximum out-of-pocket expenditures or coinsurance applicable to in-network provider fees (as opposed to Medicare's coinsurance only for Medicare-approved rates). Conversely, for the estimated 48 million people uninsured in the USA, it is likely that they do not have access to Avastin treatment.

## METHODS

Based on the economic, healthcare coverage, and reimbursement characteristics of Avastin discussed earlier, we have identified four variables of interest that could impact the ability of criminal actors to profit from the distribution and administration of counterfeit Avastin. These include the percent of Medicare enrollee population in a county (for assessing availability of Medicare-based reimbursement), the percent of the population who are living below the federal poverty line (for assessing availability of Medicaid-based reimbursement and ability to meet coinsurance payments), the percent of the uninsured population (for assessing barriers to healthcare services), and median household income of individual living in a county (for assessing ability to access and afford expensive treatments such as Avastin). These independent variables can be used to visualize geospatial associations and determine the odds ratio (e.g., the odds that a

county receives a notice given the variable of interest) of an area having been sent a counterfeit warning versus those that did not receive a notice. Areas where counterfeiting can occur could be thought to have a systemic problem where these conditions allow for healthcare providers to profit from counterfeiting.

Data to assess these associations were drawn from two sources. Geographic data on counterfeit Avastin warning notices sent by the FDA that were obtained directly from the FDA's website and then geocoded by the address of the letter recipient to specific zip codes and then joined to US counties using ARCGIS v10.3.<sup>27</sup> These addresses are derived from two separate waves of Avastin warning letter distributions to clinics and individual healthcare practitioners, first in 2012 and then in 2013.

Spatial data are frequently characterized by positive spatial autocorrelation, or the tendency for areas that are near each other in space to share similar attributes. We used Moran's I statistic to test for evidence of spatial autocorrelation in residuals from ordinary least squares regression models and did find them to have a positive spatial autocorrelation ( $p > 0.05$ ). We then conducted a hot spot analysis in ARCGIS that calculates the *Getis-Ord Gi* statistic for each variable and visualized the clustering of high (hot spot) and low (cold spot) features overlaid with individual points of counterfeit notices. This tool is a local statistic of spatial autocorrelation that identifies clusters of high/low values for each county.<sup>21</sup> A high value for the *Gi* statistic indicates high values (i.e., higher than the mean) that tend to be close to one another, while a low value indicates values lower than the mean and tend to be found together. The geospatial and statistical analyses were conducted using ARCGIS 10.3 (Esri: Redlands, CA).

Following geospatial analysis, we then conducted statistical analysis using SPSS 20 (IBM: Armonk, NY) to further explore associations observed between variables of interest. This was accomplished by calculating the odds ratio of counterfeit notice receipt in a multiple binary logistic regression model, with the four independent variables that we identified that have the potential to impact Avastin access and affordability.<sup>28</sup> Data for three of these variables were collected from the US Census Bureau for the year 2013: median household income, percent below the federal poverty line, and percent without healthcare insurance. The fourth variable, Medicare enrollees (2013), was collected directly from CMS. Total county-level population in 2012, using data from the US Census Bureau, was then used to convert count data for Medicare

enrollees to percent of the total county population. All variables were available at the county level and were entered non-sequentially so that odds ratios are controlled for the effect of other independent variables. Avastin warning notice receipt was coded as dichotomous at the county level, whereby a county had either received a notice or had not received a notice.

## RESULTS

In total, FDA Avastin warning notices from 2012 to 2013 comprised addresses for 932 distinct healthcare practitioners/clinics, corresponding to 401 distinct US counties where notices were sent. Figure 1 displays a national US map, where a dot is placed on each zip code where a warning notice was sent ( $n=791$  zip codes) by the FDA to office addresses for healthcare practitioners and clinics. County-level boundaries were added to the map in order to allow for helpful visual supplement to statistical analyses, all of which were carried out at the county level.

