UK Health Security Agency

Morbidity and mortality in hospital in-patients with invasive Panton-Valentine leukocidin *Staphylococcus aureus* infections (PVL-SA) receiving antibiotic treatment

A rapid systematic review

Contents

Main messages

1. This rapid systematic review (search up to 28 February 2025) identified and summarised evidence relating to the effect of antibiotic treatment on morbidity and mortality among hospital inpatients with invasive Panton-Valentine leukocidin *Staphylococcus aureus* (PVL-SA) infections.

2. Three observational studies (1 to 3), 14 case series (4 to 17) and 78 case reports (18 to 95) were included.

3. One observational study (1), 9 case series (7 to 10, 12 to 14, 16, 17) and 40 case reports (19, 20, 25, 27, 29, 30, 32, 33, 35, 36, 38 to 42, 45, 47, 48, 51, 52, 57, 58, 61 to 63, 66, 68, 70, 73, 75, 78, 79, 82 to 84, 87, 88, 92 to 94) involved hospitalised adults with invasive PVL-SA infections.

4. Two observational studies (2, 3), 8 case series (4 to 7, 11, 13 to 15) and 38 case reports (18, 21 to 24, 26, 28, 31, 34, 37, 43, 44, 46, 49, 50, 53 to 56, 59, 60, 64, 65, 67, 69, 71, 72, 74, 76, 77, 80, 81, 85, 86, 89 to 91, 95) involved hospitalised children with invasive PVL-SA infections.

5. Necrotising pneumonia, abscesses, osteomyelitis, and bacteraemia appeared as the most common presentations for adults and children. Clindamycin, vancomycin, linezolid and rifampicin were the most frequently administered antibiotics for adults and children. Antibiotics were most commonly administered as combinations to treat patients hospitalised with invasive PVL-SA infections. Due to the wide range of infections and antibiotics used, the main messages have been presented by outcome.

6. Morbidity in adults was documented in one observational study (1), 7 case series (7 to 9, 12 to 14, 16) and 26 case reports (19, 20, 27, 29, 33, 35, 39, 42, 48, 51, 52, 57, 58, 62, 63, 66, 70, 73, 78, 79, 82 to 84, 87, 88, 94). Intensive care unit (ICU) admission was the most common outcome measure reported, followed by intubation, mechanical ventilation and vasopressors (treatment to raise blood pressure) in adults.

7. Morbidity in children was documented in 2 observational studies (2, 3), 8 case series (4 to 7, 11, 13 to 15) and 22 case reports (18, 21, 22, 24, 26, 28, 31, 37, 44, 55, 60, 65, 67, 71, 74, 76, 77, 80, 81, 86, 90, 91). The same outcome measures were also frequently reported in children, with paediatric intensive care unit (PICU) admission being the most common, followed by mechanical ventilation and intubation.

8. Severe morbidity leading to death was documented in 22 studies in adults (1, 7 to 9, 14, 16, 20, 27, 29, 35, 39, 42, 48, 62, 63, 66, 70, 73, 79, 83, 93, 94). In the observational study, 2 out of 6 adults died (1). Across the 5 case series, 8 out of 20

adults died (7 to 9, 14, 16). Among the 40 individual case reports in adults, 16 patients died (20, 27, 29, 35, 39, 42, 48, 62, 63, 66, 70, 73, 79, 83, 93, 94).

9. Severe morbidity leading to death was documented in 10 studies in children (2, 4, 6, 11, 15, 18, 21, 67, 76, 86). In the observational study, 2 out of 2 children died (2). Across the 4 case series, 6 out of 15 children died (4, 6, 11, 15). Among the 38 individual case reports in children, 5 patients died (18, 21, 67, 76, 86). Cases that died had multiple morbidity outcomes and rapid clinical deterioration. Many of these patients experienced complications such as respiratory failure requiring mechanical ventilation, ICU admission, and in some cases, temporary life support (extracorporeal membrane oxygenation (ECMO)). Death often occurred as a consequence of sepsis or progression to multi-organ failure.

10. Patients with a history of intravenous (IV) drug use were described in 7 studies (19 patients total). One observational study involving 6 out of 6 patients (1), 3 case series involving one out of 2 (7), 2 out of 3 (12), and 7 out of 10 patients respectively (16), and 3 individual case reports (42, 83, 92) reported patients with a history of intravenous (IV) drug use. All cases except one (92) had significant morbidity including need for intubation, mechanical ventilation, haemodialysis, multi-organ failure and many were admitted to the ICU. Six out of the 19 people included in these studies died (1, 16, 42, 83).

11. Risk of bias assessment of the observational studies highlighted small sample sizes which were unlikely to be large enough to reliably determine the effect of antibiotic treatment on morbidity and mortality of hospital inpatients with invasive PVL-SA infections. The observational studies were descriptive in nature with no statistical analysis or consideration of other factors that may have affected the outcomes making it difficult to determine how the antibiotic treatment contributed to the clinical outcomes described.

12. Most of the case series and case reports described patients' medical history, symptoms, disease progression, morbidity and whether they recovered or not, indicating a low risk of bias for these study designs. However, the reporting of antibiotic treatments used was often incomplete with cases lacking detail on antibiotic dosage, route of administration, and duration. As case series and case reports are based on individual patient outcomes, they represent a low level of evidence and findings cannot be reliably generalised to the wider population.

13. In summary, the review provided descriptive evidence on antibiotic treatment for hospitalised patients with invasive PVL-SA infections. Necrotising pneumonia, abscesses, osteomyelitis, and bacteraemia appeared as the most common presentations. Most studies documented patient recovery following antibiotic treatment. Cases that were reported to have died also reported underlying conditions with

associated multiple morbidity. Due to the descriptive nature of the evidence, it was not possible to determine the effectiveness of antibiotics in reducing morbidity and mortality for invasive PVL-SA infections, nor to identify whether any specific antibiotic is more effective for a particular infection.

Purpose

The purpose of this rapid systematic review was to identify and summarise the available evidence on the effect of antibiotics on morbidity and mortality outcomes in hospital inpatients with invasive PVL-SA infection.

The review question was:

1. What is the evidence for effect of antibiotic treatment on morbidity and mortality among hospital inpatients with invasive Panton-Valentine leukocidin *Staphylococcus aureus* infections?

Methods

A rapid systematic review was conducted, following streamlined systematic methods to accelerate the review process. A literature search was undertaken to look for relevant experimental studies including randomised controlled trials, quasi-experimental studies, cross-over designs, primary observational studies including cohort, case control and cross-sectional studies and descriptive studies including case series and case reports, published up to 28 February 2025. Five databases were searched. Backwards and forwards citation searching of primary studies included during full text screening was also performed.

A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. Full details of the methodology are provided in the protocol in Annexe A. To answer the review question, the following population, exposure, and outcome definitions were used:

1. Population: Adults and children with invasive PVL-SA infections being treated as hospital inpatients. The following invasive infections, as specified by subject matter experts, were of interest for this review: osteomyelitis (a serious infection in bones that causes pain, swelling and long term damage), necrotising fasciitis (a serious infection that rapidly destroys soft tissue under the skin), pyomyositis (an infection that causes pus to collect in the muscles, leading to pain, swelling and weakness), septic arthritis (a serious joint infection that causes pain, swelling and difficulty moving the affected joint), deep-seated tissue infections or abscesses (pocket of pus caused by infection leading to pain, swelling and redness in the affected area), pneumonia (lung infection that

causes difficulty in breathing), bacteraemia (presence of bacteria in bloodstream which can lead to serious infections in other parts of the body), septicaemia (a serious bloodstream infection where bacteria spread through the blood, potentially leading to widespread inflammation, organ failure and death if not treated quickly) and purpura fulminans (a severe condition where sudden bleeding into the skin and tissues occurs due to blood clotting problems). Only studies that clearly specified the diagnostic methods used for laboratory confirmation of invasive PVL-SA infection in inpatients were included. Where studies reported multiple PVL-SA invasive infections, only data for the eligible invasive infections was extracted.

2. Exposure: Any antibiotic or combination of antibiotics taken as treatment for PVL-SA invasive infections (see Annexe B for the list of agreed antibiotics). Studies reporting any other treatment that did not include antibiotics or where antibiotics were given in combination with immunoglobulin were excluded from the review (as this intervention was covered by the rapid systematic review: Intravenous immunoglobulin in the treatment of invasive Panton-Valentine leukocidin *Staphylococcus aureus* infections). Only the final antibiotic treatment administered during hospitalisation (before discharge) has been reported in this evidence review. Full antibiotic treatment details, including any adjustments made throughout the hospital stay, are provided in Annexe E.

3. Outcome: Morbidity and mortality. Morbidity outcomes were those directly attributable to the PVL-SA infection and included: admission to an ICU or High Dependency Unit (HDU), the need for intubation (a tube to help breathing) and mechanical ventilation, use of vasopressors (medication to raise blood pressure), clinical support with oxygen, end organ dysfunction, need for renal replacement therapy (including dialysis or renal transplant), acute liver failure, and diagnosis of disseminated intravascular coagulation (DIC). Mortality was defined as the in-hospital outcome of the patient, classified as either survival (recovery) or death during the hospital stay.

Screening on title and abstract was undertaken in duplicate by 2 reviewers for 20% of the eligible studies, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and checked by a second. Data extraction was performed by one reviewer and checked by a second. Disagreement was resolved by discussion. Data related to individuals who use intravenous drugs and details on antibiotic dosage and frequency were extracted if reported by the original studies. Evidence was presented separately in this review for adults and children as subject matter experts highlighted variations related to health inequalities.

Risk of bias assessment was conducted in duplicate by 2 reviewers. The JBI tools for case series and case reports were used for critical appraisal of included studies (96). The data presented in the observational studies was descriptive in nature and resembled a case series format without any comparison group, therefore the JBI tool for case series was used for risk of bias assessment of these studies. Certainty of the evidence was planned to be

assessed using a modified Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach (97) – however, the available data was not appropriate for such an evaluation.

Evidence

In total, 4,996 studies were screened at title and abstract and 244 studies were screened at full text. Additionally, 28 studies were identified from citation searching of included studies. As a result, 272 studies were screened at full text. Of these, 95 studies met the inclusion criteria. These included 3 observational studies (1 to 3), 14 case series (4 to 17) and 78 case reports (18 to 95).

One observational study (1), 6 case series (8 to 10, 12, 16, 17) and 40 case reports (19, 20, 25, 27, 29, 30, 32, 33, 35, 36, 38 to 42, 45, 47, 48, 51, 52, 57, 58, 61 to 63, 66, 68, 70, 73, 75, 78, 79, 82 to 84, 87, 88, 92 to 94) involved adults. Two observational studies (2, 3), 5 case series (4 to 6, 11, 15) and 38 case reports (18, 21 to 24, 26, 28, 31, 34, 37, 43, 44, 46, 49, 50, 53 to 56, 59, 60, 64, 65, 67, 69, 71, 72, 74, 76, 77, 80, 81, 85, 86, 89 to 91, 95) involved children aged 17 years or below. Three case series involved both children and adults (7, 13, 14). Evidence has been presented by grouping cases based on the type of infection, with those involving multiple infections reported under a separate section.

A PRISMA diagram showing the flow of studies through the review is shown in Annexe C, and studies excluded on full text screening are available with the reasons why in Annexe D. Study characteristics are available in Annexe E, and risk of bias assessments are available in Annexe F.

Adults

Observational study

One observational study reported an outbreak of staphylococcal bacteraemia in people who inject drugs in the United Kingdom (UK). Summary information on country, invasive infections and antibiotic treatment is provided in Table 1. Additional details of cases are reported in Table E.1.

Table 1. Summary of observational evidence in adults

Study type	Time period	Number of cases (cases that meet the inclusion criteria for this review)	History of IV drug use	Country and age range of patients	Invasive PVL-SA infections	Antibiotic treatment
Observational study Beaumont, 2024 (1)	July 2018 to July 2022	8 (6) [note 1]	Yes	UK 33 to 51 years	• abscess • bacteraemia • osteomyelitis • pneumonia • sepsis	• clindamycin • cotrimoxazole • daptomycin • fusidic acid • linezolid • rifampicin • teicoplanin

Note 1: 2 patients were not PVL positive and therefore did not meet inclusion criteria.

Pneumonia

Three out of the 6 patients had pneumonia. One patient (age and sex not reported) had asthma and had previously had septic arthritis. The patient was treated with clindamycin, daptomycin and rifampicin (dosage not reported). They were admitted to the ICU, underwent intubation, mechanical ventilation, received vasopressors and subsequently developed multi-organ failure. The patient died.

One patient (age and sex not reported) had chronic kidney disease and excessive alcohol intake. They were treated with linezolid and rifampicin (dosage not reported) and survived.

One patient (age and sex not reported), who also had a groin abscess, was treated with daptomycin, rifampicin and linezolid (dosage not reported). The patient survived.

Bacteraemia

One out of the 6 patients had bacteraemia. The patient (age and sex not reported) previously had infective endocarditis and had hepatitis C and pulmonary embolus. They were treated with rifampicin and cotrimoxazole (dosage not reported) and survived.

Adults with multiple invasive PVL-SA infections

Two out of the 6 patients had multiple PVL-SA invasive infection. One patient (age and sex not reported) with a history of previous infective endocarditis and empyema had a groin abscess and sepsis. They were treated with clindamycin and teicoplanin (dosage not reported): they were admitted to the ICU and died.

One patient (age and sex not reported) had osteomyelitis and a spinal abscess. They were treated with fusidic acid and linezolid (dosage not reported): the patient survived.

In summary, rifampicin was used in 4 out of 6 patients, in combination with other antibiotics such as linezolid (3 patients), daptomycin (2 patients), clindamycin (2 patients), teicoplanin (1 patient) and fusidic acid (1 patient). Dosage of antibiotics was not reported: two patients died and 4 survived.

Case series

Nine case series were identified for inclusion which reported on 30 hospitalised adults aged 20 to 71 years with invasive PVL-SA infections receiving antibiotic treatment. Three case series were in people with a history of drug use (7, 12, 16). Summary information on country, invasive infections and antibiotic treatment is provided in Table 2. Additional details of cases are reported in Table E.2.

Table 2. Summary of case series evidence in adults

Case series	Number of cases included in review overall (number of cases reported in this section)	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Hanratty, 2015 (7)	3 (2) [note 1]	Yes	UK	• abscess • pneumonia	• flucloxacillin • linezolid • moxifloxacin
Hayakawa, 2020 (8)	2 (2)	No	Japan	• necrotising pneumonia	• azithromycin • ceftriaxone • linezolid • tazobactam-piperacillin • vancomycin
Kravitz, 2005 (9)	3 (3)	No	USA	• necrotising pneumonia • purpura fulminans	• azithromycin • cefotaxime • fluconazole • gatifloxacin • gentamicin • levofloxacin nafcillin • vancomycin
Lin, 2008 (10)	3 (3)	No	USA	• abscess • bacteraemia • osteomyelitis • pyomyositis	• trimethoprim-sulfamethoxazol • vancomycin

Case series	Number of cases included in review overall (number of cases reported in this section)	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Micek, 2005 (12)	3 (3)	Yes	USA	• necrotising pneumonia • pneumonia	• clindamycin linezolid • rifampicin • vancomycin
Osterlund, 2002 (13)	2 (1) [note 1]	No	Sweden	• pneumonia • septicaemia	• clindamycin
Peleg, 2005 (14)	7 (3) [note 1]	No	Australia	• abscess • necrotising pneumonia • septicaemia	• clindamycin • ceftriaxone • erythromycin • fusidic acid • gentamicin • vancomycin • rifampicin
Toro, 2014 (16)	10 (10)	Yes	Canada	• abscess • bacteraemia • necrotising pneumonia	• clindamycin • linezolid • trimethoprim-sulfamethoxazol • vancomycin
Young, 2008 (17)	3 (3)	No	USA	• bacteraemia • necrotising fasciitis	• clindamycin • nafcillin • penicillin G • vancomycin

Note 1: remaining cases reported in children case series section.

Necrotising pneumonia

Three case series reported on 5 hospitalised adults with necrotising pneumonia and PVL-SA receiving antibiotics (8, 12, 16).

Hayakawa and others (8) reported 2 cases with necrotising pneumonia in Japan:

- a 20 year old man was treated with intravenous tazobactam-piperacillin (4.5 grams 4 times daily), azithromycin (500 milligrams once daily) and linezolid (600 milligrams twice daily). He required mechanical ventilation, vasopressors (noradrenaline) and veno-venous ECMO: the patient died
- a 61 year old woman was treated with ceftriaxone and vancomycin (1 gram twice daily): the patient survived

Micek and others (12) reported one case with necrotising pneumonia in the USA:

- a 45 year old man was treated with linezolid and rifampicin for 14 days (dosage not reported). He required mechanical ventilation: the patient survived

Toro and others (16) reported one case with necrotising pneumonia in Canada:

- a 38 year old man with a history of illicit drug use was treated with vancomycin and linezolid (dosage not reported). He required a chest tube: the patient survived

In summary, in the case series that reported on patients with necrotising pneumonia, the most common antibiotics used were linezolid and vancomycin. One patient died and 4 survived.

Pneumonia

One case series reported on 2 hospitalised adults with pneumonia and PVL-SA receiving antibiotics in the USA (12):

- a 34 year old man with a history of cocaine and heroin use was treated with a combination of vancomycin (1 gram twice daily) and clindamycin (900 milligrams every 8 hours). He was admitted to the ICU, underwent intubation and mechanical ventilation: the patient survived
- a 40 year old man with a history of insulin-dependent diabetes and substance use was treated with linezolid (600 milligrams twice daily) and rifampicin (300 milligrams every 8 hours) for 14 days. He required ICU admission, intubation, mechanical ventilation, and haemodialysis for acute renal failure: the patient survived

In summary, in the case series that reported on patients with pneumonia, both patients received different antibiotic treatments (both type and dose). Both patients survived.

