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Health-associated quality of life impairment in people who inject drugs (PWID) after bloodstream infection

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SUMMARY

Background: People who inject drugs (PWID) have high rates of bloodstream infections (BSI) with *Staphylococcus aureus* (SA) and group A *streptococcus* (GAS). Little is known about health-related quality of life outcomes after BSI.

Methods: We performed a prospective pilot cohort study of patients with BSI due to SA or GAS. Health-related quality of life, anxiety, depression and cognitive function were assessed using validated tools (EQ5-5D-5L), Hospital Anxiety and Depression Score (HADS) and Montreal Cognitive Assessment (MOCA) at baseline, 28 days post-discharge and 6 months post-infection.

Findings: 66 patients were recruited over a 12-month period, including 17 PWID. For the whole cohort, global health rank improved from baseline to day 28 (median 40 to 60, p=0.002), with no significant improvement from day 28 to day 168 (median 60 to 75, p=0.161). At baseline, PWID had lower overall health-related quality of life than non-PWID (median 25 vs 45, p=0.229), persisting at day 28 (non-PWID median 65, PWID median 43, p=0.036) and day 168 (non-PWID median 75, PWID median 40, p=0.035). This difference was driven by worse scores in the EQ-5D-5L mental health component and HADS, with HADS scores being significantly impaired in PWID at baseline (p=0.001) and day 28 (p=0.007).

Conclusion: PWID have impaired health-related quality of life after SA and GAS BSI that persists for up to 6 months. Poor mental health is the major component of this, and further studies could clarify if this is a target for intervention.

Introduction

Bacterial infections in people who inject drugs (PWID) are a significant cause of healthcare utilisation, morbidity, and mortality. In England, PWID have high rates of bacterial infections, with the United Kingdom Health Security Agency's (UKHSA) annual 'Shooting up' report[1] highlighting both group A *Streptococcus* (GAS) and *Staphylococcus aureus* (SA) as common significant pathogens. Earlier studies[2–4] reported higher mortality, up to twice the rate of relapse in PWID with SA and GAS infections, however they included participants with high rates of HIV infection potentially confounding the results.

While a UK study[5] found 1-year survival outcomes in PWID with infective endocarditis were poor despite effective therapy and surgical intervention, a previous retrospective study[6] found that PWID have a significantly lower 30-day, 1 year and 4-year mortality than non-PWID patients with *Staphylococcus aureus* bloodstream infection.

Severe long-term impacts on quality of life (QoL), health care use and mental health after significant infections such as sepsis, COVID-19 and SABSI have been reported. Follow-up from the ADRENAL trial,[7] highlighted approximately 20% of septic shock survivors reported '*moderate to extreme problems with heath related QoL at 6 months*'. The PHOSP-COVID trial[8] found that up to 80% of those hospitalised with COVID-19 had an impacted QoL at 6 months post discharge. A qualitative study that assessed the QoL outcomes in SA BSI at 6–8 weeks post-infection[9], found that the patient's QoL remained significantly impacted despite effective medical treatment. However, this study only assessed a single time point and did not evaluate differences between PWID and non-PWID patients.

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Our pilot study aimed to compare health care outcomes in patients with *Staphylococcus aureus* or group A *Streptococcus* BSI between PWID and non-PWID, assessing changes in QoL, mental health and cognition from acute illness to 12 months following discharge.

Materials and methods

Participants and setting

We conducted a prospective pilot cohort study of adult patients aged ≥18 years, diagnosed with bloodstream infection (BSI) due to group A *Streptococcus* or *Staphylococcus aureus* at Hull University Teaching Hospitals NHS Trust, a tertiary hospital service providing all services except solid organ transplantation and allogenic stem cell transplantation, with a catchment population of 1.25 million people. The study recruited participants between May 2022 and April 2023. Participants must have been able to consent or in cases of impaired capacity, have next of kin able to provide in person informed assent, within 72 h of the blood culture becoming positive in the microbiology laboratory, to be included in the study. Polymicrobial blood cultures with more than one significant organism were excluded from the study.

Data collection

Data were collected from medical and laboratory records at time of positive blood culture, together with standardised questionaries for recording outcomes.

