

Mortality associated with bacteraemia caused by *Staphylococcus aureus*:

A cohort analysis with follow up beyond hospital discharge from the BURDEN study group

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Methods

Study population:

Adults resident in Tayside, Scotland who had a new admission to Ninewells Hospital between 1st July 2005 and 30th June 2006.

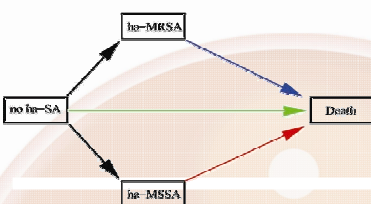
Cohort:

All patients from this population who were admitted to wards where at least one case of *S aureus* bacteraemia was admitted in the study period.

Outcome:

Mortality up to 30th September 2006 (i.e. at least 90 days after admission), from the national registry of deaths.

Multi-state model:



- Each arrow represents the hazard moving from one state to the other
- Time-dependency of exposures and outcomes is taken into account

Model outputs:

We used the model to estimate

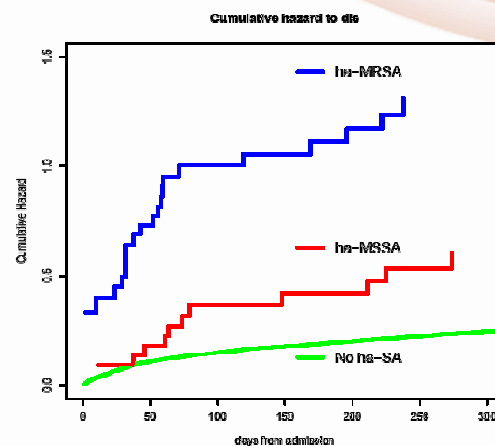
- The effect of ha-MSSA on hazard of death
- The effect of ha-MRSA on hazard of death
- Compare the hazard of death with ha-MRSA *versus* ha-MSSA

Results

The cohort included 4,397 patients of whom 34 had ha-MRSA and 27 had ha-MSSA bacteraemia 220 patients died in hospital and 1,044 died by the end of the study period.

No patient had both MRSA and MSSA bacteraemia

FIGURE



- Cumulative hazards are most suitable for time-dependent exposures
- Exposure effects can be displayed
- Estimated by Nelson-Aalen using the R-package MVNA

Univariate analysis

Variable	death HR [95% CI]
ha-MRSA vs reference	4.26 [2.67 – 6.80]
ha-MSSA vs reference	2.47 [1.40 – 4.37]
Ha-MRSA vs ha-MSSA	1.73 [0.83 – 3.58]

Multivariate analysis

Variable	death HR [95% CI]
ha-MRSA vs reference	3.49 [2.19 – 5.57]
ha-MSSA vs reference	2.71 [1.53 – 4.79]
Age	1.04 [1.03 – 1.04]
Charlson comorbidity	1.28 [1.26 – 1.31]
Sex (female vs male)	0.96 [0.85 – 1.08]
Ha-MRSA vs ha-MSSA	1.29 [0.62 – 2.68]

Details of the statistical analysis

Regression on the multistate model above:

We define two time-dependent risk factors. $ha-MRSA(t)$ is defined as

$$ha-MRSA(t) = \begin{cases} 1 & \text{if } t > \text{time}(ha-MRSA), \\ 0 & \text{if } t \leq \text{time}(ha-MRSA) \end{cases}$$

and $ha-MSSA(t)$ is defined as

$$ha-MSSA(t) = \begin{cases} 1 & \text{if } t > \text{time}(ha-MSSA), \\ 0 & \text{if } t \leq \text{time}(ha-MSSA) \end{cases}$$

We fit a standard Cox model with two time-dependent covariates

$$\lambda(t|Z(t)) = \lambda_0(t) \exp(\beta_1 ha-MRSA(t) + \beta_2 ha-MSSA(t))$$

Conclusions

Our cohort study has demonstrated that hospital acquired *S aureus* bacteraemia significantly increases mortality and that the hazard persists beyond the period of hospital stay. These effects still remain after adjusting for age, Charlson comorbidity and gender.

The results show the importance of preventing ha-MRSA and ha-MSSA bacteraemias and support efforts to reduce bacteraemias caused by MSSA as well as MRSA.