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Predictors of mortality for people aged over 65 years receiving mental health care for delirium in a South London Mental Health Trust, UK: a retrospective survival analysis

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Background: Delirium is a common phenomenon in older people. Using a large mental health care data resource, we investigated mortality rates and predictors of mortality following delirium in older people.

Methods: The South London and Maudsley NHS Foundation Trust (SLAM) Clinical Record Interactive Search (CRIS) was used to retrieve anonymised data on patients known to mental health services who were over 65 years of age and received a diagnosis of delirium during a 3-year period. Age-standardised and gender-standardised mortality rates (SMRs) were calculated, and predictors of survival were investigated considering demographic factors, health status rated on the Health of the National Outcome Scale (HoNOS), cognitive function and previous or contemporaneous diagnosed dementia.

Results: In 974 patients with delirium, 1- and 3-year mortality rates were 37.2 and 54.9% respectively, representing an SMR of 4.7 overall (95% CI: 4.3–5.1). SMR was 5.2 (95% CI: 4.6–5.7) for patients with delirium without prior dementia; SMR was 4.1 (95% CI: 3.6–4.7) for patients with dementia preceding delirium and 2.2 (2.0–2.5) excluding deaths within 6 months of the delirium diagnosis. Significant predictors of mortality in fully adjusted models were older age, male gender, white (compared with non-white) ethnicity, and HoNOS subscales measuring physical ill-health and functional impairment. No mortality associations were found with cognitive function, dementia, or psychological profile.

Conclusions: In people with delirium diagnosed by mental health services, mortality risk was high and predicted by demographic and physical health status rather than by cognitive function or psychological profile. © 2014 The Authors. International Journal of Geriatric Psychiatry published by John Wiley & Sons, Ltd.

Key words: delirium; mortality; dementia; standardised mortality ratio

Introduction

Delirium is a clinical syndrome typified by transient episodes of disturbed consciousness, cognitive function and perception. It is a major health issue with a mean prevalence of 20% of older people over 65 years in general hospitals in the UK (Royal College of Psychiatrists 2005), although ranging from 10 to 31% on admission (Siddiqi et al., 2006). Delirium is one of the most common diagnoses made by psychiatric consultation services (Bourgeois et al. 2005). It has a significant impact throughout health and social services and is associated with considerable health and socio-economic costs (Witlox et al., 2010). In the USA, it is estimated that the national health care cost for delirium ranges from $38 to 152bn per year (Leslie et al., 2008).

As well as being associated with increased risk of long-term institutionalisation (Siddiqi et al., 2009) and dementia (Potter and George, 2006), delirium is recognised to be independently associated with higher mortality in older medical inpatients (Eeles et al., 2010). However, rates of delirium and associated mortality may vary according to care settings, patient
characteristics and methods of assessments. For example, one third of patients still have symptoms of delirium after 6 months, and these patients with persistent delirium were found to be nearly three times more likely to die within a 1-year follow-up compared with those whose delirium had resolved (Kiely et al., 2009). Findings on predictors of mortality following delirium are contradictory. For example, some studies suggest that delirium is a significant predictor of increased mortality for people with dementia (Voyer et al., 2011), while other studies found lower mortality among delirium patients with dementia (Pitkala et al., 2005). The role of age and frailty is also unclear. On one hand, both are associated with higher mortality in their own right. However, both are predisposing factors for delirium, and it is possible that delirium occurring without these predispositions may reflect a more severe physical insult that itself drives a higher relative mortality in ‘lower risk’ groups.

Delirium is commonly seen by mental health services for older people, particularly where coverage is provided of acute general medical units. However, to our knowledge, there have been no British studies up to date that have obtained mortality rates in this population or investigated factors associated with this — particularly the role or not of underlying dementia. Taking a large sample of people with delirium diagnoses who had received mental health service assessment and/or aftercare, we sought to describe the relative mortality risk considering age/gender and other factors associated with this outcome.