The Index of Multiple Deprivation (IMD, last updated in 2019) was extrapolated from the participant's postcode using the UK Government and office for national statistics website. IMD measures relative rank of deprivation from the most to the least deprived, deciles 1 to 10 respectively. The IMD considers and combines 7 domains of deprivation: income; employment; education; health; crime; barriers to housing & services; and living environment.

Validated and widely used health-associated questionnaires for assessing quality of life (EuroQol5[7,8,11] -EQ5–5D-5L), comorbities (Charlson Score[10]) mental health (Hospital Anxiety and Depression Scale[12]- HADS) and cognition (Montreal Cognitive Assessment[13] blind- MoCA-BLIND) were completed at time of positive blood culture in participants providing their own consent. For those participants for whom next of kin provided assent at enrolment into the study, baseline demographics only were collected.

Participants who consented themselves, or regained capacity following enrolment, were followed up by the study team by telephone at initially 28 days post-discharge, but following a protocol amendment after the first 22 volunteers were enrolled, calls at 6 months and 12 months after discharge were included, in which repeat MoCA-BLIND, HADS and EQ5-DL questionnaires were performed.

All participants were also consented for access to medical records at 12 months from discharge to assess mortality, healthcare utilisation and antibiotic use post discharge. Antibiotic usage using available electronic prescribing records from both primary and secondary care in the 12 months post discharge was reviewed using the defined daily dosing (DDD) methodology from the World Health Organisation (WHO)[14].

Data analysis

Data were analysed using IBM SPSS (version 29.0.1.0 [171]). Student's T-Test and Mann-Whitney-U tests were performed as appropriate for linear parametric and non-parametric comparisons, respectively. Chi-squared testing was performed for categorical variables with Fisher's exact test performed when expected values were < 5. Spearman's rank correlation coefficient was performed to assess the direction and strength of the relationship between variables. Due to the small total population number and low events rate in the PWID group, multivariate analysis was not performed. Survival analysis was performed using the Kaplan-Meier methodology.

Ethics

This study was performed subject to approval from Health Research Authority and local Trust Research and Development team. The study was approved by the Wales Research Ethics Committee 1, (ref 22/WA/0088).

Results

Of 166 eligible patients screened, 66 enrolled into the study (see Fig. 1 for study consort diagram). The majority of participants (Table 1) were male (61%), with a median age of 56 years. Community-acquired SA was the predominant causative organism (86%), with 17 PWID (26%) recruited into the study. Participants came from a deprived area (3rd most deprived local authority in England out of 326) with a median deprivation index of 4 and were moderately comorbid with a median Charlson index of 3. PWID participants had non-statically significant increased rated of pre-existing anxiety or depression diagnoses compared to the non-PWID group, 24% and 12%, respectively (p=0.264). The most common focus of infection was bone and joint infection (24%) followed by line associated (17%) and vascular site (15%) infections.

PWID participants (Table 1) were younger than non-PWID (median age 40 and 62 years, respectively, p < 0.001) and were more likely to be male. Non-PWID were more comorbid than PWID, median Charlson score of 3 and 0, respectively (p=0.001). There was no statistical difference in organism or IMD score between PWID and non-PWID. No significant differences at presentation were found in severity (as assessed by National Early Warning Score) between PWID and non-PWID (supplementary table 1).

Mortality was 17% (11) deaths at 12 months post positive BSI (9 non-PWID and 2 PWID) (supplementary figure 1). There was no statistical difference in mortality between the two groups (p=0.54). Causative organism had no statistical impact on mortality (p=0.62).

EQ5-5D-5L-Health Rank

The health rank (overall global health rating) for all participants increased (improved) from baseline (day 0) to 6 Months follow-up (Day 168) with a significant improvement between baseline and 28 days (median 40 and 60 respectively, p=0.002) and baseline and 6 months (median 40 and 75 respectively, p < 0.001). Although the health rating improved between 28 days and 6 months, this was non-significant (P=0.161) (Fig. 2A).

