



EUCAST

European Committee
on Antimicrobial
Susceptibility Testing

Haemophilus influenzae

Benzylpenicillin 1 unit as screen for
beta-lactam resistance

Version 10.0
January 2026

Haemophilus influenzae

MIC and zone diameter correlates

- The following histograms present inhibition zone diameter distributions from EUCAST antimicrobial susceptibility testing. In most, the different colours of the bars indicate different MIC values. In some, the colours of the bars indicate a resistance gene or a resistance mechanism.
- The distributions include data for wild-type isolates and for isolates with acquired resistance mechanisms. A large number of isolates with MIC values close to the edge of the wild-type distribution and/or close to EUCAST clinical breakpoints were intentionally included. These distributions can not be used to infer resistance rates or the performance of the tests with routine isolates.
- For some agents, isolates were tested on more than one occasion, including parallel tests with disks and media from several manufacturers. When this is the case, data are presented as both the “number of isolates tested” and the “total number of MIC-zone diameter correlates”, including replicate tests and parallel tests with disks and media from different sources.

Haemophilus influenzae

Materials and methods

- Antimicrobial susceptibility testing was performed on a collection of *Haemophilus influenzae*, including many isolates with beta-lactam resistance. Disk diffusion was performed on MH-F media according to EUCAST methodology and MIC determination was performed with the ISO broth microdilution method using MH-F broth.
- The following graphs present inhibition zone distributions for benzylpenicillin 1 unit with MIC values for clinically important beta-lactam agents or resistance mechanisms as coloured bars. A nitrocefin-based disk test was used to analyse β -lactamase production and PCR was used to detect PBP mutations.
- The distributions in this presentation are the result of a collaboration between EUCAST, JMI Laboratories (USA), Laboratory Specialists Inc. (USA) and Sykehuset i Vestfold, Tønsberg (Norway).
- This presentation is based on EUCAST Clinical Breakpoint Tables v. 16.0.

Changes from previous version (9.0)

Changes
<ul style="list-style-type: none">• Indications updated for ampicillin and amoxicillin iv.

Haemophilus influenzae

Screen for beta-lactam resistance

- The benzylpenicillin 1 unit disk screen test shall be used to exclude beta-lactam resistance mechanisms.
- The screening breakpoint for benzylpenicillin 1 unit is $S \geq 12$ mm.
- When the screen is negative, all beta-lactam agents for which clinical breakpoints are available, including those with a “Note”, can be reported susceptible without further testing, except for oral preparations of amoxicillin, amoxicillin-clavulanic acid and cefuroxime, which if reported, should be reported “susceptible, increased exposure” (I).
- When the screen is positive, see flow chart for interpretation.

Haemophilus influenzae

Screen for beta-lactam resistance

Haemophilus influenzae: Flow chart based on the benzylpenicillin (PCG) screen test for beta-lactam resistance mechanisms to reduce the number of specific tests for beta-lactam agents

To take full advantage of the procedure, include the amoxicillin-clavulanic acid 2-1 µg disk, but read and interpret only on beta-lactamase positive isolates.

PCG 1 unit zone diameter ≥12 mm

Mechanism: excludes all beta-lactam resistance mechanisms

Report susceptible (**S**) to beta-lactam agents for which clinical breakpoints are available, including those with "Note". **Exception:** Oral amoxicillin, oral amoxicillin-clavulanic acid and oral cefuroxime are reported "susceptible, increased exposure" (**I**).

No further testing required.

PCG 1 unit zone diameter <12 mm

Mechanism: beta-lactamase and/or PBP3 mutations

Further testing: test for beta-lactamase.

For meropenem in meningitis, determine the MIC and interpret according to the clinical breakpoints.

Beta-lactamase positive

Mechanisms: beta-lactamase with or without PBP3 mutations

Report resistant (**R**) to ampicillin, amoxicillin and piperacillin (without beta-lactamase inhibitor).

For other beta-lactam agents, read the amoxicillin-clavulanic acid 2-1 µg disk and interpret as below.

Beta-lactamase negative

Mechanism: PBP3 mutations

Perform susceptibility testing for the relevant agents and interpret according to breakpoints.

For cefepime, cefpodoxime and imipenem, if PCG 1 unit <12 mm and susceptible by agent disk diffusion test, determine the MIC of the agent and interpret according to the clinical breakpoints.

Amoxicillin-clavulanic acid 2-1 µg ≥15 mm

Mechanism: beta-lactamase only

Report susceptible (**S**) to agents (other than ampicillin, amoxicillin and piperacillin) for which clinical breakpoints are available, including those with "Note". **Exception:** Oral amoxicillin-clavulanic acid and oral cefuroxime are reported "susceptible, increased exposure" (**I**).

Amoxicillin-clavulanic acid 2-1 µg <15 mm

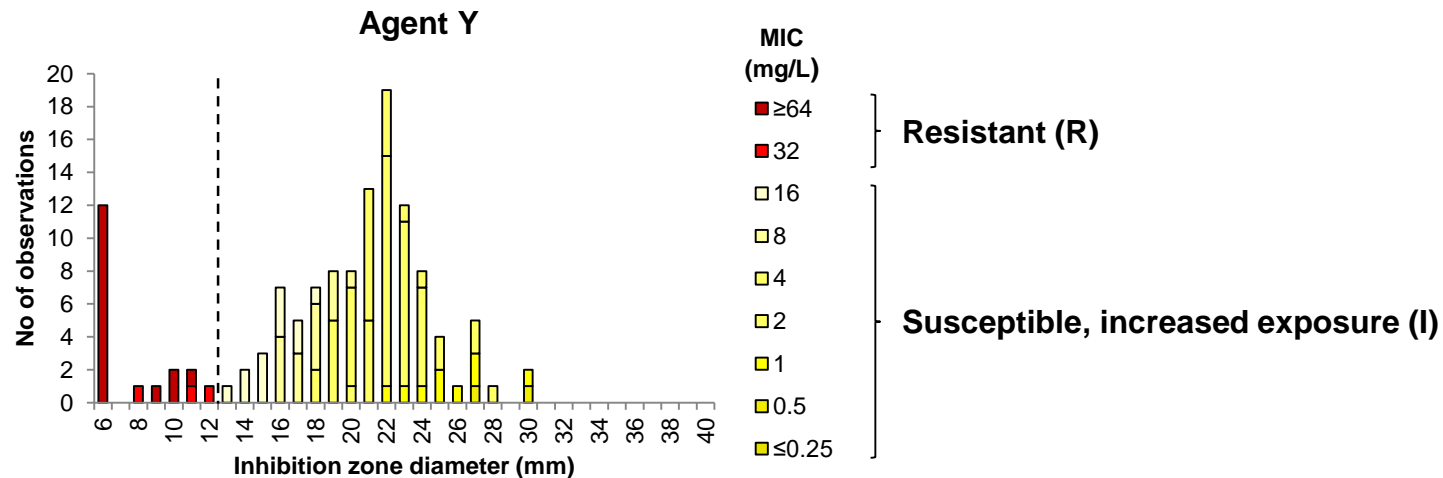
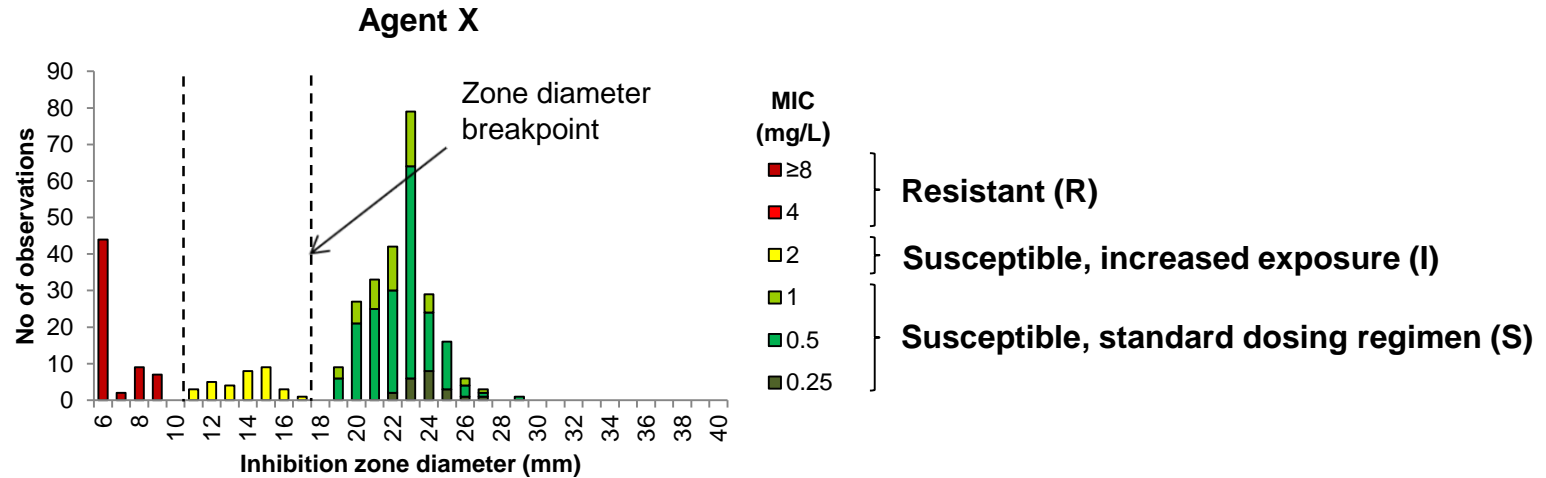
Mechanisms: beta-lactamase and PBP3 mutations

Perform susceptibility testing for the relevant agents and interpret according to breakpoints.

For cefepime, cefpodoxime and imipenem, if PCG 1 unit <12 mm and susceptible by agent disk diffusion test, determine the MIC of the agent and interpret according to the clinical breakpoints.

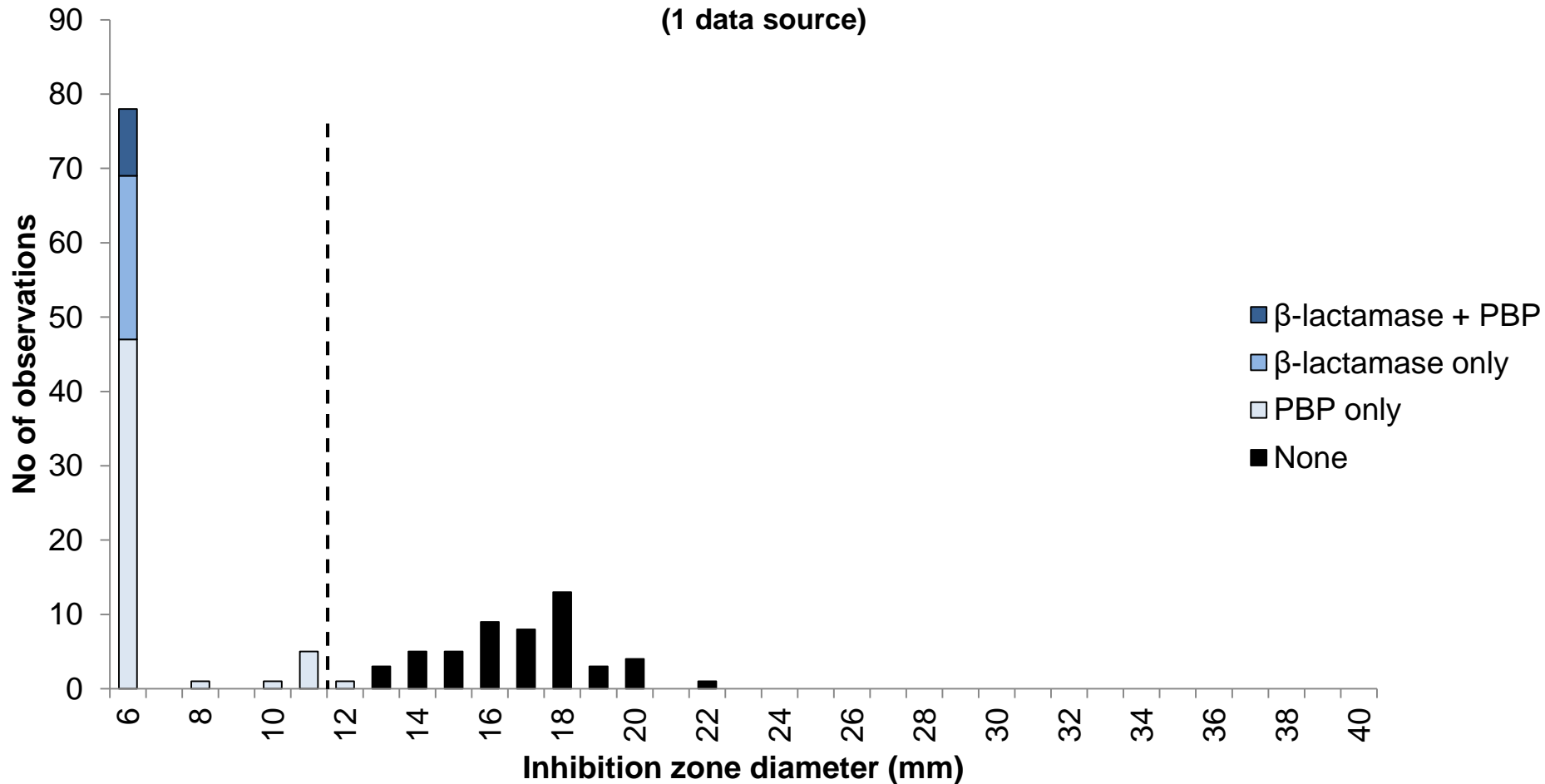
Explanation of graphs:

- These graphs show zone diameter distributions with MIC values or resistance mechanisms as coloured bars. Colours are related to current EUCAST MIC breakpoints.