Necrotising fasciitis

One case series reported on 2 hospitalised adults with necrotising fasciitis and PVL-SA receiving antibiotics in the USA (17):

- a 55 year old woman with a history of diabetes mellitus, hypertension, and coronary artery disease was treated with penicillin G, nafcillin, and clindamycin (dosage not reported): the patient survived
- a 29 year old man with a history of nephrolithiasis and depression treated with vancomycin and clindamycin (dosage not reported): the patient survived

In summary, in the case series that reported on patients with necrotising fasciitis, the most common antibiotic used was clindamycin. Both patients survived.

Purpura fulminans

One case series reported on 2 hospitalised adults with purpura fulminans and PVL-SA receiving antibiotics USA (9):

- a 40 year old woman was treated with nafcillin (2 grams every 4 hours) and levofloxacin (250 milligrams once daily). She was admitted to the ICU, required intubation and vasopressors (dopamine): the patient died
- a 34 year old woman with a history of juvenile rheumatoid arthritis was treated with vancomycin, gentamicin, gatifloxacin, and fluconazole (dosage not reported). She developed renal failure requiring haemodialysis: the patient died

In summary, in the case series that reported on patients with purpura fulminans, both patients received different antibiotic treatments. Both patients died.

Septicaemia

One case series reported on a hospitalised adult with septicaemia and PVL-SA receiving antibiotics in Australia (14):

- a 45 year old woman with a history of diabetes mellitus was treated with intravenous vancomycin followed by oral clindamycin or combination therapy with rifampicin and fusidic acid (dosage not reported): the patient survived

Abscess

One case series reported on a hospitalised adult with a lung abscess and PVL-SA receiving antibiotics in the UK (7):

- a 44 year old woman with a history of alcohol abuse and suicidal attempts admitted to the hospital for cellulitis and septic shock was treated with intravenous moxifloxacin

(500 milligrams once daily) along with flucloxacillin and linezolid. She was admitted to the ICU, required dialysis and developed multi-organ failure: the patient died

Adults with multiple invasive PVL-SA infections

Seven case series reported on 17 hospitalised adults with 2 or more PVL-SA invasive infections receiving antibiotics (7, 9, 10, 13, 14, 16, 17).

Necrotising pneumonia and bacteraemia

One case series reported on 5 hospitalised adults with necrotising pneumonia and bacteraemia (16) in Canada:

- a 34 year old woman with a history of illicit drug use and MRSA risk factors was treated with vancomycin, clindamycin and linezolid (dosage not reported). She was admitted to ICU, had a chest tube fitted and went into multiple organ failure: the patient died
- a 34 year old man with a history of illicit drug use and hepatitis C and MRSA risk factors was treated with vancomycin, clindamycin and linezolid (dosage not reported). He had a chest tube fitted: the patient survived
- a 68 year old man with a with a history of illicit drug use, MRSA risk factors, cardiac disease, diabetes mellitus and hypertension was treated with vancomycin, and linezolid (dosage not reported). He had a chest tube fitted: the patient survived
- a 41 year old woman with a with a history of illicit drug use and MRSA risk factors was treated with vancomycin and trimethoprim sulfamethoxazole (dosage not reported): the patient survived
- a 44 year old man was treated with vancomycin and linezolid (dosage not reported). He was admitted to ICU and had a chest tube fitted: the patient survived

Necrotising pneumonia and abscess

One case series reported on a hospitalised adult with necrotising pneumonia and abscess (16) in Canada:

- a 36 year old man with a with a history of illicit drug use, hepatitis C and MRSA risk factors was treated with vancomycin (dosage not reported). He was admitted to ICU, had a chest tube fitted and went into multiple organ failure: the patient died

Necrotising pneumonia and purpura fulminans

One case series reported on a hospitalised adult with necrotising pneumonia and purpura fulminans (9) in the USA:

- a 21 year old man was treated with cefotaxime, azithromycin and gatifloxacin (dosage not reported). He was admitted to ICU and was intubated: the patient died

Necrotising pneumonia and septicaemia

One case series reported on a hospitalised adult with necrotising pneumonia and septicaemia (14) in Australia:

- a 21 year old man was treated with ceftriaxone, erythromycin, gentamicin and rifampicin (dosage not reported). He was intubated and mechanically ventilated: the patient died

Necrotising pneumonia, bacteraemia and lung abscess

One case series reported on 2 hospitalised adults with necrotising pneumonia, bacteraemia and lung abscess (16) in Canada:

- a 48 year old woman with a history of illicit drug use, hepatitis C and MRSA risk factors was treated with vancomycin and linezolid (dosage not reported). She was admitted to the ICU and had a chest tube fitted: the patient survived
- a 71 year old woman was treated with vancomycin and linezolid (dosage not reported). She was admitted to the ICU: the patient survived

Necrotising pneumonia, septicaemia and abscess

One case series reported on a hospitalised adult with necrotising pneumonia, septicaemia and abscesses (14) in Australia:

- a 34 year old woman with a history of intravenous drug use was treated with intravenous vancomycin for 4 weeks. She was intubated and mechanically ventilated: the patient survived

Pneumonia and septicaemia

One case series reported on a hospitalised adult with pneumonia and septicaemia (13) in Sweden:

- a 32 year old woman who had influenza like symptoms one week before admission was treated with clindamycin (dosage not reported). She was admitted to ICU and mechanically ventilated: the patient survived

Ventilator-associated pneumonia and abscess

One case series reported on a hospitalised adult with ventilator associated pneumonia and abscess (7) in the UK:

- a 32 year old woman with a history of hepatitis C, alcohol and intravenous drug dependence was treated with piperacillin-tazobactam (4.5 grams every 8 hours), gentamicin (280 milligrams once daily) and intravenous linezolid (600 milligrams every 12 hours). She was admitted to the ICU and required mechanical ventilation: the patient survived

Necrotising fasciitis and bacteraemia

One case series reported on a hospitalised adult with necrotising fasciitis and bacteraemia (17) in the USA:

- a 32 year old man was treated with nafcillin and vancomycin (dosage not reported): the patient survived

Pyomyositis and bacteraemia

One case series reported on a hospitalised adult with pyomyositis and bacteraemia (5) in the USA:

- a 65 year old man with a history of alcoholism was treated with vancomycin (dosage not reported): the patient survived

Prostatic abscess and bacteraemia

One case series reported on a hospitalised adult with prostatic abscess and bacteraemia (5) in the USA:

- a 55 year old man with a history of hypertension, benign prostatic hypertrophy and chronic rectal haemorrhoids was treated with vancomycin (dosage not reported): the patient survived

Pyomyositis, osteomyelitis and bacteraemia

One case series reported on a hospitalised adult with pyomyositis, osteomyelitis and bacteraemia (10) in the USA:

- a 46 year old man was treated with vancomycin the switched to intravenous trimethoprim-sulfamethoxazole (due to suspected drug fever) (dosage not reported): the patient survived

In summary, in the case series that reported on patients with 2 or more invasive infections, the most common antibiotics used were linezolid and vancomycin. Four patients died and 14 patients survived.

Case reports

Forty case reports were identified in hospitalised adults aged between 20 to 92 years with invasive PVL-SA infections receiving antibiotic treatment. Summary information on country, invasive infections and antibiotic treatment is provided in Table 3. Additional details of cases are reported in Table E.3.

Table 3. Summary of case report evidence in adults

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Alonso-Tarres, 2005 (19)	Not reported	No	Spain	• necrotising pneumonia	• linezolid
Al-Talib, 2011 (20)	August 2009	No	Malaysia	• necrotising pneumonia	• ceftriaxone
Carroll, 2017 (25)	Not reported	No	Australia	• abscess	• clindamycin • vancomycin
Chen, 2024 (27)	Not reported	No	China	• necrotising pneumonia • sepsis	• linezolid • imipenem
Chetchotisakd, 2007 (29)	August 2004	No	Thailand	• necrotising pneumonia	• ceftriaxone • metronidazole
Conan, 2021 (30)	Not reported	No	France	• abscess	• clindamycin
Dhanoa, 2012 (32)	Not reported	No	Malaysia	• osteomyelitis • pyomyositis • septic arthritis • abscess • bacteraemia	• vancomycin • fusidic acid
Dubos, 2014 (33)	Not reported	No	France	• abscess sepsis	• ofloxacin • rifampicin
Enany, 2007 (35)	April 2007	No	Egypt	• abscess pneumonia	• vancomycin

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Enayet, 2006 (36)	Not reported	No	USA	• pneumonia	• vancomycin
Fahmy, 2008 (38)	Not reported	No	USA	• pyomyositis	• vancomycin
Fernandez, 2015 (39)	February 2013	No	Argentina	• necrotising pneumonia	• vancomycin • piperacillin / tazobactam • clarithromycin
Fica, 2023 (40)	2021	No	Chile	• bacteraemia	• daptomycin • cefazolin
Fogo, 2011 (41)	Not reported	No	UK	• abscess	• clindamycin • rifampicin
Frazee, 2005 (42)	February 2005	Yes	USA	• necrotising pneumonia • sepsis	• vancomycin • piperacillin / tazobactam • levofloxacin
Govindan, 2012 (45)	Not reported	No	India	• necrotising fasciitis	• clindamycin • amikacin
Higashiyama, 2010 (47)	June 2008	No	Japan	• abscess	• vancomycin • ceftriaxone
Honarpour, 2007 (48)	Not reported	No	USA	• necrotising pneumonia • sepsis	• vancomycin • piperacillin / tazobactam

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Iwanaga, 2013 (51)	Not reported	No	Japan	• necrotising pneumonia • osteomyelitis	• clindamycin • imipenem / cilastatin • vancomycin
Jung, 2008 (52)	October 2006	No	Germany	• abscess • necrotising pneumonia • sepsis	• clindamycin • rifampicin • flucloxacillin
Kuo, 2016 (57)	Not reported	No	Taiwan	• necrotising pneumonia • pyomyositis	• linezolid • oxacillin
Larsen, 2021 (58)	Not reported	No	Faroe Islands	• necrotising pneumonia	• clindamycin
Leung, 2024 (61)	January 2023	No	Hong Kong	• abscess	• vancomycin
Magira, 2007 (62)	Not reported	No	Greece	• necrotising pneumonia	• clindamycin • vancomycin • moxifloxacin • ceftriaxone
Mattu, 2024 (63)	Not reported	No	Canada	• abscess • necrotising pneumonia	• ceftriaxone • dexamethasone • azithromycin
Morimoto, 2024 (66)	Not reported	No	Japan	• pneumonia	• tedizolid

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Newell, 2023 (68)	Not reported	No	UK	• necrotising pneumonia	• linezolid • rifampicin • teicoplanin
Obed, 2006 (70)	Not reported	No	Germany	• necrotising pneumonia	• vancomycin • meropenem
Ote, 2023 (73)	Not reported	No	Japan	• bacteraemia • necrotising pneumonia • pyomyositis	• linezolid • daptomycin
Ramos, 2009 (75)	Not reported	No	Spain	• abscess • osteomyelitis	• cloxacillin
Riedweg-Moreno, 2014 (78)	November 2012	No	France	• necrotising pneumonia	• clindamycin • oxacillin
Roberts, 2008 (79)	April 2007	No	USA	• necrotising pneumonia	• ceftriaxone • moxifloxacin • gentamycin • ciprofloxacin • piperacillin / tazobactam
Schefold, 2007 (82)	Not reported	No	Germany	• abscess	• clindamycin • daptomycin

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
				• necrotising pneumonia • sepsis	
Sifri, 2007 (83)	Not reported	Yes	USA	• abscess	• vancomycin • cefepime
Soavi, 2011 (84)	January 2008	No	Italy	• necrotising pneumonia • septic shock	• clindamycin • caspofungin • linezolid
Takigawa, 2019 (87)	February 2017	No	Japan	• necrotising pneumonia	• vancomycin • linezolid
Torell, 2005 (88)	March 2005	No	Sweden	• pneumonia	• clindamycin • rifampicin
Venugopal, 2007 (92)	Not reported	Yes	USA	• abscess	• vancomycin
Wan, 2016 (93)	Not reported	No	Not reported	• pneumonia	• levofloxacin
Xia, 2020 (94)	Not reported	No	China	• pneumonia	• linezolid • mezlocillin sodium / sulbactam sodium

ICU admission was reported in 18 out of the 40 cases (19, 20, 27, 33, 35, 39, 52, 57, 58, 62, 63, 70, 73, 78, 79, 83, 84, 94), intubation in 14 out of 40 cases (27, 29, 42, 48, 57, 58, 62, 63, 70, 73, 79, 83, 84, 94) and mechanical ventilation in 13 out of 40 cases (20, 27, 39, 42, 57, 58, 62, 70, 73, 78, 82, 84, 94).

Seven out of 40 case reports documented use of vasopressors (48, 57, 62, 70, 79, 82, 94).

Clinical support with oxygen was provided in 3 out of 40 cases (66, 87, 88).

Two out of 40 cases documented both renal replacement therapy and multi-organ dysfunction (27, 63).

Two out of 40 cases reported DIC (48, 51).

One case report documented patient requiring haemodialysis (58), and one documented multi-organ failure requiring continuous veno-venous hemofiltration (84).

Fourteen out of 40 case reports did not report any morbidity outcomes relevant to the review question (25, 30, 32, 36, 38, 40, 41, 45, 47, 61, 68, 75, 92, 93). Only one case that did not report any morbidity outcomes died. This was reported to be due to cerebral infarction (93). The 13 other cases in these reports survived.

Sixteen of the 40 cases were reported to have died (20, 27, 29, 35, 39, 42, 48, 62, 63, 66, 70, 73, 79, 83, 93, 94).

Pneumonia

Five out of the 40 individual case reports were in hospitalised adults with pneumonia and PVL-SA receiving antibiotics (36, 66, 88, 93, 94):

- a 27 year old woman received intravenous vancomycin (dosage not reported): the patient survived (36)
- a 60 year old man with a medical history of hypertension and stroke received tedizolid (200 milligrams every 24 hours). He required ventilation, ECMO and ultimately died (66)
- a 24 year old woman was treated with clindamycin along with rifampicin (dosage not reported) and received clinical support with oxygen: the patient survived (88)
- a 92 year old man who also developed cerebral infarction (brain tissue damage due to blocked blood vessel) reported use of oral levofloxacin (500 milligrams every 24 hours) and ultimately died (93)
- a 68 year old man with a 15 pack year smoking history and long term alcohol use (100 grams per day) was administered linezolid along with mezlocillin sodium/sulbactam sodium (dosage not reported). He was admitted to the respiratory ICU, required

intubation, mechanical ventilation, and vasopressors (noradrenaline): the patient subsequently died (94)

In summary, in the cases reporting on adults with pneumonia, all 5 patients were treated with different antibiotics. Three of the 5 cases died.

Necrotising pneumonia

Eleven out of 40 individual cases were of hospitalised adults with necrotising pneumonia and PVL-SA receiving antibiotics (19, 20, 29, 39, 58, 62, 68, 70, 78, 79, 87):

- a 28 year old man received linezolid alone (600 milligrams every 12 hours): he was admitted to the ICU and survived (19)
- a 29 year old man who received ceftriaxone alone (1 gram twice daily) was admitted to the ICU, required mechanical ventilation and subsequently died (20)
- a 38 year old man with a medical history of human immunodeficiency virus (HIV), tuberculous colitis (bacterial infection in colon or large intestine), candida esophagitis (fungal infection in oesophagus), cryptococcus lymphadenitis (fungal infection of lymph nodes) and pulmonary rhodococcosis (bacterial infection of lungs) received intravenous ceftriaxone in combination with metronidazole (dosage not reported): he underwent intubation and ultimately died (29)
- a 50 year old man with a medical history of hypertension received vancomycin in combination with piperacillin/tazobactam and clarithromycin (dosage not reported). He was admitted to the ICU, underwent mechanical ventilation and subsequently died (39)
- a 47 year old man received intravenous clindamycin (900 milligrams 3 times daily). He was admitted to the ICU, underwent intubation, mechanical ventilation and haemodialysis: the patient survived (58)
- a 61 year old woman with a history of hypothyroidism and pulmonary tuberculosis (in her teens) was administered clindamycin in combination with vancomycin, moxifloxacin and ceftriaxone (dosage not reported). She was admitted to the ICU, underwent intubation and mechanical ventilation and received vasopressors: the patient died (62)
- a 35 year old man received linezolid in combination with rifampicin and teicoplanin (dosage not reported) and survived (68)
- a 51 year old woman with decompensated liver cirrhosis (long term condition where the liver loses its ability to function properly) due to hepatitis C infection was administered vancomycin along with meropenem (dosage not reported). She was admitted to the ICU, underwent intubation and mechanical ventilation and received vasopressors: the patient died (70)
- a 26 year old woman received clindamycin along with oxacillin (dosage not reported) and was admitted to the ICU and underwent mechanical ventilation: the patient survived (78)
- a 30 year old woman was given ceftriaxone along with moxifloxacin, gentamycin, ciprofloxacin and piperacillin/tazobactam (dosage not reported). She was admitted to the ICU, intubated and received vasopressors: the patient died (79)

- a 66 year old man with a history of acute renal failure received vancomycin (1000 milligrams per day, later increased to 1,500 milligrams per day) along with linezolid: he received clinical support with oxygen and survived (87)

In summary, in the cases reporting on adults with necrotising pneumonia, the most commonly administered antibiotics were ceftriaxone and vancomycin followed by linezolid and clindamycin. Six out of the 11 cases died.