At baseline, non-PWID had a non-significant higher health rank than PWID (median rank 45 and 25 respectively, p=0.229) (Fig. 3B). At 28 days post-discharge PWID reported significantly lower health ranks with median rank of 43, compared to a non-PWID median rank of 65 (p=0.036) (Fig. 3C). At 168 days post-discharge, PWID continued to report significantly lower health ranks compared to non-PWID, median rank 40 and 75 respectively (p=0.035) (Fig. 3D). Due to loss to follow-up or removal of consent for questionnaires, 1-year results were only available for 8 cases across the cohort and were therefore not statistically analysed.

There was a significant positive correlation between IMD score and health rank at baseline and 28 days (p=0.01 and p=0.014 receptively), which became non-significant by day 168 (supplementary figure 2).

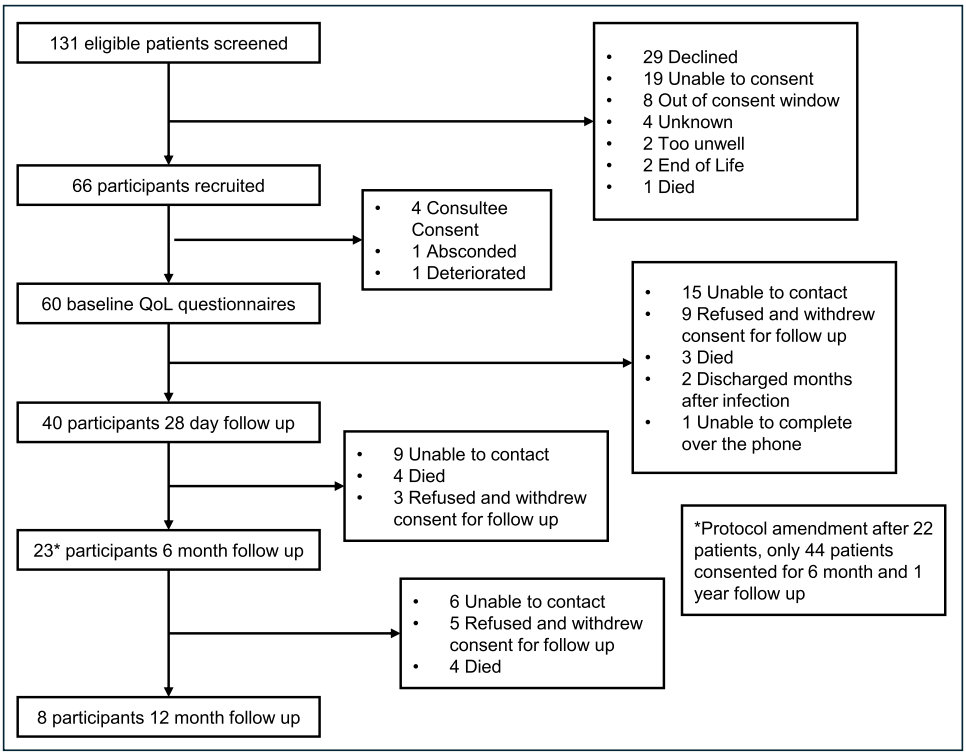

Fig. 1. Consort Diagram.

Table 1
Demographics of overall demographics and split into PWID and Non-PWID groups.

Demographics	
Male (%)	40 (61)
Age (median, range)	56 (22–69)
PWID (%)	17 (26)
Staphylococcus aureus (%)	57 (86)
Group A Streptococci (%)	9 (14)
IMD Score (median, range)	4 (1–10)
Charlson index (median, range)	3 (0–8)
Community-Acquired (%)	50 (75)
Focus of Infection	
Bone and Joint (%)	16 (24)
Line Associated (%)	11 (17)
Vascular (%)	10 (15)
Skin and Soft Tissue (%)	7 (11)
Cardiac (%)	6 (9)
Chest (%)	5 (8)
Intrabdominal (%)	3 (6)
Complicated UTI (%)	3 (6)
Head and Neck/ENT (%)	2 (3)
Blood stream(no focus) (%)	2 (3)
Metastatic focus (%)	1 (2)

Group-Specific Demographics

	PWID (n=17)	Non-PWID (n=49)	p Value
Age[a] (median, range)	40 (22–73)	62 (26–96)	< 0.001
Male (%)	12 (71)	28 (57)	0.328
SA (%)	15 (88)	42 (86)	0.578
GAS (%)	2 (12)	7 (14)	
IMD score (median, range)	1 (1–10)	4 (1–10)	0.176
Charlson index[a] (median, range)	0 (0–5)	3 (0–8)	0.001
Pre-diagnosed Anxiety or Depression (%)	4(24)	6(12)	0.264
Previous Imprisonment[a] (%)	8 (47)	1 (2)	< 0.001
Homeless[a] (%)	6 (35)	1 (2)	< 0.001
Sex Work[a] (%)	4 (24)	0 (0)	0.003
In work[a] (%)	6 (35)	40 (81)	< 0.001

[a] Significant results, IMD Score 1= most deprived, 10= least deprived.