Benzylpenicillin 1 unit vs. β -lactam resistance mechanism *H. influenzae*, 137 clinical isolates

(1 data source)



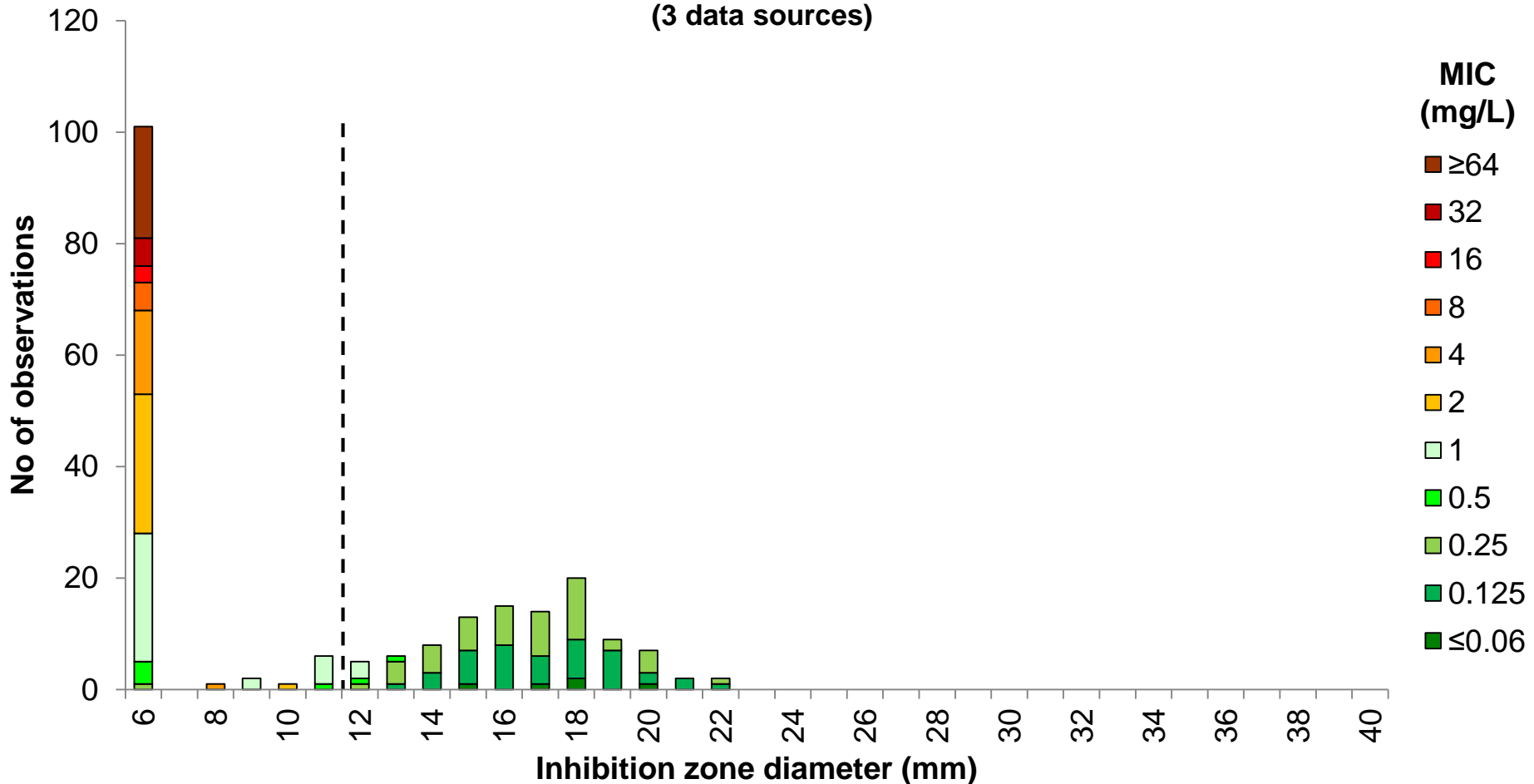
Breakpoints

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Ampicillin MIC *H. influenzae*, 167 isolates (212 correlates)

(3 data sources)



Breakpoints (non-meningitis)

Ampicillin MIC

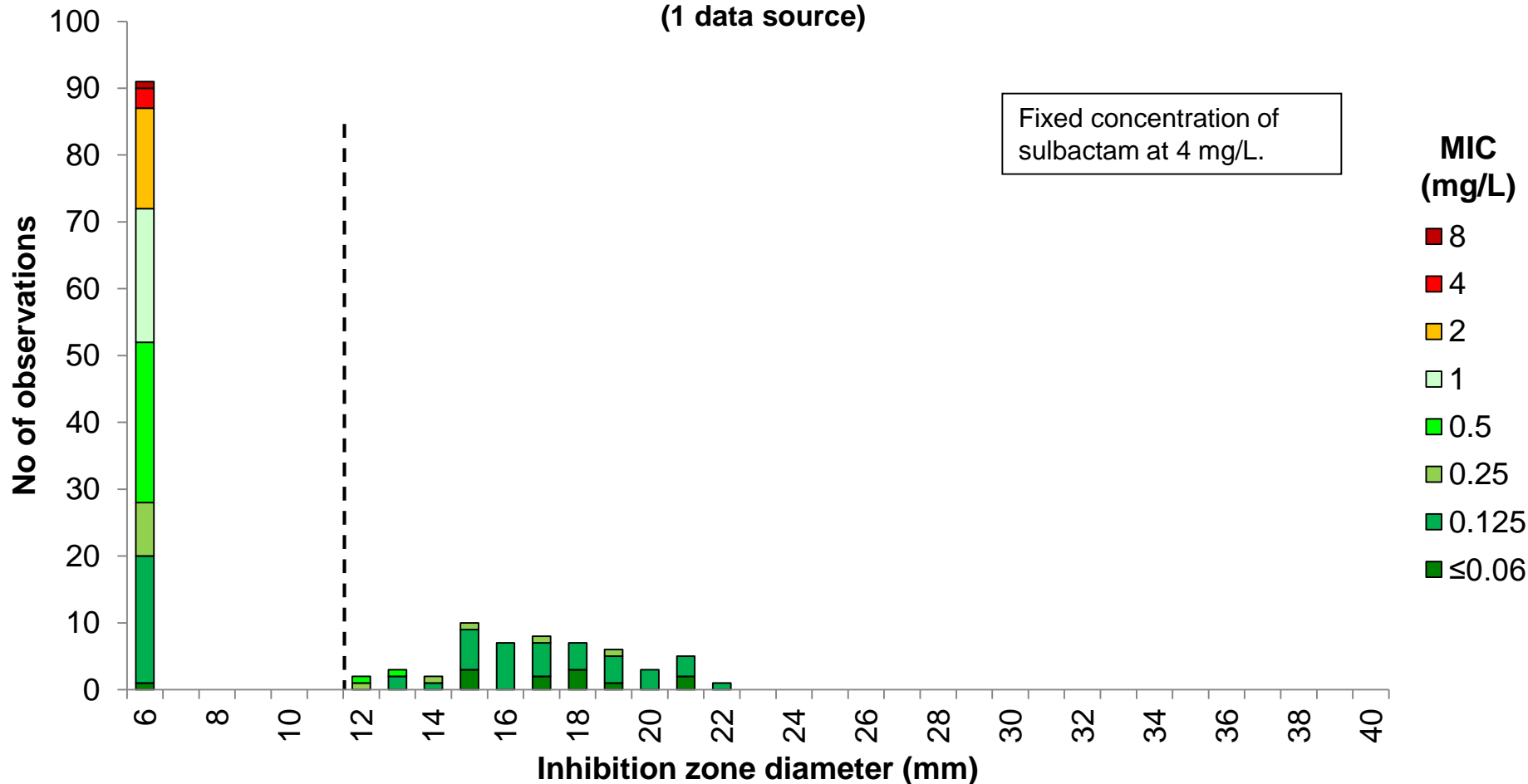
$S \leq 1$, $R > 1$ mg/L

Benzympenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Ampicillin-sulbactam MIC *H. influenzae*, 145 isolates

(1 data source)



Breakpoints

Ampicillin-sulbactam MIC

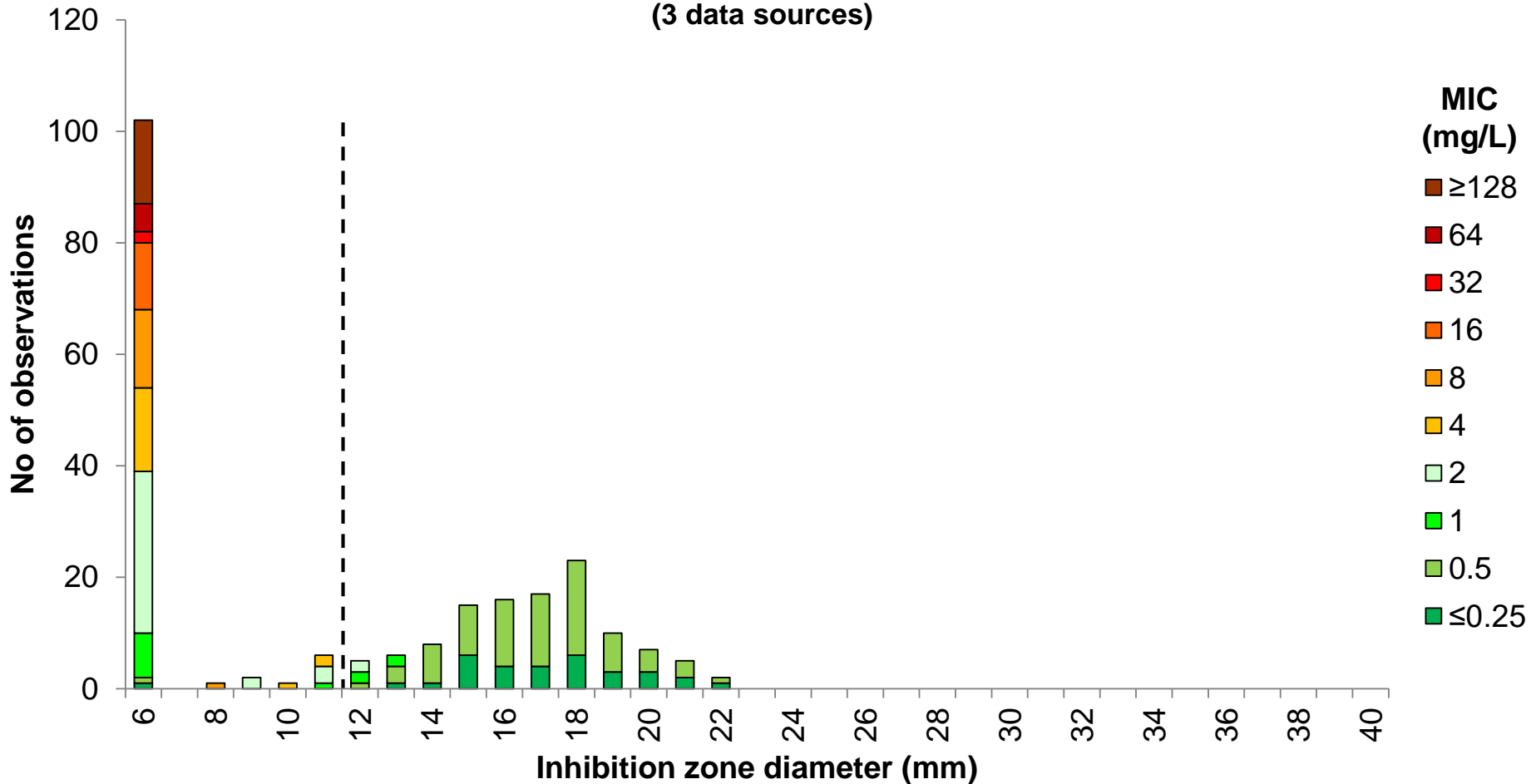
$S \leq 1$, $R > 1$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Amoxicillin MIC *H. influenzae*, 173 isolates (226 correlates)