Deep-seated abscesses

Seven out of 40 individual case reports reported deep-seated abscesses in hospitalised adults with PVL-SA receiving antibiotics (25, 30, 41, 47, 61, 83, 92):

- a 53 year old man with prostatic abscess (a pocket of pus in the prostate gland) and a history of type 2 diabetes, chronic hepatitis B infection, recurrent skin and soft tissue infections received oral clindamycin along with intravenous vancomycin (dosage not reported): the patient survived (25)
- a 20 year old woman with renal abscess (collection of pus around the kidney) received oral clindamycin (600 milligrams 3 times daily): the patient survived (30)
- a 39 year old woman with deep painful cutaneous (skin) abscess received clindamycin along with rifampicin (dosage not reported) and survived (41)
- a 25 year old woman with epidural abscess (buildup of pus between the bones of the spine and the lining of the spinal cord) was administered vancomycin along with ceftriaxone (dosage not reported): the patient survived (47)
- a 38 year old man with lung abscess received intravenous vancomycin (dosage not reported) and survived (61)
- a 37 year old woman with brain abscess and a history of injection drug use and incarceration received vancomycin with cefepime (dosage not reported) and was admitted to the ICU and intubated: the patient died (83)
- a 46 year old woman with psoas abscess (pocket of pus in a deep muscle near the spine and hips) and a history of injection drug use (heroin) received intravenous vancomycin (dosage not reported): the patient survived (92)

In summary, in the cases reporting on adults with deep-seated abscesses, the most commonly used antibiotics were vancomycin and clindamycin. One case died and 6 cases survived.

Bacteraemia

One case reported bacteraemia in a pregnant 37 year old woman with a history of hypothyroidism. She received intravenous daptomycin (500 milligrams daily) along with intravenous cefazolin (2 grams every 8 hours) and survived (40).

Pyomyositis

One case reported pyomyositis in a 39 year old man. He received intravenous vancomycin (dosage not reported) and survived (38).

Necrotising fasciitis

A 48 year old man with necrotising fasciitis received intravenous clindamycin along with amikacin (dosage not reported) and survived (45).

Adults with multiple invasive PVL-SA infections

Fourteen out of the 40 case reports documented hospitalised adults with multiple PVL-SA invasive infections receiving antibiotics (27, 32, 33, 35, 42, 48, 51, 52, 57, 63, 73, 75, 82, 84).

- a 39 year old woman with necrotising pneumonia and sepsis received linezolid along with imipenem (dosage not reported). She required ICU admission, tracheal intubation, mechanical ventilation, renal replacement therapy and developed multi-organ dysfunction: the patient died (27)
- a 31 year old man with history of alcohol and cocaine use had necrotising pneumonia and sepsis. He received vancomycin along with piperacillin / tazobactam and levofloxacin (dosage not reported) and underwent intubation and mechanical ventilation: the patient died (42)
- another 48 year old woman with necrotising pneumonia and sepsis was administered vancomycin along with piperacillin / tazobactam (dosage not reported). She was admitted to the ICU with DIC, requiring intubation and vasopressors and subsequently died (48)
- a 49 year old woman with necrotising pneumonia and septic shock received clindamycin with caspofungin and linezolid (dosage not reported). She was admitted to the ICU, underwent intubation and mechanical ventilation, required continuous veno-venous hemofiltration and had multi-organ failure: the patient survived (84)
- a 29 year old woman with necrotising pneumonia and abscesses received ceftriaxone with dexamethasone and azithromycin (dosage not reported). She was admitted to the ICU, underwent intubation and continuous renal replacement therapy progressing to multi-organ failure: the patient died (63)
- a 23 year old woman with necrotising pneumonia, muscle abscess and sepsis received clindamycin (600 milligrams 3 times daily) along with rifampicin (600 milligrams) and intravenous flucloxacillin (4 grams 3 times daily) and was admitted to the ICU: the patient survived (52)
- a 51 year old man with necrotising pneumonia, soft tissue abscesses and sepsis was administered clindamycin in combination with daptomycin (dosage not reported): he underwent mechanical ventilation, received vasopressors and survived (82)

- a 28 year old man who was a regular smoker with osteomyelitis, septic arthritis, pyomyositis, deep-seated tissue abscesses and bacteraemia received intravenous vancomycin (1 gram twice daily) with fusidic acid: the patient survived (32)
- a 20 year old man with a history of allergic asthma and recurrent furuncles (painful, red, swollen bumps on the skin) developed prostatic abscess and sepsis. He received ofloxacin and oral rifampicin (dosage not reported) and was admitted to the ICU: the patient survived (33)
- a 50 year old man with a history of chronic hepatitis and diabetes developed brain abscess and pneumonia. He received vancomycin (1 gram every 12 hours) and was admitted to the ICU: the patient died (35)
- a 34 year old man with osteomyelitis and brain abscess received intravenous cloxacillin (2 grams every 4 hours) and survived (75)
- a 31 year old man with necrotising pneumonia and osteomyelitis was administered intravenous clindamycin (600 milligrams every 12 hours) along with intravenous (imipenem/cilastatin 0.5 grams every 6 hours) and intravenous vancomycin (2 grams) added later: he had DIC and survived (51)
- a 23 year old man with necrotising pneumonia and pyomyositis was administered intravenous linezolid (600 milligrams every 12 hours) along with intravenous oxacillin (2 grams every 4 hours). He was admitted to the ICU, underwent intubation, mechanical ventilation and received vasopressors: the patient survived (57)
- a 25 year old man with necrotising pneumonia, pyomyositis and bacteraemia received linezolid (600 milligrams every 12 hours) along with daptomycin (700 milligrams) every 24 hours: he was admitted to the ICU, underwent intubation and mechanical ventilation and subsequently died (73)

In summary, linezolid, vancomycin, and clindamycin were the most frequently used antibiotics in cases reporting adults with multiple invasive PVL-SA infections, often administered in combination with other antibiotics depending on clinical severity and infection site. Six out of the 14 cases died while all others survived.

Children

Observational studies

Two observational studies were identified in hospitalised children with invasive PVL-SA infections receiving antibiotic treatment. Summary information on country, invasive infections and antibiotic treatment is provided in Table 4. Additional details of cases are reported in Table E.4.

Table 4. Summary of observational evidence in children

Study type	Time period	Number of cases (cases that meet the inclusion criteria for this review)	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Multicentre cohort study Nygaard, 2022 (2)	January 2016 to November 2021	11 (2) [note 1]	No	Denmark	• bacteraemia • necrotising pneumonia	• amoxicillin • meropenem
Outbreak report Tang, 2007 (3)	April 2006 to May 2006	9 (1) [note 2]	No	Vietnam	• necrotising fasciitis • abscess	• vancomycin • imipenem

Note 1: details of antibiotic treatment given to the 9 other children was not reported and therefore did not meet inclusion criteria.
Note 2: invasive PVL-SA infections were not reported in the 8 other children and therefore did not meet inclusion criteria.

Necrotising pneumonia and septic shock

Nygaard and others (2) reported on a 2 year old girl exposed to SARS-Cov-2, parainfluenza and rhinovirus with necrotising pneumonia and septic shock. She was treated with amoxicillin (dosage not reported). The patient died.

Necrotising pneumonia, septic shock and necrotising abscess

Nygaard and others (2) reported on a 15 year old adolescent boy exposed to influenza A also developed necrotising pneumonia complicated by pulmonary necrotising abscess (infected lung abscess with dead tissue) and septic shock. He was treated with meropenem (dosage not reported) and required mechanical ventilation, fluid resuscitation (giving fluids to prevent shock) and ionotropic support (medication to help the heart pump stronger). The patient died.

Necrotising fasciitis and necrotising abscess

Tang and others (3) reported on a 17 month old boy hospitalised with necrotising fasciitis and a necrotic abscess severe which developed at the injection site following an out-patient vaccination. He was treated with vancomycin and imipenem (dosage not reported) and required vasopressor treatment with dopamine and noradrenaline. The patient survived.

Case series

Eight case series were identified for inclusion which reported on 23 hospitalised children aged 25 weeks to 16 years with invasive PVL-SA infections receiving antibiotic treatment. Information on country, invasive infections and antibiotic treatment is provided in Table 5. Additional details of cases are reported in Table E.5.

Table 5. Summary of case series evidence in children

Case series	Number of cases included in review overall (number of cases reported in this section)	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Adem, 2005 (4)	3 (3)	No	USA	• bacteraemia • necrotising pneumonia • purpura fulminans • sepsis	• ceftriaxone • vancomycin

Case series	Number of cases included in review overall (number of cases reported in this section)	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Bybeck Nielsen, 2020 (5)	2 (2)	No	Denmark	• abscess • bacteraemia • necrotising fasciitis • osteomyelitis	• clindamycin
Cunnington, 2009 (6)	7 (7)	No	UK	• abscess • necrotising pneumonia • sepsis • osteomyelitis • pyomyositis • septic arthritis	• cephalosporin • clindamycin • flucloxacillin • linezolid • rifampicin
Hanratty, 2015 (7)	3 (2) [note 1]	No	UK	• abscess	• amoxicillin • flucloxacillin
McAdams, 2008 (11)	2 (2)	No	USA	• bacteraemia • necrotising pneumonia	• amikacin • clindamycin • piperacillin-tazobactam • vancomycin
Osterlund, 2002 (13)	2 (1) [note 1]	No	Sweden	• pneumonia	• cefuroxime • clindamycin

Case series	Number of cases included in review overall (number of cases reported in this section)	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Peleg, 2005 (14)	7 (4) [note 1]	No	Australia	• abscess • necrotising pneumonia • osteomyelitis • septic arthritis • septicaemia	• clindamycin • fusidic acid • rifampicin • vancomycin
Schwartz, 2012 (15)	3 (3)	No	Australia	• bacteraemia • necrotising pneumonia	• clindamycin • flucloxacillin • linezolid • rifampicin

Note 1: remaining cases reported in adult case series section.

Necrotising pneumonia

Two case series reported on 3 hospitalised children with necrotising pneumonia and PVL-SA receiving antibiotics (6, 15). Schwartz and others (15) reported 2 cases with necrotising pneumonia in Australia:

- an 8 month old girl was treated with clindamycin, linezolid and rifampicin (dosage not reported). She was intubated and medically ventilated: the patient survived
- a 5 month old boy was treated with linezolid, lincomycin and rifampicin (dosage not reported). He was medically ventilated: the patient survived

Cunnington and others (6) reported one case with necrotising pneumonia in the UK:

- a 10 year old boy was treated with clindamycin and flucloxacillin (dosage not reported). He was admitted to PICU: the patient survived

In summary, the case series that reported on patients with necrotising pneumonia and PVL-SA, the most common antibiotics used were clindamycin, linezolid and rifampicin. All 3 patients survived.

Pneumonia

One case series reported on a hospitalised child with pneumonia and PVL-SA receiving antibiotics in the Sweden (13):

- a 13 year old girl was treated with cefuroxime and clindamycin (dosage not reported). She was admitted to ICU and was ventilated: the patient survived

Septic arthritis

One case series reported on 2 hospitalised children with septic arthritis and PVL-SA receiving antibiotics in the UK (6):

- a 10 year old boy was treated with intravenous cephalosporin and clindamycin (dosage not reported): the patient survived
- a 13 year old boy was treated with intravenous cephalosporin and clindamycin (dosage not reported): the patient survived

In summary, the case series that reported on patients with septic arthritis and PVL-SA, the most common antibiotics used was clindamycin. Both patients survived.

Bacteraemia

One case series reported on a hospitalised child with bacteraemia and PVL-SA receiving antibiotics in the UK (6):

- a 26 week old girl who was born premature and have a central venous line, was treated with vancomycin, amikacin, clindamycin (dosage not reported). She was admitted to neonatal intensive care unit (NICU): the patient survived

Osteomyelitis

One case series reported on a hospitalised child with osteomyelitis and PVL-SA receiving antibiotics in the UK (6):

- a 6 year old girl was treated with flucloxacillin, clindamycin and rifampicin (dosage not reported). She was admitted to PICU: the patient survived

Pyomyositis

One case series reported on a hospitalised child with pyomyositis and PVL-SA receiving antibiotics in the UK (6):

- a 5 year old boy was treated with clindamycin, rifampicin and linezolid (dosage not reported): the patient survived

Retropharyngeal abscess

One case series reported on a hospitalised child with retropharyngeal abscess and PVL-SA receiving antibiotics in the UK (6):

- a 7 month old girl was treated with intravenous cephalosporin and clindamycin (dosage not reported). She was admitted to PICU: the patient survived

Submandibular abscess

One case series reported on a hospitalised child with submandibular abscess and PVL-SA receiving antibiotics in the UK (7):

- a 13 year old boy with a history of latent tuberculosis was treated with amoxicillin and intravenous flucloxacillin (dosage not reported). He was admitted to high dependency unit and was ventilated: the patient survived

Children with multiple invasive PVL-SA infections

Seven case series reported on 12 hospitalised children with 2 or more PVL-SA invasive infections receiving antibiotics (4 to 6, 11, 13 to 15).

Necrotising pneumonia and bacteraemia

Two case series reported on 2 cases of hospitalised children with necrotising pneumonia and bacteraemia in the USA (11) and in Australia (15):

- a 25 week old boy who was born prematurely and had a central venous line was treated with vancomycin, amikacin and piperacillin-tazobactam (dosage not reported). He was admitted to NICU: the patient died (11)
- a 5 month old boy was treated with linezolid, lincomycin and rifampicin (dosage not reported). He was mechanically ventilated: the patient survived (15)

Necrotising pneumonia and sepsis

One case series reported on a case of a hospitalised child with necrotising pneumonia and sepsis in the USA (4):

- a 9 month old girl with was treated with vancomycin and ceftriaxone (dosage not reported). She was admitted to the ICU, required intubation and ECMO and suffered multiorgan system failure: the patient died

Necrotising pneumonia, sepsis and bacteraemia

One case series reported on a case of a hospitalised child with necrotising pneumonia, sepsis and bacteraemia in the USA (4):

- a 15 month old girl with was treated with vancomycin and ceftriaxone. She experienced multiorgan system failure: the patient died

Necrotising pneumonia, sepsis and purpura fulminans

One case series reported on a case of a hospitalised child with necrotising pneumonia, sepsis and purpura fulminans in the USA (4):

- a 17 month old boy with a history of reactive airway disease and pharyngitis was treated with vancomycin and ceftriaxone. He required intubation and ECMO and experienced multiorgan system failure: the patient died

Necrotising fasciitis and bacteraemia

One case series reported on a case of a hospitalised child with necrotising fasciitis and bacteraemia in Denmark (5):

- a 14 year old (sex not reported) child was treated with clindamycin (dosage not reported). The patient required mechanical ventilation, DIC and dialysis: the patient survived

Septicaemia and osteomyelitis

One case series reported on 2 cases of hospitalised children with septicaemia and osteomyelitis in Australia (14):

- a 4 year old girl was treated with intravenous vancomycin followed by oral clindamycin or combination therapy with rifampicin and fusidic acid (dosage and specific treatment not reported): the patient survived
- a 16 year old boy was treated with intravenous vancomycin followed by oral clindamycin or combination therapy with rifampicin and fusidic acid (dosage and specific treatment not reported): the patient survived

Septicaemia and paraspinal abscess

One case series reported on a case of a hospitalised child with septicaemia and paraspinal abscess in Australia (14):

- a 12 year old boy was treated with intravenous vancomycin followed by oral clindamycin or combination therapy with rifampicin and fusidic acid (dosage and specific treatment not reported): the patient survived

Septicaemia and septic arthritis

One case series reported on a case of a hospitalised child with septicaemia and septic arthritis in Australia (14):

- a 9 year old boy was treated with intravenous vancomycin followed by oral clindamycin or combination therapy with rifampicin and fusidic acid (dosage and specific treatment not reported): the patient survived

Septic arthritis and nosocomial sepsis

One case series reported on a case of a hospitalised child with septic arthritis and nosocomial sepsis in the UK (6):

- a 3 year old girl was treated with intravenous cephalosporin and flucloxacillin (dosage not reported). She was admitted to PICU and required continuous veno-venous hemodiafiltration (a treatment that filters and cleans the blood when kidneys are not working properly) as they had renal failure: the patient died

Osteomyelitis, bacteraemia and abscesses

One case series reported on a case of a hospitalised child with osteomyelitis, bacteraemia and multiple abscesses in Denmark (5):

- a 10 year old (sex not reported) patient was treated with clindamycin (dosage not reported): the patient survived

In summary, in the case series that reported on children with 2 or more invasive PVL-SA infections, the most common antibiotics used were vancomycin and clindamycin. Five patients died and 7 patients survived.

Case reports

Thirty-eight case reports described hospitalised children aged between 7 days to 17 years with invasive PVL-SA infections receiving antibiotic treatment. Summary information on country, invasive infections and antibiotic treatment is provided in Table 6. Additional details of cases are reported in Table E.6.