EQ5-5D-5L-Pain

Reported levels of pain in the entire cohort from the EQ5–5D-5L questionnaire improved over time with a significant improvement between baseline (median 3) and 168 days (median 1, p=0.001), however, between baseline (median 3) and day 28 (median 3), there was no significant improvement (supplementary figure 3 A).

At baseline, PWID had a non-significant higher level of pain compared to non-PWID, median scores of 4 and 3, respectively (p=0.223). PWID status had no significant impact on EQ5 pain scores at both 28 (PWID median 3, non-PWID 3, p=1) and 168 days (PWID median 1, non-PWID 1, p=0.409) (supplementary figure 3B-D).

EQ5-5D-5L-Mental Health and Hospital Anxiety and Depression Scale-HADS

Levels of reported anxiety and depression within the EQ5–5D-5L questionnaire amongst the entire cohort improved from baseline (median 2) to 168 days (median 1, p=0.027). When comparing PWID (median 3) and non-PWID (median 2) participants, at baseline, there was no statistical difference (p=0.077) in mental health scores, however at 28 days, PWID reported significantly worse EQ5–5D-5L mental health scores with a median score of 3 compared to non-PWID score of 2 (p=0.042). At 168 days this difference remained between PWID and non-PWID, median score of 2 and 1, respectively, but was not significant (p=0.116) (Fig. 3A-D).

The total combined anxiety and depression score as part of the HADS significantly improved over time between baseline and day 168 for the whole cohort, with a median score 17 and 5, respectively (p=0.001). PWID (median 23) reported significantly more anxiety and depression at baseline compared to non-PWID (median 16, p=0.003). This significant difference between PWID (median 29) and non-PWID (median 8) in HADS total score continued at day 28