Methods

Source of data

Data for this study was obtained from the South London and Maudsley NHS Foundation Trust (SLaM), a large mental health provider serving a geographic catchment of four south London boroughs (Lambeth, Southwark, Lewisham and Croydon) and approximately 1.2 million residents. Since 2006, SLaM has used an electronic health record in all services. The Clinical Record Interactive Search (CRIS) was developed to enable this electronic health record data to be used in research and contains full but anonymised information from over 220,000 mental health service users with a robust patient-led governance framework (Stewart et al., 2009). CRIS was developed in 2008 and has supported a large number of projects including a programme of work on mortality in mental disorder (Hayes et al., 2011). The CRIS system received ethical approval from the Oxfordshire Research Ethics Committee C as an anonymised data resource.

Sample

People over 65 years of age who received a diagnosis of delirium from SLaM services within the 3-year period between 1 January 2008 and 31 December 2010 were identified using CRIS. Diagnoses of delirium were ascertained both from structured International Classification of Diseases, Tenth Revision (ICD-10) codes (World Health Organisation, 2010) using diagnoses that are recorded routinely in Electronic Patient Journey System (ePJS) and from an information extraction application developed by the CRIS team, which brings back text strings associated with a ICD-10 diagnosis statement in clinical correspondence. Dementia diagnoses were obtained in the same way, and mortality in the case sample was stratified according to whether or not a diagnosis of dementia had been recorded either before or contemporaneously with the delirium diagnosis.

Measurements

Data were also extracted on age (at delirium diagnosis), gender and ethnicity (white British/Irish vs non-white). Health of the Nation Outcome Scale for older people (HoNOS65+) is routinely administered in SLaM services, and the following HoNOS65+ subscale scores were extracted closest to the delirium diagnosis within 3 months of before or after the index delirium diagnosis for this analysis: agitated behaviour, cognitive problems, physical illness, hallucinations/delusions, depressed mood and daily living problems (Burns et al., 1999). Each of the HoNOS items are rated from 0 (no problem) to 4 (severe problem). The recorded mini-mental state examination (MMSE) (Folstein et al., 1975) numerator score closest to the delirium diagnosis within 3 months of delirium diagnosis date was then extracted. Mortality up to 31 October 2012 was obtained from the UK Office for National Statistics (ONS) and analysed as the primary outcome with date of death available from routine SLaM checks of patient records (active and inactive).

Statistical analysis

Mortality in cases with delirium was compared with expected rates within the England and Wales population.
Predictors of mortality for delirium patients aged over 65 years

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in 2011 (Office of National Statistics, 2011). Standardised mortality rates (SMRs) were calculated, with expected numbers of deaths estimated from age-specific and gender-specific death rates for England and Wales. There is slight variation in SMR from one region to another in England and Wales. For example, highest SMR for regions in England and Wales during 2011 was 12% higher in North East of England and lowest SMR was 8% lower in London and South Central England compared with England and Wales (Office of National Statistics, 2011). SMRs were stratified by age group, gender and presence or not of prior/contemporaneous dementia. Sensitivity analyses were repeated excluding deaths within 6 months of the delirium diagnosis.

Stata 12 software was used for the remaining analyses. Cox proportional hazard regression analyses were used to investigate factors associated with mortality for delirium cases with the following covariates: age, gender, ethnicity, MMSE numerator score and HoNOS65+ subscale scores (agitated behaviour, cognitive problems, physical illness, hallucinations, depressed mood and daily living problems).

Results

A total of 1089 patients with a diagnosis of delirium were identified of whom 986 were over 65 years of age at diagnosis. Of these, 12 patients were excluded because of insufficient data, resulting in an analysed sample of 974, 407 (41.8%) of whom had documented prior or contemporaneous dementia. Out of those 407, 137 patients had Alzheimer’s disease, 159 had vascular dementia, 71 with mixed type and 40 diagnosed with other types of dementia, diagnosed using ICD-10 (World Health Organisation, 2010). Those with dementia were older, more likely to be living alone, more likely to be in socio-economically deprived groups, and had higher cognitive and functional impairment (Table 1). Most of patients had contacts with either psychiatric liaison teams (48%), Community Mental Health Teams (50%) or inpatient services (2%) at the point of delirium diagnosis. The crude mortality rates within 1 and 3 years were 37.2 and 54.9% respectively for all delirium cases, 33.2 and 53.8% for those with concurrent/preceding dementia and 40.0 and 55.7% for patients with no history of dementia. Table 2 summarises mortality rates by covariate level during the study period that were observed to be higher with increased age, in males compared with females, in white compared with non-white ethnic groups, with increased HoNOS subscale scores in daily living problem and physical illness, and with lower MMSE score. However, there was no substantial variation by scores of agitated behaviour, psychotic symptoms, or depressive symptoms and no substantial difference between those with or without dementia.