Figure 2 displays the hot spot analysis of counterfeit warning notices by county at the 99%, 95%, and 90% confidence interval. Based on these visualizations, it is clear that certain areas of the USA, primarily the southwest (California and Arizona), northeast (New York), Florida, and parts of the mid-west, received the most counterfeit Avastin warning notices and may have been at heightened risk of exposure. When conducting our hot spot analysis we found that when looking at the variables individually, income, poverty, and insurance status all had significant associations

with counterfeit warning notices (Figures 3–5). In the southern region of the USA, there was a positive association with low income, low insurance coverage, and high poverty and counterfeit warnings. The only significant hot spot for Medicare enrollees was found to be in the Hawaiian Islands. The Moran's I test for spatial autocorrelation showed a statistically significant rate of clustering for counterfeit warnings (index=0.043 and  $z=27.90$ ).

In our multivariable logistic regression model, we found three statistically significant relationships with independent variables. Specifically, the odds of a counterfeit warning receipt were 2.698 times higher per \$10 000 increase in county median household income ( $p<0.0001$ ), 0.874 times lower per 10% increase in Medicare enrollees ( $p=0.0121$ ), and 2.990 times higher per 10% increase in impoverished population ( $p<0.0001$ ). While not significant ( $p=0.3121$ ), odds of counterfeit warning in this regression model were 1.124 times higher per 10% increase in uninsured population.

Overall, these results indicate that counterfeit Avastin notices were more likely to be associated with US counties that had higher household incomes, lower percent of Medicare enrollees, and higher percent of impoverished individuals. Generally, these results support the possibility that counties with greater ability to pay higher rates of Avastin reimbursement (versus a lower reimbursement or higher coinsurance under Medicare as explained further later) may have been at higher risk to receive a counterfeit Avastin warning notice.