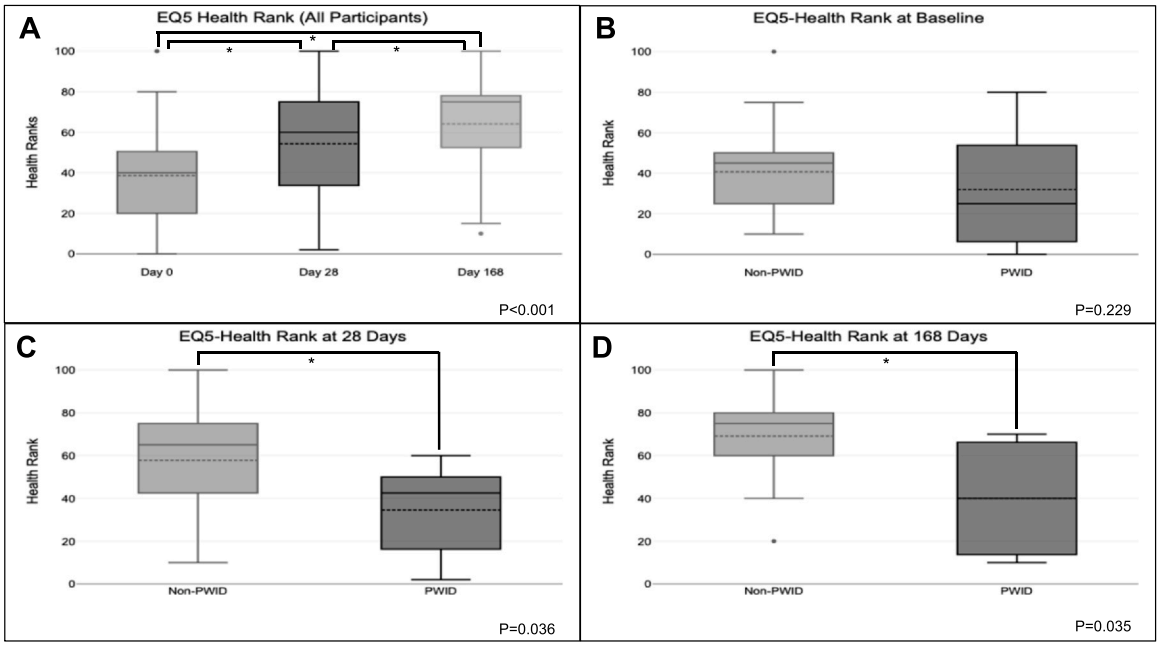

Fig. 2. **A**) EQ5-Health rank (all participants) Median: Baseline: 40, Day 28: 60 and Day 168: 75 **B**) EQ5-Health Rank at baseline PWID (median 25) vs Non-PWID (median 45) **C**) EQ5-Health Rank at 28 days PWID (median 43) vs Non-PWID (median 65) **D**) EQ5-Health Rank at 168 Days PWID (median 40) vs Non-PWID (median 75). **Key** = Dashed line- mean value, solid line- median value, Shaded box-interquartile range, whiskers- 95% confidence intervals. *=significant results.

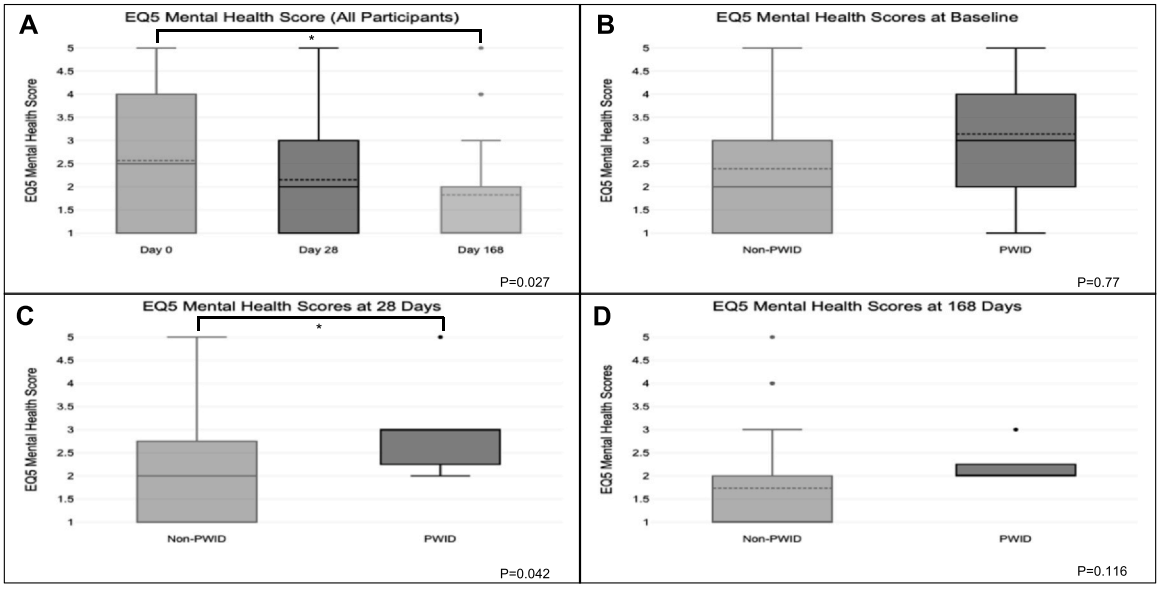

Fig. 3. **A**) EQ5-Mental Health score (all participants) Median: Baseline: 2, Day 28: 2 and Day 168: 1 **B**) EQ5-Mental Health score at baseline PWID (median 3) vs Non-PWID (median 2) **C**) EQ5-Mental Health score at 28 days PWID (median 3) vs Non-PWID (median 2) **D**) EQ5-Mental Health score at 168 Days PWID (median 2) vs Non-PWID (median 1) **Key** = Dashed line- mean value, solid line- median value, Shaded box-interquartile range, whiskers- 95% confidence intervals. *=significant results.