(3 data sources)



Breakpoints (iv, non-meningitis)

Amoxicillin MIC

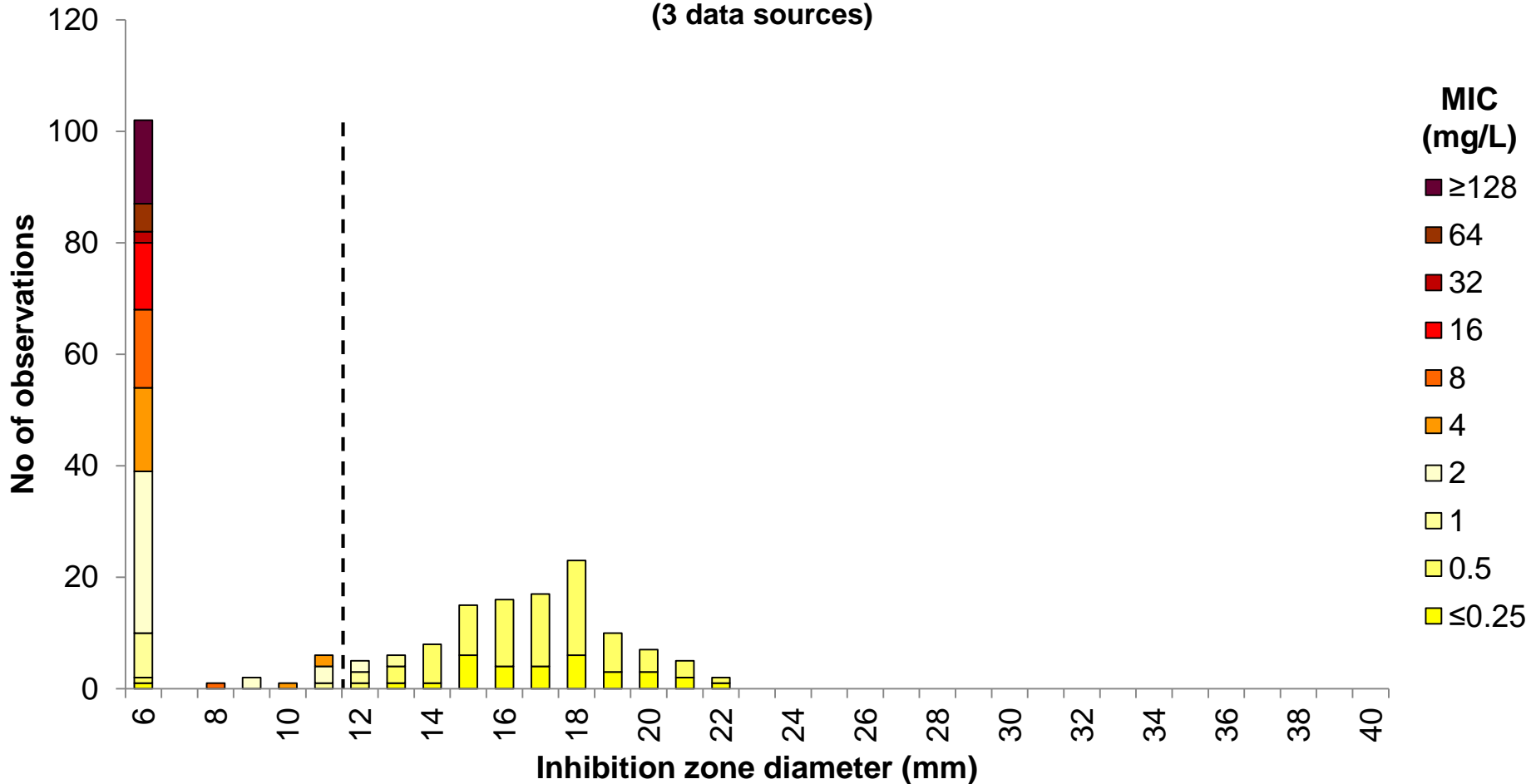
$S \leq 2$, $R > 2$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Amoxicillin MIC *H. influenzae*, 173 isolates (226 correlates)

(3 data sources)



Breakpoints (oral)

Amoxicillin MIC

$S \leq 0.001$, $R > 2$ mg/L

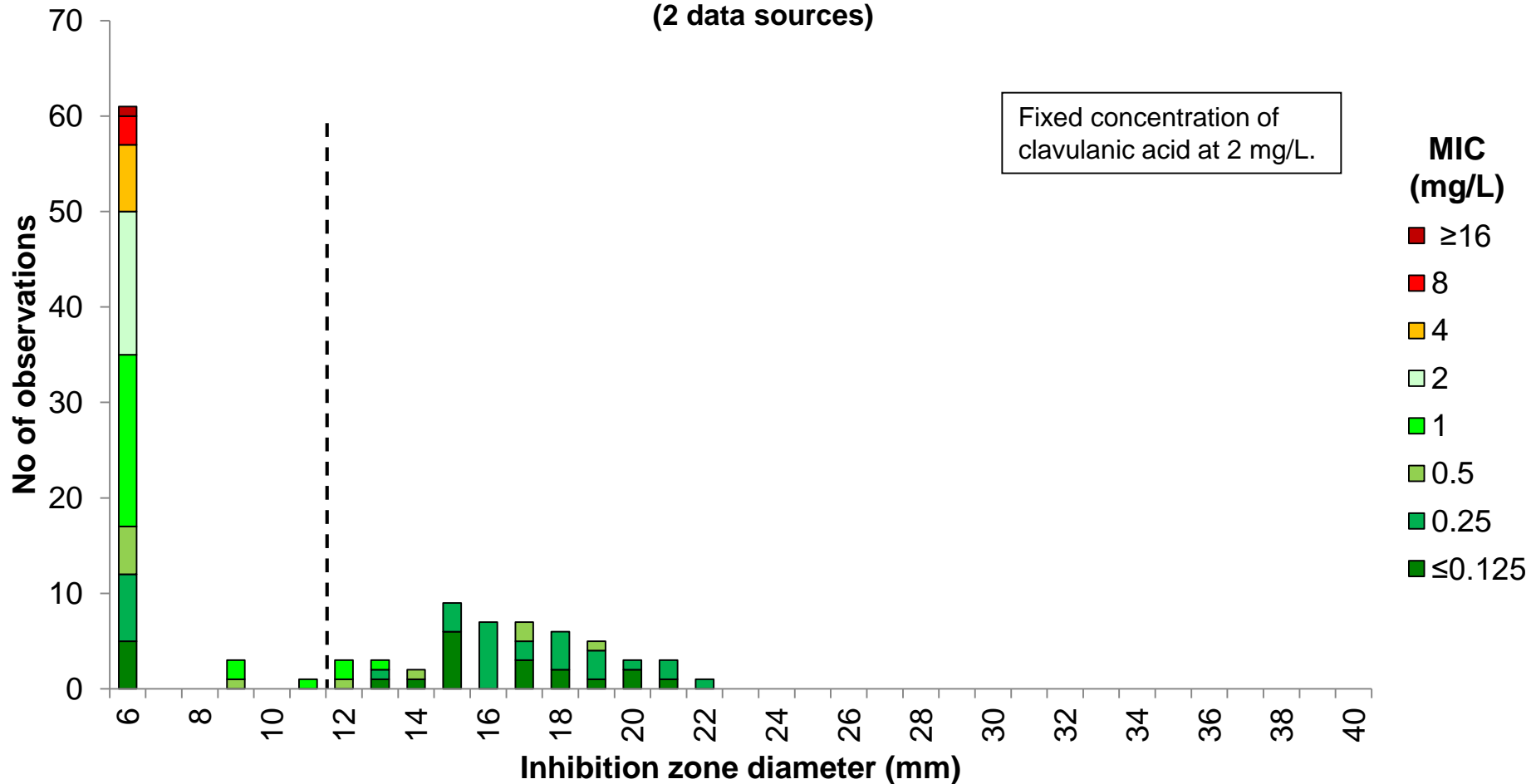
Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Amoxicillin-clavulanic acid MIC

H. influenzae, 114 isolates

(2 data sources)



Breakpoints (iv)

Amoxicillin-clavulanic acid MIC

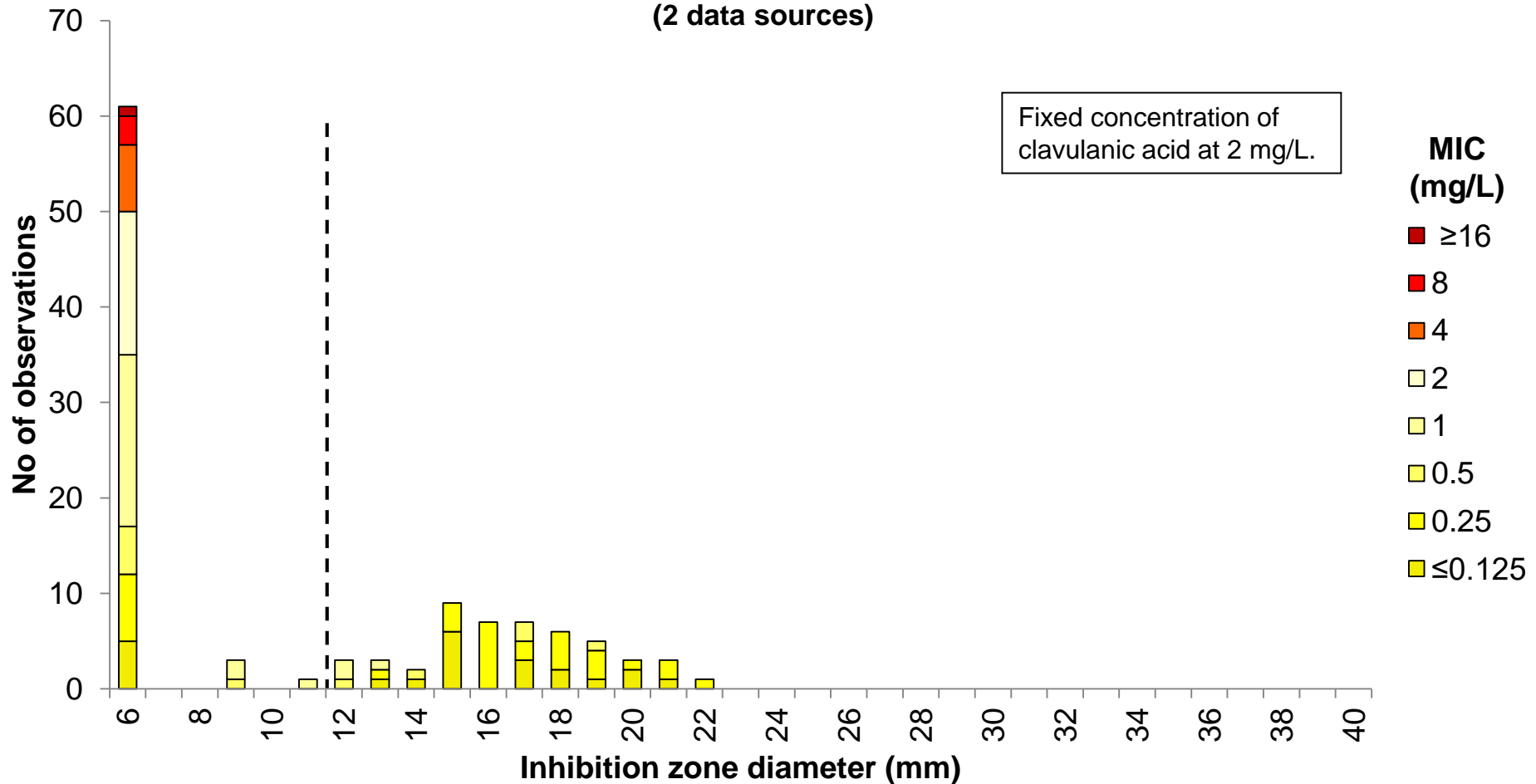
$S \leq 2$, $R > 2$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Amoxicillin-clavulanic acid MIC *H. influenzae*, 114 isolates

(2 data sources)



Breakpoints (oral)