Table 6. Summary of case report evidence in children

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Akpaka, 2011 (18)	Not reported	No	Trinidad and Tobago	• septic arthritis • necrotising fasciitis • septicaemia	• clindamycin • ceftriaxone • vancomycin • cloxacillin
Ambrozova, 2013 (21)	December 2008	No	Czech Republic	• pneumonia	• clindamycin • gentamicin • oxacillin
Balis, 2007 (22)	Not reported	No	Greece	• pneumonia • bacteraemia	• linezolid • moxifloxacin
Bukhari, 2012 (23)	Not reported	No	Saudi Arabia	• osteomyelitis • abscess	• clindamycin • cloxacillin
Camargo, 2013 (24)	December 2010	No	Brazil	• pneumonia	• vancomycin • imipenem
Castellazzi, 2021 (26)	Not reported	No	Italy	• osteomyelitis abscess	• clindamycin • ceftaroline • daptomycin
Chen, 2014 (28)	Not reported	No	China	• necrotising pneumonia	• teicoplanin • fosfomycin
Cupane, 2010 (31)	November 2009	No	Latvia	• pneumonia	• clindamycin • ceftriaxone • oxacillin

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Elledge, 2014 (34)	Not reported	No	UK	• osteomyelitis	• flucloxacillin • rifampicin
Esteves, 2010 (37)	Not reported	No	Portugal	• pneumonia • septic arthritis	• flucloxacillin
Garbo, 2024 (43)	June 2023	No	Italy	• necrotising pneumonia • osteomyelitis	• clindamycin • daptomycin • fosfomycin
Goemanne, 2022 (44)	February 2021	No	Belgium	• abscess	• flucloxacillin
Harada, 2023 (46)	Not reported	No	Japan	• osteomyelitis • septic arthritis	• clindamycin • vancomycin
Irenji, 2018 (49)	Not reported	No	UK	• pneumonia • osteomyelitis • sepsis • abscess	• linezolid • clindamycin
Isobe, 2013 (50)	October 2004	No	Japan	• osteomyelitis • abscess	• vancomycin • fosfomycin
Karli, 2016 (53)	Not reported	No	Turkey	• abscess	• linezolid • clindamycin
Karli, 2016 (54)	Not reported	No	Turkey	• osteomyelitis • abscess	• linezolid • clindamycin

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Kefala-Agoropoulou, 2010 (55)	2007	No	Greece	• osteomyelitis • pyomyositis	• clindamycin • teicoplanin
Kim, 2023 (56)	Not reported	No	South Korea	• necrotising fasciitis	• vancomycin
Laurens, 2008 (59)	Not reported	No	USA	• osteomyelitis	• clindamycin • vancomycin
Lehman, 2010 (60)	Not reported	No	USA	• septic arthritis • osteomyelitis • necrotising fasciitis • myositis	• oxacillin
Miyashita, 2002 (64)	Not reported	No	Japan	• bacteraemia	• cefazolin
Montagnani, 2013 (65)	Not reported	No	Italy	• necrotising pneumonia	• clindamycin • linezolid
Mushtaq, 2008 (67)	Not reported	No	UK	• necrotising pneumonia • purpura fulminans	• cefotaxime • gentamicin
Ng, 2018 (69)	Not reported	No	Malaysia	• bacteraemia	• cloxacillin • gentamicin
Ogawa, 2022 (71)	2017	No	Japan	• abscess	• clindamycin
Oshima, 2021 (72)	Not reported	No	Japan	• necrotising pneumonia • abscess	• linezolid

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
Perbet, 2010 (74)	Not reported	No	France	• necrotising fasciitis • sepsis	• clindamycin • oxacillin
Ravishankar, 2016 (76)	Not reported	No	USA	• necrotising pneumonia	• vancomycin • ceftriaxone
Reichert, 2005 (77)	Not reported	No	UK	• abscess	• flucloxacillin
Rovira, 2015 (80)	Not reported	No	Mozambique	• necrotising pneumonia • osteomyelitis	• vancomycin • gentamicin
Rozenbaum, 2009 (81)	January, 2007	No	Brazil	• osteomyelitis • septic shock	• teicoplanin
Swaminathan, 2006 (85)	Not reported	No	Australia	• osteomyelitis • septic arthritis • abscesses	• flucloxacillin
Székely, 2010 (86)	March 2007	No	Romania	• necrotising pneumonia	• meropenem • ciprofloxacin • teicoplanin
Uda, 2020 (89)	Not reported	No	Japan	• septic arthritis	• vancomycin
Valentini, 2008 (90)	Not reported	No	Italy	• necrotising pneumonia • abscess • bacteraemia	• linezolid • teicoplanin • rifampicin
Vanbiervliet, 2022 (91)	Not reported	No	Belgium	• osteomyelitis • pyomyositis	• clindamycin • flucloxacillin

Case report	Time period	History of IV drug use	Country	Invasive PVL-SA infections	Antibiotic treatment
					• levofloxacillin • linezolid
Yonezawa, 2015 (95)	Not reported	No	Japan	• osteomyelitis • necrotising • fasciitis • necrotising pneumonia • bactaeremia • sepsis	• linezolid • meropenem

Sixteen of the 38 case reports described hospitalised children with invasive PVL-SA infections who experienced no morbidity outcomes of interest during their hospital stay and survived (23, 34, 43, 46, 49, 50, 53, 54, 56, 59, 64, 69, 72, 85, 89, 95).

PICU admission was reported in 15 out of 38 case reports (18, 21, 22, 24, 26, 31, 37, 44, 67, 71, 74, 76, 81, 90, 91), mechanical ventilation in 11 out of 38 cases (18, 21, 22, 24, 31, 60, 67, 76, 81, 86, 91), intubation in 10 out of 38 cases (18, 21, 22, 60, 67, 71, 76, 81, 86, 91), clinical support with oxygen in 6 out of 38 cases (28, 55, 65, 76, 77, 80), use of vasopressors in 5 out of 38 cases (21, 22, 67, 76, 91), renal failure in one case (77), continuous veno-venous haemodialysis in one (91) and multiple organ failure in 2 out of 38 cases (67, 91).

Five out of 38 cases were reported to have died (18, 21, 67, 76, 86).

Pneumonia

Three out of 38 individual cases reported on hospitalised children with pneumonia and PVL-SA receiving antibiotics (21, 24, 31):

- a 10 month old boy who was admitted to the PICU, was treated with clindamycin along with gentamicin and oxacillin (dosage not reported). He underwent intubation and mechanical ventilation and received vasopressors (intravenous noradrenaline): the patient died (21)
- a 16 year old boy was treated with vancomycin along with imipenem (dosage not reported). He was admitted to the ICU and mechanically ventilated: the patient survived (24)
- a 15 year old boy was treated with clindamycin and intravenous ceftriaxone and oxacillin (dosage not reported): he was admitted to PICU, required mechanical ventilation and survived (31)

In summary, in the cases that reported on children with pneumonia and PVL-SA, the most common antibiotics given were clindamycin and oxacillin. One case died while the other 2 survived.

Necrotising pneumonia

Four out of 38 individual cases reported necrotising pneumonia in hospitalised children with PVL-SA receiving antibiotics (28, 65, 76, 86):

- a 15 year old girl was treated with teicoplanin and fosfomycin (dosage not reported): she received clinical support with oxygen and survived (28)
- a 3 month old boy was treated with clindamycin along with linezolid (dosage not reported): he received clinical support with oxygen and survived (65)
- a 10 year old girl was treated with intravenous vancomycin (1 gram) in combination with intravenous ceftriaxone (2 grams). She was admitted to PICU, underwent intubation, mechanical ventilation and required dopamine and epinephrine infusions: the patient died (76)
- a 4 year old girl received a combination of 3 antibiotics including meropenem, ciprofloxacin, and teicoplanin (dosage not reported). She underwent orotracheal intubation and mechanical ventilation: the patient died (86)

In summary, in the cases that reported on children with necrotising pneumonia and PVL-SA, the most common antibiotic was teicoplanin. Two out of these 4 cases died.

Deep-seated abscesses

Four out of 38 cases reported deep-seated abscesses in hospitalised children with PVL-SA receiving antibiotics (44, 53, 71, 77):

- a 21 month old girl with parapharyngeal abscess (a deep neck infection that causes a pocket of pus near the throat) was treated with intravenous flucloxacillin (200 milligrams per kilogram per day or mg/kg/d). She was admitted to the PICU: the patient survived (44)

- a 13 year old boy with gluteal abscess (a pocket of pus in the hip area) was treated with linezolid (30 mg/kg/d) along with clindamycin (40 mg/kg/d): the patient survived (53)
- a one year old girl with parapharyngeal abscess was treated with clindamycin monotherapy (dosage not reported). She was admitted to the PICU and intubated: the patient survived (71)
- a 15 year old boy with a history of insulin dependent diabetes mellitus developed an abscess in the hip area and was treated with flucloxacillin (1 gram every 6 hours). He was admitted to local HDU, required oxygen support and developed renal failure: the patient survived (77)

In summary, in the cases that reported on children with deep-seated abscesses and PVL-SA, clindamycin and flucloxacillin were the most frequently used antibiotics. All cases survived following antibiotic treatment.

Osteomyelitis

Two case reports described hospitalised children with osteomyelitis and PVL-SA receiving antibiotics (34, 59):

- a 10 year old boy received linezolid in combination with intravenous flucloxacillin and rifampicin (dosage not reported) (34) and another 10 year old boy received intravenous clindamycin along with intravenous vancomycin (dosage not reported) (59): both cases survived

Bacteraemia

Two case reports reported bacteraemia in hospitalised children with PVL-SA receiving antibiotics (64, 69):

- a 17 year old boy received cefazolin (3 grams per day) (64)
- a 19 month old girl received intravenous cloxacillin and gentamicin (dosage not reported) (69)

Both cases survived.

Necrotising fasciitis

One case reported necrotising fasciitis in a 7 day old girl. She received vancomycin alone (dosage not reported) and survived (56).

Septic arthritis

One case reported septic arthritis in a 3 year old girl. She was treated with intravenous vancomycin (dosage not reported) and survived (89).

Children with multiple PVL-SA infections

Twenty-one out of 38 case reports identified hospitalised children with multiple invasive PVL-SA infections receiving antibiotics (18, 22, 23, 26, 37, 43, 46, 49, 50, 54, 55, 60, 67, 72, 74, 80, 81, 85, 90, 91, 95):

- a 17 year old boy with pneumonia and bacteraemia was treated with linezolid along with moxifloxacin (dosage not reported). He was admitted to the PICU, received vasopressors (noradrenaline 100 micrograms per minute) and required intubation and mechanical ventilation: the patient survived (22)
- a 14 year old boy with pneumonia and septic arthritis was treated with intravenous flucloxacillin (dosage not reported): he was admitted to the PICU and survived (37)
- a 10 year old boy with necrotising pneumonia and osteomyelitis received clindamycin with daptomycin and fosfomycin (dosage not reported): the patient survived (43)
- a one month old boy with necrotising pneumonia and deep-seated abscesses received linezolid monotherapy (10 mg/kg 3 times daily) and survived (72)
- a 14 year old boy with necrotising pneumonia and purpura fulminans was given intravenous cefotaxime and gentamicin as part of antibiotic therapy (dosage not reported). He was admitted to the intensive therapy unit (ITU), required intubation, mechanical ventilation, vasopressors and subsequently developed multi-organ failure: the patient died (67)
- a 6 year old boy with necrotising pneumonia and osteomyelitis was treated with intravenous vancomycin along with gentamicin (dosage not reported): he required oxygen support and survived (80)
- a 15 year old boy with necrotising pneumonia, lung abscess and bacteraemia was treated with intravenous linezolid (600 milligrams twice daily) in combination with intravenous teicoplanin (400 milligrams twice daily) and rifampicin (600 milligrams once daily): he was admitted to the PICU for 18 hours and survived (90)
- a 9 month old girl with osteomyelitis and femur abscess (pocket of pus around the thigh bone) received intravenous clindamycin (40 mg/kg/d every 8 hours) along with cloxacillin (150 mg/kg/d every 6 hours): the patient survived (23)
- a 17 year old girl with osteomyelitis and multiple abscesses received vancomycin (2 grams per day) in combination with intravenous fosfomycin (4 grams per day) and survived (50)
- a 6 month old boy with a history of recurrent respiratory infections and 4 hospitalisations in the first 5 months of life developed multiple muscle abscesses and osteomyelitis. He was treated with intravenous clindamycin (30 mg/kg/d) in combination with ceftaroline (24 mg/kg/d) and daptomycin (12 mg/kg/d): he was admitted to the PICU and survived (26)
- a 12 year old boy with osteomyelitis and psoas abscess received intravenous linezolid (30 mg/kg/d) followed by oral clindamycin (30 mg/kg/d): the patient survived (54)
- a 10 year old girl with osteomyelitis and pyomyositis was treated with clindamycin in combination with teicoplanin (dosage not reported): she required clinical support with oxygen and survived (55)

- a 6 year old boy with septic arthritis, osteomyelitis and necrotising fasciitis and myositis was treated intravenous oxacillin monotherapy (dosage not reported). He required intubation and mechanical ventilation: the patient survived (60)
- a 13 year old boy with pneumonia, osteomyelitis, sepsis and psoas abscess received linezolid and clindamycin (dosage not reported) and survived (49)
- a 14 year old boy with a medical history of mild asthma developed deep tissue abscesses, osteomyelitis and septic arthritis: he received flucloxacillin monotherapy (2 grams every 4 hours) and survived (85)
- a 13 year old boy with septic arthritis, necrotising fasciitis and septicaemia was treated with clindamycin in combination with ceftriaxone, vancomycin, and cloxacillin (dosage not reported). He was admitted to the ICU and underwent intubation and mechanical ventilation: the boy died (18)
- a 10 year old boy with septic arthritis and osteomyelitis received clindamycin and vancomycin (dosage not reported) and survived (46)
- a 16 year old girl with necrotising fasciitis and sepsis was treated with clindamycin (600 milligrams every 6 hours) along with oxacillin (2g every 6 hours): she was admitted to PICU and survived (74)
- a 10 year old girl with osteomyelitis and septic shock was treated with teicoplanin monotherapy (dosage not reported). She was admitted to PICU, required tracheal intubation, mechanical ventilation and insertion of a chest tube to drain pleural empyma (collection of pus in the space around lungs): the patient survived (81)
- a 12 year old boy with osteomyelitis and pyomyositis was treated with clindamycin in combination with flucloxacillin, levofloxacillin and linezolid (dosage not reported). He was admitted to the PICU, underwent intubation and mechanical ventilation, required vasopressor and ionotropic support, continuous veno-venous hemofiltration later replaced by intermittent dialysis and developed multi-organ failure: the patient survived (91)
- a 23 month old girl with osteomyelitis, necrotising pneumonia, necrotising fasciitis, bacteraemia and sepsis received intravenous linezolid (10 mg/kg/d every 8 hours) and intravenous meropenem (40 mg/kg 3 times daily for 3 weeks): the patient survived (95)

In summary, clindamycin and linezolid were the most frequently used antibiotics in cases reporting children with multiple invasive infections and PVL-SA. Two out of the 21 cases died while all other cases survived.

Critical appraisal of evidence

There were a number of concerns relating to risk of bias in the observational studies. All studies were descriptive in nature, lacking statistical analysis, and were presented in the form of case series. Limited demographic and clinical details were reported, and the sample sizes were small.

All of the evidence from case series was also considered at high risk of bias. Most of the included case series did not provide clearly defined eligibility criteria for the inclusion of patients. In some case series, it was unclear if patient selection was complete and whether there was consecutive inclusion of participants in the given time period.

Case reports are considered a low level of evidence as they report on selected individual cases only. The included case reports described individual patient demographics including age, sex, medical history, symptoms, disease progression and clinical outcomes. In most case reports, the antibiotics used were not described with sufficient detail. There was no information provided on the dosage, route of administration or duration of the antibiotic. Additionally, only a few case reports explicitly noted whether any antibiotic-related adverse events or harms occurred.

Information on ethnicity, psychosocial history, and underlying conditions was often missing or only briefly mentioned in the evidence identified for this review.

The evidence was from reports with small sample sizes across all study types, meaning findings cannot be generalised to the wider population.

Due to the descriptive nature of the case series, case reports, and non-comparative observational studies, and the lack of data on effect size and variance, a GRADE assessment of the overall certainty of evidence could not be conducted (97). However, the quality of evidence was generally considered low and at high risk of bias.

Health inequalities

The evidence presented in this review was almost equally split between adults and children with one observational study, 9 case series and 40 case reports in adults and 2 observational studies, 8 case series and 38 case reports in children.

There were differences in participants between studies identified including the invasive infections patients had, their underlying conditions and the antibiotic treatment received. Twenty-six out of 76 hospitalised adults with invasive PVL-SA infections died and 12 out of 64 hospitalised children with invasive PVL-SA died across all study types. Adults more

commonly had underlying conditions, which may have influenced clinical outcomes. Although the rate appears higher in adults from the included studies, the differences in invasive infections, antibiotics used, and underlying comorbidities of patients, means that conclusions can't be drawn and this evidence should not be relied on to inform differences between the 2 populations, and none of the included studies performed analysis to compare the 2 groups.

Patients with a history of intravenous (IV) drug use were described in 7 studies (19 patients total). One observational study involving 6 patients (1), 3 case series involving one (7), 2 (12), and 7 patients respectively (16), and 3 individual case reports (42, 83, 92) described patients with a history of intravenous drug use. Among these, 6 people died (1, 16, 42, 83). All cases with a history of drug use except one (92) experienced morbidity outcomes including need for intubation, mechanical ventilation, haemodialysis and multi-organ failure and many were admitted to the ICU. However, it was not possible from this evidence to determine if outcomes were different from people without a history of drug use as direct comparisons weren't made. One study highlighted that there were difficulties in intravenous access amongst people who injected drugs, and the management had to be tailored to select oral antibiotics with good bioavailability as well as anti-PVL toxin cover, such as linezolid or rifampicin (1).