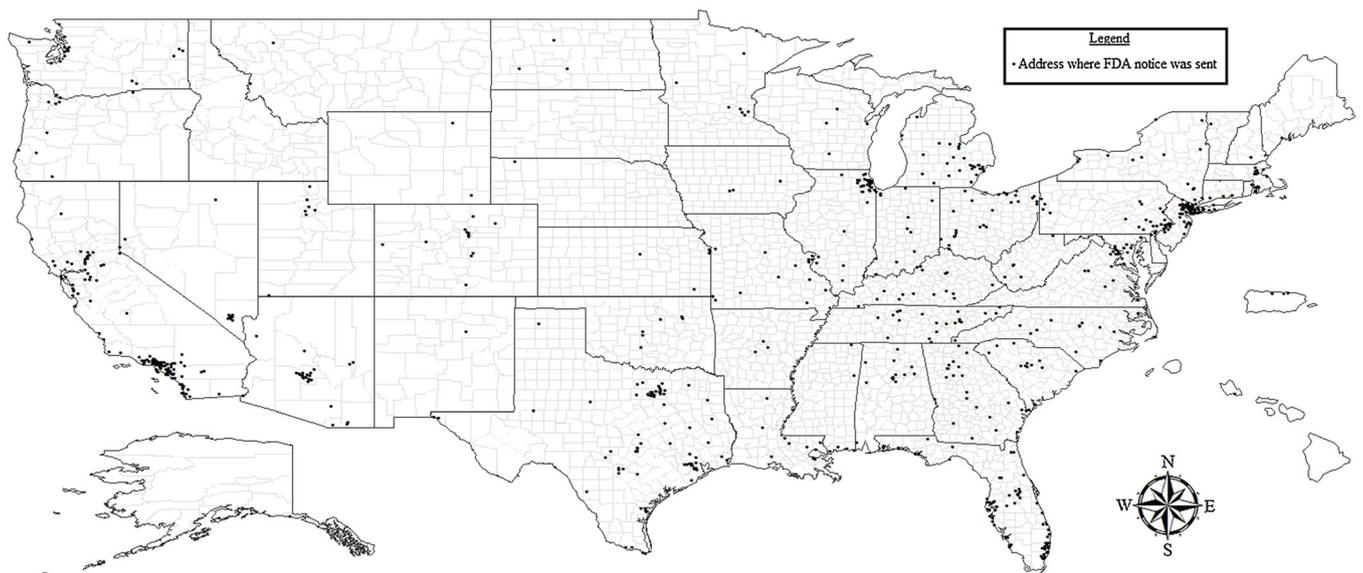


Figure 1. Locations where counterfeit Avastin warning notices were received

THE ECONOMICS OF COUNTERFEIT AVASTIN  
Counterfeit Drug Detection by County

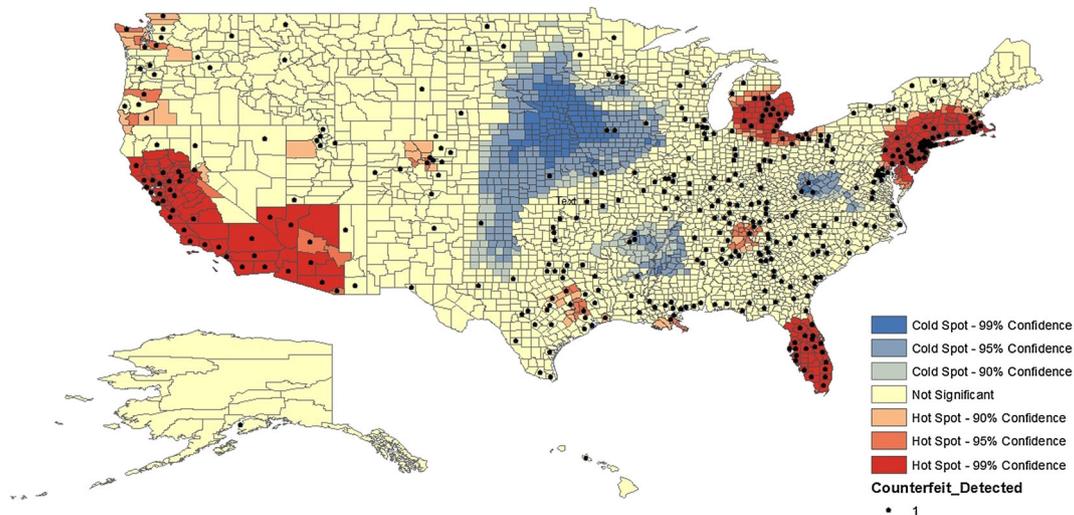


Figure 2. County-level hotspot analysis of Avastin warning notice distribution

Counterfeit Drug Detected and Median Household Income

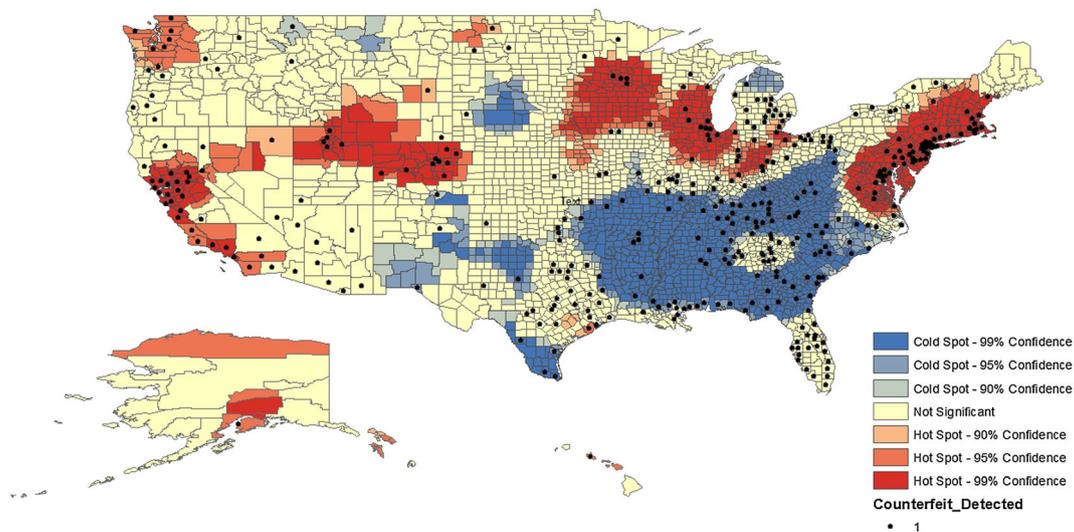


Figure 3. County-level hotspot analysis of median household income, overlaid upon counterfeit warning notice hotspots