Amoxicillin-clavulanic acid MIC

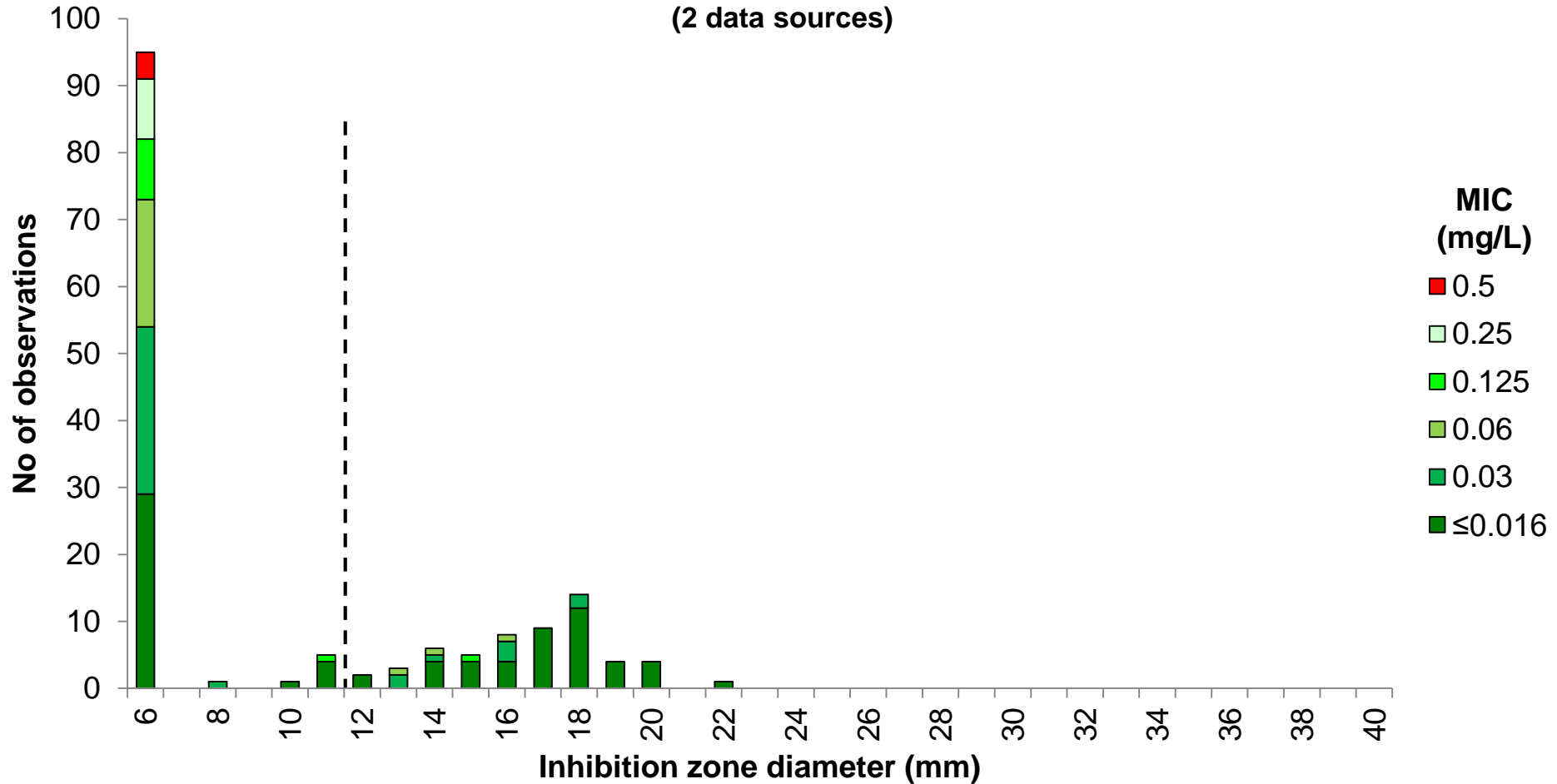
$S \leq 0.001$, $R > 2$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Piperacillin-tazobactam MIC *H. influenzae*, 158 isolates

(2 data sources)



Breakpoints

Piperacillin-tazobactam MIC

$S \leq 0.25$, $R > 0.25$ mg/L

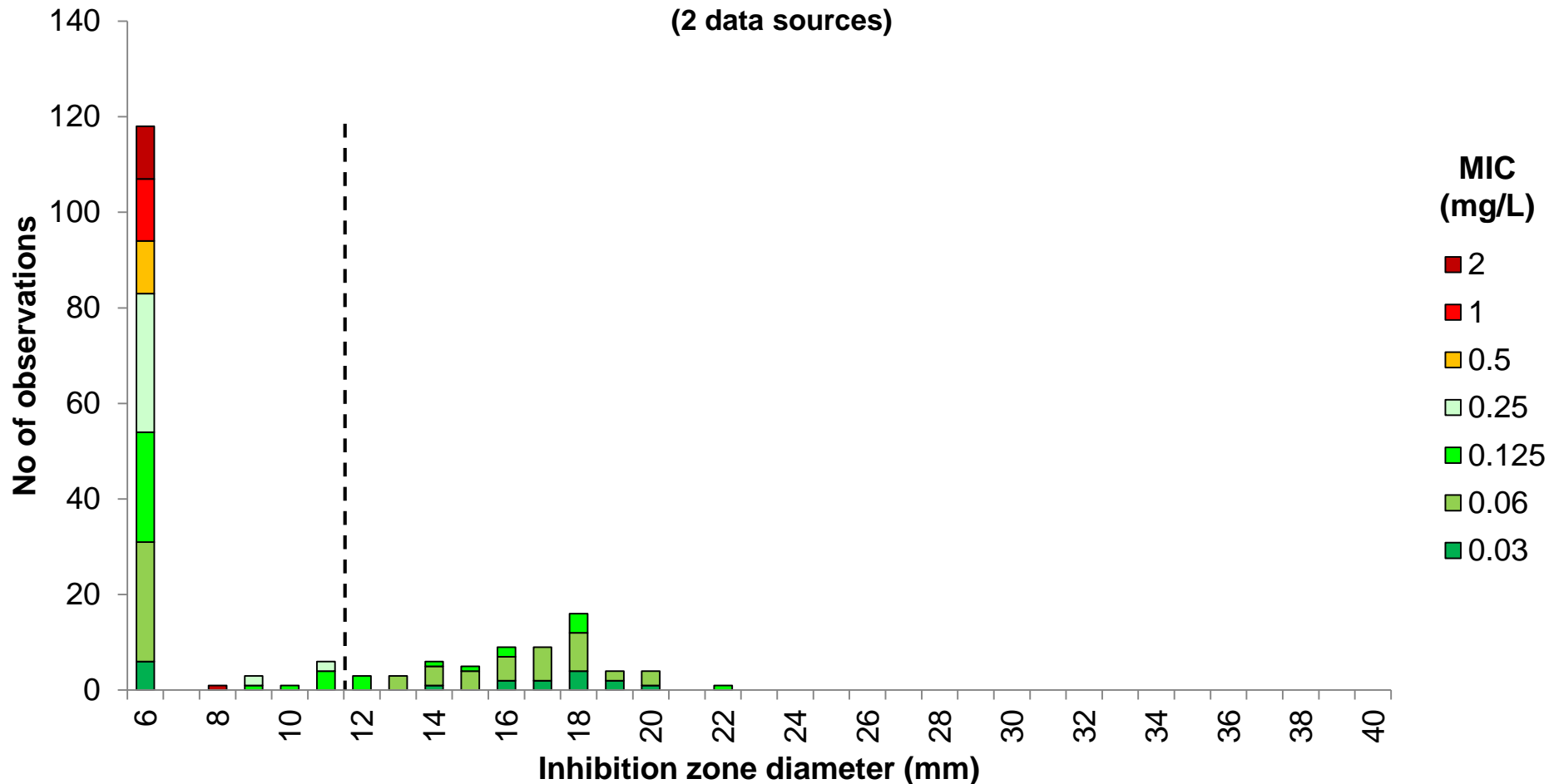
Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Cefepime MIC

H. influenzae, 189 isolates

(2 data sources)



Breakpoints

Cefepime MIC

$S \leq 0.25$, $R > 0.25$ mg/L

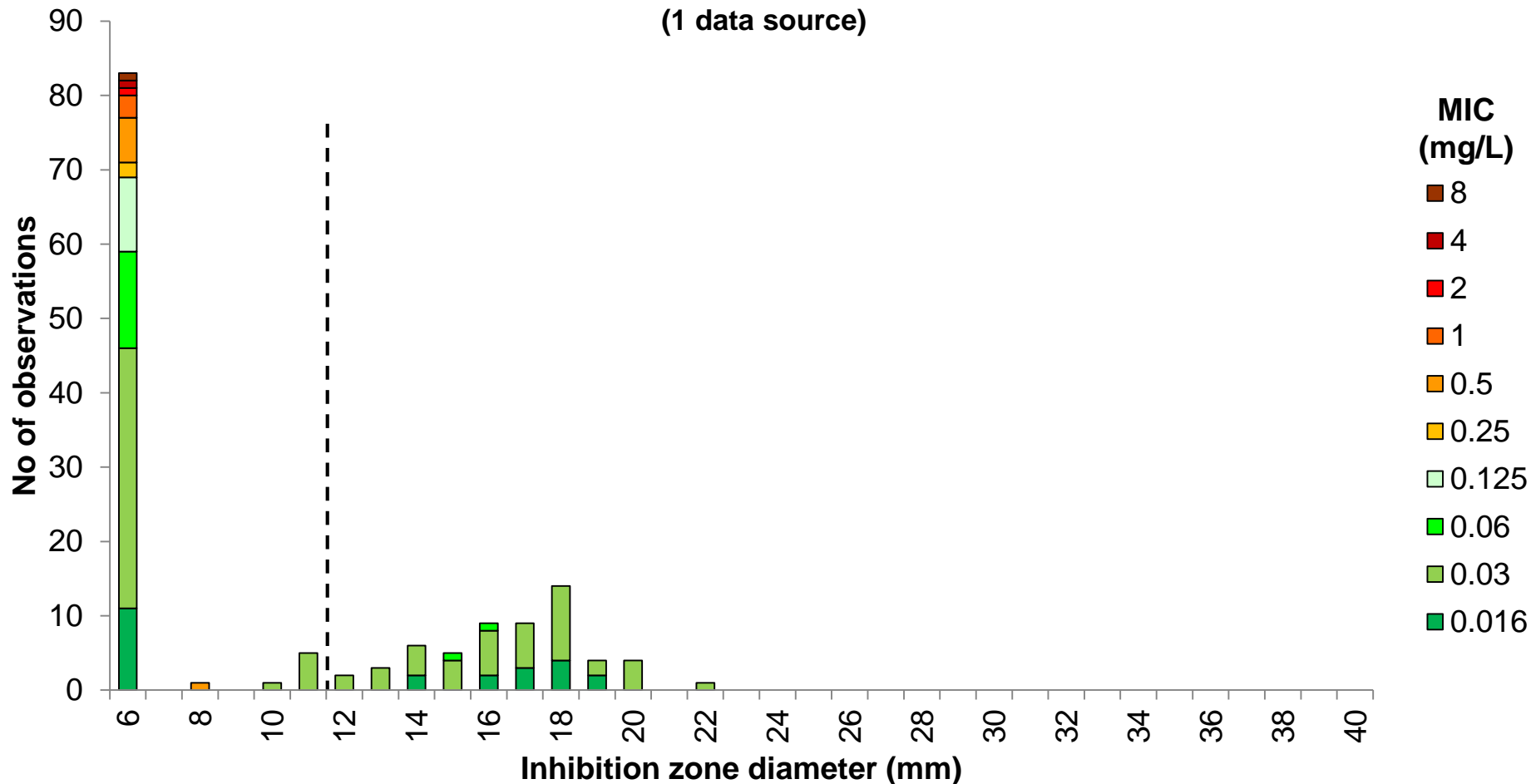
Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Cefixime MIC

H. influenzae, 147 isolates

(1 data source)



