CALIFORNIA SENATE BILL 1311

An Evaluation Proposal

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BACKGROUND

The benefits of antimicrobials are undeniable: since the discovery of penicillin in 1928,(“American Chemical Society International Historic Chemical Landmarks. Discovery and Development of Penicillin.,” 1999) antibiotics have been used for the treatment of life-threatening infections like Meningitis and Tuberculosis. The overuse and misuse of antibiotics however, have resulted in the development of antibiotic resistance. A recent report by the Centers for Diseases Control and Prevention showed that up to 50% of all antibiotics are either overprescribed or not optimally prescribed.(Centers for Disease Control and Prevention, 2013) The report estimated that at least 2 million people acquire serious infections with resistant bacteria and at least 23,000 people die as a direct result of these infections each year in the United States. The projected economic burden of antimicrobial resistance is as high as $20 billion in the United States.

Antimicrobial stewardship refers to promoting the optimal use of antimicrobials achieved through coordinated efforts in the healthcare setting.(“Infectious Diseases Society of America : Antimicrobial Stewardship,” 2011) The success of antimicrobial stewardship programs (ASPs) has been well documented.(Davey et al., 2017) Several studies that were compiled into a systematic review have shown that interventions through stewardship programs decrease the overall duration of antimicrobials prescribed (from 11 days to 9 days) and also improve appropriate antimicrobial prescribing (from 43% to 58%).

The importance of dedicated antimicrobial stewardship efforts within the healthcare setting have been recognized, leading to concerted national and statewide

efforts to promote the development of ASPs within every hospital. In 2014, the Centers for Disease Control and Prevention (CDC) issued the “Core Elements of Hospital Antibiotic Stewardship”.(“CDC. Core Elements of Hospital Antibiotic Stewardship Programs.,” 2014) The seven core elements include: 1) leadership commitment, 2) program accountability, 3) drug expertise, 4) systemic action, 5) tracking of antimicrobial use and resistance, 6) regular reporting of information to doctors and nurses and 7) educating clinicians about resistance and optimal prescribing techniques.

The antimicrobial stewardship efforts in the state of California have long preceded national efforts. Chapter 526 of Senate Bill 739 was passed in September 2006 and required acute care hospitals within the state to develop a process of evaluating the judicious use of antibiotics and monitor results by January 2008.(Speier, 2006) A review of the impact of this legislation showed that while hospitals improved their antimicrobial use, only 22% of the responding hospitals were influenced by the bill to develop ASPs. (Trivedi & Rosenberg, 2013) The state further passed Senate Bill 1311 in September 2014, to build on and address the shortcomings of the previous bill on antimicrobial stewardship.(Hill, 2014) The impact of Senate Bill 1311 on development of ASPs and antimicrobial resistance in the state has not been evaluated to date.

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OUTCOMES OF INTEREST

We aim to evaluate the impact of the California Senate Bill 1311 (Hospitals: Antimicrobial Stewardship) which was passed in September 2014.(Hill, 2014) More specifically, we would like to determine the impact of the bill in acute care hospitals within Los Angeles County on the following two outcomes:

1. The development of ASPs within hospitals that met all the Core Elements outlined by the CDC.
2. The rates of antimicrobial resistance.

HYPOTHESES

Causal Hypothesis:

High rates of antimicrobial resistance in California are due to inappropriate antimicrobial prescribing secondary to inadequate legislation around the development of antimicrobial stewardship programs (ASPs) within hospitals.

Intervention Hypothesis:

Passing legislation (California Senate Bill 1311) that requires all hospitals to establish formal ASPs, will reduce inappropriate antimicrobial prescribing and therefore reduce antimicrobial resistance within the state of California.

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METHODS

The Intervention:

The intervention of interest is the California Senate Bill 1311, passed in September 2014.(Hill, 2014) Around the time, there was national interest in combating antimicrobial resistance, evidenced by the signing of an Executive Order to combat antibiotic-resistant bacteria by President Obama.(Combating Antibiotic-Resistant Bacteria, 2014) With the passage of Senate Bill 1311(sec1288.85), California became the first state to require presence of formal ASPs within all acute care hospitals in the state as a commitment to prevent the spread of antimicrobial resistant organisms. Hospitals were expected to develop an antimicrobial stewardship policy based on guidelines issued by professional organizations and the federal government. In addition, hospitals were required to have a physician-led multidisciplinary committee consisting of at least one physician or pharmacist trained in antimicrobial stewardship. Finally, the bill required stewardship program activities to be reported to the respective quality improvement committee. Hospitals were given until July 1st, 2015 to adopt and implement an antimicrobial stewardship policy. The California Department of Public Health (CDPH) provided technical support and education to hospitals to implement the requirements of this new law.

