

National Prevalence of Extended Spectrum Beta-lactamase-Producing Enterobacteriaceae (ESBL) in the Ambulatory and Acute Care Settings in the United States in 2015-2016

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Abstract

BACKGROUND: In 2013 the CDC classified infections caused by ESBL organisms as a serious threat. The purpose of this study was to estimate the number of national ESBL events in outpatient and hospitalized patients based on the determination of ESBL episodes in the Becton Dickinson research database.

METHODS: Susceptibility data from non-duplicate organisms including *E. coli*, *K. pneumoniae*, and *P. mirabilis* were collected from 348 hospitals. ESBL was identified per NHSN definitions. Organisms were classified into ambulatory, admission, and hospital-onset (HO) periods based on collection time. The raking method was applied per CMS national hospital distribution by location, teaching status, urban/rural status, and bed size to project to national event estimates.

RESULTS: Of 878,777 isolates tested, 60,932 were ESBL and the national projected total of ESBL events was 538,452 (see Table). The ESBL rates were highest in the hospital onset period, followed by admission and ambulatory. National projections for ESBL for each region were: ambulatory (4.6%, 6.5%, 6.2%, & 5.9%), admission (8.3%, 10.0%, 9.0% & 8.8%) and hospital-onset (10.9%, 16.4%, 13.0% & 14.2%) for the Midwest, Northeast (NE), South & West regions, respectively.

| Period Tested | Observed Events (348 hospitals) | | | National Projection | | |
|----------------|---------------------------------|----------------|-------------|---------------------|----------------|-------------|
| | Isolates tested | Confirmed ESBL | % ESBL | Isolates tested | ESBL Events | % ESBL |
| Ambulatory | 682,409 | 39,317 | 5.8% | 6,319,175 | 360,202 | 5.7% |
| Admission | 109,746 | 10,062 | 9.2% | 912,212 | 81,345 | 8.9% |
| Hospital-onset | 86,622 | 11,553 | 13.3% | 736,300 | 96,906 | 13.2% |
| Total | 878,777 | 60,932 | 6.9% | 7,967,687 | 538,452 | 6.8% |
| Regions | | | | | | |
| Midwest | 242,065 | 13,157 | 5.4% | 2,348,457 | 130,637 | 5.6% |
| NE | 128,383 | 9,673 | 7.5% | 1,146,354 | 91,151 | 8.0% |
| South | 373,503 | 28,357 | 7.6% | 3,002,689 | 216,535 | 7.2% |
| West | 134,826 | 9,745 | 7.2% | 1,470,187 | 100,130 | 6.8% |
| Total | 878,777 | 60,932 | 6.9% | 7,967,687 | 538,452 | 6.8% |

CONCLUSION: These data estimate that national hospital onset ESBL rates in July 2015 to June 2016 were higher than previously reported. Although the highest prevalence of ESBL events occurred in the HO period, ESBL events were highest in frequency in the ambulatory period. The highest rates of ESBL events were in the NE and South regions among all periods tested.

Introduction

Extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (*Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis*) are traditionally nosocomial pathogens, but have begun to emerge in the outpatient setting. Approximately 19% of healthcare-associated infections (HAIs) due to Enterobacteriaceae are caused by ESBL-producing Enterobacteriaceae.¹ Additionally, HAIs caused by ESBLs often result in high mortality and economic burden.² According to the National Healthcare Safety Network (NHSN) report of antimicrobial resistance patterns for HAIs in 2009-2010, extended-spectrum cephalosporin-resistant *Klebsiella* spp. and *E. coli* were found in 3% of catheter-associated urinary tract infections, central line-associated infections, ventilator associated bacterial pneumonia and surgical site infections in the United States (US).³ The CDC estimates ~17,000 infections and 9,000 HAIs caused by ESBL-producing *Klebsiella* spp. and *E. coli*, respectively, occur annually in the US.