Breakpoints

Cefixime MIC

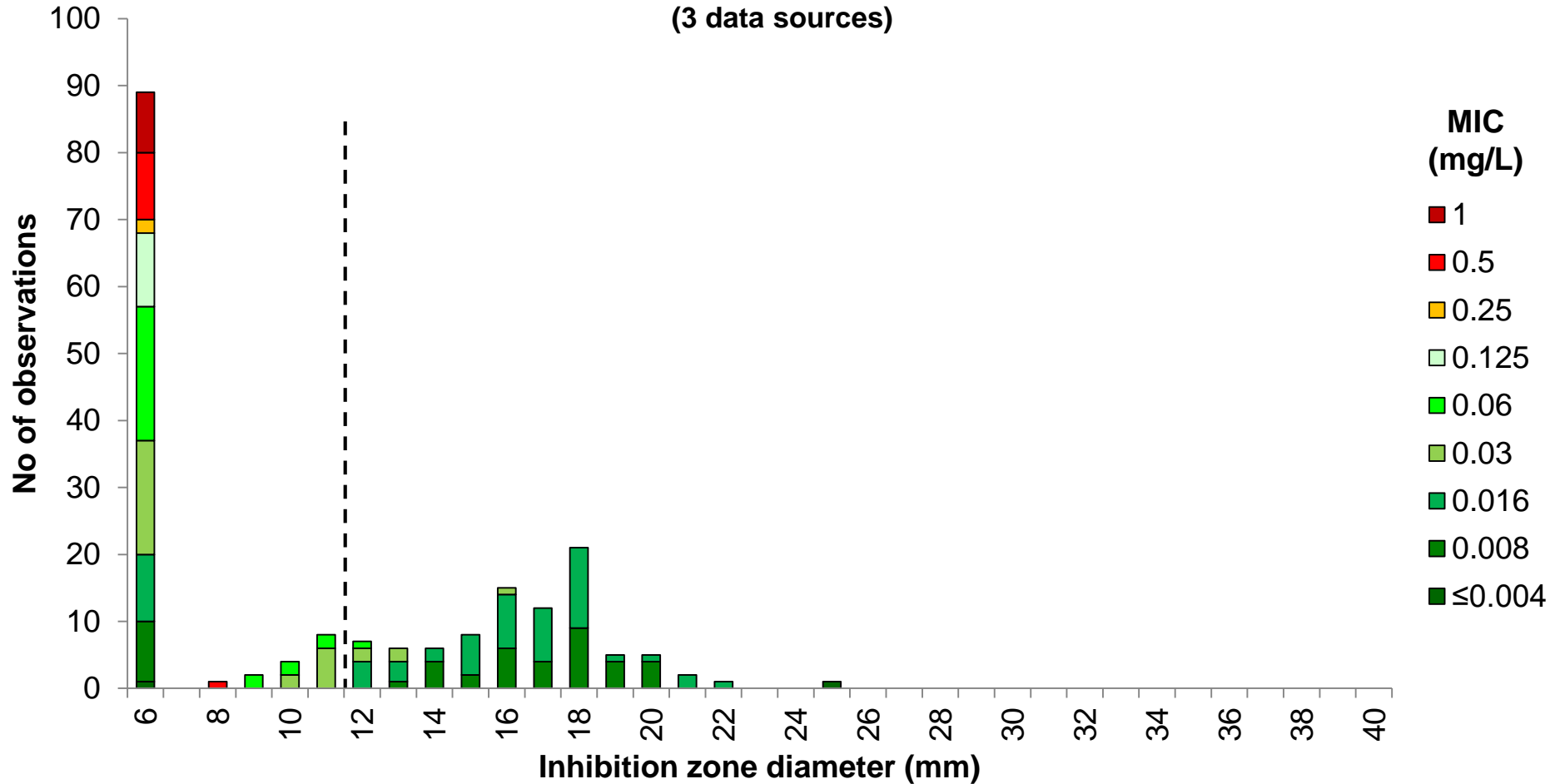
$S \leq 0.125$, $R > 0.125$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Cefotaxime MIC *H. influenzae*, 161 isolates (193 correlates)

(3 data sources)



Breakpoints

Cefotaxime MIC

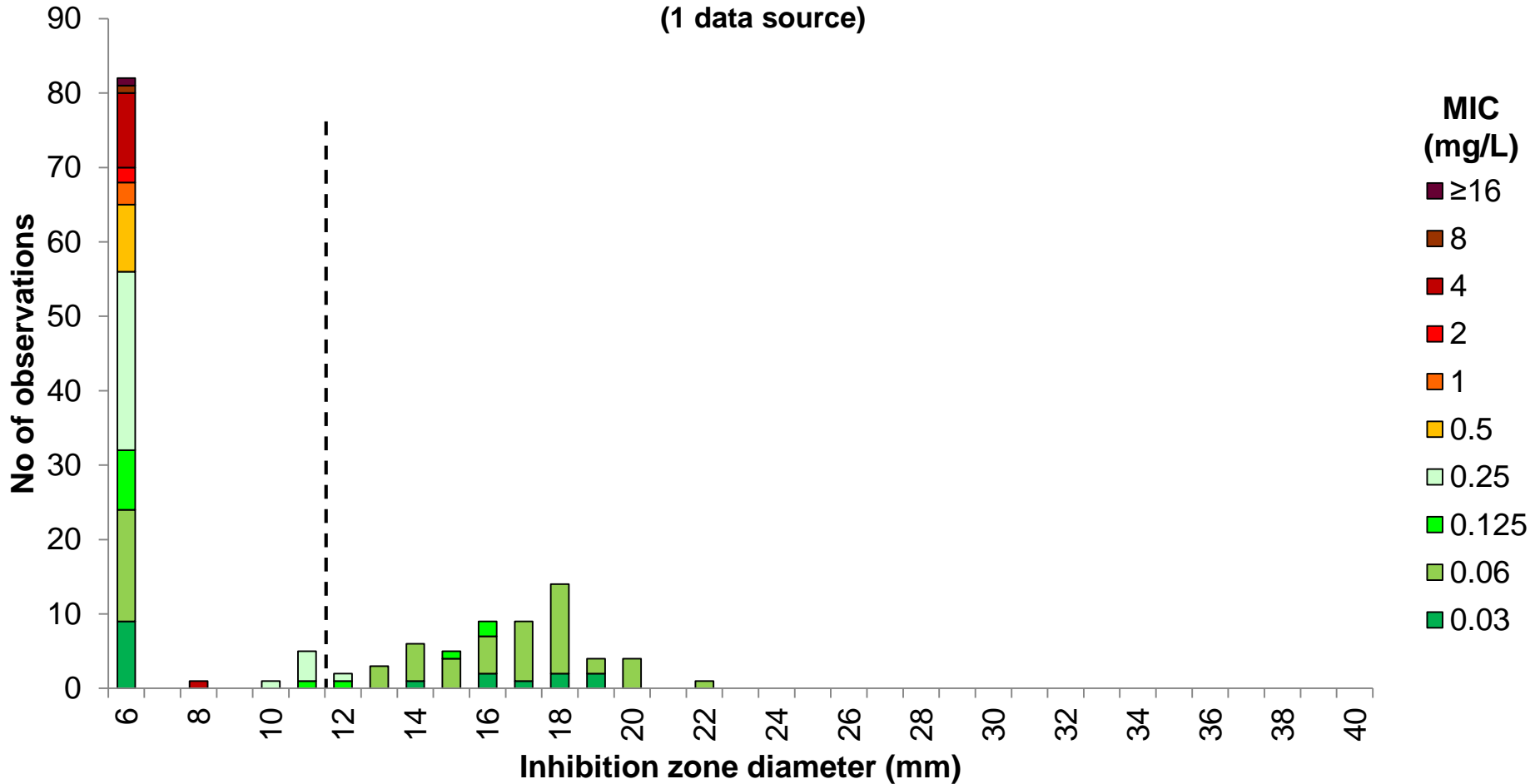
$S \leq 0.125$, $R > 0.125$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Cefpodoxime MIC *H. influenzae*, 146 isolates

(1 data source)



Breakpoints

Cefpodoxime MIC

$S \leq 0.25$, $R > 0.25$ mg/L

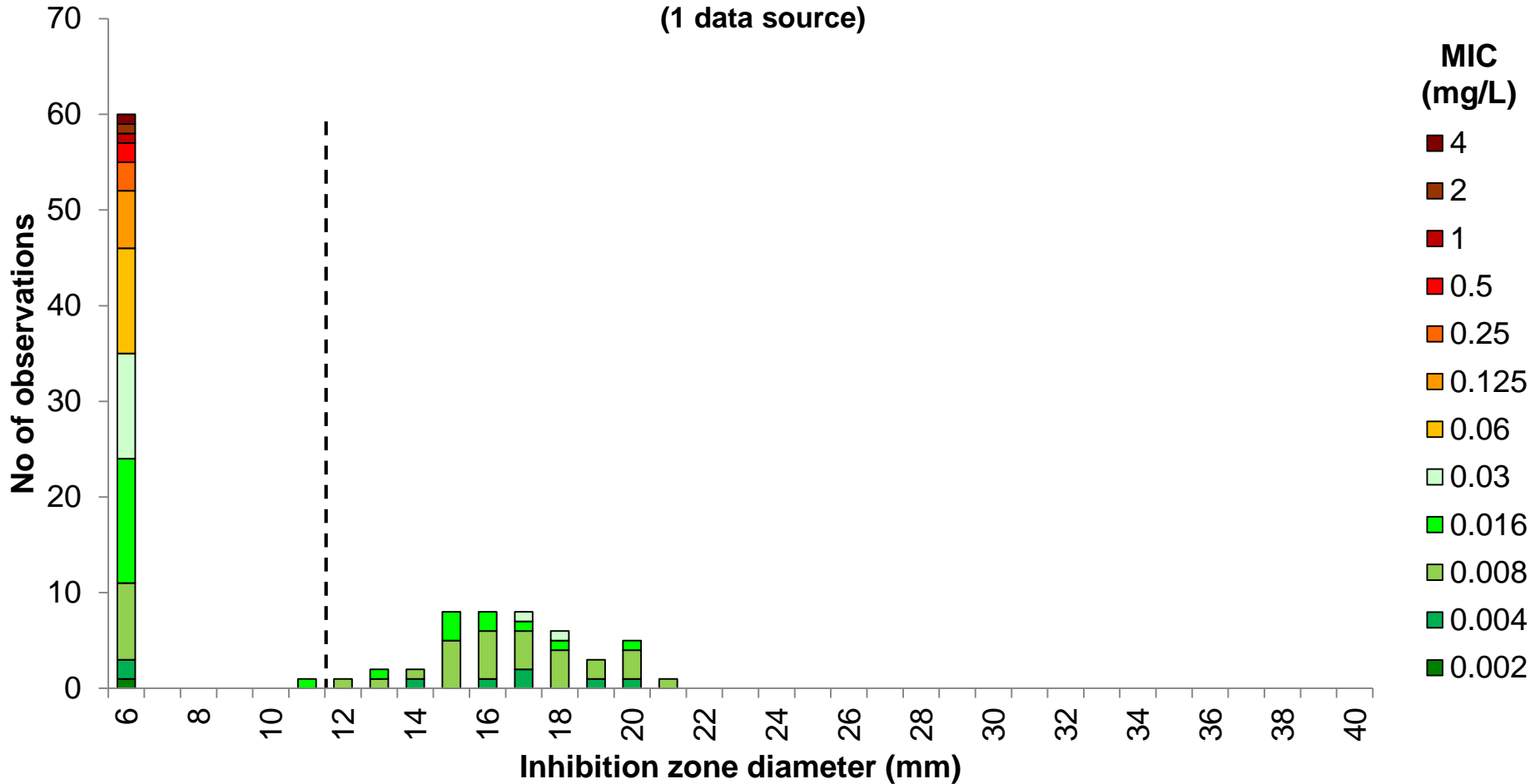
Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Ceftaroline MIC

H. influenzae, 105 isolates

(1 data source)



Breakpoints

Ceftaroline MIC

$S \leq 0.03$, $R > 0.03$ mg/L

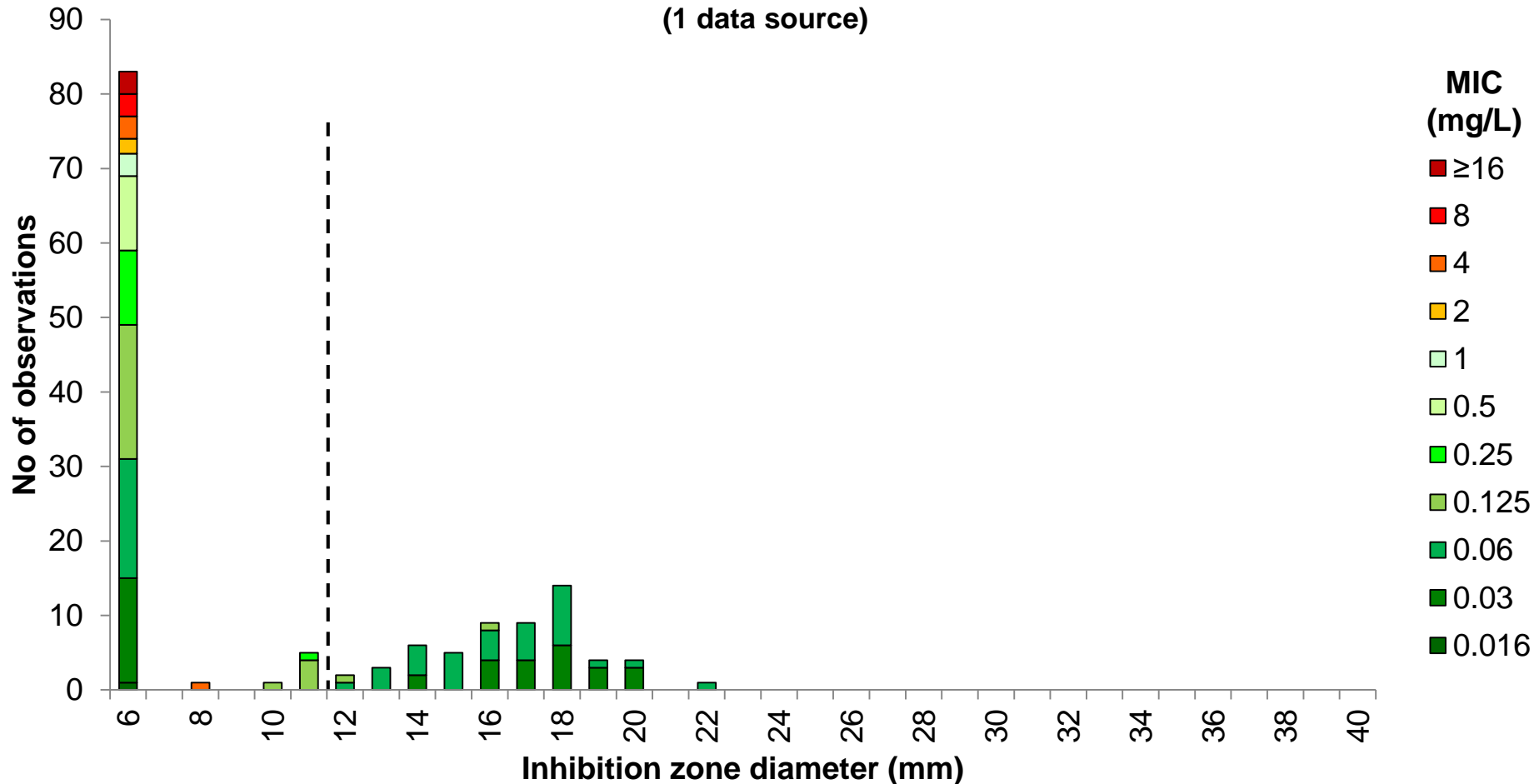
Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Ceftibuten MIC

