

TECHNICAL REPORT

Derivation of event probabilities

The natural history of catheter-associated *S. aureus* bacteremia was estimated by pooling clinical data with data from the literature. The pooled estimates were used as point estimates in the base-case analysis. For sensitivity analyses, the wider range of reported values was used rather than the 95% confidence intervals. Table 1 presents the pooled estimate of mortality in patients with catheter-associated *S. aureus* bacteremia uncomplicated by endocarditis. Mortality in this group of patients, estimated at 14.2%, reflects both the grave consequences of staphylococcal bacteremia and the severity of underlying illness in patients who develop catheter-associated *S. aureus* bacteremia.

Secondary event rates in patients who developed endocarditis also were estimated by pooling clinical data with data from the literature. Endocarditis event rates in patients who developed infection secondary to an intravascular catheter were assumed to be the same as event rates reported for *S. aureus* endocarditis from any cause. Stroke rates in *S. aureus* endocarditis were estimated at 21.4% (Table 2). Because the combined sample of *S. aureus* endocarditis patients with stroke was less than 100 patients, stroke mortality rates were estimated from studies reporting stroke mortality in patients with endocarditis from any infectious microorganism (Table 3). Table 4 presents the valve replacement rates in endocarditis. It is important to note that, although we used pooled estimates for the valve replacement rate, this rate will vary dramatically depending upon how aggressively centers surgically manage patients with active infective endocarditis. Because the combined sample of surgically managed *S. aureus* endocarditis patients for whom mortality rates were reported was less than 100 patients, valve replacement mortality rates were estimated from studies reporting on patients with endocarditis from any infectious

microorganism (Table 5). Table 6 presents the combined overall mortality rate of 30.5% in patients with *S. aureus* endocarditis. A mortality rate of 29% for patients with *S. aureus* endocarditis and no event (stroke or valve replacement) was calculated based on the overall endocarditis mortality rate and the rates of and mortality rates associated with each of the two modeled endocarditis complications.

Bayes theorem

Using the standard epidemiologic terms reported in the manuscript (sensitivity, specificity, prevalence), Bayes theorem was applied to calculate the following model probabilities:

1) The probability of a positive TEE =

$$(prevalence)(sensitivity) + (1 - prevalence)(1 - specificity)$$

1.1) The probability of endocarditis given a positive TEE (true positive rate) =

$$\frac{(prevalence)(sensitivity)}{(prevalence)(sensitivity) + (1 - prevalence)(1 - specificity)}$$

1.2) The probability of no endocarditis given a positive TEE (false positive rate) =

$$\frac{(1 - prevalence)(1 - specificity)}{(prevalence)(sensitivity) + (1 - prevalence)(1 - specificity)}$$

2) The probability of a negative TEE =

$$(prevalence)(1 - sensitivity) + (1 - prevalence)(specificity)$$

2.1) The probability of endocarditis given a negative TEE (false negative rate) =

$$\frac{(prevalence)(1 - sensitivity)}{(prevalence)(1 - sensitivity) + (1 - prevalence)(specificity)}$$

2.2) The probability of no endocarditis given a negative TEE (true negative rate) =

$$\frac{(1 - prevalence)(specificity)}{(prevalence)(1 - sensitivity) + (1 - prevalence)(specificity)}$$

Probabilities in three-part nodes

Two different types of three-part nodes were used in the decision model. The first three-part node assigns the probabilities of stroke, valve replacement, and no event given that endocarditis is present. In this node, sensitivity analyses allowed the 'no event' rate to vary up or down as the stroke and valve replacement rates varied (i.e. $p(\text{no event}) = 1 - [p(\text{stroke}) + p(\text{valve replacement})]$). Thus, complication rates were varied independently. A check was set such that the sum of the three probabilities always equalled 1.

The second three-part node assigns the probabilities of die, relapse, and cure given that some event occurred (stroke, valve replacement, or no event) in the setting of endocarditis being treated with a set duration (2 vs. 4 weeks) of therapy. Again all probabilities added to 1. In this case, the death rate always superseded the other probabilities. The mortality rate always equalled the $p(\text{die})$ (base-case or sensitivity analysis rates). The relapse rate was assigned $p(\text{relapse})$ unless the sum of the relapse and mortality rates exceeded 1 during sensitivity analyses; in those cases $p(\text{relapse})$ was set at $1 - p(\text{die})$. The cure rate was calculated as $1 - [p(\text{die}) + p(\text{relapse})]$.

Table 1. Mortality in patients with catheter-associated *S. aureus* bacteremia uncomplicated by endocarditis.

Study (Reference)	N	Deaths	Mortality Rate
Mylotte et al, 1987 (13)	38	17	44.7%
Rahal et al, 1986 (38)	36	12	33.3%
Libman et al, 1984 (12)	20	4	20.0%
Dugdale et al, 1990 (15)	37	6	16.2%
Watanakunakorn et al, 1977 (9)	13	2	15.4%
Malanoski et al, 1995 (18)	50	5	10.0%
Raad et al, 1992 (2)	51	3	5.9%
Knudsen et al, 1993 (16)	86	5	5.8%
Iannini et al, 1976 (39)	22	1	4.5%
Bayer et al, 1980 (17)	9	0	0%
Institutional clinical data	196	24	12.2%
Total	558	79	14.2%
Estimate (95% confidence interval)		14.2% (11.3-17.1%)	

