Nationwide data from 2011 implicated Kentucky as the state with the highest outpatient antibiotic prescribing rate in the United States (Hicks, 2015). Inappropriate use of antibiotics can lead to antibiotic resistance, one of the world’s most urgent health threats. Appropriate antibiotic use requires a joint effort between prescribers, the public, and pharmacists. This report presents an analysis of data from two sources to help illuminate outpatient antibiotic prescribing practices in Kentucky.
Foreword

The Healthcare-Associated Infection (HAI) Prevention Program at the Kentucky Department for Public Health uses a multifaceted approach to promote the health of Kentuckians by preventing HAI.s and slowing the spreading of antibiotic-resistant organisms in the Commonwealth. The Centers for Disease Control and Prevention (CDC) has outlined four core actions to combat antibiotic resistance, one of which is to improve antibiotic prescribing. An initial step in improving antibiotic prescribing in the Commonwealth is to better understand current prescribing practices in the outpatient setting. This understanding will allow educational opportunities for prescribers regarding appropriate antibiotic use and public health messages to be tailored to meet the needs of Kentucky residents.
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Background information

Antibiotics

Antibiotics are medications used for the treatment of bacterial infections. Following the first use of penicillin to treat infections in 1942 (Dawson, 1943) and later identification of additional antibiotics, morbidity and mortality associated with bacterial infections have been significantly reduced (Shapiro, 2013). Antibiotic use, however, is not without risk. Antibiotics have been associated with adverse drug reactions (Dantes 2015; Bell 2014) and increased risk of Clostridium difficile infections (Brown 2013; Deshpande 2013). In the United States, C. difficile infections result in almost 250,000 hospitalizations and an estimated 14,000 deaths each year (Centers for Disease Control, 2013).

Additionally, inappropriate antibiotic use is a core contributor to the development of antibiotic-resistant organisms, resulting in poorer health outcomes and increased health care costs. In the United States, an estimated 2 million people develop serious bacterial infections that are resistant to one or more antibiotics every year (CDC, 2013). Almost 23,000 deaths occur each year as a direct result of antibiotic-resistant bacteria and additional deaths occur from conditions that were complicated by infections with these organisms (CDC, 2013). Antibiotic resistance presents a challenge in the delivery of appropriate health care across the continuum of care.

There are many factors that drive inappropriate antibiotic use, including agricultural practices (Teuber, 2001). From the human perspective, both patient and caregiver expectations are associated with inappropriate prescribing of antibiotics (Mustafa 2014; Little 2004). Studies have shown that to maintain or establish positive relationships with their patients, physicians prescribe antibiotics according to their perceptions of patient expectations (Cals 2007; Andre 2010). Additional research has suggested that patient socioeconomic factors, such as income and education, have an impact on antibiotic prescribing rates (Masiero 2010; Marra 2010). By some estimates, over half of antibiotic prescribing in the outpatient setting may be unnecessary or inappropriate (Shapiro, 2014); a significant portion of this is related to the management of acute respiratory infections, such as sinusitis (Shapiro, 2014) and bronchitis (Gonzales, 1999). Antibiotics prescribed incorrectly offer limited, if any, benefits to patients and lead to potential complications. Clinical practice guidelines for common infections (e.g., the American Academy of Pediatrics guidelines for sinusitis (Wald, 2013) and otitis (Lieberthal, 2013), and adult sinusitis (Rosenfeld, 2015)) help establish standards of care, focus quality improvement efforts, and improve patient outcomes.
Antibiotic stewardship

Antibiotic stewardship is concerned with “optimizing clinical outcomes while minimizing unintended consequences of antimicrobial use...” (Dellit, 2001). Antibiotic stewardship programs include activities and commitments that encourage appropriate use of antibiotics, reduce antibiotic resistance, improve patient outcomes, and decrease the spread of infections caused by drug-resistant organisms. The adoption of stewardship programs, regardless of the health care setting, requires active participation by all who prescribe antibiotics and care for those requiring treatment. An overarching goal of antibiotic stewardship is to promote adherence to clinical practice guidelines, especially with regard to antibiotic use.