The target population was all acute care hospitals within the state of California. The state however, had not mandated simultaneous regional antimicrobial resistance monitoring activities. The overall impact of the bill on resistance patterns in the state can therefore, not be well-estimated. On the other hand, antimicrobial resistance within Los Angeles County has been monitored more closely through the Regional Antibiogram

Project. In brief, the project collected resistance data from acute care hospitals as well as long-term acute care hospitals (details outlined below). We will use this data to study the impact of the state-wide intervention on antimicrobial resistance in Los Angeles County.

Needs Assessment:

The current Senate Bill 1311 evolved from a previous bill in California, Senate Bill 739 (Health and Safety Code §§ 1288.5-1288.9, 2006).(Trivedi & Rosenberg, 2013) The impact evaluation of Senate Bill 739 served as a needs assessment for the Senate Bill 1311.(Trivedi & Rosenberg, 2013) The assessment used data from a voluntary web-based survey. Of the 223 hospitals that responded (~50% response rate), 50% of hospitals had an ASP. Among the remaining hospitals, 30% reported planning ASPs while 20% reported no ASPs. Only 22% of 135 hospitals felt that Senate Bill 739 influenced them to initiate ASPs in their hospitals. Some of the barriers to development of ASPs elicited in the survey included staffing constraints (47%), lack of availability of a formal proposal (42% of hospitals) and lack of administrative support (18%).

In order for individual hospitals to develop formal ASPs, there was need for greater guidance and support. Results from the assessment as well as growing evidence from the CDC and the World Health Organization about antimicrobial resistance as a public health crisis shaped the development of Senate Bill 1311.(Hill, 2014) Technical support to adhere to the legislation was provided by the CDPH.

Monitoring Activities:

The bill text calls for a report on compliance in 2017 which will be completed by the Licensing and Certification Program of the CDPH.(Hill, 2014) Details of the report are not widely known. We would recommend the compliance report collect the following:

1. Data on the number of hospitals who meet the seven core elements of antimicrobial stewardship outlined by the CDC.
2. Data on how/in what manner do hospitals meet the seven core elements, i.e., the specific structure of the ASP.
3. Data on the problems faced in implementation and sustaining ASPs after passage of the legislation.

Data for part 1 can be obtained from the National Healthcare Safety Network (NHSN) public reporting of antimicrobial stewardship activities. Data for parts 2 and 3 could be collected through a survey administered to all acute care hospitals within the state.

Evaluation Design:

The design of this evaluation study will be a “One-Group Pretest-Posttest Design”, represented as “O X O”.(D.T. Campbell & Stanley, 1966) The “X” refers to the intervention, which in this case is the passage of California Senate Bill 1311 (sec1288.85). The first “O” represents the pre-intervention outcome measurement and the second “O” refers to the post-intervention outcome measurement. As previously noted, though the target population for the intervention was all acute care hospitals within the state of California, we will evaluate the impact of the bill locally in Los Angeles County. Our sample will consist of all the acute care hospitals located in Los Angeles County.

We choose this study design because of data availability limitations. The systematic collection of “Core Elements” data from the NHSN started in 2014. Similarly, the collection of antimicrobial resistance data by Los Angeles County through the Regional Antibiogram Project started in 2013. We therefore have only one “pre-intervention” data point. Some of the threats to validity could be eliminated using a control group. However, Los Angeles County is the only county we know of, that has undertaken the systematic monitoring of antimicrobial resistance and therefore obtaining a control group will be near impossible.

There will be two main outcome measures that will be studied. The first outcome will be the adoption of the CDC’s seven Core Elements in the acute care hospitals in Los Angeles County. The second outcome will be resistance rates for four of the biggest antimicrobial resistance threats: carbapenem-resistant Enterobacteriaceae, extended-spectrum beta-lactamase producing bacteria, methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* species. We will collect supplemental data on individual hospital characteristics which will serve as control variables during our analysis.

Data Sources/Outcome Measures:

We will obtain data required for the evaluation study from multiple reliable sources.

1. Data on the adoption of the Core Elements will be obtained from the NHSN database. At the start of every new year, individual hospitals complete an online survey on whether their facility met the Core Elements for the prior

year. Reporting of Core Elements first began in the year 2015, reflecting results from the prior year 2014. Results for the year 2014 and 2015 will serve as pre-test and post-test outcomes data respectively. A minor drawback is the outcomes data are collected annually and therefore some of the pre-intervention data would actually represent post-intervention data since the bill was passed in September 2014.