DISCUSSION

Given the high cost of Avastin and variable coverage for cancer patients, there may be situations where providers are particularly cost-sensitive in their procurement of Avastin. A provider may therefore change his or her drug procurement and prescribing habits based on the capability of his or her patient population (and their insurance) to pay for Avastin. As a result, individuals more capable of accessing the high cost of Avastin may be more likely to be prescribed Avastin and therefore more

likely to receive a counterfeit version. Previous research has focused primarily on profit-motivated medical providers increasing their share of profits by lowering the cost of acquiring Avastin; this may indeed be justification enough for them to turn to an illegitimate distributor. However, as profit is derived from both revenue and cost, further study was required to assess the likelihood of potential counterfeit Avastin receipt based on economically associated demographic factors.

Specifically, in order to better understand the high profit that can be attained by providers who source

## Counterfeit Drug Detected and Percent of Population Below the Poverty Line

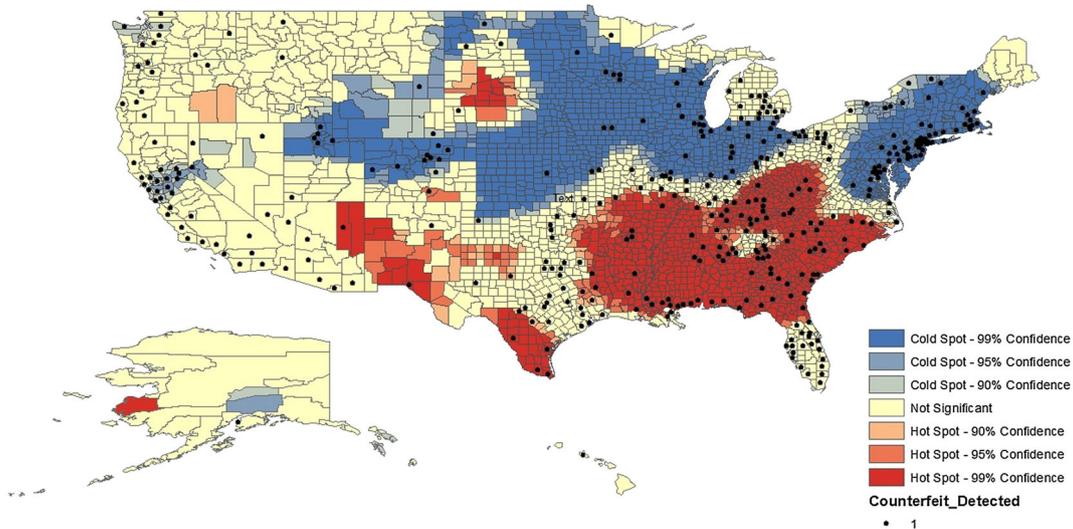


Figure 4. County-level hotspots analysis of percent below poverty line, overlaid upon counterfeit warning notice hotspots