Collecting and making publicly available data regarding antibiotic use and resistance patterns is critical in guiding and evaluating efforts to combat resistance. While many of the most highly resistant infections develop within the hospital setting, any approach to combating resistance and the spread of resistant organisms must include these types of surveillance across the continuum of care.

All stewardship programs require certain elements to be successful. The CDC has defined “Core Elements” for stewardship programs across the continuum of care including both inpatient (CDC, 2014) and outpatient settings (Sanchez, 2016). The seven core elements for hospital-based stewardship are as follows:

- **Leadership Commitment**: Dedicating necessary human, financial and information technology resources
- **Accountability**: Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective
- **Drug Expertise**: Appointing a single pharmacist leader responsible for working to improve antibiotic use
- **Action**: Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (e.g., “antibiotic time out” after 48 hours)
- **Tracking**: Monitoring antibiotic prescribing and resistance patterns
- **Reporting**: Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff
- **Education**: Educating clinicians about resistance and optimal prescribing
In 2016, 69 of the 71 acute care hospitals in Kentucky completed the patient safety survey through the National Healthcare Safety Network (NHSN). Of those 69, 64% reported that they met each of CDC’s seven elements of antibiotic stewardship, up from 41% in 2015. In both 2015 and 2016, only two facilities reported meeting none of the elements and two reported meeting only one of the elements. In 2016, facilities that did not meet each of the seven core elements most commonly reported that they did not have leadership commitment (13 of 64, or 20%, reported this absence), an antibiotic tracking process (20%), or stewardship education (20%). Regarding the least commonly reported deficiencies, only four facilities reported that they did not have drug expertise and four reported not taking at least one recommended action related to stewardship.

In addition to strengthening antibiotic stewardship in the hospital setting, improving prescribing practices in the outpatient setting is also important. Outpatient prescribing is the focus of the remainder of this report. The concept of outpatient antibiotic stewardship refers to coordinated efforts to promote appropriate prescribing of antibiotics for non-hospitalized patients in clinics, private offices, and emergency departments. Once again, the engagement of all stakeholders is necessary for success. The CDC’s core elements for stewardship in the outpatient setting are as follows:

- **Commitment**: Demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety
- **Action for policy and practice**: Implement at least one policy or practice to improve antibiotic prescribing, assess whether it is working, and modify as needed
- **Tracking and reporting**: Monitor antibiotic prescribing practices and offer regular feedback to clinicians, or have clinicians assess their own antibiotic prescribing practices themselves
- **Education and expertise**: Provide educational resources to clinicians and patients on antibiotic prescribing, and ensure access to needed expertise on optimizing antibiotic prescribing

The Kentucky Department for Public Health (KDPH) has not previously conducted an evaluation of antibiotic stewardship activities in Kentucky’s outpatient settings. However, analyses conducted by the KDPH and the University of Louisville have identified potential targets for outpatient stewardship interventions.
Data from Kentucky

I. Antibiotic prescriptions in the outpatient setting

*Data Source*

The Kentucky Department for Public Health used IMS Government Solutions antimicrobial data to conduct a descriptive analysis of 10.4 million outpatient prescriptions for antimicrobials written by Kentucky-based providers, including all professionals with the authority to prescribe to humans, in 2013–2014. The collection of these data is described in detail elsewhere (Hicks, 2015). An analysis of IMS data collected in 2011 revealed that Kentucky led the nation in outpatient antibiotic prescriptions with 1281 antibiotic prescriptions per 1000 person-years (Hicks, 2015).

*Analyses*

KDPH staff calculated the frequency of antimicrobial-specific prescriptions, assessed provider characteristics such as professional specialty (defined by the American Medical Association categorization scheme), and, using U.S. Census data, calculated prescription rates by patient gender. A secondary analysis considered variation across the different regions of Kentucky. Sampling error was not included in the calculations.