The SMR for the overall sample with delirium was 4.7 (95% CI: 4.3–5.1) (Figure 1). This was similar for males (95% CI: 5.2; 4.6–5.8) and females (95% CI: 4.3; 3.8–4.8) but decreased quite markedly with increasing age (Figure 2). The SMR was 5.2 (95% CI: 4.6–5.7) in those with no recorded dementia and 4.1 (95% CI: 3.6–4.7) in those with previous/contemporaneous dementia. Within the overall cohort, after exclusion of deaths within 6 months of the delirium diagnosis (number of patients = 674, number of deaths = 253), the SMR remained raised at 2.2 (95% CI: 2.0–2.5).

In unadjusted Cox regression models, the hazard of death was significantly associated with demographic factors including increased age and white ethnicity as well as with some of the HoNOS subscale scores such as physical illness, daily living problems, depressed mood and MMSE score; however, it was not significantly associated with the presence of dementia (Table 3). In fully adjusted models, mortality was significantly associated with age, male gender, white ethnicity, worse physical health and functional impairment. Dementia and cognitive function (MMSE score), on the other hand, were not substantial predictors in adjusted models. Associations with age, gender and ethnicity persisted when earlier mortality (within 6 months of the delirium diagnosis) was excluded, but those with worse physical health and functional impairment persisted.

Discussion

In a large sample of patients with delirium seen by mental health services over a 3-year period, overall age-standardised and gender-standardised mortality was 4.7 times that expected and remained 2.2-fold higher after a 6-month interval. The mortality difference was substantially stronger in younger compared with older cases. However, if anything, mortality was higher for those with no previous dementia diagnosis (SMR 5.5) than for those with dementia (SMR 4.1). Considering the delirium cases as a whole, mortality was independently associated with increased age, male gender, white (compared with non-white) ethnicity and with worse physical health and functional impairment on the HoNOS instrument, although the last two of these were not independent predictors of mortality after 6 months. Agitated behaviour,
hallucinations, and depressed mood on the HoNOS instrument were not predictors of mortality and neither were MMSE score or dementia diagnosis.

The overall level of mortality following a delirium diagnosis was high with over a third having died within 1 year and over a half dead within 3 years. Although the SMR was substantially reduced when deaths within 6 months were excluded, it remained over 2-fold higher than that expected in the population. Gonzalez et al. (2009) in a short-term mortality study reported a mortality of 25.9%, 3 months after delirium in an inpatient sample in Chile. Although not significant, the excess risk of mortality following delirium was if anything lower rather than higher in cases with dementia, concurring with some previous studies suggesting that delirium in dementia might have a better prognosis than delirium alone (Pitkala et al., 2005; Tsai et al., 2012a). Dementia is a widely recognised predisposing factor for delirium, and the lower risk of mortality might well reflect more minor physical illnesses precipitating delirium in this context. Conversely, delirium occurring in the absence of dementia might have required more severe and acute underlying physical illness associated with higher mortality. In our cohort, patients with delirium but no dementia were slightly younger (mean (SD) age 80.2 (8.1) years) compared with those with both delirium and dementia (82.0 (7.1) years). Although 2 years is a relatively small difference, it is also possible that younger patients had required more severe precipitating health events to result in delirium. Thus, although increased age was an independent predictor of mortality in cases with delirium, consistent with other studies (St.John and Montgomery, 2009), the excess mortality associated with delirium was higher in younger compared with older cases—i.e. illustrating an absolute mortality risk increasing with age but a relative mortality risk that decreases. As well as the threshold issue described in the preceding texts, competing causes of death in older age groups may dilute the impact of delirium itself.