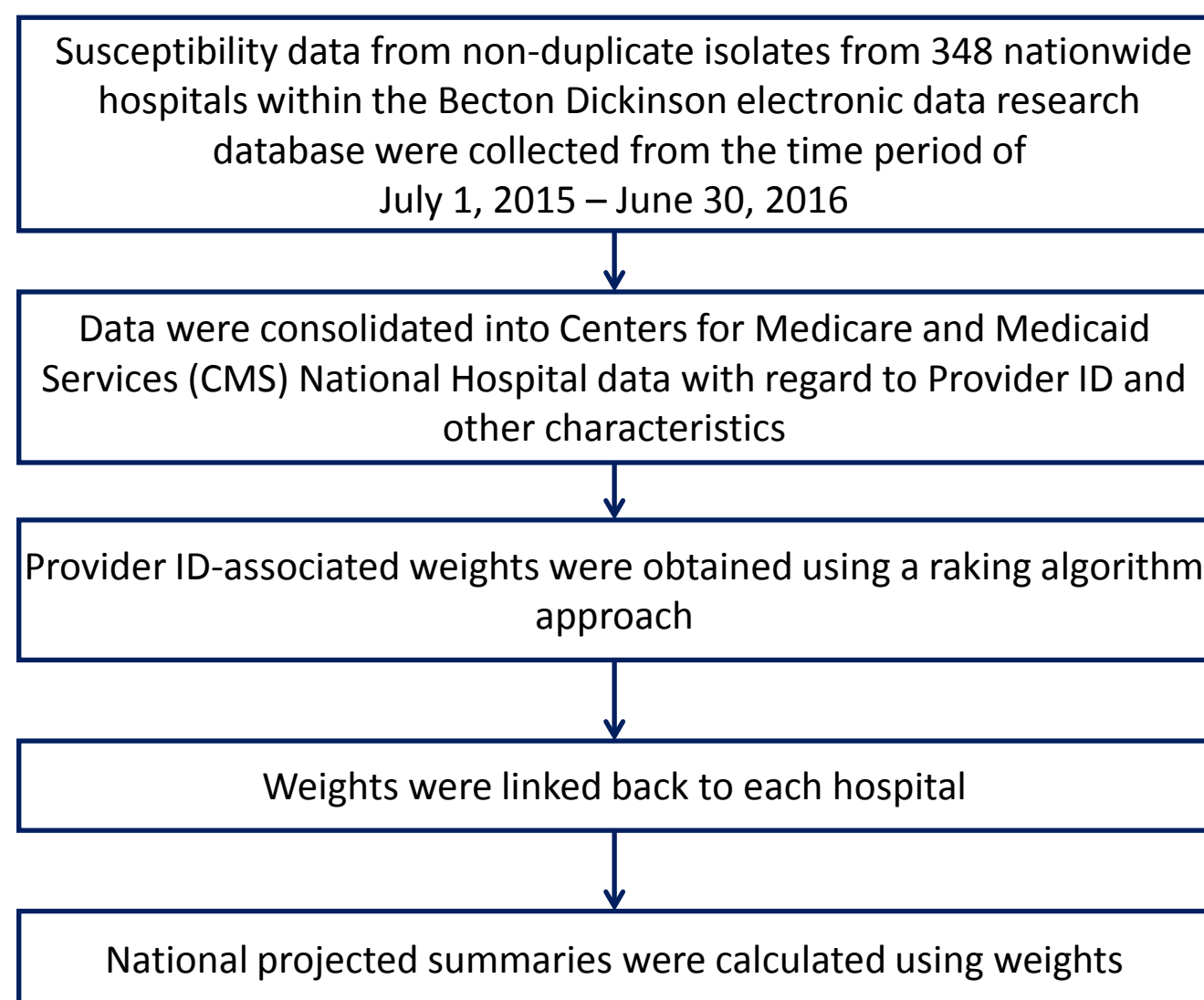
The purpose of this study was to estimate the national prevalence of ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* events in the acute care and ambulatory settings in the US from July 2015 to June 2016 based on a large database from Becton Dickinson & Company.