## Counterfeit Detected and Percent of Population Uninsured

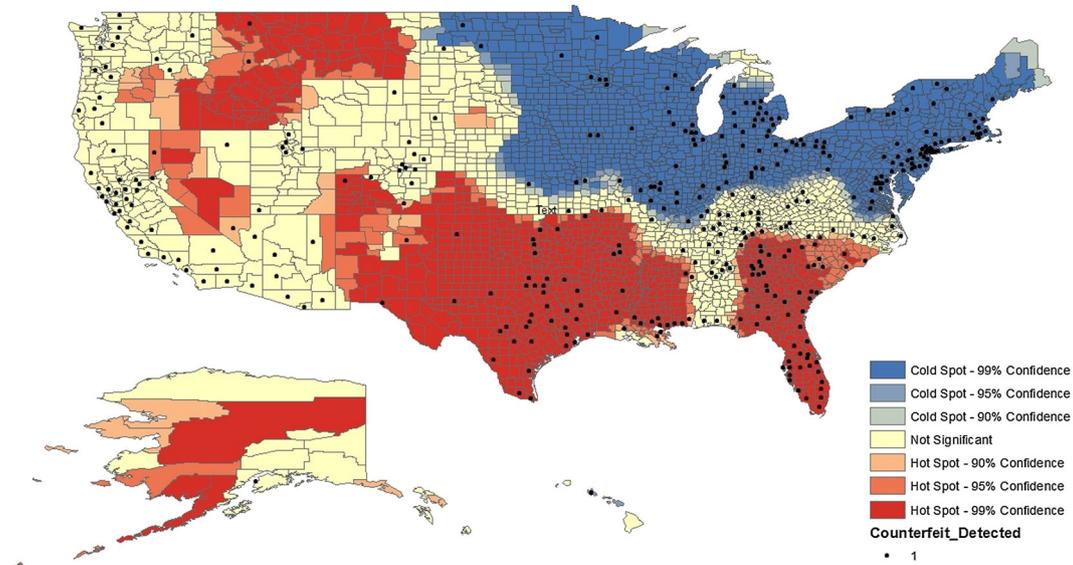


Figure 5. County-level hotspot analysis of percent population uninsured, overlaid upon counterfeit warning notice hotspots

counterfeit Avastin and bill for its high cost, it is useful to consider examples of Avastin reimbursement situations. The billing code for 10 mg of Avastin is 1 unit under billing code HCPCS J9035.<sup>29</sup> In 2008, the Medicare-approved amount for this billing code was \$57.46.<sup>30</sup> As previously discussed, the estimated yearly dose of 18 200 mg for treatment of glioblastoma would equate to a total cost of \$104 577 for Avastin (Appendix Table S1). In this scenario, CMS would pay \$83 662, and the beneficiary would pay the 20%

coinsurance of \$20 915. For patients with household incomes below \$75 000, Genentech also provides a patient assistance program that pays for all beneficiary charges after the patient has paid for 10 000 mg of Avastin.<sup>31</sup> The patient would then actually be charged \$11 492, while CMS pays \$83 662 and Genentech pays \$9423. Given the high cost of Avastin, the association observed in this study between counterfeit notices and Medicare-eligible populations may be partially explained. At a reimbursement rate of only

\$57.46 and high percent coinsurance from patient under Medicare, providers may have less opportunity to profit from Avastin, even if they seek to gain additional profits by acquiring lower-cost counterfeit versions.

In the more likely scenario that a provider charges \$70.00 per 10 mg of Avastin,<sup>32</sup> a higher amount than the Medicare-approved rate, CMS will still pay \$83 662, Genentech will still pay \$9423, but the patient now pays \$34 315. Assuming that the provider paid a reasonable estimate of about \$2300 per 400 mg vial of Avastin, the provider's cost of acquiring Avastin will be \$104 650 and his net profit would be \$22 823. If the patient is unable to pay his or her share (\$34 315) of the bill, then the provider has a net profit of -\$11,565. Given the high financial responsibility of the patient, the associations observed in this study between counterfeit notices with median household income and with poverty rate may also be partially explained.

It is also important to compare this scenario with one where a patient has a private plan, which would apply to insured persons under the age of 65 years. Therefore, imagining a 63-year-old glioblastoma patient with the Anthem Blue Cross plan<sup>33</sup> from Table 1, this patient would have a maximum out-of-pocket expense of \$6350. If the provider continues to bill at the same rate of \$70 per 10 mg Avastin, then the provider would make a profit over \$15 000 regardless of whether this privately insured individual is capable of paying his or her share (\$6450) of the cost.