The gender difference in mortality may reflect generally better survival in female compared with male inpatients regardless of delirium (Campbell et al., 2004), although this is in contrast to another study finding no such association (Tsai et al., 2012b). Of other demographic factors, white ethnicity was independently associated with higher risk. To our knowledge, this is a novel finding and requires replication, although white ethnicity was also a risk factor for mortality found by Gambassi et al. (1999) in an American study of patients with Alzheimer’s...
disease living in nursing homes. If anything, cardio-
vascular and cerebrovascular disease tends to be 
higher in UK minority ethnic groups, particularly 
South Asian and African Caribbean groups 
(Chanturvedi, 2003). The relatively low risk of mortal-
ity following delirium in this group might re
fl
ex
survival bias or might possibly re
fl
ex more cohesive 
and supportive family structures after discharge,
particularly as the association persisted largely 
altered in strength when mortality within 6 months 
was excluded.

A range of subscale scores from the HoNOS instru-
ment were evaluated as predictors of mortality in this 
sample. Physical ill-health and functional impairment 
(problems with activities of daily living) were both 
important factors in primary analyses. Acute illness 
leading to hospitalisation often leads to functional 
decline and is a predictor of mortality (Gonzalez 
et al., 2009). The associations of both poor physical

Table 2 Risk of death for those patients with delirium exposed to various levels of risk factors that were identified in Table 3, during the study period

| Risk factor                  | No. of deaths | No. of patients | Mortality rate per 1000 (95% CI) |
|------------------------------|--------------|----------------|---------------------------------|
| Age                          |              |                |                                 |
| 65–69                        | 31           | 77             | 402.6 (273.5–571.5)             |
| 70–74                        | 76           | 145            | 524.1 (413–656)                 |
| 75–79                        | 91           | 186            | 489.3 (393.9–600.7)             |
| 80–84                        | 126          | 221            | 570.1 (474.9–678.8)             |
| 85–89                        | 123          | 207            | 594.2 (493.8–709.0)             |
| 90+                          | 104          | 132            | 787.9 (643.8–954.6)             |
| Gender                       |              |                |                                 |
| Female                       | 296          | 533            | 555.4 (493.9–622.4)             |
| Male                         | 255          | 435            | 586.2 (516.5–662.7)             |
| Ethnicity                    |              |                |                                 |
| Non-white                    | 69           | 148            | 466.2 (362.7–590.0)             |
| White                        | 465          | 796            | 584.2 (532.3–639.8)             |
| HoNOS daily living problem score* |          |                |                                 |
| 0                            | 38           | 85             | 447.1 (316.4–613.6)             |
| 1                            | 48           | 123            | 390.2 (287.7–517.4)             |
| 2                            | 156          | 268            | 582.1 (494.3–680.9)             |
| 3                            | 190          | 311            | 610.9 (527.1–704.2)             |
| 4                            | 88           | 131            | 671.8 (538.8–827.6)             |
| HoNOS physical illness score* |              |                |                                 |
| 0                            | 12           | 39             | 307.7 (159.0–537.5)             |
| 1                            | 36           | 88             | 409.1 (286.5–566.4)             |
| 2                            | 129          | 250            | 516 (430.8–613.1)               |
| 3                            | 215          | 353            | 609.1 (530.4–696.1)             |
| 4                            | 134          | 198            | 676.8 (567.0–801.5)             |
| HoNOS agitated behaviour score* |          |                |                                 |
| 0                            | 169          | 321            | 526.5 (450.1–612.1)             |
| 1                            | 126          | 202            | 623 (519.6–742.7)               |
| 2                            | 141          | 234            | 602.6 (507.2–710.6)             |
| 3                            | 77           | 146            | 527.4 (416.2–659.2)             |
| 4                            | 13           | 25             | 520 (276.9–889.2)               |
| HoNOS hallucinations score*   |              |                |                                 |
| 0                            | 295          | 512            | 576.2 (512.3–645.8)             |
| 1                            | 54           | 97             | 558.7 (418.2–726.4)             |
| 2                            | 96           | 175            | 548.6 (444.3–669.9)             |
| 3                            | 55           | 100            | 550 (414.3–715.9)               |
| 4                            | 6            | 18             | 333.3 (122.3–725.5)             |
| HoNOS depressed mood score*   |              |                |                                 |
| 0                            | 272          | 508            | 535.4 (473.7–603.0)             |
| 1                            | 158          | 268            | 589.6 (501.2–680.9)             |
| 2                            | 58           | 97             | 597.9 (454.0–773.0)             |
| 3                            | 28           | 42             | 666.7 (443.0–963.5)             |
| 4                            | 13           | 3              | 333.3 (8.4–1857.2)              |
| MMSE score                   |              |                |                                 |
| >24                          | 68           | 164            | 414.6 (322.0–525.6)             |
| 21–24                        | 67           | 122            | 549.2 (425.6–697.4)             |
| 10–20                        | 179          | 315            | 568.3 (488.1–657.9)             |
| 0–9                          | 61           | 101            | 604 (462.0–773.8)               |
| Unknown                      | 176          | 266            | 661.7 (567.5–767.0)             |
| Previous/current dementia    |              |                |                                 |
| Absent                       | 324          | 564            | 574.5 (513.6–640.6)             |
| Present                      | 227          | 404            | 561.9 (491.2–639.9)             |