2. The second outcome of resistance rates will be obtained from the Los Angeles County Regional Antibiogram Project for the years 2013 and 2015, which will serve as pre-intervention and post-intervention outcomes data respectively. The Los Angeles County Department of Public Health has conducted a cross-sectional voluntary survey of all acute care and long-term acute care hospitals in the county. This survey requests for hospital-level antibiograms. An antibiogram is a document representing yearly aggregates of antimicrobial resistance data of most organisms (including the four organisms of interest) tested in the hospital (see example below).

Gram negative organisms, % SUSCEPTIBLE:

	N	Amp	Amp/ Sul	Ceftri ax	Ceftaz	Cefe pime	Ami kacin	Gent	Cipro flox	Levo flox	Tri/ Sulf	Nitro furan	Merop enem	Pip- tazo
Acinetobacter baumannii	77	0	64	8	42	38	-	55	51	51	60	0	53	-
Citrobacter freundii	86	-	-	72	72	98	100	86	83	83	80	94	99	73
Citrobacter koseri	59	-	-	100	100	100	100	100	100	100	100	88	100	100
Enterobactor aerogenes	110	-	-	86	86	100	99	100	97	96	98	14	100	85
Enterobacter cloacae	175	-	-	79	79	98	100	99	97	98	92	28	99	80
Escherichia coli (non-ESBL)	2757	45	53	99	99	100	100	90	78	78	53	93	100	-
Escherichia coli (ESBL (+))	528	0	0	0	0	2	99	49	11	11	34	49	99	85
Klebsiella oxytoca	105	0	64	100	100	100	100	96	100	100	91	80	99	97
Kleb. pneumoniae (non-ESBL)	509	0	85	100	100	100	100	99	98	98	87	23	100	-
Kleb. pneumoniae (ESBL (+))	65	0	0	0	0	2	97	51	46	55	37	6	97	65
Morganella morganii	59	0	0	98	92	100	100	75	70	73	53	0	100	100
Proteus mirabilis	367	81	88	96	97	96	100	88	85	86	79	0	100	100
Proteus vulgaris	33	0	79	88	100	100	97	97	97	97	82		100	100
Pseudomonas aeruginosa	456	0	-	0	86	87	99	95	84	80	-	-	90	98
Salmonella spp.	14	64	71	100	100	100	0	0	100	100	93	-	100	100
Shigella spp.	5	100	100	100	100	100	0	0	100	100	0		100	100
Serratia marcescens	68	-	-	94	100	100	100	100	99	99	100	0	97	-
Stenotrophomonas maltophilia	84	-	-	-	-	-	-	-	-	89	97	-	-	-

While the antibiogram itself is fairly standardized across hospitals, the laboratory testing of various organisms is not, which may affect the outcome results.

3. Hospital characteristics will be obtained from the Hospital Annual Utilization Report from the Office of Statewide Health Planning and Development (OSHPD). Variables of interest will include data on size of the hospital, volume of patients treated, case-mix index, number of intensive-care beds, emergency room traffic and service planning area information. Data from years 2013 and 2015 will be used.

Analysis:

Data from multiple sources will be combined into a single dataset. The number of hospitals that have adopted all the seven Core Elements will be aggregated and compared before and after the intervention using the Chi-Square test. Similarly, the number of hospitals adopting individual core elements will also be compared pre- and post-intervention. The resistance rates for CRE, ESBL, MRSA and VRE will be aggregated from hospital-level data and compared pre- and post- intervention using the independent *t*-test. Multivariable logistic and linear regression models will be constructed, controlling for hospital characteristics to identify predictors of adoption of Core Elements and low resistance rates.

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THREATS TO VALIDITY

Based on the study design, there are several threats to both internal and external validity of the evaluation study as outlined by Campbell and Stanley.(Donald T. Campbell & Stanley, 1963)

Threats to Internal Validity

1. History: The study design does not control for this threat. The threat of history is a considerable in this study. Over the past few years there has been great emphasis laid on antimicrobial stewardship in the medical and political communities in the United States. At the national level, the CDC published a summary document on the core-elements of ASP in 2014.(“CDC. Core Elements of Hospital Antibiotic Stewardship Programs.,” 2014) In March 2015, the White House released a National Action Plan for Combating Resistant Bacteria which outlined the importance of hospital-level antimicrobial stewardship.(The White House, 2015) In California itself, following the passage of Senate Bill 1311, the CDPH established a state-wide antimicrobial stewardship collaborative from January-December 2015 to support and enhance the development of ASPs in the state.(“California Antimicrobial Stewardship Program Initiative,” 2017) The external events occurred around the same time the intervention of interest was introduced could serve as a threat to internal validity.