Methods

- Non-duplicate isolates (first isolate of a species per 30-day period) were collected from 348 US hospitals (hospital characteristics listed in Table 1). Sources were respiratory, blood, urine, skin, intra-abdominal, and other, and ESBLs were identified per the following criteria:
 - E. coli*, *K. pneumoniae*, *P. mirabilis* confirmed as ESBL-positive per commercial panels or reported as intermediate or resistant to any of the four extended spectrum cephalosporins (ceftriaxone, cefotaxime, ceftazidime or cefepime).
- Isolates were categorized into three settings by the specimen collection time totals:
 - Admission:** Within 3 days of an inpatient admission and no previous admission within 14 days
 - Hospital-onset:** 3 days or more post-admission or within 14 days of discharge
 - Ambulatory:** Neither a or b.

- All data were linked with publicly available CMS (Centers for Medicare and Medicaid Services) National Hospital Data using Provider IDs
- The raking method was applied per CMS national hospital distribution by location, teaching status, urban/rural status, and bed size to project the national prevalence estimates. Raking has been borrowed from survey research methods. Raking uses an iterative proportional fitting algorithm to force estimates to match known underlying distribution totals.
- Figure 1 demonstrates the projection methodology for determining national prevalence estimates.

Figure 1. Projection Methodology for determining national prevalence estimates



Results

- For the 348 facilities 878,777 non-duplicate *E. coli*, *K. pneumoniae*, and *P. mirabilis* isolates were identified and tested for susceptibility in 745,182 patients
 - 60,932 (6.9%) of the isolates were determined to be ESBL-producing organisms (Table 2) in 44,165 patients
 - The proportion of observed ESBL-producing organisms was highest in the hospital onset period (13.3%), followed by admission (9.2%) and ambulatory (5.8%) settings (Table 2)
- The top three sources of ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* isolates were: urine (79.6% of isolates), skin (7.9% of isolates), and blood (6.0% of isolates) (Figure 2)
- The national projection of ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* was 538,452 (6.8%) (Table 2)
- National projections for ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* for each region were: ambulatory (4.6%, 6.5%, 6.2%, & 5.9%), admission (8.3%, 10.0%, 9.0% & 8.8%) and hospital-onset (10.9%, 16.4%, 13.0% & 14.2%) for the Midwest, Northeast, South & West regions, respectively (Table 3)

Table 1. Hospital Characteristics

| Hospital Characteristics | BD Database N=348 Hospitals | CMS Database N=4,650 Hospitals |
|---------------------------|--------------------------------|-----------------------------------|
| Teaching Status | | |
| Major | 12.9% | 9.6% |
| Limited | 19.3% | 13.2% |
| Graduate | 4.6% | 2.8% |
| No Affiliation | 63.2% | 74.5% |
| Bed Size | | |
| <100 beds | 22.8% | 50.8% |
| 100-300 beds | 41.3% | 30.3% |
| ≥300 beds | 35.8% | 19.0% |
| Urban/Rural Status | | |
| Urban | 75.9% | 57.8% |
| Rural | 24.1% | 42.2% |
| Region | | |
| Northeast | 9.5% | 8.9% |
| South | 47.7% | 41.1% |
| Midwest | 27.0% | 30.1% |
| West | 15.8% | 19.9% |

BD= Becton Dickinson; CMS= Centers for Medicare and Medicaid Services

Figure 2: Source distribution for ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* (N=60,932) from 348 facilities