*Results*

**Statewide:** The overall prescription rate was 1182 antimicrobial prescriptions per 1000 person-years (py). The most common antimicrobial prescribed was amoxicillin (n=2,071,233, 19.8% of prescriptions) followed by azithromycin (n=1,781,694, 17.1%). The most common categories of antimicrobials prescribed were aminopenicillins (n=2,091,173, 20.0%), extended spectrum macrolides (n=1,880,807, 18.0%), and cephalosporins (n=1,583,235, 15.2%). Among professional specialties, family medicine providers prescribed the highest absolute number of antimicrobials (n=2,314,069, 22.2%), but dermatologists had the highest average number of prescriptions written per provider per year (Figure 1). The annual number of prescriptions per provider was highest among dermatologists, family medicine providers, and urologists. Across age categories, females received more prescriptions (Figure 2). Counties in southern and eastern Kentucky generally had higher annual prescription rates per 1,000 people than elsewhere in the state (Figure 3).
Figure 1. Antibiotic Prescription Rates for Outpatients in Kentucky, by Provider Specialty, 2013—2014

Figure 2. Antibiotic Prescriptions for Outpatients in Kentucky by Patient Age and Sex, 2013—2014
Regional data: The data were also analyzed by region. Table 1 presents the findings from this analysis.

Table 1. Outpatient Prescription Data by Region\(^a\) in Kentucky, 2013—2014.

<table>
<thead>
<tr>
<th>Provider type(^b)</th>
<th>Eastern</th>
<th>Western</th>
<th>North</th>
<th>South Central</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialty(^c)</td>
<td>Nurse Practitioners</td>
<td>Nurse Practitioners</td>
<td>Doctors of Osteopathy</td>
<td>Nurse Practitioners</td>
</tr>
<tr>
<td>Most commonly</td>
<td>Amoxicillin</td>
<td>Azithromycin</td>
<td>Amoxicillin</td>
<td>Amoxicillin</td>
</tr>
<tr>
<td>prescribed drug</td>
<td>Rate per 1000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>person-years</td>
<td>1485</td>
<td>1145</td>
<td>1068</td>
<td>1222</td>
</tr>
<tr>
<td>Total Rx</td>
<td>1,715,174</td>
<td>2,565,874</td>
<td>3,342,983</td>
<td>2,812,808</td>
</tr>
</tbody>
</table>


\(^b\) Highest average number of annual prescriptions per provider

\(^c\) Included specialties with more than one provider

Limitations

There is no information on the number of visits any specific provider conducts throughout the year.

Data on prescriptions per 1000 visits would be more informative, but these data are not currently
available. A provider that has a higher number of visits may appear to be a “high prescriber” and that may erroneously indicate that the provider is over-prescribing antibiotics; in turn, identification of specific providers as “high prescribers” is problematic. Additionally, because there is no information on the reasons that the prescription was written, the appropriateness of any particular prescription cannot be determined.

Conclusions
An outpatient antimicrobial stewardship program in Kentucky may need to target specific provider types, such as nurse practitioners, and professional specialties, such as dermatologists. The development of curriculum that provides education on prescribing in the context of known antimicrobial resistance patterns may also be of value. Variations in prescribing rates by provider location and patient’s sex may reflect both differences in the health of the population and differences in health-seeking behaviors; this should be further explored to determine if these factors should be considered when designing a stewardship program.
II. Antibiotic prescriptions in the pediatric Kentucky Medicaid population

The Child and Adolescent Health Services Research Design and Support (CAHRDS) Unit housed within the Department of Pediatrics at the University of Louisville has collaborated with Kentucky Medicaid to improve the quality of care of pediatric Medicaid recipients. In 2016, this initiative expanded to include an assessment of antibiotic prescribing. Research reported in this section was supported, in part, by the Cabinet for Health and Family Services, Department for Medicaid Services under Agreement titled “Improving Care Quality for Children Receiving Kentucky Medicaid,” Norton Healthcare, and the University of Louisville.

Data Source
Because rates of outpatient antibiotic use are highest in children (Hicks, 2015), and nearly one half of children in Kentucky are covered by Medicaid, we selected pharmacy claims from pediatric recipients (age <20 years) of Kentucky Medicaid from 2012 –2015 to analyze.