One case reported history of incarceration (83) and one reported history of homelessness (10). Alcohol dependence or abuse was reported in 7 cases (7, 10, 12, 42, 61, 94), of whom 3 cases died (7, 42, 94). This highlights that people from inclusion health groups (people experiencing homelessness, people with drug and/or alcohol dependence) with invasive PVL-SA infections were represented in the evidence but whether their outcomes differ compared to the general population remains unclear.

Most studies did not examine or report on socioeconomic factors, psychosocial history, ethnicity or race, or geographic disparities in patients with hospitalised patients with invasive PVL-SA infections receiving antibiotics, limiting the ability to address health inequalities. Differences in healthcare system capacity such as access to ICU care, renal replacement therapy, haemodialysis, continuous veno-venous hemofiltration, ECMO, early diagnostic methods for PVL-SA invasive infections, antibiotic availability could influence the risk of morbidity and mortality, but this factor was not explored in the included studies.

Limitations

This rapid systematic review used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted and most article screening was completed without duplication, so it is possible relevant evidence may have been missed.

No experimental studies were identified for inclusion. Most of the evidence came from case series and case reports which described individual clinical presentations and outcomes. The observational studies were descriptive with small sample sizes and lack of comparator, limiting the generalisability to the wider population even if they have the same characteristics. Across the evidence base, reporting was often inconsistent and incomplete and lacked sufficient demographic and clinical information. Details on antibiotic regimens including dosage, route, frequency and duration were frequently incomplete. Morbidity outcomes were not always linked to antibiotic treatment timelines. Cases were not followed up following hospital discharge so no information on long-term outcomes was available.

With the evidence being mostly non-comparative descriptive evidence, no conclusions could be drawn about the effectiveness of antibiotics to reduce or prevent morbidity and mortality in hospitalised patients with invasive PVL-SA infections.

Although planned in the protocol, it was not possible to undertake a GRADE assessment for quality of evidence as none of the observational studies reported effect sizes and variance, and the remainder of the evidence was from reports of individual cases.

Evidence gaps

There were a limited number of observational studies on the effect of antibiotic treatment on morbidity and mortality in hospital inpatients with invasive PVL-SA infections, with 2 of them classified as outbreak investigation reports (1, 3). The multicentre cohort study (2) lacked any comparison groups or statistical analysis. No experimental studies were identified in adults or children.

Conclusion

In summary, the review documented descriptive evidence on effect of antibiotic treatment on morbidity and mortality in hospitalised patients with invasive PVL-SA infections. Necrotising pneumonia, osteomyelitis and bacteraemia appeared to be the most common presentation in hospital inpatients with PVL-SA. Clindamycin, vancomycin and linezolid were the most frequently used antibiotics often in combination regimens or as monotherapy. While most cases survived following treatment with these antibiotics, others experienced morbidity demonstrated by ICU admission, intubation, mechanical ventilation, multi-organ failure or ultimately died, highlighting that outcomes were more strongly influenced by severity of invasive infection and underlying conditions. With the evidence being non-comparative descriptive evidence, no conclusions could be drawn about the effectiveness of antibiotics to reduce or prevent morbidity and mortality in hospitalised patients with invasive PVL-SA infections. However, the review does identify evidence of antibiotic use for these infections including evidence of patients recovering following treatment. When death was reported, it

was often as a consequence of sepsis or progression to multi-organ failure. Cases that died often had multiple morbidity outcomes, underlying conditions and rapid clinical deterioration. Many of these patients experienced complications such as respiratory failure requiring mechanical ventilation, ICU admission, and in some cases, temporary life support (ECMO). However, it should be highlighted that the evidence was at high risk of bias so may not be a reliable representation of the outcomes, and it also cannot inform how the outcomes would compare if antibiotic treatment had not been given, or if a different treatment had been used.

Acknowledgments

We would like to thank colleagues within the All Hazards Public Health Response division who either reviewed or input into aspects of the review.

Disclaimer

UKHSA's rapid reviews and evidence summaries aim to provide the best available evidence to decision makers in a timely and accessible way, based on published peer-reviewed scientific papers, and papers on preprint servers. Please note that the reviews:

- use accelerated methods and may not be representative of the whole body of evidence publicly available
- have undergone an internal independent peer review but not an external peer review
- are only valid as of the date stated on the review

In the event that this review is shared externally, please note additionally, to the greatest extent possible under any applicable law, that UKHSA accepts no liability for any claim, loss or damage arising out of, or connected with the use of, this review by the recipient or any third party including that arising or resulting from any reliance placed on, or any conclusions drawn from, the review.

References

1. Beaumont M and others. 'Clinical impact and public health challenges of a PVL-MRSA bacteraemia outbreak amongst people who inject drugs in South Yorkshire, UK' Access Microbiology 2024: volume 6, issue 2
2. Nygaard U and others. 'Fatal SARS-CoV-2-Associated Panton-Valentine Leukocidin-producing Staphylococcal Bacteremia: A Nationwide Multicenter Cohort Study' Pediatric Infectious Disease Journal 2022: volume 41, issue 4, pages e142 to e145
3. Tang CT and others. 'An outbreak of severe infections with community-acquired MRSA carrying the Panton-Valentine leukocidin following vaccination' PLoS ONE [Electronic Resource] 2007: volume 2, issue 9, page e822
4. Adem PV and others. 'Brief report: *Staphylococcus aureus* sepsis and the waterhouse-friderichsen syndrome in children' New England Journal of Medicine 2005: volume 353, issue 12, pages 1,245 to 1,251
5. Bybeck Nielsen A and others. 'Clinical manifestations in children with Staphylococcal bacteremia positive for Panton-Valentine Leucocidin: a nationwide survey in a low methicillin-resistance setting' Pediatric Infectious Disease Journal 2020: volume 39, issue 9, pages e274 to e276
6. Cunnington A and others. 'Severe invasive Panton-Valentine Leucocidin positive *Staphylococcus aureus* infections in children in London, UK' Journal of Infection 2009: volume 59, issue 1, pages 28 to 36
7. Hanratty J and others. 'Panton-Valentine leukocidin positive Staphylococcal aureus infections of the head and neck: case series and brief review of literature' Journal of Oral and Maxillofacial Surgery 2015: volume 73, issue 4, pages 666 to 670
8. Hayakawa K and others. 'Two cases of intrafamilial transmission of community-acquired methicillin-resistant *Staphylococcus aureus* producing Both PVL and TSST-1 causing fatal necrotizing pneumonia and sepsis' Infection and Drug Resistance 2020: volume 13, pages 2,921 to 2,927
9. Kravitz GR and others. 'Purpura fulminans due to *Staphylococcus aureus*' Clinical Infectious Diseases 2005: volume 40, issue 7, pages 941 to 947
10. Lin MY and others. 'Septic pulmonary emboli and bacteremia associated with deep tissue infections caused by community-acquired methicillin-resistant *Staphylococcus aureus*' Journal of Clinical Microbiology 2008: volume 46, issue 4, pages 1,553 to 1,555
11. McAdams RM and others. 'Spread of methicillin-resistant *Staphylococcus aureus* USA300 in a neonatal intensive care unit' Pediatrics International 2008: volume 50, issue 6, pages 810 to 815
12. Micek ST and others. 'Pleuropulmonary complications of Panton-Valentine leukocidin-positive community-acquired methicillin-resistant *Staphylococcus aureus*: importance of treatment with antimicrobials inhibiting exotoxin production' Chest 2005: volume 128, issue 4, pages 2,732 to 2,738

13. Osterlund A and others. 'Intrafamilial spread of highly virulent *Staphylococcus aureus* strains carrying the gene for Panton-Valentine leukocidin' Scandinavian Journal of Infectious Diseases 2002: volume 34, issue 10, pages 763 to 764
14. Peleg AY and others. 'Life-threatening community-acquired methicillin-resistant *Staphylococcus aureus* infection in Australia' European Journal of Clinical Microbiology and Infectious Diseases 2005: volume 24, issue 6, pages 384 to 387
15. Schwartz KL and others. 'Panton-Valentine leukocidin-associated *Staphylococcus aureus* necrotizing pneumonia in infants: a report of four cases and review of the literature' European Journal of Pediatrics 2012: volume 171, issue 4, pages 711 to 717
16. Toro CM and others. 'Community-associated methicillin-resistant *Staphylococcus aureus* necrotizing pneumonia without evidence of antecedent viral upper respiratory infection' Canadian Journal of Infectious Diseases and Medical Microbiology 2014: volume 25, issue 3, pages E76 to E82
17. Young LM and others. 'Community-acquired methicillin-resistant *Staphylococcus aureus* emerging as an important cause of necrotizing fasciitis' Surgical Infections 2008: volume 9, issue 4, pages 469 to 474
18. Akpaka PE and others. 'Methicillin sensitive *Staphylococcus aureus* producing Panton-Valentine leukocidin toxin in Trinidad and Tobago: a case report' Journal of Medical Case Reports [Electronic Resource] 2011: volume 5, page 157
19. Alonso-Tarres C and others. 'Favorable outcome of pneumonia due to Panton-Valentine leukocidin-producing *Staphylococcus aureus* associated with hematogenous origin and absence of flu-like illness' European Journal of Clinical Microbiology and Infectious Diseases 2005: volume 24, issue 11, pages 756 to 759
20. Al-Talib H and others. 'Fatal necrotizing pneumonia caused by Panton-Valentine leukocidin-producing hospital-acquired *Staphylococcus aureus*: a case report' Japanese Journal of Infectious Diseases 2011: volume 64, issue 1, pages 58 to 60
21. Ambrozova H and others. 'The first case of fatal pneumonia caused by Panton-Valentine leukocidin-producing *Staphylococcus aureus* in an infant in the Czech Republic' Folia Microbiologica 2013: volume 58, issue 3, pages 225 to 228
22. Balis E and others. 'Community-acquired pneumonia and bacteremia due to methicillin-resistant *Staphylococcus aureus* carrying Panton-Valentine-leukocidin gene in Greece: two case reports and literature review' Journal of Chemotherapy 2007: volume 19, issue 6, pages 703 to 708
23. Bukhari EE and others. 'Panton-Valentine leukocidin *Staphylococcus aureus* osteomyelitis of the femur in a Saudi child' Saudi Medical Journal 2012: volume 33, issue 2, pages 201 to 204
24. Camargo CH and others. 'Systemic CA-MRSA infection following trauma during soccer match in inner Brazil: clinical and molecular characterization' Diagnostic Microbiology and Infectious Disease 2013: volume 76, issue 3, pages 372 to 374
25. Carroll DE and others. '*Staphylococcus aureus* Prostatic abscess: a clinical case report and a review of the literature' BMC Infectious Diseases 2017: volume 17, issue 1, page 509

26. Castellazzi ML and others. 'Panton-valentine leukocidin *Staphylococcus aureus* severe infection in an infant: a case report and a review of the literature' Italian Journal of Pediatrics 2021: volume 47, issue 1, page 158
27. Chen H and others. 'Necrotizing pneumonia secondary to Influenza A (H1N1) coinfection with *Staphylococcus aureus*: A case report' IDCases 2024: volume 37, page e02066
28. Chen J and others. 'Community-acquired necrotizing pneumonia caused by methicillin-resistant *Staphylococcus aureus* producing Panton-Valentine leukocidin in a Chinese teenager: case report and literature review' International Journal of Infectious Diseases 2014: volume 26, pages 17 to 21
29. Chetchotisakd P and others. 'A rapidly fatal case of Panton-Valentine leukocidin-positive *Staphylococcus aureus* necrotizing pneumonia in an HIV-infected patient' Southeast Asian Journal of Tropical Medicine and Public Health 2007: volume 38, issue 4, pages 690 to 694
30. Conan PL and others. 'Renal abscess caused by Panton-Valentine leukocidin-producing *Staphylococcus aureus*: report of an unusual case and review of the literature' Infectious Diseases 2021: volume 53, issue 2, pages 131 to 136
31. Cupane L and others. 'Methicillin-susceptible Panton-Valentine leukocidin-positive S. aureus pneumonia in a child with novel influenza H1N1 infection' Acta Chirurgica Latviensis 2010: volume 10, issue 2, pages 127 to 130
32. Dhanoa A and others. 'Acute haematogenous community-acquired methicillin-resistant *Staphylococcus aureus* osteomyelitis in an adult: case report and review of literature' BMC Infectious Diseases 2012: volume 12, page 270
33. Dubos M and others. 'Prostatic abscesses and severe sepsis due to methicillin-susceptible *Staphylococcus aureus* producing Panton-Valentine leukocidin' BMC Infectious Diseases 2014: volume 14, page 466
34. Elledge RO and others. 'Panton-Valentine leukocidin-positive *Staphylococcus aureus* osteomyelitis of the tibia in a 10-year-old child' Journal of Pediatric Orthopaedics, Part B 2014: volume 23, issue 4, pages 358 to 363
35. Enany S and others. 'Brain abscess caused by Panton-Valentine leukocidin-positive community-acquired methicillin-resistant *Staphylococcus aureus* in Egypt, April 2007' Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles- European Communicable Disease Bulletin 2007: volume 12, issue 9, pages E070927.070922
36. Enayet I and others. 'Community-associated methicillin-resistant *Staphylococcus aureus* causing chronic pneumonia' Clinical Infectious Diseases 2006: volume 42, issue 7, pages e57 to e60
37. Esteves I and others. 'Septic pulmonary embolism case report: optimal outcome after insertion of an inferior vena cava filter in a patient with *Staphylococcus aureus* bacteraemia' International Journal of Pediatrics 2010: volume 2010, page 651023
38. Fahmy S and others. 'Community-acquired methicillin-resistant *Staphylococcus aureus* USA 300 genotype causing pyomyositis and Kikuchi-Fujimoto disease' Infectious Diseases in Clinical Practice 2008: volume 16, pages 321 to 323

39. Fernandez S and others. 'Community-acquired necrotizing pneumonia caused by methicillin-resistant *Staphylococcus aureus* ST30-SCCmecIVc-spat019-PVL positive in San Antonio de Areco, Argentina' Revista Argentina de Microbiologia 2015: volume 47, issue 1, pages 50 to 53
40. Fica A and others. 'Successful use of daptomycin and cefazolin in a case of persistent bacteremia caused by community acquired-methicillin resistant *Staphylococcus aureus* in a pregnant woman. Case report' Revista Medica de Chile 2023: volume 151, pages 1,631 to 1,635
41. Fogo A and others. 'PVL positive *Staphylococcus aureus* skin infections' BMJ (Online) 2011: volume 343
42. Frazee BW and others. 'Fatal community-associated methicillin-resistant *Staphylococcus aureus* pneumonia in an immunocompetent young adult' Annals of Emergency Medicine 2005: volume 46, issue 5, pages 401 to 404
43. Garbo V and others. 'Severe Panton–Valentine leukocidin-positive *Staphylococcus aureus* infections in pediatric age: a case report and a literature review' Antibiotics 2024: volume 13
44. Goemanne S and others. 'Severe *Staphylococcus aureus* infections in children: case reports and management of positive Panton-Valentine leucocidin cases' Frontiers in Pediatrics 2022: volume 10, 1003708
45. Govindan S and others. 'Necrotizing fasciitis caused by a variant of epidemic methicillin-resistant *Staphylococcus aureus* - 15' Indian Journal of Medical Microbiology 2012: volume 30, issue 4, pages 476 to 479
46. Harada N and others. 'Acute osteomyelitis/septic pulmonary embolism associated with familial infections caused by PVL-positive ST6562 MRSA-IVa, a presumptive variant of USA300 clone' IJID Regions (Online) 2023: volume 8, pages 16 to 18
47. Higashiyama M and others. 'Epidural abscess caused by community-associated methicillin-resistant *Staphylococcus aureus* strain USA300 in Japan' Journal of Infection and Chemotherapy 2010: volume 16, issue 5, pages 345 to 349
48. Honarpour N and others. 'A case of fatal community-acquired necrotizing pneumonia caused by Panton-Valentine leukocidin-positive methicillin-sensitive *Staphylococcus aureus*' Current Respiratory Medicine Reviews 2007: volume 3, pages 49 to 51
49. Irenji N and others. 'Serious life-threatening multifocal infection in a child, caused by Panton-Valentine leucocidin-producing *Staphylococcus aureus* (PVL-MSSA)' BMJ Case Reports 2018: volume 5, page 5
50. Isobe H and others. 'Recurrence of pelvic abscess from Panton-Valentine leukocidin-positive community-acquired ST30 methicillin-resistant *Staphylococcus aureus*' Pediatrics International 2013: volume 55, issue 1, pages 120 to 123
51. Iwanaga N and others. 'Necrotizing pneumonia due to femoral osteomyelitis caused by community-acquired methicillin-resistant *Staphylococcus aureus*' Internal Medicine 2013: volume 52, issue 13, pages 1,531 to 1,536
52. Jung N and others. 'Necrotizing pneumonia caused by Panton-Valentine leucocidin-producing *Staphylococcus aureus* originating from a Bartholin's abscess' Infectious Diseases in Obstetrics and Gynecology 2008: volume 2008, 491401