2. Secular trend: The study design does not control for this threat. There are two important trends that might affect the internal validity of the study. One, antimicrobial resistance depends on several factors particularly related to patient movement which drive the underlying rate of resistance in a given region. Two, hospitals with a greater antimicrobial resistance might allocate greater resources to developing ASPs. Since we do not have a baseline trend of rates of resistance and rates of ASP adoption in Los Angeles County, the threat of secular trends is significant.

3. Maturation: The study design does not control for this threat. The data for the evaluation is collected over a span of three years. However, since the study population is the entire county, younger providers enter practice as older providers age and retire. Maturation would therefore not be a major threat in this case as the age-mix of physicians remains constant overall.

4. Testing: The study design does not control for this threat. The current study is a retrospective study using existing data and therefore testing is not a threat.

5. Instrumentation: The study design does not control for this threat. Instrumentation is a significant threat to internal validity in the current study. There were no major changes in the NHSN survey on Core Elements or the OSHPD survey data. However, there were changes between 2013 and 2015 in antimicrobial resistance testing. Standards for microbiologic testing of organisms

in hospitals and laboratories are set by the Clinical and Laboratory Standards Institute (CLSI).(“CLSI Press Releases - CLSI News & Events”) These standards are modified and updated regularly. While individual laboratories are encouraged to keep up-to-date with these standards, it is not mandatory, resulting in some early adopters and some late adopters. For example, in 2013 the CLSI updated testing/interpretation criteria for some of the organisms of interest (*Staphylococcus* spp., Enterobacteriaceaea).(Hindler, 2013) The antimicrobial resistance results in our study could be influenced by this change rather than the intervention depending on how many laboratories were early or late adopters of the 2013 CLSI standards.

6. Regression: While the study design does not control for this threat, it is not a major concern in this study. Our sample includes all types of acute care hospitals within Los Angeles County and not only those with extreme antimicrobial resistance patterns.

The study design uses a single group pre-test and post-test and therefore selection (and selection interactions) and mortality are not considered threats to internal validity.

<u>Threats to External Validity</u>

1. Interaction of selection and X: The study design does not control for this threat. The selected sample population are the acute care hospitals within Los Angeles

County. The Los Angeles County Department of Public Health has been actively involved in antimicrobial stewardship in the community and therefore, the effect of the intervention on this sample population may be unique. The uptake of the ASPs in Los Angeles County may have been quicker because of the support from Department of Public Health. Generalizability to other settings, even within the state, might not result in similar findings.

2. Interaction of history of X(Grembowski, 2001): The study design does not control for this threat. As outlined earlier, there were national, state and local efforts taken in improving antimicrobial stewardship when Senate Bill 1311 was passed which may have resulted in the hospitals and clinicians being more receptive to adopting the bill. Generalizability to a different setting and at a future time may not result in similar results.

3. Reactive arrangements: The threat does not exist for this study since this is a retrospective study and there are no “experimental conditions” which might lead to reactive arrangements by study participants.

4. Multiple X interface: Our study is evaluating the impact of a single Senate Bill and therefore does not suffer from having to tease out the effect of a single intervention from multiple possible ones.

5. Interaction of testing and X: The study did not use any experimental testing and hence does not suffer from the threat of testing and X.

IMPLICATIONS

The results from this evaluation study will have several potential implications.

1. For Los Angeles County Department of Public Health: Results from the study will show the impact of California Senate Bill 1311 on antimicrobial stewardship practices across the county. While several hospitals had already adopted the CDC Core Elements, many required formalized guidance regarding the essential elements of an ASP which was offered by this bill. The ultimate goal of creating robust ASPs is to reduce antimicrobial resistance rates. While changes in antimicrobial resistance patterns might take years, this study will estimate the early impact of a state law on county-level antimicrobial resistance patterns.
2. For other similar public health departments: Both positive and negative evaluation results will serve as learning opportunities for other public health departments who have been burdened with high rates of antimicrobial resistance. If the evaluation shows a positive impact of the bill, similar initiatives maybe undertaken in other areas. Negative results will highlight the need for more intensive public health efforts in antimicrobial stewardship which are not necessarily achieved by solely passing a bill.

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