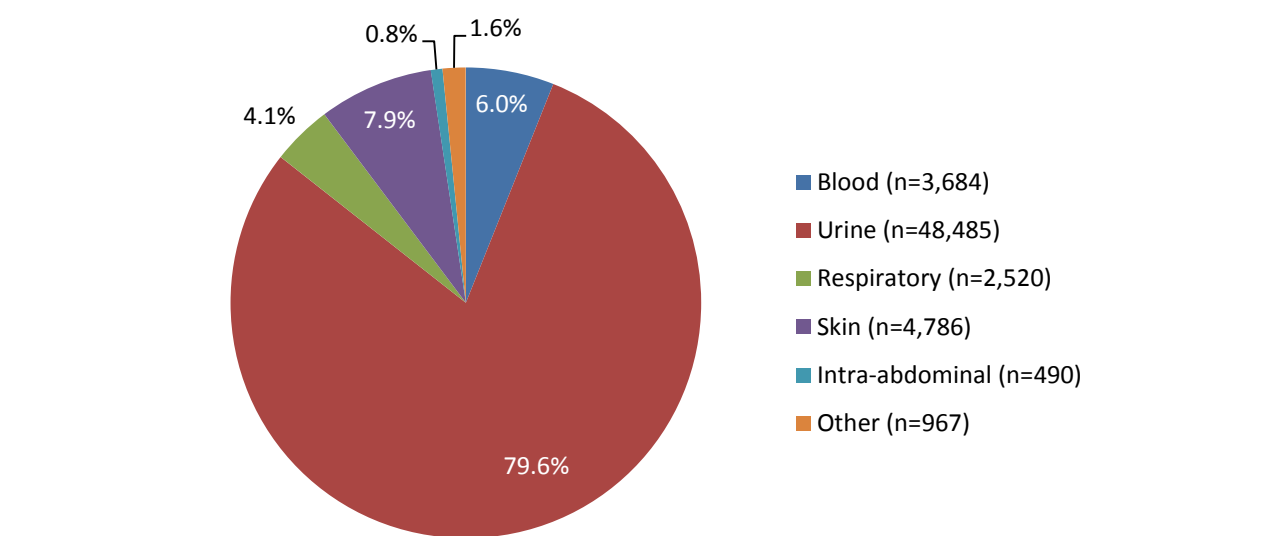


Figure 3: Source distribution of ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* for projections of national prevalence by setting type