53. Karli A and others. 'Panton-Valentine leukocidin-positive *Staphylococcus aureus* infection in childhood: a case report' Turkish Journal of Pediatrics 2016: volume 57, pages 615 to 617
54. Karli A and others. 'Disseminated Panton-Valentine leukocidin-positive *Staphylococcus aureus* infection in a child' Archivos Argentinos de Pediatria 2016: volume 114, issue 2, pages e75 to e77
55. Kefala-Agoropoulou K and others. 'Life-threatening infection due to community-acquired methicillin-resistant *Staphylococcus aureus*: case report and review' European Journal of Pediatrics 2010: volume 169, issue 1, pages 47 to 53
56. Kim YH and others. 'The first neonatal case of Panton-Valentine leukocidin-positive *Staphylococcus aureus* causing severe soft tissue infection in Korea' Pediatric Infection and Vaccine 2023: volume 30, pages 152 to 158
57. Kuo PH and others. 'Pyomyositis and necrotizing pneumonia in a young soldier caused by methicillin-susceptible *Staphylococcus aureus* of sequence type 59 lineage' Journal of Internal Medicine of Taiwan 2016: volume 27, pages 49 to 54
58. Larsen SAH and others. 'Life-threatening necrotizing pneumonia with Panton-Valentine leukocidin-producing, methicillin-sensitive *Staphylococcus aureus* in a healthy male co-infected with influenza B' Infectious Disease Reports 2021: volume 14, issue 1, pages 12 to 19
59. Laurens MB and others. 'MRSA with progression from otitis media and sphenoid sinusitis to clival osteomyelitis, pachymeningitis and abducens nerve palsy in an immunocompetent 10-year-old patient' International Journal of Pediatric Otorhinolaryngology 2008: volume 72, issue 7, pages 945 to 951
60. Lehman D and others. '*Staphylococcus aureus* Panton-Valentine leukocidin targets muscle tissues in a child with myositis and necrotizing fasciitis' Clinical Infectious Diseases 2010: volume 50, issue 1, pages 69 to 72
61. Leung CCD and others. 'A single lung abscess caused by Panton-Valentine leukocidin-producing methicillin-resistant *Staphylococcus aureus*' Cureus 2024: volume 16, issue 6, page e61845
62. Magira EE and others. 'Community-acquired methicillin-resistant *Staphylococcus aureus* carrying Panton-Valentine leukocidin genes: a lethal cause of pneumonia in an adult immunocompetent patient' Scandinavian Journal of Infectious Diseases 2007: volume 39, issue 5, pages 466 to 469
63. Mattu PS and others. 'Necrotizing pneumonia and septic shock caused by methicillinsensitive *Staphylococcus aureus* producing Panton-Valentine leukocidin after surgical treatment of Bartholin gland abscess: A case report and literature review' Canadian Journal of Pathology 2024: volume 16, issue 4, pages 9 to 16
64. Miyashita T and others. 'Destructive pulmonary embolism in a patient with community-acquired staphylococcal bacteremia' Journal of Infection and Chemotherapy 2002: volume 8, issue 1, pages 99 to 102
65. Montagnani C and others. 'Severe infections caused by Panton-Valentine leukocidin-positive *Staphylococcus aureus* in infants: report of three cases and review of literature' Acta Paediatrica 2013: volume 102, issue 6, pages e284 to e287

66. Morimoto S and others. 'Adult severe community-acquired pneumonia with bloodstream infection caused by psiUSA 300: A case report' Diagnostic Microbiology and Infectious Disease 2024: volume 111, issue 3,116630
67. Mushtaq F and others. 'Necrotizing haemorrhagic pneumonia proves fatal in an immunocompetent child due to Panton-Valentine Leucocidin, toxic shock syndrome toxins 1 and 2 and enterotoxin C-producing *Staphylococcus aureus*' Acta Paediatrica 2008: volume 97, issue 7, pages 985 to 987
68. Newell R and others. 'Panton–Valentine leucocidin *Staphylococcus aureus* necrotising pneumonia in a clinically well patient' 2023: volume 84, pages 1 to 4
69. Ng DCE and others. 'Panton-valentine leukocidin positive methicillin-susceptible *Staphylococcus aureus*: a case report of two pediatric patients with thrombotic complications' Pediatric Infection and Vaccine 2018: volume 25, pages 50 to 53
70. Obed A and others. 'Fatal pneumonia caused by Panton-Valentine leucocidine-positive methicillin-resistant *Staphylococcus aureus* (PVL-MRSA) transmitted from a healthy donor in living-donor liver transplantation' Transplantation 2006: volume 81, issue 1, pages 121 to 124
71. Ogawa E and others. 'Retropharyngeal abscess caused by community-acquired MRSA USA300 clone in a 1-year-old Japanese girl' Japanese Journal of Infectious Diseases 2022: volume 75, issue 4, pages 403 to 406
72. Oshima N and others. 'Panton-Valentine leukocidin-positive novel sequence type 5959 community-acquired methicillin-resistant *Staphylococcus aureus* meningitis complicated by cerebral infarction in a 1-month-old infant' Journal of Infection and Chemotherapy 2021: volume 27, issue 1, pages 103 to 106
73. Ote H and others. 'A fatal case of disseminated infection caused by community-associated methicillin-resistant *Staphylococcus aureus* USA300 Clone' Japanese Journal of Infectious Diseases 2023: volume 76, issue 4, pages 251 to 254
74. Perbet S and others. 'Multifocal community-acquired necrotizing fasciitis caused by a Panton-Valentine leukocidin-producing methicillin-sensitive *Staphylococcus aureus*' Infection 2010: volume 38, issue 3, pages 223 to 225
75. Ramos A and others. 'Brain abscess due to Panton-Valentine leukocidin-positive *Staphylococcus aureus*' Infection 2009: volume 37, issue 4, pages 365 to 367
76. Ravishankar S and others. 'Enterovirus D68 and Panton-Valentine leukocidin-positive *Staphylococcus aureus* respiratory coinfection with fatal outcome' Pediatric and Developmental Pathology 2016: volume 19, issue 1, pages 80 to 85
77. Reichert B and others. 'Severe non-pneumonic necrotising infections in children caused by Panton-Valentine leukocidin-producing *Staphylococcus aureus* strains' Journal of Infection 2005: volume 50, issue 5, pages 438 to 442
78. Riedweg-Moreno K and others. 'Successful management of Panton-Valentine leukocidine-positive necrotising pneumonia and A/H1N12009 influenzavirus coinfection in adult' BMJ Case Reports 2014: volume 16, page 16
79. Roberts JC and others. 'Fatal necrotizing pneumonia due to a Panton-Valentine leukocidin-positive community-associated methicillin-sensitive *Staphylococcus aureus*

and influenza co-infection: a case report' Annals of Clinical Microbiology and Antimicrobials 2008: volume 7, page 5

80. Rovira G and others. 'The challenge of diagnosing and treating *Staphylococcus aureus* invasive infections in a resource-limited sub-Saharan Africa setting: a case report' Journal of Tropical Pediatrics 2015: volume 61, issue 5, pages 397 to 402
81. Rozenbaum R and others. 'The first report in Brazil of severe infection caused by community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA)' Brazilian Journal of Medical and Biological Research 2009: volume 42, issue 8, pages 756 to 760
82. Schefold JC and others. 'Therapy-refractory Panton-Valentine leukocidin-positive community-acquired methicillin-sensitive *Staphylococcus aureus* sepsis with progressive metastatic soft tissue infection: a case report' Journal of Medical Case Reports [Electronic Resource] 2007: volume 1, page 165
83. Sifri CD and others. 'Fatal brain abscess due to community-associated methicillin-resistant *Staphylococcus aureus* strain USA300' Clinical Infectious Diseases 2007: volume 45, issue 9, pages E113 to E117
84. Soavi L and others. 'Linezolid and clindamycin improve the outcome of severe, necrotizing pneumonia due to community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA)' Infezioni in Medicina 2011: volume 19, issue 1, pages 42 to 44
85. Swaminathan A and others. 'Fulminant methicillin-sensitive *Staphylococcus aureus* infection in a healthy adolescent, highlighting 'Panton-Valentine leucocidin syndrome'' Internal Medicine Journal 2006: volume 36, issue 11, pages 744 to 747
86. Székely E and others. 'Fatal sepsis due to community-associated methicillin-resistant *Staphylococcus aureus*: a case report' Revista Romana De Medicina De Laborator 2010: volume 18, issue 2, pages 29 to 33
87. Takigawa Y and others. 'Rapidly progressive multiple cavity formation in necrotizing pneumonia caused by community-acquired methicillin-resistant *Staphylococcus aureus* positive for the Panton-Valentine leucocidin gene' Internal Medicine 2019: volume 58, issue 5, pages 685 to 691
88. Torell E and others. 'Community-acquired pneumonia and bacteraemia in a healthy young woman caused by methicillin-resistant *Staphylococcus aureus* (MRSA) carrying the genes encoding Panton-Valentine leukocidin (PVL)' Scandinavian Journal of Infectious Diseases 2005: volume 37, issue 11, pages 902 to 904
89. Uda K and others. 'A pediatric case of septic arthritis caused by methicillin-resistant *Staphylococcus aureus* with Panton-Valentine leukocidin and toxic shock syndrome toxin-1' Japanese Journal of Infectious Diseases 2020: volume 73, issue 3, pages 259 to 262
90. Valentini P and others. 'An uncommon presentation for a severe invasive infection due to methicillin-resistant *Staphylococcus aureus* clone USA300 in Italy: a case report' Annals of Clinical Microbiology and Antimicrobials 2008: volume 7, page 11
91. Vanbiervliet V and others. 'A case report: septic shock due to (tropical) pyomyositis and multiple metastatic embolisms caused by Panton-Valentine Leukocidin-positive

methicillin-sensitive *Staphylococcus aureus* in a 12-year-old boy' Acta Clinica Belgica 2022: volume 77, issue 2, pages 421 to 424

92. Venugopal AA and others. 'Community-associated methicillin-resistant *Staphylococcus aureus* causing psoas abscess and empyema' Infectious Diseases in Clinical Practice 2007: volume 15, pages 60 to 62
93. Wan TW and others. 'Emerging ST121/agr4 community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) with strong adhesin and cytolytic activities: trigger for MRSA pneumonia and fatal aspiration pneumonia in an influenza-infected elderly' New Microbes and New Infections 2016: volume 13, pages 17 to 21
94. Xia H and others. 'Community-acquired pneumonia caused by methicillin-resistant *Staphylococcus aureus* in a Chinese adult: a case report' Medicine 2020: volume 99, issue 26, page e20914
95. Yonezawa R and others. 'Invasive community-acquired methicillin-resistant *Staphylococcus aureus* in a Japanese girl with disseminating multiple organ infection: a case report and review of Japanese pediatric cases' Case Reports in Pediatrics 2015: volume 2015, 291025
96. JBI. 'JBI Critical appraisal tools' 2020
97. TGW G. 'GRADE handbook for grading quality of evidence and strength of recommendations' 2013

Annexe A. Protocol

Review question

The review question is:

1. What is the evidence for effect of antibiotic treatment on morbidity and mortality among hospital inpatients with invasive Panton-Valentine leukocidin *Staphylococcus aureus* (PVL-SA) infections?

A search for primary evidence to answer this review question will be conducted up to 28 February 2025.

Eligibility criteria

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	Adults and children with laboratory confirmed invasive PVL-SA (confirmed through any laboratory method) being treated as hospital inpatients Invasive PVL-SA infections will be defined as: • osteomyelitis • necrotising fasciitis • pyomyositis • septic arthritis • deep-seated tissue infections or abscesses • pneumonia • bacteraemia • abscesses • purpura fulminans • septicaemia	• adults and children with laboratory confirmed invasive PVL-SA infections who are not hospital inpatients • adults and children with non-invasive PVL-SA infections • animals
Context	Any	
Settings	Hospitals	• laboratories • community

	Included	**Excluded**
Intervention or exposure	Any antibiotic or combination of antibiotics taken as treatment for PVL-SA invasive infections (see Annexe D for the list of agreed antibiotics)	Any form of treatment that does not include an antibiotic Antibiotic given in combination with immunoglobulin
Comparator	None required	
Outcomes	• mortality (as reported by the study) • morbidity, as measured by the following (and directly linked to having the infection): • intensive care or high dependency unit admission: - need for intubation and ventilation - need for vasopressors - clinical support with oxygen • end organ dysfunction: - need for renal replacement therapy (to include dialysis and renal transplant) - evidence of acute liver failure - diagnosis of disseminated intravascular coagulation (DIC)	
Language	English	Non-English language studies
Date of publication	Up to 28 February 2025	
Study design	Experimental studies including randomised-controlled trials, quasi-experimental studies, cross-over designs, before-and-after studies Observational studies including cohort studies, case control studies, cross sectional studies Descriptive studies including case series or case reports	• qualitative research • mixed methods • modelling studies • reviews (all types)

	Included	Excluded
Publication type	Peer-reviewed published research	• conference abstracts or presentations • editorials • letters • news articles • grey literature • reports (for example, from governments, world health organisation) • preprints

Identification of studies

The following databases and trial registries will be searched for studies published up to 28 February 2025: Ovid Medline, Ovid Embase, Cochrane Central Register of Controlled Trials, Web of Science Core Collection (Science Citation Index) and CINAHL. The search strategy is presented below.

Backwards and forwards citation searching will be carried out using references that are included at full text screening as seed papers. Citation searching will use Lens.org via CitationChaser.

Screening

Title and abstract screening will be undertaken in duplicate by 2 reviewers for at least 20% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion or with involvement of a third reviewer where necessary.

Screening on full text will be undertaken by one reviewer and checked by a second.

References retrieved through citation searching will be cross checked against the results of the database search, and duplicates will be removed. The remaining references will be screened by one reviewer.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information to be extracted will include country, study period, study design, intervention or exposure, participant demographics, results, and any relevant contextual data. This will be undertaken by one reviewer and checked by a second.

Risk of bias assessment

We will perform risk of bias assessment at the primary study level using the relevant JBI checklist (96). Risk of bias will be assessed by 2 reviewers independently with disagreements resolved through discussion or with a third reviewer.

Certainty of evidence

If appropriate, the certainty of evidence identified within this review will be assessed using a modified version of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework (97).

Certainty of evidence will be assessed at the outcome level, and be rated as one of 4 levels:

- **very low** (the true effect is probably different from the estimated effect)
- **low** (the true effect might be different from the estimated effect)
- **moderate** (the true effect is probably close to the estimated effect)
- **high** (the authors are confident that the true effect is similar to the estimated effect)

The certainty of evidence will be assessed by one reviewer (and checked by a second) for each outcome across 4 domains:

1. **Risk of bias**: where results may not represent the true effect because of limitations in the design or conduct of the study.
2. **Inconsistency**: where studies show different effects for the same outcome of interest (only assessed where there are 2 or more studies measuring the same outcome). Inconsistency will be rated down if the point estimates are not similar, or the confidence intervals do not overlap.
3. **Indirectness**: where elements of the study differ from the intended elements in the review question (for example, the outcome of interest has not been directly measured). This will be rated down if the population, intervention, comparator, or outcome of interest have not been directly measured.
4. **Imprecision**: a measure of how uncertain the estimate is. Imprecision will be rated down if the confidence intervals cross the line of no effect, or if the reviewer judges that the confidence intervals are overly wide and so the true effect is likely to be different at the upper versus the lower end of the confidence interval.

Publication bias will not be used to assess the quality of the evidence in this review.

Evidence may be downgraded one or 2 levels following the assessment of quality or upgraded if there is a large magnitude of effect or clear dose-response gradient.

Synthesis

Where studies are similar enough to combine and present data in a consistent format, a narrative synthesis will be produced to interpret the findings. The number of studies, the number of participants in each study, effect size and variance and a summary of the risk of bias across studies reporting each outcome will be synthesised and presented. Alternatively, if studies present methodological differences that would make synthesis inappropriate, a narrative summary of each study will be provided.

Health inequalities

Variations among individuals experiencing health inequalities will be taken into account, as these factors may influence treatment outcomes for PVL-SA-associated invasive infections, particularly in those individuals who use intravenous (IV) drugs. Where available, data for children aged 17 years or below will be presented separately to that of individuals aged 18 years or above.