*Health of the Nation Outcome Scale (HoNOS) subscales—hazard ratios calculated per score increment on a 0–4 scale, where 0 is least severe and 4 is most severe status.

Figure 1 Comparison of SMR (95% CI) for patients with different cohorts of delirium patients compared with the England general population.

Figure 2 Standardised mortality rates for patients with delirium compared with the England and Wales general population by age and prior/contemporaneous dementia diagnosis.
Table 3  Unadjusted and adjusted hazard ratio showing predictors of mortality (95% confidence interval) for those patients with delirium

| Adjustment/Variable            | All delirium patients | Delirium patients excluding those who deceased within 6 months |
|-------------------------------|-----------------------|---------------------------------------------------------------|
|                               | Unadjusted (n = 968)  | Model 1 (n = 896) | Model 2 (n = 874) | Model 3 (n = 650) | Model 4 (n = 650) | Model 5 (n = 499) | Model 6 (n = 499) |
| One year increase in age      | 1.03 (1.02, 1.04)     | 1.03 (1.02, 1.05) | 1.04 (1.02, 1.06) | 1.05 (1.03, 1.07) | 1.05 (1.03, 1.07) |
| Male gender                   | 1.10 (0.93, 1.24)     | 1.21 (1.05, 1.34) | 1.23 (1.04, 1.38) | 1.30 (1.06, 1.49) | 1.31 (1.06, 1.49) |
| White ethnicity               | 1.29 (1.08, 1.45)     | 1.27 (1.04, 1.44) | 1.28 (1.05, 1.46) | 1.40 (1.17, 1.68) | 1.41 (1.06, 1.63) |
| Daily living problem*         | 1.27 (1.17, 1.38)     | 1.15 (1.05, 1.26) | 1.13 (1.01, 1.27) | 1.14 (1.01, 1.28) | 1.09 (0.93, 1.27) |
| Physical illness*             | 1.39 (1.27, 1.52)     | 1.28 (1.16, 1.42) | 1.22 (1.08, 1.37) | 1.21 (1.07, 1.37) | 1.06 (0.90, 1.24) |
| Agitated behaviour*           | 1.01 (0.94, 1.09)     | 1.01 (0.93, 1.10) | 1.01 (0.91, 1.11) | 1.00 (0.87, 1.15) | 1.00 (0.88, 1.15) |
| Hallucinations/delusions*     | 1.06 (0.99, 1.13)     | 1.07 (0.99, 1.15) | 1.07 (0.97, 1.16) | 1.04 (0.90, 1.16) | 1.02 (0.88, 1.15) |
| Depression*                   | 1.12 (1.02, 1.23)     | 1.04 (0.94, 1.16) | 1.00 (0.87, 1.12) | 1.04 (0.87, 1.12) | 0.96 (0.76, 1.13) |
| MMSE (per unit decrease)      | 1.02 (1.01, 1.04)     | 1.01 (0.99, 1.03) | 0.95 (0.80, 1.25) | 1.01 (0.99, 1.03) | 1.00 (0.98, 1.03) |
| Presence of dementia          | 0.92 (0.77, 1.09)     |                   |                   |                   |                   |

*Health of the Nation Outcome Scale (HoNOS) subscales—hazard ratios calculated per score increment on a 0–4 scale.
health conditions and higher levels of functional impairment with mortality are therefore not surprising although interestingly remained relatively independent of each. Symptoms of delirium affect activities of daily living including mobility, meaning patients are unlikely to engage in therapeutic activities that promote recovery and functional rehabilitation (Buurman et al., 2011). In addition, physical illnesses directly or indirectly contributing to delirium are often likely themselves to be predictors of increased mortality (Lundstrom et al., 2003). Both physical illness ratings and functional impairment reduced substantially as predictors of post-delirium mortality after 6 months, suggesting primarily acute rather than longer lasting effects on risk.