(p=0.007), becoming non-significant at 168 days (PWID median 17, non-PWID 3.5, p=0.141) (Fig. 4 A-D).

Breaking HADS down into its individual anxiety and depression scores, PWID (median 13) also reported significantly higher rates of baseline anxiety than non-PWID (median 8, p=0.002). Levels of anxiety at day 28 were also significantly higher in PWID (median 12) than in non-PWID (median 3, p=0.016), whereas at 168 days, although PWID had higher levels of anxiety when compared to non-PWID, median 9 and 2 retrospectively, this was not significant (p=0.118).

Older people reported less anxiety than younger members of the cohort. There was a significant negative correlation between age and anxiety level at baseline and day 28, $p < 0.001$, $r=-0.46$ and p=0.045, $r=-0.033$, respectively. However, this association had weakened by day 168 (p=0.19, $r=-0.29$).

As with the anxiety scores, separate HADS depression scores for the cohort improved over time (median day 0: 8, day 28: 6, day 168: 3, p=0.009). PWID reported significantly higher levels of depression (median 12) compared to non-PWID (median 7) at baseline (p=0.017), which continued to day 28 (median 14 and 5, respectively, p=0.006). Levels of depression in the PWID cohort remained higher (median 9) at day 168 compared to non-PWID (median 2) but were non-significant (p=0.118).

There was no significant association between deprivation and mental health scores at any timepoint (supplementary figure 4).