Search strategy

Ovid MEDLINE(R) ALL (1946 to 27 February 2025)

1. Leukocidins/ (1,759)
2. leukocidin*.tw,kf. (2,259)
3. leucocidin*.tw,kf. (572)
4. leukotoxi*.tw,kf. (1,114)
5. leucotoxi*.tw,kf. (75)
6. Panton Valentine.tw,kf. (2,359)
7. PVL.tw,kf. (5,219)
8. LukS.tw,kf. (380)
9. LukF.tw,kf. (336)
10. Luk pv.tw,kf. (49)
11. Bacterial Toxins/ and (exp Staphylococcal Infections/ or exp Staphylococcus aureus/) (3,613)
12. or/1-11 (10,013)
13. Soft Tissue Infections/ (4,467)
14. Superinfection/ (2120)
15. (superinfect* or super infect*).tw,kf. (7,992)
16. (superinvas* or super invas*).tw,kf. (44)
17. ((deep or invasiv*) adj3 infect*).tw,kf. (30,004)
18. ((deep or invasiv*) adj3 staph*).tw,kf. (481)
19. ((deep or invasiv*) adj3 s aureus).tw,kf. (245)
20. ((deep or invasiv*) adj3 "s.aureus").tw,kf. (4)

21. ((deep or invasiv*) adj3 bacter*).tw,kf. (3,820)
22. (deep tissue* adj3 infect*).tw,kf. (328)
23. (deep tissue* adj3 invasiv*).tw,kf. (88)
24. (deep tissue* adj3 staph*).tw,kf. (6)
25. (deep tissue* adj3 s aureus).tw,kf. (6)
26. (deep tissue* adj3 "s.aureus").tw,kf. (0)
27. (deep tissue* adj3 bacter*).tw,kf. (66)
28. (soft tissue* adj3 infect*).tw,kf. (11,507)
29. (soft tissue* adj3 invasiv*).tw,kf. (344)
30. (soft tissue* adj3 staph*).tw,kf. (96)
31. (soft tissue* adj3 s aureus).tw,kf. (73)
32. (soft tissue* adj3 "s.aureus").tw,kf. (0)
33. (soft tissue* adj3 bacter*).tw,kf. (523)
34. exp Osteomyelitis/ (25,353)
35. osteomyelit*.tw,kf. (28,967)
36. (Mastoiditis or Petrositis or Pott Puffy Tumo?r).tw,kf. (2,485)
37. (bone* adj3 (invasiv* or infect* or staph* or bacter*)).tw,kf. (11,514)
38. (bone* adj3 S aureus).tw,kf. (148)
39. (bone* adj3 "S.aureus").tw,kf. (0)
40. Fasciitis, Necrotizing/ (3,487)
41. necroti* fasciitis.tw,kf. (5,634)
42. flesh eating bacter*.tw,kf. (42)
43. necroti* bacter*.tw,kf. (55)
44. (fascia adj3 (invasiv* or infect* or staph* or bacter*)).tw,kf. (119)
45. (fascia adj3 S aureus).tw,kf. (0)
46. (fascia adj3 "S.aureus").tw,kf. (0)
47. Pyomyositis/ (471)
48. (intramusc* adj3 (invasiv* or infect* or staph* or bacter*)).tw,kf. (571)
49. (intramusc* adj3 S aureus).tw,kf. (12)
50. (intramusc* adj3 "S.aureus").tw,kf. (0)
51. ((muscle* or muscular) adj3 (invasiv* or infect* or staph* or bacter*)).tw,kf. (13,640)
52. ((muscle* or muscular) adj3 S aureus).tw,kf. (11)
53. ((muscle* or muscular) adj3 "S.aureus").tw,kf. (0)
54. pyomyositis.tw,kf. (1,301)
55. Myositis/ (10,316)
56. myositis.tw,kf. (13,571)
57. infectious myositides.tw,kf. (1)
58. focal myositides.tw,kf. (0)
59. exp Arthritis, Infectious/ (16,443)
60. (bacter* adj3 arthriti*).tw,kf. (869)
61. (septic* adj3 arthriti*).tw,kf. (7,689)
62. (suppurat* adj3 arthriti*).tw,kf. (305)
63. (infect* adj3 arthriti*).tw,kf. (3,064)

64. (staph* adj3 arthriti*).tw,kf. (322)
65. (S aureus adj3 arthriti*).tw,kf. (134)
66. ("S.aureus" adj3 arthriti*).tw,kf. (5)
67. exp Tissues/ (2082757)
68. Pneumonia, Staphylococcal/ (2,104)
69. exp Pneumonia/ (392,310)
70. pneumoni*.tw,kf. (248,608)
71. ((lung or lungs or pulmonary) adj3 infection*).tw,kf. (31,146)
72. ((lung or lungs or pulmonary) adj3 inflam*).tw,kf. (31,885)
73. ((lung or lungs or pulmonary) adj3 (invasiv* or bacter* or staph*)).tw,kf. (11,754)
74. ((lung or lungs or pulmonary) adj3 S aureus).tw,kf. (159)
75. ((lung or lungs or pulmonary) adj3 "S.aureus").tw,kf. (3)
76. exp Lung/ and Necrosis/ (1,380)
77. ((pulmonary or lung*) adj3 necro*).tw,kf. (2,350)
78. ((Alveolar* or airway* or respiratory* or lung* or bronch*) adj3 h?emorrhag*).tw,kf. (6,359)
79. ((Alveolar* or airway* or respiratory* or lung* or bronch*) adj3 bleed*).tw,kf. (1,749)
80. ((Alveolar* or airway* or respiratory* or lung* or bronch*) adj3 blood).tw,kf. (22,946)
81. (multi lobar infiltrat* or multilobar infiltrat*).tw,kf. (80)
82. Respiratory Distress Syndrome/ (26,300)
83. exp Respiratory Insufficiency/ (70,635)
84. (respiratory adj (collapse* or distress or insufficiency or failure)).tw,kf. (108,347)
85. (lung* adj (collapse* or distress or insufficiency or failure)).tw,kf. (1,863)
86. (pulmonary adj (collapse* or distress or insufficiency or failure)).tw,kf. (2,863)
87. Influenza, Human/ (61,017)
88. (influenza* or flu).tw,kf. (157,514)
89. Hemoptysis/ (6,874)
90. h?emoptys#s.tw,kf. (13,575)
91. Leukopenia/ or Neutropenia/ (27,587)
92. (leu#ocytop?eni* or leu#op?eni*).tw,kf. (20794)
93. neutrop?eni*.tw,kf. (50,555)
94. Oxygen Saturation/ (1,239)
95. Oxygen/ and exp Blood/ (9,970)
96. oxygen saturation.tw,kf. (36,599)
97. (blood adj (oxygen or o2)).tw,kf. (10,413)
98. SPo2.tw,kf. (9,321)
99. exp Sepsis/ (149,769)
100. exp Bacteremia/ (34,426)
101. (Bacteria/ or exp Staphylococcus aureus/ or Bacterial Infections/ or exp Staphylococcal Infections/) and exp Blood/ (16,482)
102. ((bacter* or "S.aureus" or S aureus or staph*) and blood*).tw,kf. (93,591)
103. bacter?emi*.tw,kf. (41,233)
104. seps#s.tw,kf. (135,168)

105. septic*.tw,kf. (9,4622)
106. (infect* adj3 (blood or bloodstream)).tw,kf. (3,8454)
107. (poison* adj3 (blood or bloodstream)).tw,kf. (578)
108. (bacter* adj3 (blood or bloodstream)).tw,kf. (6,399)
109. (S aureus adj3 (blood or bloodstream)).tw,kf. (499)
110. ("S.aureus" adj3 (blood or bloodstream)).tw,kf. (5)
111. (Staph* adj3 (blood or bloodstream)).tw,kf. (1,413)
112. septic?emi*.tw,kf. (24,314)
113. py?emi*.tw,kf. (265)
114. pyoh?emi*.tw,kf. (16)
115. exp Abscess/ (60,960)
116. abscess*.tw,kf. (94,377)
117. Purpura Fulminans/ (366)
118. (purpura adj1 fulmina*).tw,kf. (1,172)
119. h?emorrhagic vasculitis.tw,kf. (201)
120. henoch purpura*.tw,kf. (382)
121. henoch schoenlein purpura*.tw,kf. (181)
122. nonthrombocytopenic purpura*.tw,kf. (37)
123. non-thrombocytopenic purpura*.tw,kf. (37)
124. nonthrombopenic purpura*.tw,kf. (5)
125. non-thrombopenic purpura*.tw,kf. (4)
126. purpura h?emorrhagica.tw,kf. (265)
127. rheumatoid purpura*.tw,kf. (159)
128. or/13-127 (358,1353)
129. 12 and 128 (3,469)
130. limit 129 to (comment or editorial or letter) (107)
131. 129 not 130 (3,362)

Embase 1974 to 27 February 2025

1. leukocidin/ (1,009)
2. Panton Valentine leukocidin/ (2,779)
3. leukocidin*.tw,kf. (2,746)
4. leucocidin*.tw,kf. (658)
5. leukotoxi*.tw,kf. (1,184)
6. leucotoxi*.tw,kf. (83)
7. Panton Valentine.tw,kf. (2,917)
8. PVL.tw,kf. (7,922)
9. LukS.tw,kf. (496)
10. LukF.tw,kf. (419)
11. Luk pv.tw,kf. (56)
12. bacterial toxin/ and (exp Staphylococcus aureus/ or exp Staphylococcus infection/) (1,529)
13. or/1-12 (12,453)

14. exp staphylococcal pneumonia/ (1,238)
15. exp superinfection/ (11,811)
16. soft tissue infection/ (16,771)
17. (superinfect* or super infect*).tw,kf. (9,697)
18. (superinvas* or super invas*).tw,kf. (47)
19. ((deep or invasiv*) adj3 infect*).tw,kf. (40,239)
20. ((deep or invasiv*) adj3 staph*).tw,kf. (606)
21. ((deep or invasiv*) adj3 s aureus).tw,kf. (344)
22. ((deep or invasiv*) adj3 "s.aureus").tw,kf. (3)
23. ((deep or invasiv*) adj3 bacter*).tw,kf. (4,668)
24. (deep tissue* adj3 infect*).tw,kf. (388)
25. (deep tissue* adj3 invasiv*).tw,kf. (88)
26. (deep tissue* adj3 staph*).tw,kf. (8)
27. (deep tissue* adj3 s aureus).tw,kf. (6)
28. (deep tissue* adj3 "s.aureus").tw,kf. (0)
29. (deep tissue* adj3 bacter*).tw,kf. (78)
30. (soft tissue* adj3 infect*).tw,kf. (15,581)
31. (soft tissue* adj3 invasiv*).tw,kf. (454)
32. (soft tissue* adj3 staph*).tw,kf. (130)
33. (soft tissue* adj3 s aureus).tw,kf. (102)
34. (soft tissue* adj3 "s.aureus").tw,kf. (1)
35. (soft tissue* adj3 bacter*).tw,kf. (715)
36. exp osteomyelitis/ (50,067)
37. osteomyelit*.tw,kf. (33,536)
38. (Mastoiditis or Petrositis or Pott Puffy Tumo?r).tw,kf. (2,535)
39. (bone* adj3 (invasiv* or infect* or staph* or bacter*)).tw,kf. (14,480)
40. (bone* adj3 S aureus).tw,kf. (169)
41. (bone* adj3 "S.aureus").tw,kf. (0)
42. necrotizing fasciitis/ (8,399)
43. necroti* fasciitis.tw,kf. (7,113)
44. flesh eating bacter*.tw,kf. (61)
45. necroti* bacter*.tw,kf. (67)
46. (fascia adj3 (invasiv* or infect* or staph* or bacter*)).tw,kf. (155)
47. (fascia adj3 S aureus).tw,kf. (0)
48. (fascia adj3 "S.aureus").tw,kf. (0)
49. pyomyositis/ (1,748)
50. (intramusc* adj3 (invasiv* or infect* or staph* or bacter*)).tw,kf. (630)
51. (intramusc* adj3 S aureus).tw,kf. (13)
52. (intramusc* adj3 "S.aureus").tw,kf. (0)
53. ((muscle* or muscular) adj3 (invasiv* or infect* or staph* or bacter*)).tw,kf. (22,606)
54. ((muscle* or muscular) adj3 S aureus).tw,kf. (12)
55. ((muscle* or muscular) adj3 "S.aureus").tw,kf. (0)
56. pyomyositis.tw,kf. (1,514)

57. exp myositis/ (57,115)
58. myositis.tw,kf. (20,662)
59. infectious myositides.tw,kf. (1)
60. focal myositides.tw,kf. (0)
61. bacterial arthritis/ (12453)
62. (bacter* adj3 arthriti*).tw,kf. (1,105)
63. (septic* adj3 arthriti*).tw,kf. (9,937)
64. (suppurat* adj3 arthriti*).tw,kf. (289)
65. (infect* adj3 arthriti*).tw,kf. (4,054)
66. (staph* adj3 arthriti*).tw,kf. (362)
67. (S aureus adj3 arthriti*).tw,kf. (154)
68. ("S.aureus" adj3 arthriti*).tw,kf. (7)
69. exp *tissues/ (1,186,369)
70. exp pneumonia/ (432,070)
71. pneumoni*.tw,kf. (355,477)
72. ((lung or lungs or pulmonary) adj3 infection*).tw,kf. (47,387)
73. ((lung or lungs or pulmonary) adj3 inflam*).tw,kf. (46,136)
74. ((lung or lungs or pulmonary) adj3 (invasiv* or bacter* or staph*)).tw,kf. (16,945)
75. ((lung or lungs or pulmonary) adj3 S aureus).tw,kf. (240)
76. ((lung or lungs or pulmonary) adj3 "S.aureus").tw,kf. (12)
77. exp *lung/ and necrosis/ (495)
78. ((pulmonary or lung*) adj3 necro*).tw,kf. (3,495)
79. ((Alveolar* or airway* or respiratory* or lung* or bronch*) adj3 h?emorrhag*).tw,kf. (10,778)
80. ((Alveolar* or airway* or respiratory* or lung* or bronch*) adj3 bleed*).tw,kf. (3,130)
81. ((Alveolar* or airway* or respiratory* or lung* or bronch*) adj3 blood).tw,kf. (30,553)
82. (multi lobar infiltrat* or multilobar infiltrat*).tw,kf. (138)
83. exp *respiratory distress syndrome/ (46,210)
84. exp *respiratory failure/ (28,836)
85. (respiratory adj (collapse* or distress or insufficiency or failure)).tw,kf. (168,418)
86. (lung* adj (collapse* or distress or insufficiency or failure)).tw,kf. (2,792)
87. (pulmonary adj (collapse* or distress or insufficiency or failure)).tw,kf. (3,752)
88. exp *influenza/ (60,293)
89. (influenza* or flu).tw,kf. (184,437)
90. exp hemoptysis/ (35,628)
91. h?emoptys#s.tw,kf. (23,882)
92. leukopenia/ or neutropenia/ (181,893)
93. (leu#ocytop?eni* or leu#op?eni*).tw,kf. (33,042)
94. neutrop?eni*.tw,kf. (96,170)
95. oxygen saturation/ (97,242)
96. oxygen/ and exp blood/ (26,099)
97. oxygen saturation.tw,kf. (55,636)
98. (blood adj (oxygen or o2)).tw,kf. (13,236)

99. SPo2.tw,kf. (19,537)
100. exp sepsis/ (37,0853)
101. exp bacteremia/ (67,480)
102. (bacterium/ or exp Staphylococcus aureus/ or exp Staphylococcus infection/ or exp *bacterial infection/) and exp *blood/ (18,316)
103. ((bacter* or S aureus or "S.aureus" or staph*) and blood*).tw,kf. (134,690)
104. bacter?emi*.tw,kf. (56,800)
105. seps#s.tw,kf. (212,106)
106. septic*.tw,kf. (131,480)
107. (infect* adj3 (blood or bloodstream)).tw,kf. (53,446)
108. (poison* adj3 (blood or bloodstream)).tw,kf. (564)
109. (bacter* adj3 (blood or bloodstream)).tw,kf. (8,578)
110. (S aureus adj3 (blood or bloodstream)).tw,kf. (702)
111. ("S.aureus" adj3 (blood or bloodstream)).tw,kf. (19)
112. (Staph* adj3 (blood or bloodstream)).tw,kf. (2,038)
113. septic?emi*.tw,kf. (27,371)
114. py?emi*.tw,kf. (147)
115. pyoh?emi*.tw,kf. (2)
116. exp abscess/ (133,506)
117. abscess*.tw,kf. (119,943)
118. fulminating purpura/ (1,619)
119. (purpura adj1 fulmina*).tw,kf. (1,495)
120. h?emorrhagic vasculitis.tw,kf. (160)
121. henoch purpura*.tw,kf. (456)
122. henoch schoenlein purpura*.tw,kf. (300)
123. nonthrombocytopenic purpura*.tw,kf. (41)
124. non-thrombocytopenic purpura*.tw,kf. (42)
125. nonthrombopenic purpura*.tw,kf. (1)
126. non-thrombopenic purpura*.tw,kf. (2)
127. purpura h?emorrhagica.tw,kf. (34)
128. rheumatoid purpura*.tw,kf. (106)
129. or/14-128 (3,216,413)
130. 13 and 129 (4,009)
131. limit 130 to (conference abstract or conference paper or "conference review" or editorial or letter) (887)
132. 130 not 131 (3,122)

CINAHL

Date of search: 28 February 2025

#	Query	Results
S1	leukocidin*	292
S2	leucocidin*	80
S3	leukotoxi*	47
S4	leucotoxi*	5
S5	"Panton Valentine"	351
S6	PVL	766
S7	LukS	65
S8	LukF	11
S9	"Luk pv"	3
S10	(MH "Bacterial Toxins+") AND ((MH "Staphylococcal Infections+") OR (MH "Staphylococcus aureus+"))	333
S11	(MH "Pneumonia, Bacterial+")	5,436
S12	(MH "Soft Tissue Infections") or superinfect* OR "super infect*" OR superinvas* OR "super invas*"	2,492
S13	((deep or invasiv*) N3 infect*)	6,708
S14	((deep or invasiv*) N3 staph*)	121
S15	((deep or invasiv*) N3 "s aureus")	42
S16	((deep or invasiv*) N3 "s.aureus")	0
S17	((deep or invasiv*) N3 bacter*)	560
S18	(("deep tissue*" OR "soft tissue") N3 infect*)	3,601
S19	(("deep tissue*" OR "soft tissue") N3 invasiv*)	98
S20	(("deep tissue*" OR "soft tissue") N3 staph*)	71
S21	(("deep tissue*" OR "soft tissue) N3 s aureus)	26
S22	(("deep tissue*" OR "soft tissue") N3 "s.aureus")	0
S23	(("deep tissue*" OR "soft tissue") N3 bacter*)	130
S24	(MH "Osteomyelitis")	4,523
S25	osteomyelit* OR Mastoiditis or Petrositis or "Pott Puffy Tumo#r"	7,161
S26	(bone* N3 (invasiv* or infect* or staph* or bacter*))	2,484
S27	(bone* N3 "S aureus")	21
S28	(bone* N3 "S.aureus")	0