In contrast, other measures showed no substantial influences on mortality risk. Visual hallucinations and agitation are common symptoms with both delirium and dementia patients (Hodges, 2007) but were not statistically significant predictors of survival in this study. Furthermore, although depressed mood was a significant predictor in the unadjusted analysis, this association was reduced substantially in strength following adjustment for other covariates. Other studies have reported that hypoactive symptoms of delirium are associated with increased mortality rates (Ely et al., 2004) and depressive symptoms have been found to be associated with mortality in older people more generally (Teng et al., 2013). However, it should be borne in mind that hypoactive delirium may not have been adequately represented in this sample and depressive symptoms rated on the HoNOS may not have been sufficiently accurate exposure definition. Finally, although patients with delirium often experience persistent cognitive impairment following delirium and are up to three times more likely to develop dementia (Potter and George, 2006), no association was found in our study, between MMSE score and mortality after adjustment for other covariates, consistent with the lack of difference in SMR between those with and without a dementia diagnosis (and the lack of association between dementia diagnosis and mortality within those with delirium). However, delirium in older people may be the first indicator of dementia and possibly expose an insidiously progressive cognitive decline (Rahkonen et al. 2000).

This study highlights the substantially raised mortality in people with delirium seen in routine mental health care, as well as defining subgroups at particularly high risk. A key question requiring further evaluation is the extent to which survival might be improved in these groups. For example, implementing early detection strategies and assessment tools for those at high risk of developing delirium has been suggested as a mechanism leading to earlier psychiatric consultation and improved outcomes (Tennen et al., 2009). Consequently, developing protocols and providing clear guidance to clinicians in view of improving survival in these delirium patients will be vital, with prevention focussing on physical illness and functional decline.

Strengths of this study include the complete outcome ascertainment and the large sample size drawn from an essentially monopoly mental health care provider for a socially and ethnically diverse population, maximising the representativeness of the sample to its source population. A key consideration, however, is that this 'source population'—people who had received mental health contact and a diagnosis of delirium—cannot be assumed to be itself representative of all people with delirium. Inouye (1994) suggested that missed diagnosis rates for delirium were between 32 and 67%. It is likely that those referred to and recognised by mental health services contained more hyperactive compared with hypoactive syndromes. Because, as described in the preceding texts, hypoactive delirium has been found to be associated with increased mortality, overall rates might have been underestimated. Additional limitations are those of routine data; delirium was defined on the basis of a recorded clinician diagnosis rather than a structured instrument, and several of the covariates relied on brief routine assessments that will have been less accurate or consistent than a research instrument. Although the HoNOS is a widely used routine measure of clinical outcome in mental health services and was thus available on a large sample in this study, it is important to bear in mind that its subscales (for example, that covering physical illness) are relatively crude measures and unable to provide the level of detail that might be ascertained in a smaller scale but specific research project. Furthermore, the data did not include physical health records from acute secondary care or primary care; therefore, it was not feasible to identify more discrete subcohorts with specific medical conditions to examine relative contribution of risk factors associated with study outcomes. Thus, although the sample had broad generalisability to referrals received by mental health services, it was highly heterogeneous. Finally, adjustments in regression models were limited to available data, and it was not, for example, possible to take into account detailed symptomatology or interactions with health care staff or the clinical environment.
Conflict of interest

None declared.

Key points

- Overall SMRs for those delirium patients were 4.7 compared with England and Wales general population.
- Mortality risk was predicted by increase in age, male gender, white ethnicity, deteriorating physical health and functional impairment for those delirium patients.
- Cognitive function measured by MMSE scores and presence of dementia were not significant predictors in the adjusted models.
- When people who died within 6 months of delirium diagnosis were excluded, the reduced SMR may indicate that people with delirium often die within the acute phase of their physical illness.

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Description of author’s roles

Analyses were carried out by GW and GP. The manuscript was finalised by RS with substantial text contributions from GW and GP. RS also oversaw the planning and development of the SLAM BRC Case Register.

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