These calculations help to explain why counties with high median household incomes and counties with high poverty rates are both more likely to receive counterfeit Avastin notices. When providers order discounted counterfeit Avastin, there is a larger difference between the cost of acquiring the counterfeit Avastin and the revenue from high billing of wealthier patients. For instance, if providers bill a patient under the privately insured example from Table 1, the provider would about double his or her annual profits if ordering Avastin at 20% discount. This represents a very high profit potential, which can represent extraordinary motivation to order discounted, potentially counterfeit medicine. Conversely, these calculations also show that providers in counties with high poverty rates ordering legitimate Avastin would be hard-pressed to find a patient mix that will allow them to financially break even. Table 1 illustrates several examples where the provider would lose over \$10 000 for every patient that is unable to pay coinsurance. These steep losses would be converted to profits if the provider was to obtain Avastin at 20% discount. This represents a very different (although also very powerful) motivator for ordering discounted, potentially counterfeit versions of Avastin.

This variation in cost-benefit may also act synergistically with the variation in perceived penalties among healthcare practitioners and their reimbursement coverage when dispensing counterfeit medicines. For counterfeit Avastin reimbursements billed to Medicare or Medicaid, CMS and the US Federal Government has a robust set of fraud and abuse laws and prevention

Table 1. Annual costs of annual Avastin regimen in the USA by select health insurance plans

Insurer	Anthem Blue Cross of California	Medicare*	Medicare
Plan name	Anthem Essential DirectAccess—cbno	Part B	Part B
Plan type	preferred provider organization	N/A	N/A
Provider billing rate <sup>†</sup>	\$70.00 per 10 mg	\$57.46 per 10 mg <sup>‡</sup>	\$70.00 per 10 mg
Bill for Avastin treatment <sup>¶</sup>	\$127 400	\$104 577	\$127 400
Coinsurance	20%	20%	20%
Maximum cost of Avastin for patient <sup>  </sup>	\$6350	\$11 494	\$11 494
Patient payment to provider	\$6350	\$11 494	\$34 315
Manufacturer payment to provider	\$0	\$9 423	\$9423
Payer payment to provider	\$121 132	\$83 662	\$83 662
Cost for provider**	\$104 650	\$104 650	\$104 650
Revenue for provider if patient pays	\$127 400	\$104 577	\$104 577
Profit for provider if patient pays	<b>\$22 750</b>	<b>-\$73</b>	<b>\$22 750</b>
Revenue for provider if patient does not pay	\$121 132	\$93 085	\$93 085
Profit for provider if patient does not pay	<b>\$16 482</b>	<b>-\$11 565</b>	<b>-\$11 565</b>

Numbers in bold indicate final profit for healthcare provider administering Avastin, for both patient payment scenarios.

\*Does not include Medicare Advantage Plans.

<sup>†</sup>In-network provider for Anthem plan.

<sup>‡</sup>Represents the Medicare-approved rate.

<sup>§</sup>For individuals with incomes under \$85 000.

<sup>¶</sup>Assuming one dose every 2 weeks at 10 mg/kg for a 70-kg person.

<sup>||</sup>Derived from Anthem maximum out-of-pocket payment or Genentech's 10 000 mg maximum.

\*\*Assumes acquisition cost of \$2300 per 400 mg vial from a legitimate distributor of Avastin.

programs (such as the False Claims Act, the Anti-kickback Statute) that encourages the pursuit of civil and criminal prosecution of providers defrauding the government through billing for and dispensing of counterfeit medicines. Conversely, providers who only bill private insurers for counterfeit Avastin are likely not subject to the same legal scrutiny as federal or state reimbursed providers. Although seeking reimbursement for fraudulent charges under private insurance reimbursement can lead to exclusion from future participation, federal fraud and abuse laws may not apply (although individual state Anti-kickback laws might be applicable) resulting in a perceived lower level of risk for private pay providers seeking to source counterfeit Avastin. The greater enforcement of fraudulent charges may partly explain the significant negative association that we found between percent Medicare enrollees and odds of receiving a counterfeit warning notice.