H. influenzae, 147 isolates

(1 data source)



Breakpoints

Ceftibuten MIC

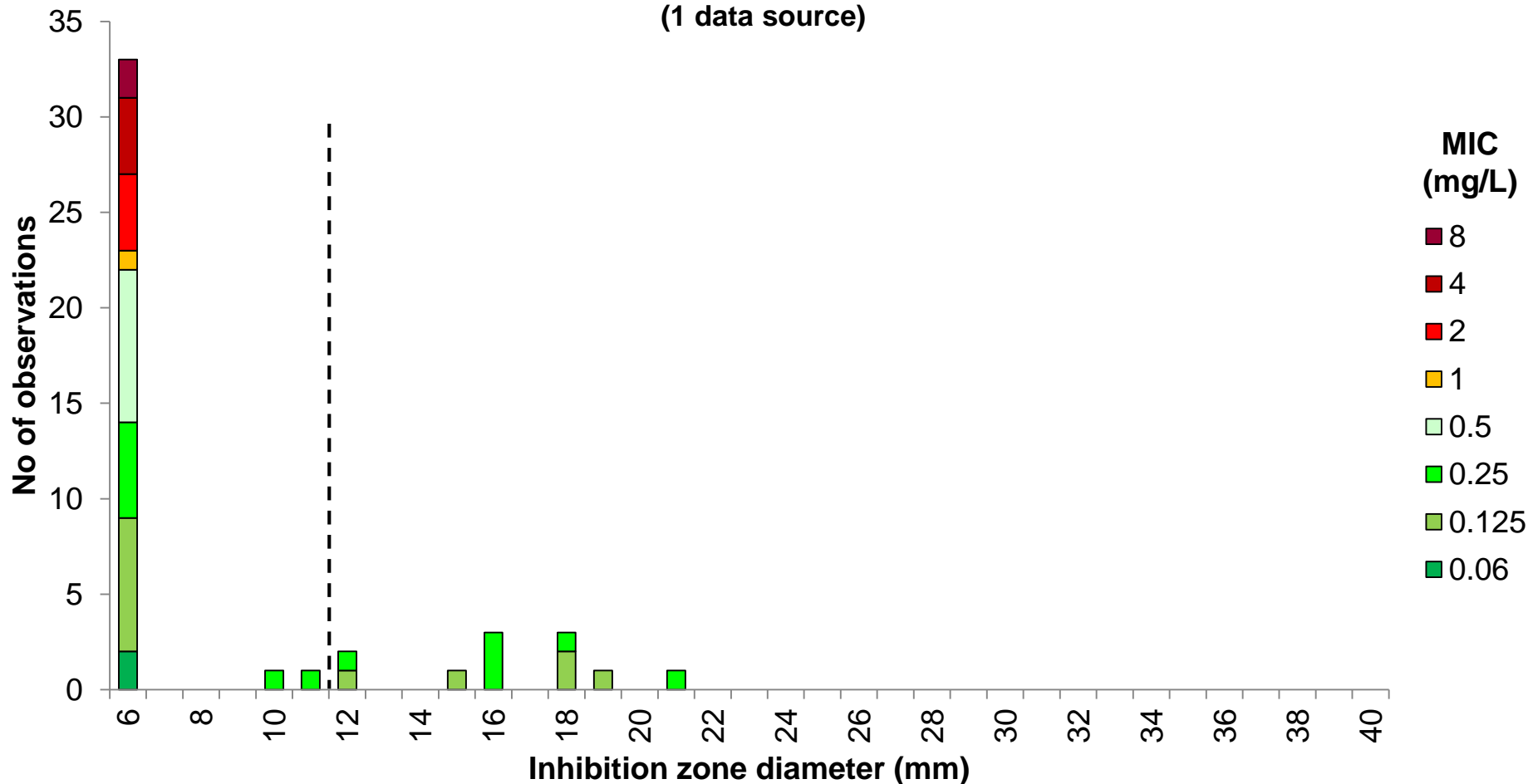
$S \leq 1$, $R > 1$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Ceftolozane-tazobactam MIC *H. influenzae*, 46 isolates

(1 data source)



Breakpoints (pneumonia)

Ceftolozane-tazobactam MIC

$S \leq 0.5$, $R > 0.5$ mg/L

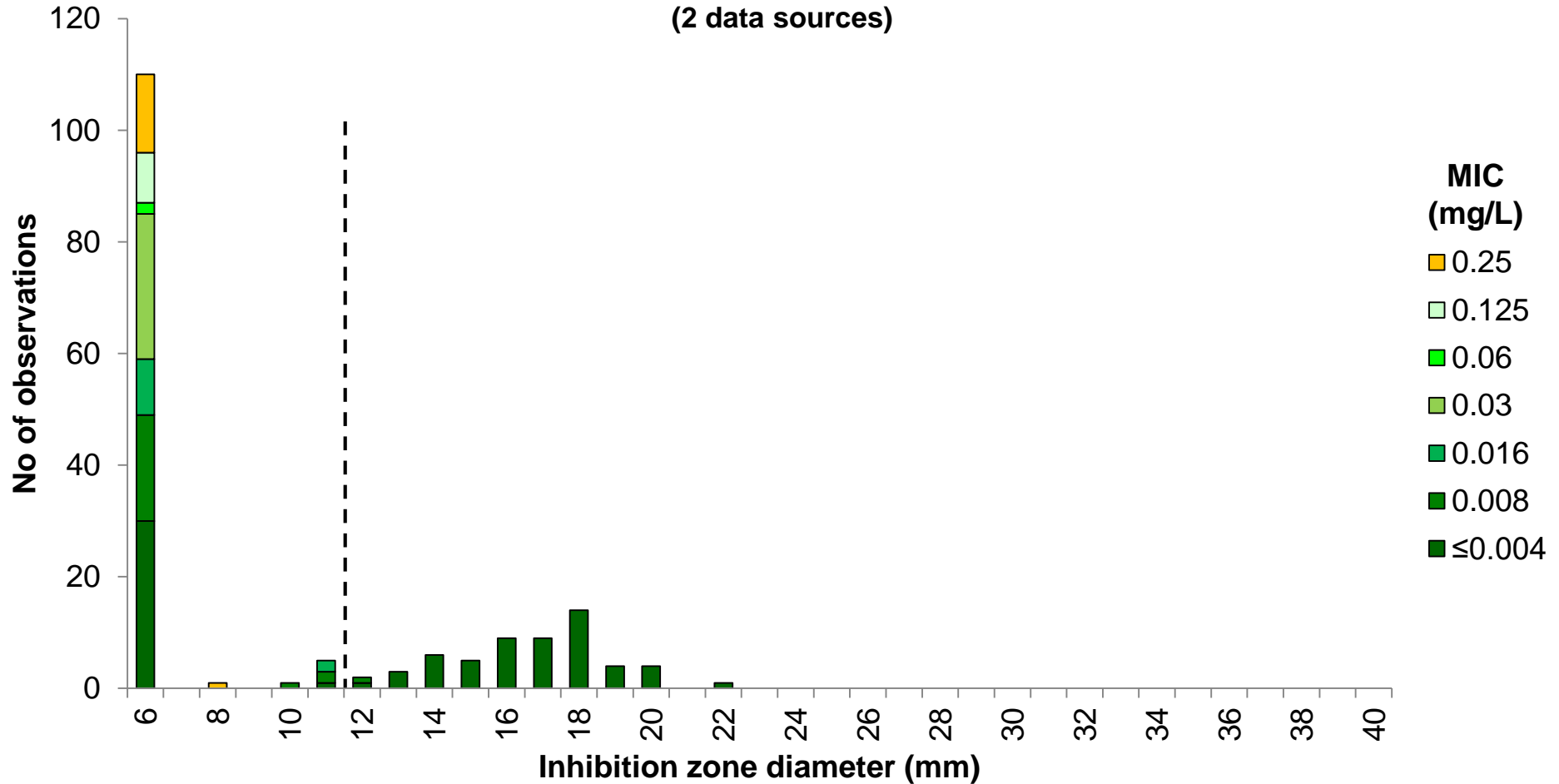
Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Ceftriaxone MIC

H. influenzae, 174 isolates

(2 data sources)



Breakpoints

Ceftriaxone MIC

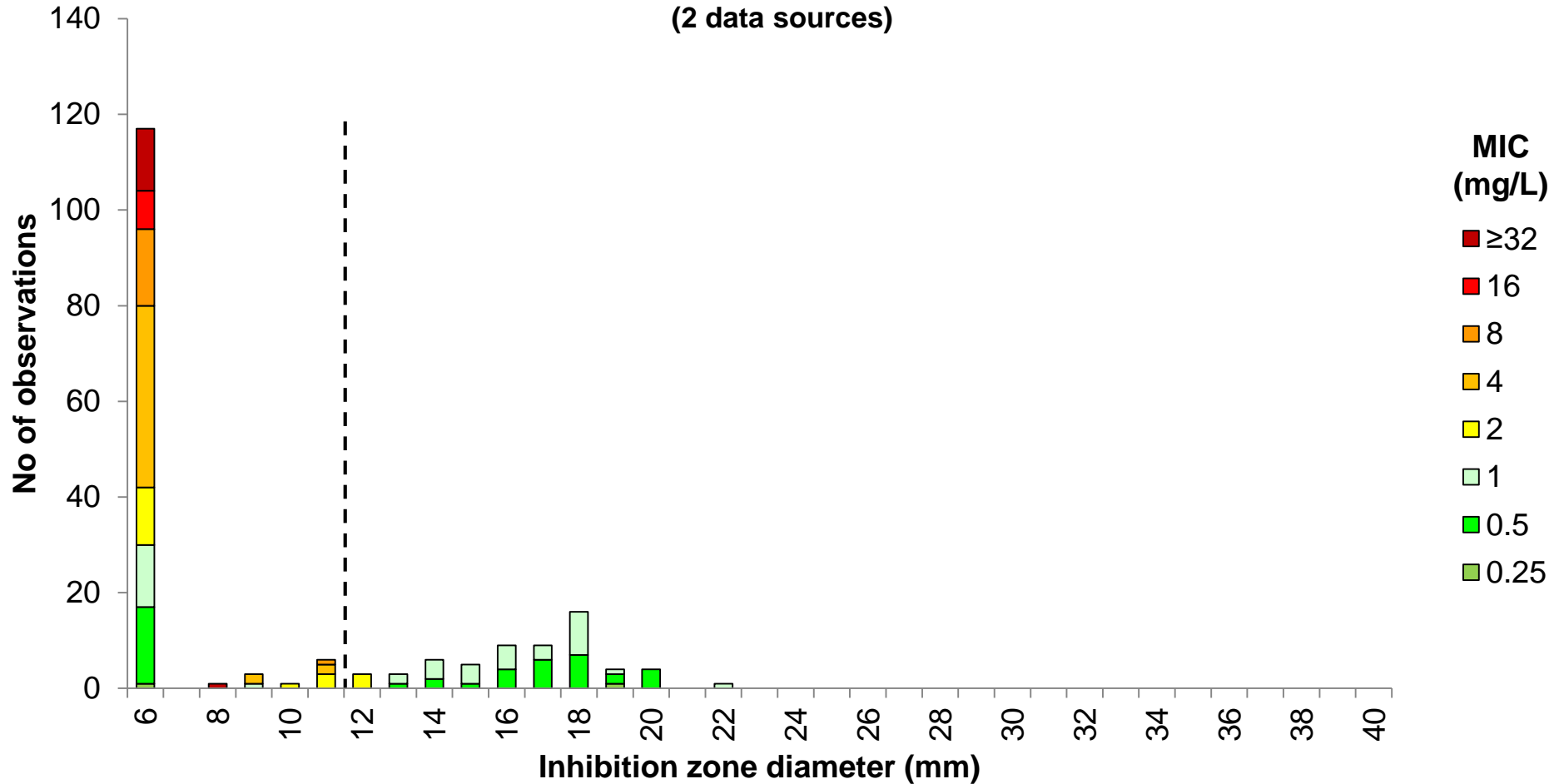
$S \leq 0.125$, $R > 0.125$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Cefuroxime MIC *H. influenzae*, 188 isolates