Table 2. Stroke in patients with *S. aureus* endocarditis

Study (Reference)	N	Strokes	Stroke Rate
Le Cam et al, 1984 (40)	35	18	51.4%
Chambers et al, 1983 (6)	35	11	31.4%
Roder et al, 1997 (41)	260	52	20.0%
Korzeniowski et al, 1982 (42)	78	14	17.9%
Hedstrom et al, 1983 (43)	19	1	5.3%
Instituional clinical data	60	8	13.3%
Total	487	104	21.4%
Estimate (95% confidence interval)		21.4% (17.7-25.0%)	

Table 3. Stroke mortality rate in patients with endocarditis*

Study (Reference)	Total strokes (N)	Deaths	Mortality Rate
Pruitt et al, 1978 (44)	41	33	80.5%
Jones et al, 1969 (45)	55	32	58.2%
Pelletier et al, 1977 (46)	22	12	54.5%
Verheul et al, 1993 (47)	26	7	26.9%
Matsushita et al, 1993 (48)	30	8	26.7%
Chambers et al, 1983 (6)	11	1	9.1%
Korzeniowski et al, 1982 (42)	14	1	7.1%
Institutional clinical data [†]	8	5	62.5%
Total	207	99	47.8%
Estimate (95% confidence interval)	47.8% (41.0-54.6%)		

*Because stroke mortality specifically for *S. aureus* endocarditis was reported for a pooled group of less than 100 patients, the above estimates are for stroke mortality in patients with endocarditis from any infectious microorganism.

[†]Clinical data are only from patients with *S. aureus* endocarditis.

Table 4. Valve replacement rates in *S. aureus* endocarditis

Study (Reference)	N	Surgeries	Valve Replacement Rate
Richardson et al, 1978 (49)	28	14	50.0%
Sanabria et al, 1990 (50)	45	17	37.8%
Austin et al, 1973 (51)	8	3	37.5%
Chambers et al, 1983 (6)	35	4	11.4%
Watanakunakorn, 1994 (52)	99	7	7.1%
Korzeniowski et al, 1982 (42)	78	5	6.4%
Institutional clinical data	60	3	5.0%
Total	353	53	15.0%
Estimate (95% confidence interval)		15.0% (11.3-18.7%)	

Table 5. Valve replacement mortality rate in patients with endocarditis*

Study (Reference)	N	Deaths	Mortality Rate
Austin et al, 1973 (51)	3	2	66.7%
Korzeniowski et al, 1982 (42)	5	3	60.0%
Pelletier et al, 1977 (46)	28	12	42.9%
Koyanagi et al, 1985 (53)	9	3	33.3%
Sanabria et al, 1990 (50)	22	7	31.8%
Tornos et al, 1992 (54)	48	15	31.3%
Verheul et al, 1993 (47)	43	12	27.9%
D'Agostino et al, 1985 (55)	63	12	19.0%
Miller, 1989 (56)	63	12	19.0%
Kimose et al, 1990 (57)	76	13	17.1%
Schulz et al, 1996 (58)	59	9	15.3%
Soma et al, 1991 (59)	57	8	14.0%
Richardson et al, 1978 (49)	81	11	13.6%
Eishi et al, 1995 (60)	893	121	13.5%
Dehler et al, 1994 (61)	70	9	12.9%
Nihoyannopoulos et al, 1985 (62)	19	2	10.5%
Wilson et al, 1979 (63)	138	14	10.1%
Croft et al, 1983 (64)	23	2	8.7%
Siddiq et al, 1996 (65)	24	2	8.3%
Olaison et al, 1996 (66)	26	2	7.7%

Bogers et al, 1991 (67)	31	2	6.5%
Larbalestier et al, 1992 (68)	109	7	6.4%
Fujita et al, 1985 (69)	32	2	6.3%
Symbas et al, 1982 (70)	19	1	5.3%
Yoshida et al, 1991 (71)	48	2	4.2%
d'Udekem et al, 1997 (72)	76	3	3.9%
Middlemost et al, 1991 (73)	203	8	3.9%
David et al, 1990 (74)	38	0	0%
Institutional clinical data [†]	3	1	33.3%
Total	2309	297	12.9%
Estimate (95% confidence interval)	12.9% (11.5-14.2%)		

*Because valve replacement mortality specifically in *S. aureus* endocarditis was reported for a pooled group of less than 100 patients, the above estimates are for valve replacement mortality in patients with endocarditis from any infectious microorganism.

[†]Clinical data are only from patients with *S. aureus* endocarditis.

Table 6. Overall mortality rate in *S. aureus* endocarditis

Study (Reference)	N	Deaths	Mortality Rate
Knudsen et al, 1993 (16)	2	2	100%
Hedstrom et al, 1983 (43)	19	13	68.4%
Finkelstein et al, 1984 (75)	14	9	64.3%
Austin et al, 1973 (51)	8	5	62.5%
Julander, 1985 (76)	31	19	61.3%
Raad et al, 1992 (2)	4	2	50.0%
Bryan et al, 1984 (77)	19	9	47.4%
Esperson et al, 1986 (7)	54	19	35.2%
Sanabria et al, 1990 (50)	29	10	34.5%
Cooper et al, 1982 (11)	12	4	33.3%
Pelletier et al, 1977 (46)	36	12	33.3%
Shah M et al, 1979 (10)	21	6	28.6%
Watanakunakorn, 1994 (52)	106	27	25.5%
Chambers et al, 1983 (6)	35	7	20.0%
Rajashekaraiah et al, 1980 (78)	50	10	20.0%
Nolan et al, 1976 (79)	26	4	15.4%
Korzeniowski et al, 1982 (42)	78	8	10.3%
Institutional clinical data	60	18	30.0%
Total	604	184	30.5%
Estimate (95% confidence interval)		30.5% (26.8-34.1%)	