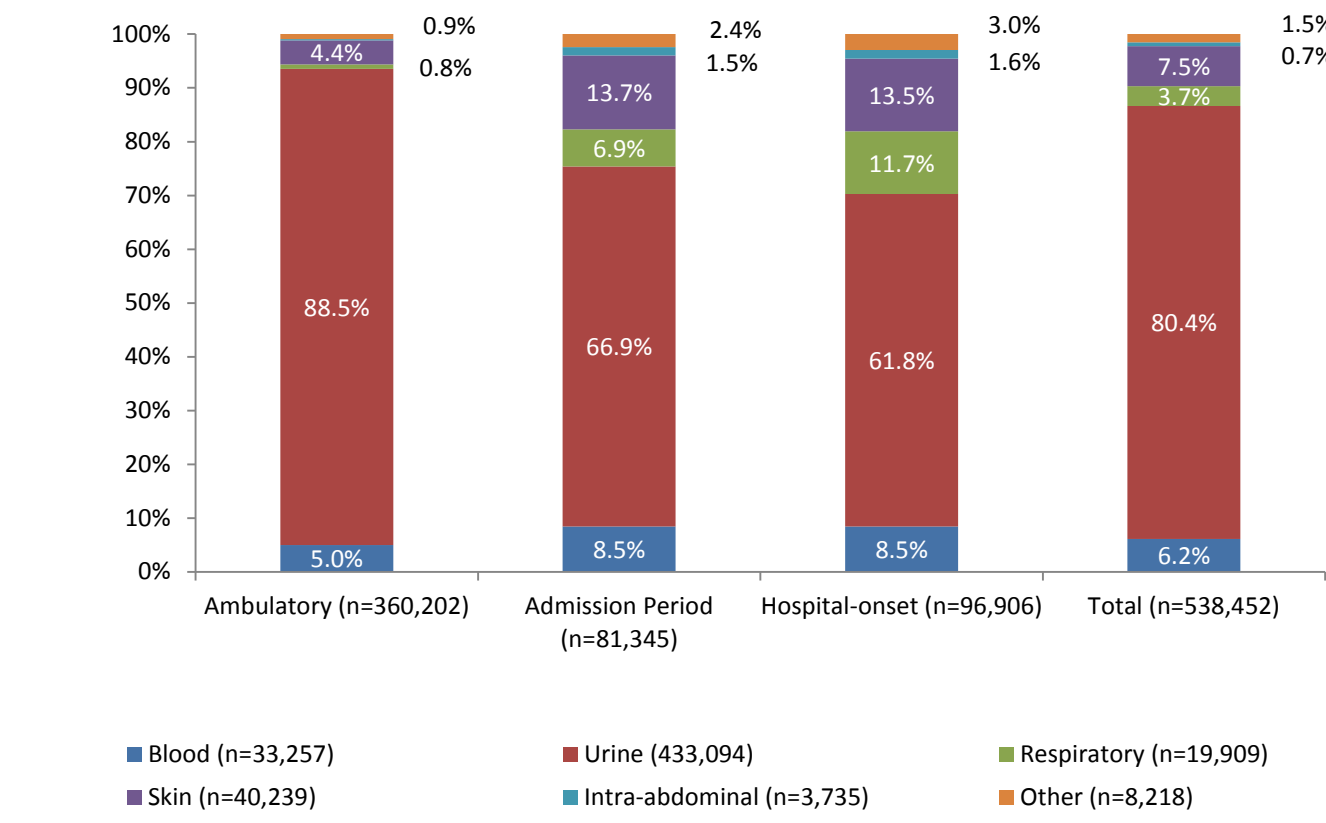


Table 2. National projection of ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* events estimated from observed events from the 348 hospitals in the BD database

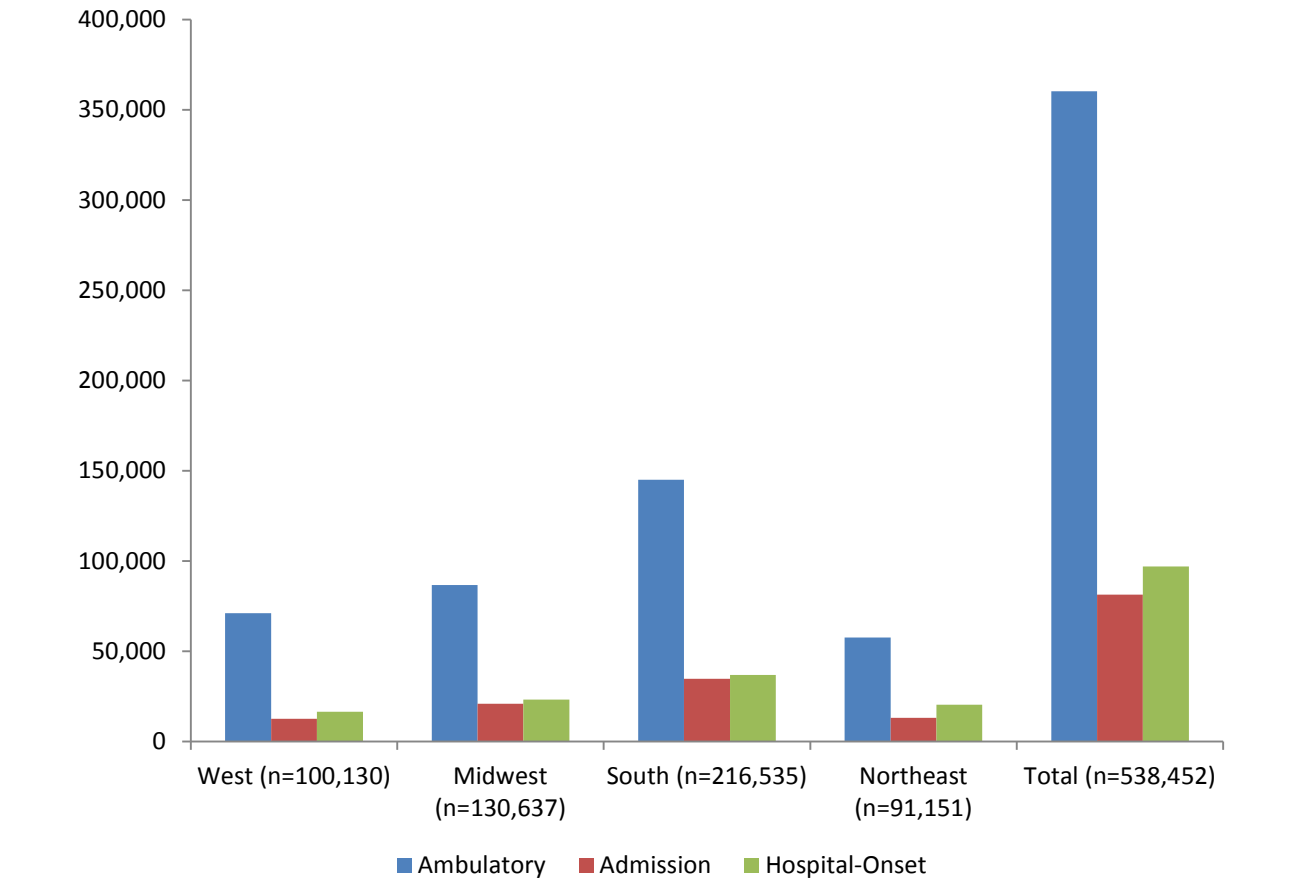
| Period | 348 Facilities Observed | | | NATIONAL PROJECTIONS | | |
|--------------------|-------------------------|---------------|-------------|-------------------------|-------------------|------------------|
| | Total Tested, N | ESBL, N | % ESBL | Projected Org Tested, N | Projected ESBL, N | Projected % ESBL |
| Ambulatory | 682,409 | 39,317 | 5.8% | 6,319,175 | 360,202 | 5.7% |
| Admission | 109,746 | 10,062 | 9.2% | 912,212 | 81,345 | 8.9% |
| Hospital-Onset | 86,622 | 11,553 | 13.3% | 736,300 | 96,906 | 13.2% |
| Grand Total | 878,777 | 60,932 | 6.9% | 7,967,687 | 538,452 | 6.8% |