(2 data sources)



Breakpoints (iv)

Cefuroxime MIC

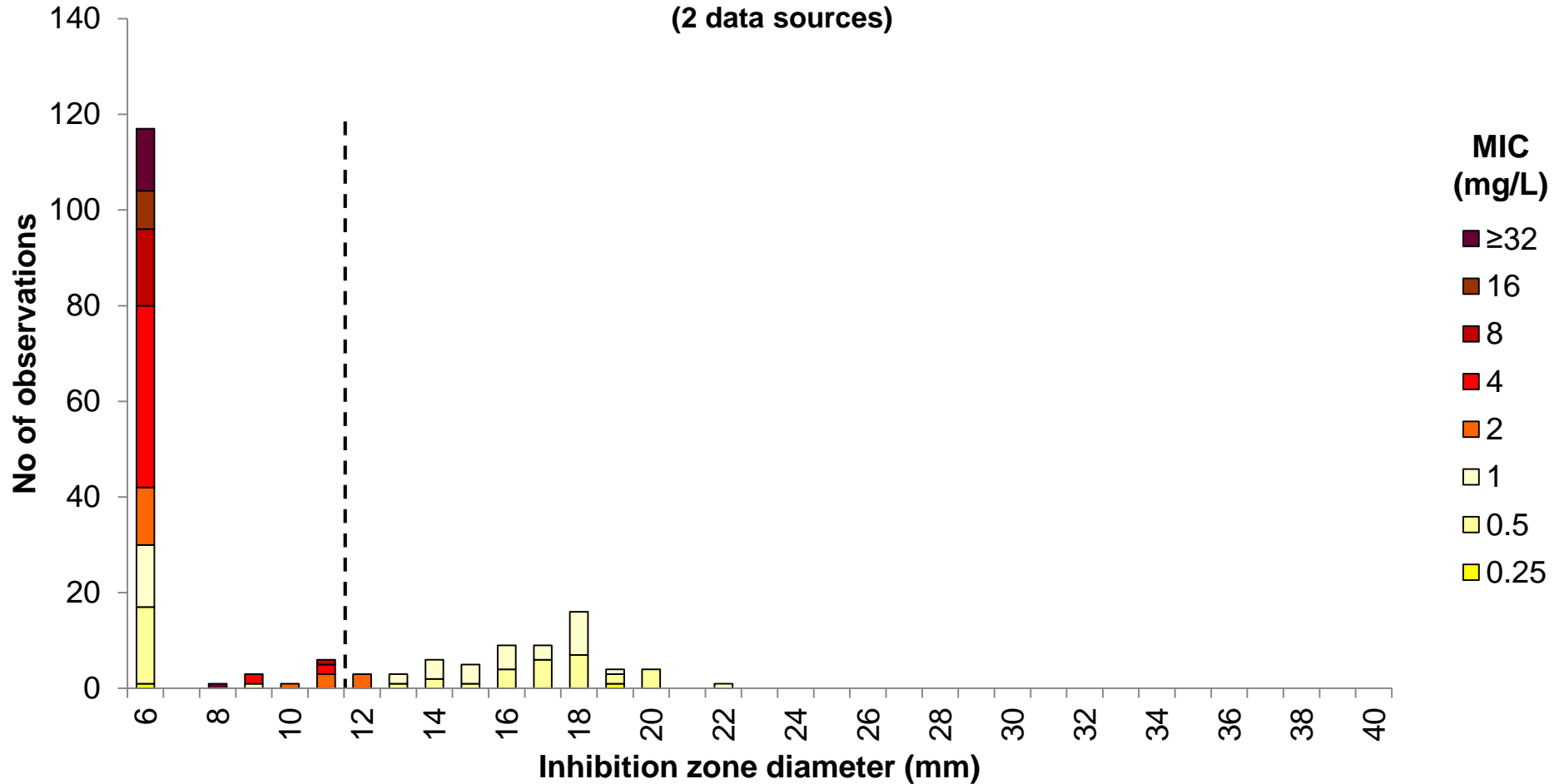
$S \leq 1$, $R > 2$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylopenicillin 1 unit vs. Cefuroxime MIC *H. influenzae*, 188 isolates

(2 data sources)



Breakpoints (oral)

Cefuroxime MIC

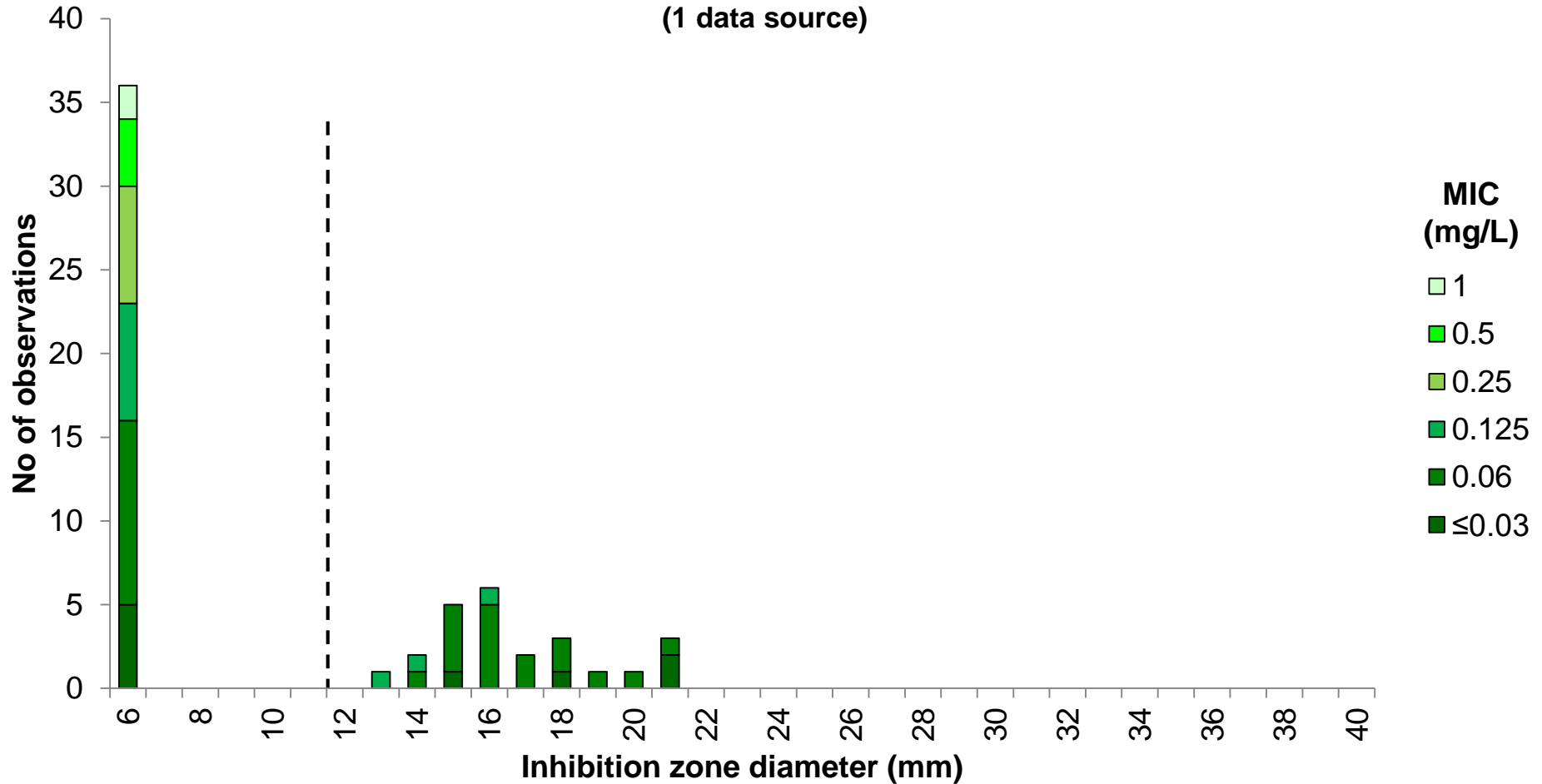
$S \leq 0.001$, $R > 1$ mg/L

Benzylopenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Doripenem MIC *H. influenzae*, 60 isolates

(1 data source)



Breakpoints

Doripenem MIC

$S \leq 1$, $R > 1$ mg/L

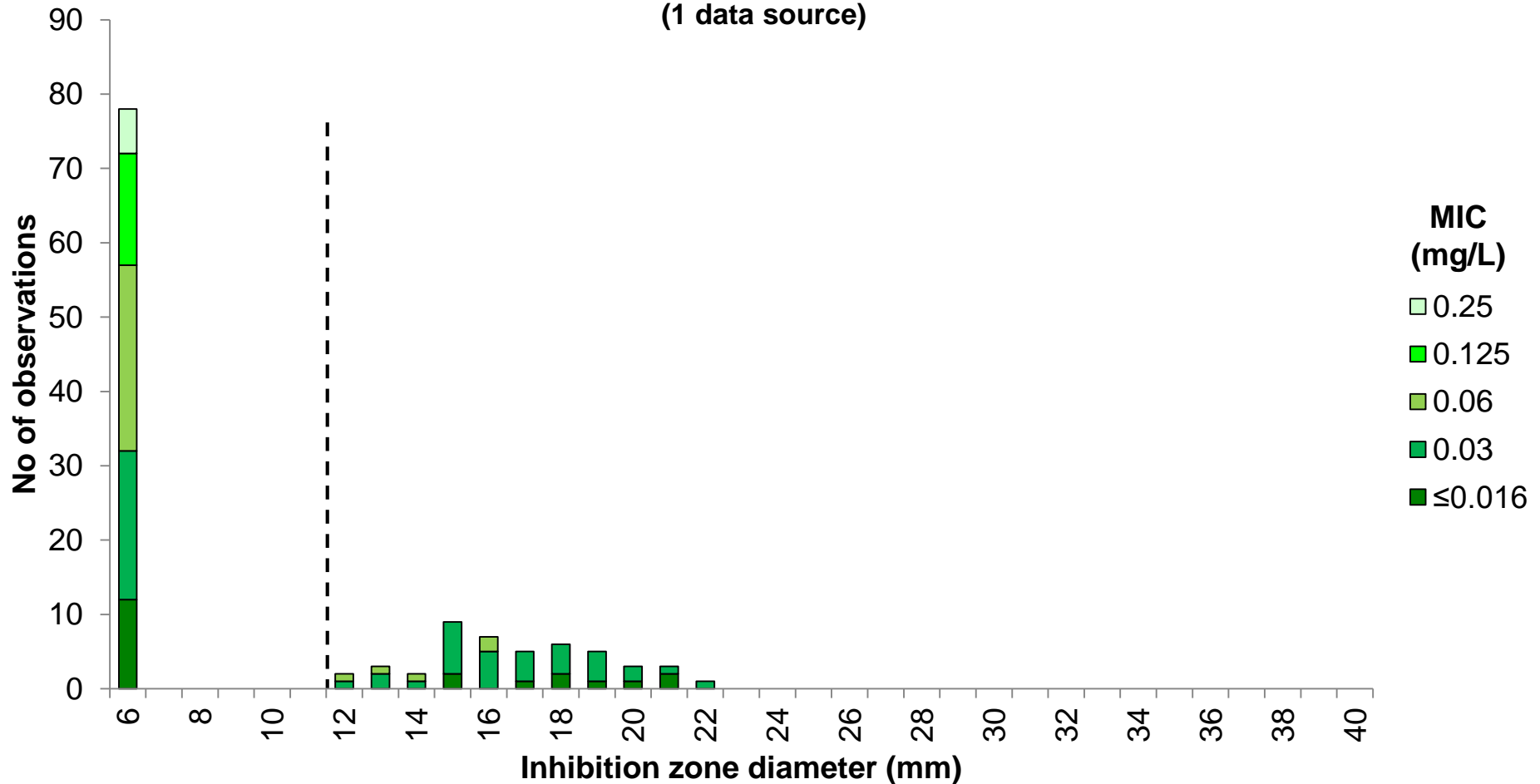
Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Ertapenem MIC