### *Limitations*

The primary limitation of this study is that the key outcome, county-level receipt of a counterfeit Avastin notice, is treated as an indicator that counterfeit Avastin was sent to a provider in that county. While these are the best data available, there has not been separate confirmation by FDA or law enforcement officials that counterfeit Avastin was actually validated as purchased and/or administered to patients, due in part to current limitations in drug safety surveillance. Furthermore, the independent variables used in this study, particularly those that serve as indicators of wealth and poverty, may not be comprehensive. Indeed, additional economic factors (such as cost of living in a county or overall healthcare coverage/access) might also explain the likelihood of receiving counterfeit medicines, and some variables examined may also confound with each other (e.g., areas with high percentage of Medicare-eligible individuals may report low rates of income but may nevertheless have a high concentration of wealth because of retirement savings that is not accurately reflected in the data). It should also be noted that results of this study may be limited in its generalizability to other counterfeit drug incidents and their associated populations at risk. For the purposes of this study, results may only be interpretable for expensive prescription physician-administered biologic cancer drugs with reimbursement characteristics similar to Avastin. Additionally, the relationships assessed in this study may correspond to underlying characteristics that describe an associated latent trait, such as degree of urbanization. These findings were

based on the distribution of warning notices across hundreds of US counties; they were likely strongly influenced by Tobler's first law of geography, given that we found evidence of autocorrelation. Further, this is a study involving statistical analysis to detect geospatial-economic associations, so these results may not be generalizable to individuals. Nevertheless, we believe that this type of limitation does not constrain the use of these findings to bolster future surveillance efforts for counterfeit cancer medications.

*Strengths.* This is the first study to use demographic and economic data in an attempt to explain potential associations regarding the risk of a cancer patient for potentially being exposed to a counterfeit cancer drug in the USA. Such a perspective may be critical in future considerations to better detect and prevent patient exposure to similar counterfeit drugs that impact similar patient populations, as financial incentives are a critical motivating factor for criminal providers and organizations, as implicated by the case study of counterfeit Avastin in the US drug supply chain.

### CONCLUSION

The results of this study, which examines the potential relationship between economic and demographic characteristics and the receipt of counterfeit Avastin warning notices from the FDA, indicate that medical professionals are more likely to order discounted and potentially counterfeit cancer medicine when their patient mix is either higher income or below the poverty line. Additionally, the study helps confirm a common observed theme in the public health crisis of the global counterfeit medicines trade: Criminals look for the most vulnerable, lowest-risk, and profitable areas in the healthcare system to target—this clearly includes high-cost cancer medications and commercial insurance-covered populations. Other characteristics that could potentially be associated with counterfeit drug exposure, such as sales volume of counterfeited drug, FDA recall notices, or areas with higher percentage of cancer patients, also should be examined in future studies attempting to identify additional counterfeit cancer drug risk factors. However, it is noteworthy in this study that significant associations were found between counterfeit warnings and population-standardized variables in our multiple regression model, thereby indicating that population-independent characteristics may represent a specific set of variables warranting further exploration. While

preliminary, this study provides the opportunity for more detailed analysis of domestic and global counterfeit drug events from a pharmacoeconomic perspective. This in turn can enable public health officials, clinicians, consumer/patient advocate groups, law enforcement, and policymakers to better design drug safety surveillance systems, identify potential patient populations at heightened risks, and enact future policies that discourage economic incentives that can be exploited by criminals and risk the lives of cancer patients.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## KEY POINTS

- We found that countries with higher proportions of Medicare enrollees had lower odds of receiving a counterfeit Avastin warning notice, while countries with higher median income and poverty rates had higher odds of being sent a notice.
- Geospatial tests suggest that poverty influences counterfeit Avastin receipt in Southern states, whereas high income levels influence counterfeit receipt in Northeast states and California.
- Our statistical analyses strongly suggest that the economic environment influences receipt of counterfeit cancer medication.

## ETHICS STATEMENT

The authors state that no ethical approval was needed.

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