Analyses
A team at the University of Louisville conducted a descriptive analysis to describe patterns of outpatient antibiotic use including patient characteristics (age, sex, race, zip code, date of service) and provider characteristics (type and specialty). The team calculated prescription rates (the total number of prescriptions per 1,000 Medicaid enrollees each year) for the overall pediatric population and for selected demographic groups. National Drug Codes were used to identify systemic antibacterial agents.

Results
Table 2 documents the rates of antibiotic use per 1000 children per year in the Kentucky pediatric Medicaid population from 2012–2015 compared to nationally representative data for children from 2011. Consistent with the literature (Hicks, 2015), Kentucky children received much higher rates of antibiotics compared to national estimates. Across all years, females had slightly higher rates of prescription compared to males. Additionally, rates of antibiotic use decreased with age, with the highest prescription rates found in infants and young children. Nationally representative data are not available for comparison, but within the Kentucky Medicaid population from 2012–2015, black children were less likely to be prescribed antibiotics as compared to white children or children of other races. Finally, antibiotic use was less common in the urban as compared to non-urban setting. This geographic variation is further explored in Table 3, which stratifies antibiotic use by Medicaid region (Figure 4). Across years, rates of prescribing were consistently highest in region 8, southeast Kentucky. The lowest
rates are in regions 3, 5 and 6 which include the metro areas of Louisville, Lexington and Cincinnati, respectively.

Table 2. Antibiotic Use in the Kentucky Medicaid Population, 2012–2015

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>National*</th>
<th>Kentucky Medicaid Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2011</td>
<td>2012</td>
</tr>
<tr>
<td>Overall</td>
<td>889</td>
<td>1,446</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>841</td>
<td>1,342</td>
</tr>
<tr>
<td>Female</td>
<td>941</td>
<td>1,483</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–2</td>
<td>1287</td>
<td>1,936</td>
</tr>
<tr>
<td>3–9</td>
<td>1018</td>
<td>1,445</td>
</tr>
<tr>
<td>10–19</td>
<td>691</td>
<td>1,129</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>Not available</td>
<td>1,521</td>
</tr>
<tr>
<td>Black</td>
<td>Not available</td>
<td>900</td>
</tr>
<tr>
<td>Other</td>
<td>Not available</td>
<td>1,127</td>
</tr>
<tr>
<td>Urban</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>Not available</td>
<td>1,268</td>
</tr>
<tr>
<td>No</td>
<td>Not available</td>
<td>1,516</td>
</tr>
</tbody>
</table>

*Based on data from Hicks et al, 2015

Table 3. Antibiotic Prescriptions per 1000 Children per year by Medicaid Region, Kentucky, 2012–2015

<table>
<thead>
<tr>
<th>Medicaid Region</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,574</td>
<td>1,496</td>
<td>1,350</td>
<td>1,455</td>
</tr>
<tr>
<td>2</td>
<td>1,338</td>
<td>1,266</td>
<td>1,150</td>
<td>1,233</td>
</tr>
<tr>
<td>3</td>
<td>1,132</td>
<td>929</td>
<td>860</td>
<td>912</td>
</tr>
<tr>
<td>4</td>
<td>1,647</td>
<td>1,527</td>
<td>1,344</td>
<td>1,375</td>
</tr>
<tr>
<td>5</td>
<td>1,188</td>
<td>1,104</td>
<td>976</td>
<td>1,054</td>
</tr>
<tr>
<td>6</td>
<td>1,082</td>
<td>974</td>
<td>854</td>
<td>933</td>
</tr>
<tr>
<td>7</td>
<td>1,618</td>
<td>1,515</td>
<td>1,357</td>
<td>1,378</td>
</tr>
<tr>
<td>8</td>
<td>1,893</td>
<td>1,847</td>
<td>1,676</td>
<td>1,725</td>
</tr>
</tbody>
</table>
Table 4 presents provider type data for antibiotic prescriptions from 2012–2015. Although the analysis focused exclusively on pediatric patients, general practitioners were the most common prescribers (36–39%), followed by nurse practitioners (25–32%). General pediatricians prescribed only 11–12% of antibiotics prescribed to children.

Figure 4. Kentucky Medicaid Regions
Image provided by the Kentucky Department For Medicaid Services.