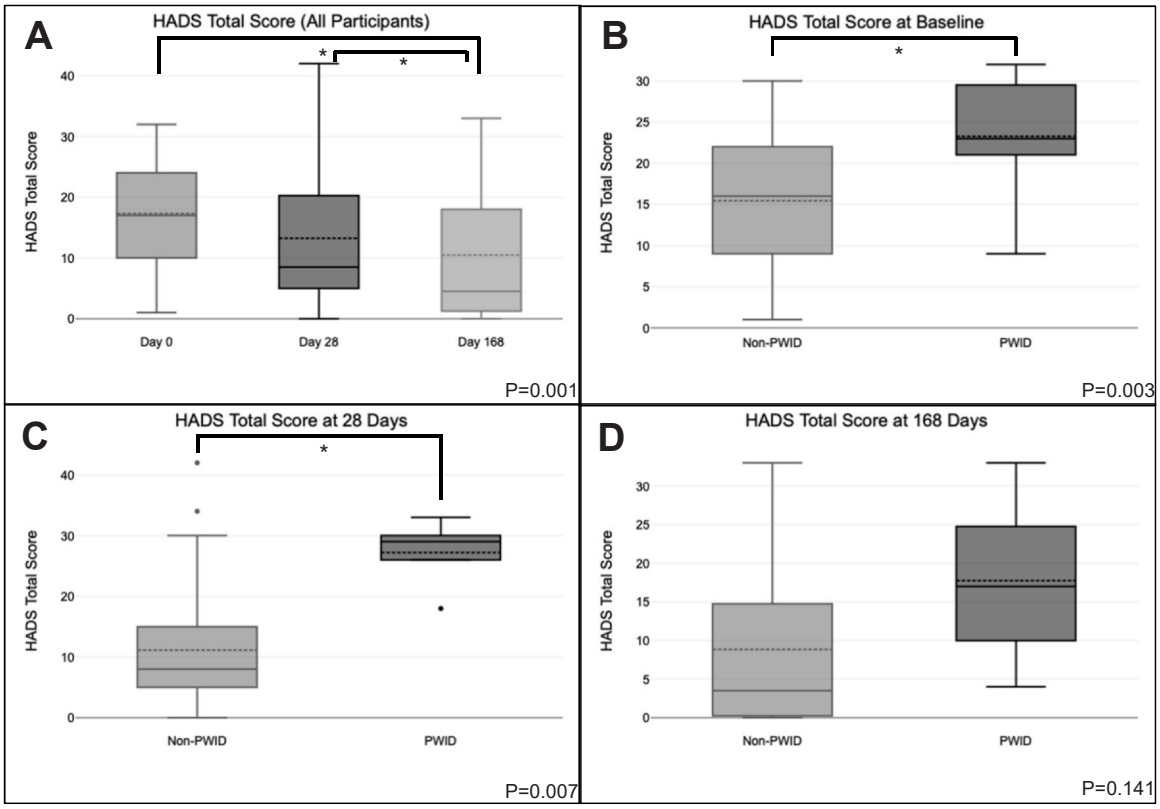

Fig. 4. **A**) HADS total score (all participants) Median: Baseline: 17, Day 28: 10 and Day 168: 5 **B**) HADS Total Score at baseline PWID (23) vs Non-PWID (median 23) **C**) HADS total score at 28 days PWID (median 29) vs Non-PWID (median 8) **D**) HADS total score at 168 Days PWID (median 17) vs Non-PWID (median 3.5) **Key**= Dashed line- mean value, solid line- median value, Shaded box- interquartile range, whiskers- 95% confidence intervals. *=significant results.

EQ5-5D-5L- Mobility

Globally, there was an improvement in EQ5–5D-5L mobility scores from baseline to 6 months, median score 4 and 2 respectively ($p < 0.001$) with a significant improvement between baseline (median 4) and 28 days (median 3, p=0.028). There was no difference in mobility scores comparing PWID and non-PWID participants at any of the timepoints (supplementary figure 5).

EQ5-5D-5L- Self-care

There was a significant difference in overall EQ5–5D-5L Self-care ratings between baseline (median score 4) and 6 months (median score 1, $p < 0.001$), with the largest improvement being between 28 days (median 3) and 6 months (median 1, p=0.001). PWID status had no influence on reported self-care scores (supplementary table 6).

EQ5-5D-5L- Usual activities

Overall, there was a significant improvement in the reported EQ5–5D-5L Usual Activities score between baseline and 6 months (median score 3 and 2, respectively, p=0.002), with the largest improvement being between baseline and 28 days ($p < 0.001$). Like mobility and self-care, PWID status had no impact on the reported usual activities score (supplementary figure 7).

Montreal Cognitive Assessment (MoCA)

Overall MOCA-BLIND improved significantly over time between baseline and 168 days, median score 20 and 22 retrospectively (p=0.001). MOCA-BLIND scores were not different between PWID and non-PWID at any time point (supplementary figure 8).

Healthcare utilisation

There was no difference in the median number of total secondary care admissions in the 12 months post-discharge for either PWID (median 1) or non-PWID (median 1, p=0.737). This was the case for both infective and non-infective indications for admission. Non-PWID (median 1) had a higher primary care usage when compared to PWID (median 0, p=0.044). The causative organism, either SA or GAS, had no statistical impact on admission to secondary care, but participants with SA BSI (median 1) were more likely to attend primary care, compared to GAS BSI (median 0, p=0.015) with the main reason for attendance being cellulitis.

In the PWID cohort, the mean average antibiotic consumption for all infective diagnoses in defined daily doses (DDD) was 9.83 DDD compared to 9.86 for the non-PWID cohort. There was no difference between PWID and non-PWID in antibiotic consumption (p=0.698) in the 12-month follow-up period.

Discussion

This descriptive, pilot study captured in-depth data on patient's quality of life experiences in the 12 months post-discharge after serious Gram-positive blood stream infections. Repeated follow-up post discharge and use of validated questionnaires encompassing different aspects of health-related quality of life, allowed the dynamics of patient recovery to be studied, an area where data are few. Understanding the lived experiences of patients with such infections is crucial for a holistic approach to the management of BSI.

Overall, PWID reported lower levels of overall health in the EQ5–5D-5L questionnaire at baseline, 28-day and 168-day follow-up, compared to non-PWID despite significantly fewer medical co-morbidities. Both PWID and non-PWID patients had markedly

impaired EQ5–5D-5L score compared to a general population study,[15] with an older UK study showing a general health ranking score of 82.5,[16] markedly higher than scores obtained in our study, with an overall health rank of 75 by 6 months across all participants. This is in spite of the findings of recent studies[17,18] of *Staphylococcus aureus* BSI that found lower mortality related to PWID-acquired infection. This finding highlights that PWID feel 'sicker' and continue to feel 'sicker' for longer compared to non-PWID,[15] despite being younger, which in general population studies is associated with higher quality of life health ranking.[15,16] It is of note that non-PWID patients had markedly greater improvement of both overall health rank in EQ5–5D-5L and HADS scores from baseline through to day 168, whilst PWID had very slow to no improvement in these measures over this period.