H. influenzae, 124 isolates

(1 data source)



Breakpoints

Ertapenem MIC

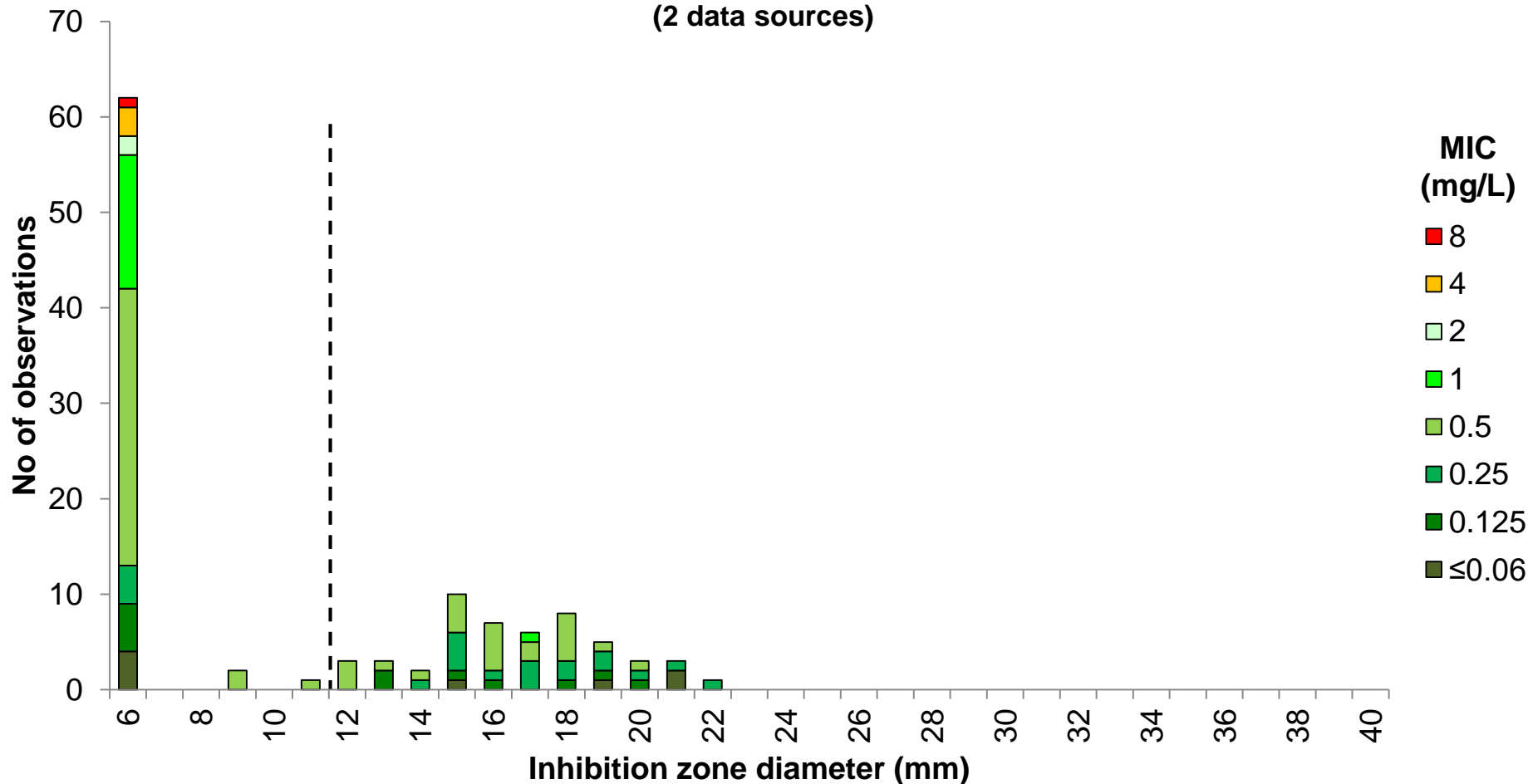
S≤0.5, R>0.5 mg/L

Benzylpenicillin zone diameter (screen)

S≥12 mm

Benzylpenicillin 1 unit vs. Imipenem MIC *H. influenzae*, 116 isolates

(2 data sources)



Breakpoints

Imipenem MIC

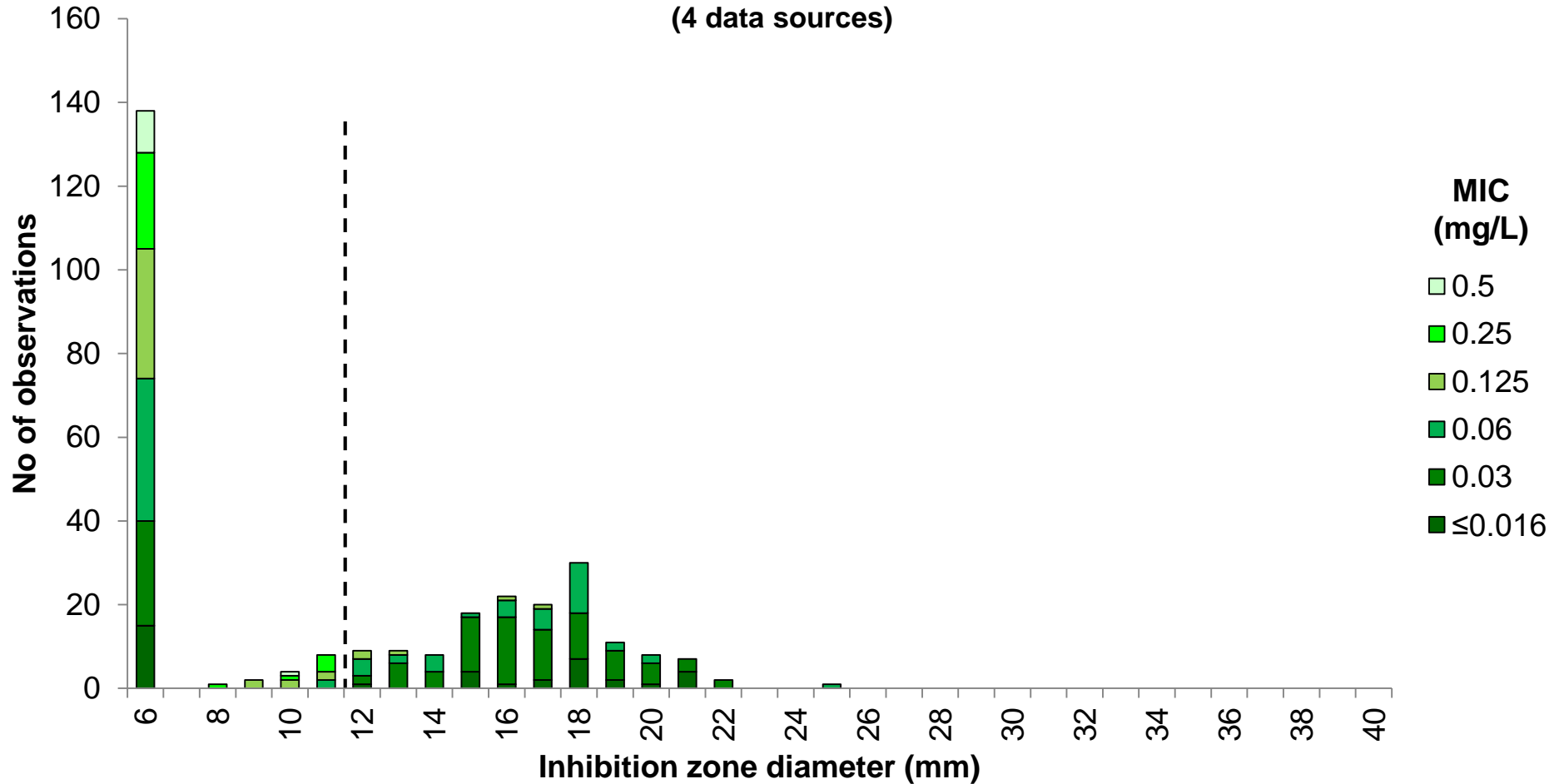
$S \leq 2$, $R > 2$ mg/L

Benzylpenicillin zone diameter (screen)

$S \geq 12$ mm

Benzylpenicillin 1 unit vs. Meropenem MIC *H. influenzae*, 200 isolates (298 correlates)

(4 data sources)



Breakpoints (non-meningitis)

Meropenem MIC

$S \leq 2$, $R > 2$ mg/L

Benzylpenicillin zone diameter (screen)

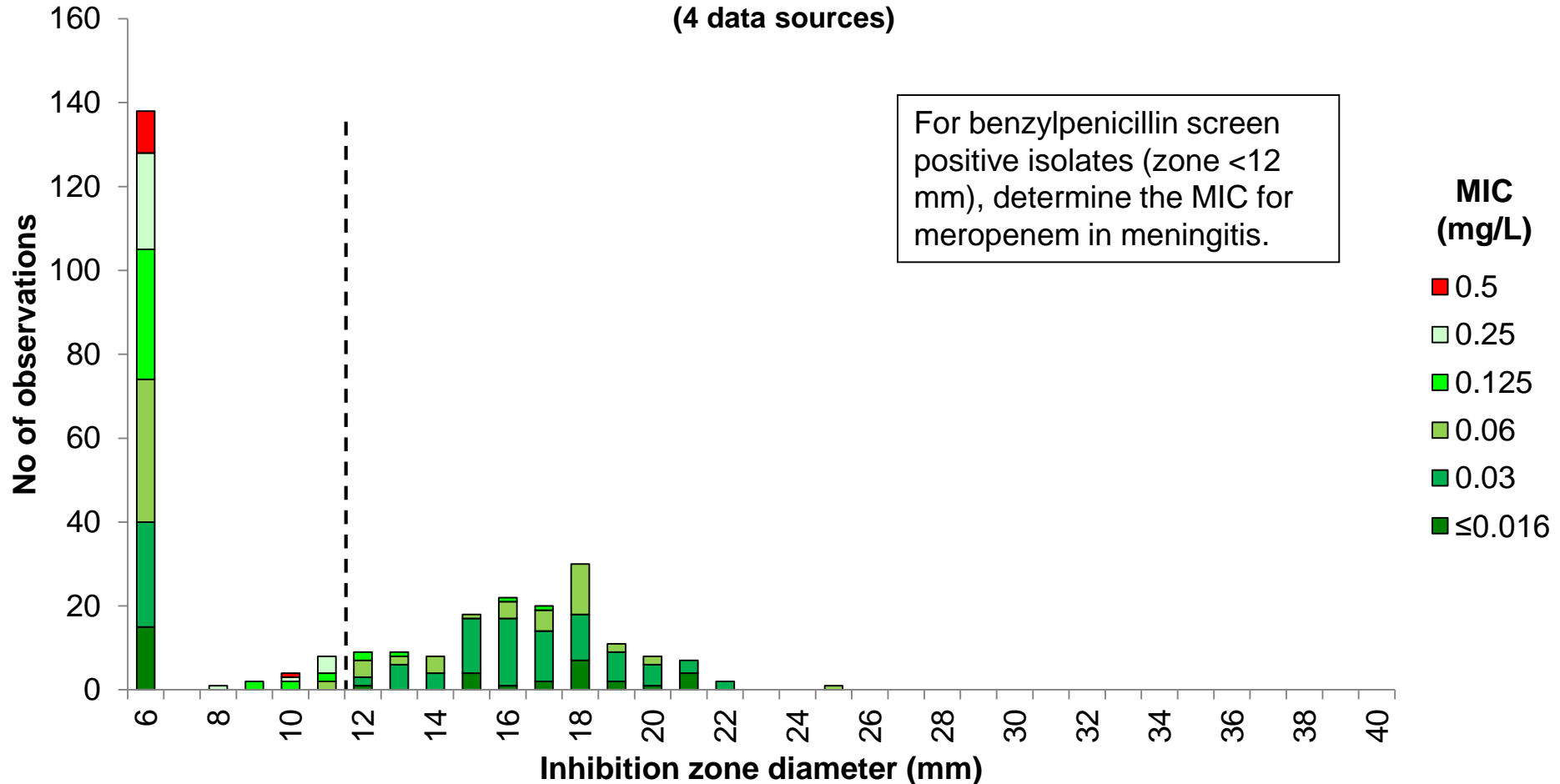
$S \geq 12$ mm

Haemophilus influenzae

Distributions with separate
breakpoints for meningitis

Benzylpenicillin 1 unit vs. Meropenem MIC *H. influenzae*, 200 isolates (298 correlates)

(4 data sources)



Breakpoints (meningitis)

Meropenem MIC

S≤0.25, R>0.25 mg/L

Benzylpenicillin zone diameter (screen)

S≥12 mm



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