<table>
<thead>
<tr>
<th>Provider Type</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Practitioners</td>
<td>39</td>
<td>39</td>
<td>38</td>
<td>36</td>
</tr>
<tr>
<td>Nurse Practitioners</td>
<td>25</td>
<td>28</td>
<td>30</td>
<td>32</td>
</tr>
<tr>
<td>General Pediatricians</td>
<td>12</td>
<td>12</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Physician Assistants</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Other</td>
<td>17</td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

Table 5 provides data for the four most commonly prescribed antibiotics in the Kentucky Medicaid population from 2012–2015 as compared to national data. The top four prescribed antibiotics in Kentucky and the United States overall were the same. Amoxicillin and Azithromycin predominated, followed by Cefdinir (Omnicef®) and Amoxicillin-Clavulanate (Augmentin®). From 2012 through 2015, the use of Cefdinir increased and it became the third most commonly prescribed antibiotic in the KY Medicaid population in 2014.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Prescriptions per 1000 Children</th>
<th>National*</th>
<th>Kentucky Medicaid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2011</td>
<td>2012</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>300</td>
<td>502</td>
</tr>
<tr>
<td>Azithromycin</td>
<td></td>
<td>183</td>
<td>354</td>
</tr>
<tr>
<td>Cefdinir</td>
<td></td>
<td>74</td>
<td>114</td>
</tr>
<tr>
<td>Amoxicillin-Clavulanate</td>
<td></td>
<td>87</td>
<td>144</td>
</tr>
</tbody>
</table>

*Based on data from Hicks et al, 2015

Conclusions
These results are consistent with the high rates of antibiotic use reported in Kentucky from nationally representative data (Hicks, 2015). The annual rate of prescriptions varied by patient demographics. This variation may be related to a combination of factors including differences in the underlying health of these sub-populations, differences in health seeking behavior of their parents/guardians, and/or differences in prescribing practices. Preliminary data suggest that the majority of prescriptions were for upper respiratory infections – formal linkage studies of pharmacy and medical claims have been initiated.

Providing targeted information to families of children more likely to receive an antibiotic (e.g., parents of young children or parents in non-urban areas) may be of use. The majority of prescriptions for children were written by general practitioners or nurse practitioners; education of appropriate antibiotic prescribing practices should include, and perhaps initially focus on, these groups.
Recommendations

Kentucky must proactively address inappropriate use of antibiotics in the Commonwealth. Though this should include continued analysis of existing data and identification of additional data sources to tailor activities moving forward, this effort can begin now and should be done across the continuum of care. Addressing inappropriate antibiotic prescribing in the outpatient setting should use a multifaceted approach. The Kentucky Department for Public Health should work with healthcare partners to do the following:

1. **Support the development/improvement of antibiotic stewardship programs for outpatient facilities that do not meet the four Core Elements of stewardship in the outpatient setting.**

2. **Disseminate materials to, and host educational programs for, providers with an emphasis on reaching nurse practitioners, general practitioners, and pediatricians.** Both the IMS and Kentucky Medicaid data show that highest rates of antibiotic prescribing are in southeastern Kentucky. This may reflect underlying differences in the health of population, however this region should be an area of focus.

3. **Disseminate guidelines on the appropriate use of the most commonly prescribed drugs (amoxicillin, azithromycin, and cephalosporin).**

4. **Increase public awareness of risks associated with inappropriate antibiotic use.**
References


Appendix A: Resources for Providers and the Community

_The Centers for Disease Control and Prevention Get Smart: Know When Antibiotics Work_

The Centers for Disease Control and Prevention (CDC) have developed a campaign to educate patients, prescribers, and pharmacists on appropriate use of antibiotics.

[https://www.cdc.gov/antibiotic-use/index.html](https://www.cdc.gov/antibiotic-use/index.html)


_Infectious Diseases Society of America Practice Guidelines:_


_Clinical Guidelines and Recommendations from the American College of Physicians:_

[https://www.acponline.org/clinical-information/guidelines](https://www.acponline.org/clinical-information/guidelines)

_American Academy of Pediatrics Clinical Practice Guidelines:_