Table 3. National projections of ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* events by region and setting in the US

| Region | Setting | ESBL % (n) |
|-----------------|----------------|---------------------------------|
| West | Ambulatory | 5.9% (71,008/1,211,156) |
| | Admission | 8.8% (12,608/142,764) |
| | Hospital-Onset | 14.2% (16,514/116,267) |
| Subtotal | | 6.8% (100,130/1,470,187) |
| Midwest | Ambulatory | 4.6% (86,575/1,884,816) |
| | Admission | 8.3% (20,904/252,003) |
| | Hospital-Onset | 10.9% (23,157/211,637) |
| Subtotal | | 5.6% (130,637/2,348,457) |
| South | Ambulatory | 6.2% (144,994/2,332,858) |
| | Admission | 9.0% (34,702/386,125) |
| | Hospital-Onset | 13.0% (36,839/283,707) |
| Subtotal | | 7.2% (216,535/3,002,689) |
| Northeast | Ambulatory | 6.5% (57,624/890,346) |
| | Admission | 10.0% (13,132/131,320) |
| | Hospital-Onset | 16.4% (20,395/124,689) |
| Subtotal | | 8.0% (91,151/1,146,354) |

ESBL= extended-spectrum beta-lactamase

Figure 4. National projections of ESBL-producing *E. coli*, *K. pneumoniae*, and *P. mirabilis* events (n) by period tested and region



Total "N" represents number of projected events

Conclusions

- These data suggest that national hospital onset ESBL rates in the 12 months ending June 2016 may be higher than previously reported estimates with urine being the primary source of ESBL-producing organisms.¹⁻³
- The highest rates of projected ESBL events occur in the hospital-onset period, however 67% of ESBL events occur in the ambulatory period
- The highest rates of ESBL are in the Northeast but the highest projected cases are in the Midwest and South regions
- The limitations to this study include that many methodologies are available to determine projections, and projections beyond the underlying data sample always have underlying assumptions and carry some risk

References

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Acknowledgements

This study is supported by Tetraphase Pharmaceuticals, Watertown, MA. We would like to thank Jason Till, MPH and John Murray, MPH for their efforts to create the dataset and analyses to support this work.

Author Disclosure Information

V. Gupta: D. Employee; Self; BD; M Olesky: D. Employee; Self; Tetraphase Pharmaceuticals; J Mohr: D. Employee; Self; Medical Affairs Strategic Solutions, LLC; K Luepke: D. D. Former Employee; Self; Tetraphase Pharmaceuticals; H Hoffman-Roberts: D. Employee; Self; Theravance Biopharma; YP Tabak: D. Employee; Self; BD; RS Johannes: D. Employee; Self; BD;