This study also demonstrates previously documented inequalities in health-associated quality of life in respect to deprivation.[19,20] Those from a more deprived area (lower IMD decile) were more likely to report lower levels of health at baseline and 28-day follow-up. The association between deprivation and mortality from infection has been reported previously,[20,21] and our findings suggest that this association may extend to quality of life.

The interplay between physical health and mental health is often overlooked in the management of serious infections, particularly amongst PWID. This study shows that PWID report more issues with their mental health than non-PWID. Interestingly, in this study, there was a difference in the results of the EQ5–5D-5L and HADS questionnaires, where EQ5 only finds a significant difference at 28 days, whereas the latter finds a significant difference in reported mental health-associated quality of life at baseline and 28-day follow-up. EQ5 only has a single question specific to the mental health domain, unlike HADS, which focuses on the different aspects of anxiety and depression, with greater granularity of data from HADS.

PWID have significantly higher rates of depression and anxiety compared to non-PWID and remain worse at follow-up than non-PWID. However, we cannot comment on the direction of causation, as PWID may be more depressed and anxious because of their drug use or conversely, poor mental health might be a reason for their drug use, with further drug use often causing (directly or indirectly) damage to mental health which further results in increased drug use. In our study, homelessness, imprisonment, not being in work and sex work were significantly more common among PWID, with these factors also likely to play a role in poor mental health. Studies[19] have attempted to understand this complex relationship but have been unable to unpick the relationship between mental health and drug use. Further research into these factors may provide targets for intervention, pharmacological or non-pharmaceutically, in attempting to break this vicious cycle. Severe infection as a result of drug use is evidence of harm resulting from addiction and should be an indication for intensive intervention. All healthcare attendances both to primary and secondary care are opportunities to intervene and address not only the physical issues but the psychosocial ones too. Healthcare workers can offer support links to support and homelessness services.

Taking opportunities to gain more secure housing for the PWID group could have a profoundly positive impact on their QoL. Reports from 'Everyone In[23]' campaign in 2020 highlighted an important potential holistic intervention in improving the QoL for PWID that resulted in a large reduction in PWID related infections.

When mental health is subdivided in the HADS questionnaire into its constituent domains, older people report lower levels of anxiety than younger participants, which aligns with Charlson comorbidity index, suggesting older more individuals feel and report less anxiety than younger, less co-morbid counterparts. This may be confounded due to PWID being on average younger than non-PWID. At baseline, age and depression scores appear to have a similar relationship i.e. older individuals report less depression; this does not continue throughout the follow-up. Further study to understand the relationship between age, PWID status and mental health is key to improving mental health outcomes in this cohort.

This pilot study has several limitations, in particular small numbers from a single geographic site. Those who were enrolled into the study tended to be less unwell than the general BSI population, as those who were severely unwell or unable to consent for the study were not followed up or did not record baseline questionnaires. Reported mortality in this study is lower than previously reported in the literature.[6,17,18] Time constraints from positive blood culture to time of consent resulted in the study team being unable to offer to include many patients within the consent window. Twelve months follow-up was especially difficult for the PWID participant group as PWID tend to have less secure housing, and to change address and contact details more often,[19,22] resulting in loss to follow-up.

Identifying strategies in improving PWID cohort follow-up would be key in future work, with possible solutions including working with pre-existing services that have systems designed to work with the PWID cohort in the community such as hepatitis C or methadone clinics.

These data suggest that quality of life after BSI with *Staphylococcus aureus* or group A *Streptococcus* is markedly impaired, and recovery is significantly slower in PWID patients. This is driven by poor mental health and clarification of this finding in other cohorts or differing infections would be of interest. Interventions to improve quality of life after BSI, especially in PWID could be an area of future study.

Author contributions

AR – Data collection, analysis, drafting of manuscript. IM, PB, EP – data collection, review of manuscript. GB, NE – Critical revision of manuscript, assistance with conceptualisation. PJL – initial idea, ethical approvals, data collection, analysis, drafting of manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2024.106375.

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