#	Query	Results
S29	(MH "Fasciitis, Necrotizing")	1,466
S30	"necroti* fasciitis"	1,414
S31	"flesh eating bacter*"	17
S32	"necroti* bacter*"	6
S33	(fascia N3 (invasiv* or infect* or staph* or bacter*))	56
S34	fascia N3 "S aureus"	0
S35	fascia N3 "S.aureus"	0
S36	(intramusc* N3 (invasiv* or infect* or staph* or bacter*))	48
S37	(intramusc* N3 S aureus)	1
S38	(intramusc* N3 "S.aureus")	0
S39	((muscle* or muscular) N3 (invasive* or infect* or staph* or bacter*))	2,920
S40	((muscle* or muscular) N3 S aureus)	3
S41	((muscle* or muscular) N3 "S.aureus")	0
S42	pyomyositis	242
S43	(MH "Myositis+")	4,608
S44	myositis OR "infectious myositides" OR "focal myositides"	3,927
S45	(MH "Arthritis, Infectious")	2,340
S46	(bacter* N3 arthriti*)	161
S47	septic* N3 arthriti*	1,683
S48	suppurat* N3 arthriti*	27
S49	infect* N3 arthriti*	2,853
S50	staph* N3 arthriti*	51
S51	"S aureus" adj3 arthriti*	0
S52	("S.aureus" N3 arthriti*)	1
S53	(MH "Pneumonia+")	34,868
S54	pneumoni*	61,874
S55	((lung or lungs or pulmonary) N3 infection*)	4,710
S56	((lung or lungs or pulmonary) N3 inflam*)	4,384
S57	((lung or lungs or pulmonary) N3 (invasiv* or bacter* or staph*))	2,346
S58	((lung or lungs or pulmonary) N3 S aureus)	11
S59	((lung or lungs or pulmonary) N3 "S.aureus")	0
S60	(MH "Lung+") AND (MH "Necrosis+")	217
S61	((pulmonary or lung*) N3 necro*)	377

#	Query	Results
S62	((Alveolar* or airway* or respiratory* or lung* or bronch*) N3 h#emorrhag*)	1,542
S63	((Alveolar* or airway* or respiratory* or lung* or bronch*) N3 bleed*)	405
S64	((Alveolar* or airway* or respiratory* or lung* or bronch*) N3 blood)	7,793
S65	("multi lobar infiltrat*" or "multilobar infiltrat*")	9
S66	(MH "Respiratory Distress Syndrome, Acute")	8,928
S67	(MH "Respiratory Failure+")	17,711
S68	(respiratory N1 (collapse* or distress or insufficiency or failure))	35,403
S69	(lung* N1 (collapse* or distress or insufficiency or failure))	732
S70	(pulmonary N1 (collapse* or distress or insufficiency or failure))	985
S71	(MH "Influenza, Human+")	9,987
S72	influenza* OR flu	38,137
S73	(MH "Hemoptysis")	1,583
S74	h#emoptys?s	3,149
S75	(MH "Leukopenia")	882
S76	(MH "Neutropenia+")	5,207
S77	leu?op#eni* OR leu?cytoop#eni* OR neutrop#eni*	13,543
S78	(MH "Oxygen Saturation")	6,088
S79	(MH "Oxygen") AND (MH "Blood+")	381
S80	"oxygen saturation"	12,596
S81	(blood N1 (oxygen or o2))	7,207
S82	SPo2	2,300
S83	(MH "Sepsis+")	33,259
S84	(MH "Bacteremia")	6,663
S85	(MH "Blood+") AND ((MH "Bacteria+") OR (MH "Staphylococcus aureus+") OR (MH "Staphylococcal Infections+") OR (MH "Bacterial Infections+"))	4,545
S86	((bacter* or "S aureus" or "S.aureus" OR staph*) and blood*)	20,060
S87	bacter#emi*	10,327
S88	seps?s	37,816
S89	septic*	18,800
S90	(infect* N3 (blood or bloodstream))	13,355
S91	(poison* N3 (blood or bloodstream))	374

#	Query	Results
S92	(bacter* N3 (blood or bloodstream))	3,150
S93	(("S aureus" OR "S.aureus") N3 (blood or bloodstream))	97
S94	(Staph* N3 (blood or bloodstream))	416
S95	septic#emi*	2,059
S96	py#emi*	8
S97	pyoh#emi*	0
S98	(MH "Abscess+")	8,386
S99	abscess*	15,427
S100	(MH "Purpura, Schoenlein-Henoch")	1,011
S101	(purpura N1 fulmina*)	242
S102	"h#emorrhagic vasculitis"	1
S103	"henoch purpura*"	871
S104	"henoch schoenlein purpura*"	873
S105	"nonthrombocytopenic purpura*"	866
S106	"non-thrombocytopenic purpura*"	5
S107	"nonthrombopenic purpura*"	0
S108	"non-thrombopenic purpura*"	0
S109	"purpura h#emorrhagica"	2
S110	"rheumatoid purpura*"	866
S111	(MH "Pneumonia+")	34,868
S112	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10	1,195
S113	S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111	287,536

#	Query	Results
S114	S112 AND S113	402

Cochrane Central Register of Controlled Trials

Date run: 28 February 2025

ID	Search	Hits
#1	MeSH descriptor: [Leukocidins] explode all trees	8
#2	leukocidin*	20
#3	leucocidin*	5
#4	leukotoxi*	5
#5	leucotoxi*	0
#6	"Panton Valentine"	20
#7	PVL	484
#8	LukS	43
#9	LukF	0
#10	"Luk pv"	0
#11	MeSH descriptor: [Bacterial Toxins] explode all trees	4,169
#12	MeSH descriptor: [Staphylococcal Infections] explode all trees	1,527
#13	MeSH descriptor: [Staphylococcus aureus] explode all trees	1,154
#14	#12 OR #13	2,000
#15	#11 AND #14	20
#16	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #15	555
#17	MeSH descriptor: [Pneumonia, Staphylococcal] explode all trees	44
#18	MeSH descriptor: [Soft Tissue Infections] explode all trees	184
#19	MeSH descriptor: [Superinfection] explode all trees	58
#20	(superinfect* or super NEXT infect*)	677
#21	(superinvas* or super NEXT invas*)	0
#22	((deep or invasiv*) NEAR/3 infect*)	2,254
#23	((deep or invasiv*) NEAR/3 staph*)	14
#24	((deep or invasiv*) NEAR/3 s aureus)	15
#25	((deep or invasiv*) NEAR/3 s.aureus).	0
#26	((deep or invasiv*) NEAR/3 bacter*)	198

ID	Search	Hits
#27	(deep tissue* NEAR/3 infect*)	174
#28	(deep tissue* NEAR/3 invasiv*)	14
#29	(deep tissue* NEAR/3 staph*)	1
#30	(deep tissue* NEAR/3 s aureus)	1
#31	(deep tissue* NEAR/3 "s.aureus")	1
#32	deep tissue* NEAR/3 bacter*	40
#33	(soft tissue* NEAR/3 infect*)	973
#34	(soft tissue* NEAR/3 invasiv*)	24
#35	(soft tissue* NEAR/3 staph*)	76
#36	(soft tissue* NEAR/3 s aureus)	1
#37	(soft tissue* NEAR/3 "s.aureus")	2
#38	(soft tissue* NEAR/3 bacter*)	84
#39	MeSH descriptor: [Osteomyelitis] explode all trees	211
#40	osteomyelit*	849
#41	Mastoiditis or Petrositis or Pott Puffy Tumor	107
#42	(bone* NEAR/3 (invasiv* or infect* or staph* or bacter*))	1,047
#43	(bone* NEAR/3 S aureus)	3
#44	(bone* NEAR/3 "S.aureus")	1
#45	MeSH descriptor: [Fasciitis, Necrotizing] explode all trees	22
#46	necroti* fasciitis	120
#47	flesh eating bacter*	4
#48	necroti* bacter*	880
#49	(fascia NEAR/3 (invasiv* or infect* or staph* or bacter*))	21
#50	(fascia NEAR/3 S aureus)	0
#51	(fascia NEAR/3 "S.aureus")	0
#52	MeSH descriptor: [Pyomyositis] explode all trees	1
#53	(intramusc* NEAR/3 (invasiv* or infect* or staph* or bacter*))	186
#54	intramusc* NEAR/3 S aureus	1
#55	(intramusc* NEAR/3 "S.aureus")	1
#56	((muscle* or muscular) NEAR/3 (invasiv* or infect* or staph* or bacter*))	2,140
#57	((muscle* or muscular) NEAR/3 S aureus)	0
#58	((muscle* or muscular) NEAR/3 "S.aureus")	0
#59	pyomyositis	18

ID	Search	Hits
#60	MeSH descriptor: [Myositis] explode all trees	309
#61	myositis	787
#62	infectious myositides	0
#63	focal myositides	0
#64	MeSH descriptor: [Arthritis, Infectious] explode all trees	155
#65	(bacter* NEAR/3 arthriti*)	210
#66	(septic* NEAR/3 arthriti*)	182
#67	(suppurat* NEAR/3 arthriti*)	9
#68	(infect* NEAR/3 arthriti*)	375
#69	(staph* NEAR/3 arthriti*)	9
#70	(S aureus NEAR/3 arthriti*)	2
#71	("S.aureus" NEAR/3 arthriti*)	2
#72	MeSH descriptor: [Tissues] explode all trees	43,902
#73	pneumoni*	26,322
#74	((lung or lungs or pulmonary) NEAR/3 infection*)	3,735
#75	((lung or lungs or pulmonary) NEAR/3 inflam*)	2,570
#76	((lung or lungs or pulmonary) NEAR/3 (invasiv* or bacter* or staph*))	786
#77	((lung or lungs or pulmonary) NEAR/3 S aureus)	5
#78	((lung or lungs or pulmonary) NEAR/3 "S.aureus")	2
#79	MeSH descriptor: [Lung] explode all trees	6,288
#80	MeSH descriptor: [Necrosis] explode all trees	18,747
#81	#79 AND #80	20
#82	((pulmonary or lung*) Near/3 necro*)	199
#83	((Alveolar* or airway* or respiratory* or lung* or bronch*) NEAR/3 hemorrhage*)	723
#84	((Alveolar* or airway* or respiratory* or lung* or bronch*) NEAR/3 haemorrhage*)	156
#85	((Alveolar* or airway* or respiratory* or lung* or bronch*) NEAR/3 bleed*)	503
#86	((Alveolar* or airway* or respiratory* or lung* or bronch*) NEAR/3 blood)	6,469
#87	(multi lobar infiltrat* or multilobar infiltrat*)	30
#88	MeSH descriptor: [Respiratory Distress Syndrome] explode all trees	3,,576
#89	MeSH descriptor: [Respiratory Insufficiency] explode all trees	3945

ID	Search	Hits
#90	(respiratory NEAR/1 (collapse* or distress or insufficiency or failure))	16,853
#91	(lung* NEAR/1 (collapse* or distress or insufficiency or failure))	818
#92	(pulmonary NEAR/1 (collapse* or distress or insufficiency or failure))	407
#93	MeSH descriptor: [Influenza, Human] explode all trees	3629
#94	influenza* OR flu	13,893
#95	MeSH descriptor: [Hemoptysis] explode all trees	44
#96	hemoptysis OR haemoptysis OR hemoptyses OR haemoptyses	938
#97	MeSH descriptor: [Leukopenia] explode all trees	3,124
#98	MeSH descriptor: [Neutropenia] explode all trees	2,224
#99	leukopeni* OR leukopaeni* OR leucopeni* OR leucopaeni*	6,623
#100	neutropeni* OR neutropaeni*	16,699
#101	MeSH descriptor: [Oxygen Saturation] explode all trees	178
#102	MeSH descriptor: [Oxygen] explode all trees	7,495
#103	MeSH descriptor: [Blood] explode all trees	20,850
#104	#102 AND #103	241
#105	oxygen saturation	20,464
#106	(blood NEAR/1 (oxygen or o2))	3,065
#107	SPo2	8,055
#108	MeSH descriptor: [Sepsis] explode all trees	6,480
#109	MeSH descriptor: [Bacteremia] explode all trees	1,298
#110	MeSH descriptor: [Bacteria] this term only	2,299
#111	MeSH descriptor: [Staphylococcus aureus] explode all trees	1,154
#112	MeSH descriptor: [Bacterial Infections] explode all trees	23,019
#113	MeSH descriptor: [Staphylococcal Infections] explode all trees	1,527
#114	#110 OR #111 OR #112 OR #113	25,165
#115	MeSH descriptor: [Blood] explode all trees	20,850
#116	#114 AND #115	578
#117	((bacter* or S aureus OR "S.aureus" or staph*) and blood*)	14,718
#118	bacteremi*	2858
#119	bacteraemi*	775
#120	sepsis OR septic* OR sepses	19,564
#121	(infect* NEAR/3 (blood or bloodstream))	4,058
#122	(poison* NEAR/3 (blood or bloodstream))	219

ID	Search	Hits
#123	(bacter* NEAR/3 (blood or bloodstream))	1,806
#124	(S aureus NEAR/3 (blood or bloodstream))	69
#125	("S.aureus" NEAR/3 (blood or bloodstream))	33
#126	(Staph* NEAR/3 (blood or bloodstream))	95
#127	septicemi* OR septicaemi*	1,300
#128	pyemi* OR pyaemi*	16
#129	pyohemi* OR pyohaemi*	6
#130	MeSH descriptor: [Abscess] explode all trees	817
#131	abscess*	5,205
#132	MeSH descriptor: [Purpura Fulminans] explode all trees	0
#133	(purpura NEAR/1 fulmina*)	19
#134	hemorrhagic vasculitis	25
#135	haemorrhagic vasculitis	19
#136	henoch purpura*	143
#137	henoch schoenlein purpura*	12
#138	nonthrombocytopenic purpura*	7
#139	non-thrombocytopenic purpura*	5
#140	nonthrombopenic purpura*	0
#141	non-thrombopenic purpura*	0
#142	purpura h*emorrhagica	0
#143	rheumatoid purpura*	71
#144	MeSH descriptor: [Pneumonia] explode all trees	13,253
#145	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #116 OR #117 OR #118 OR #119 OR #120 OR #121 OR #122 OR #123 OR #124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133 OR #134 OR	189,568

ID	Search	Hits
	#135 OR #136 OR #137 OR #138 OR #139 OR #140 OR #141 OR #142 OR #143 OR #144	
#146	#16 AND #145	275

Results filtered to CENTRAL only: 169

Web of Science Core Collection (Science Citation Index)

Date of search: 28 February 2025

TS=(leukocidin*) OR TS=(leucocidin*) OR TS=(leukotoxi*) OR TS=(leucotoxi*) OR TS=("Panton Valentine") OR TS=(PVL) OR TS=(LukS) OR TS=(LukF) OR TS=("Luk pv")

AND

TS=((superinfect* or "super infect*")) OR TS=((superinvas* or "super invas*")) OR TS=(((deep or invasiv*) NEAR/2 infect*)) OR TS=(((deep or invasiv*) NEAR/2 staph*)) OR TS=(((deep or invasiv*) NEAR/2 "s aureus")) OR TS=(((deep or invasiv*) NEAR/2 "s.aureus")) OR TS=(((deep or invasiv*) NEAR/2 bacter*)) OR TS=(("deep tissue*" NEAR/2 infect*)) OR TS=(("deep tissue*" NEAR/2 invasiv*)) OR TS=(("deep tissue*" NEAR/2 staph*)) OR TS=(("deep tissue*" NEAR/2 "s aureus")) OR TS=(("deep tissue*" NEAR/2 "s.aureus")) OR TS=(("deep tissue*" NEAR/2 bacter*)) OR TS=(("soft tissue*" NEAR/2 infect*)) OR TS=(("soft tissue*" NEAR/2 invasiv*)) OR TS=(("soft tissue*" NEAR/2 staph*)) OR TS=(("soft tissue*" NEAR/2 "s aureus")) OR TS=(("soft tissue*" NEAR/2 "s.aureus")) OR TS=(("soft tissue*" NEAR/2 bacter*)) OR TS=(osteomyelit*)

OR

TS=((Mastoiditis or Petrositis or "Pott Puffy Tumo$r")) OR TS=((bone* NEAR/2 (invasiv* or infect* or staph* or bacter*))) OR TS=((bone* NEAR/2 "S aureus")) OR TS=((bone* NEAR/2 "S.aureus")) OR TS=("necroti* fasciitis") OR TS=("flesh eating bacter*") OR TS=("necroti* bacter*") OR TS=((fascia NEAR/2 (invasiv* or infect* or staph* or bacter*))) OR TS=((fascia NEAR/2 "S aureus")) OR TS=((fascia NEAR/2 "S.aureus")) OR TS=((intramusc* NEAR/2 (invasiv* or infect* or staph* or bacter*))) OR TS=((intramusc* NEAR/2 "S aureus")) OR TS=((intramusc* NEAR/2 "S.aureus")) OR TS=(((muscle* or muscular) NEAR/2 (invasiv* or infect* or staph* or bacter*))) OR TS=(((muscle* or muscular) NEAR/2 "S aureus"))

OR

TS=(((muscle* or muscular) NEAR/2 "S.aureus")) OR TS=(pyomyositis) OR TS=(myositis) OR TS=("infectious myositides") OR TS=("focal myositides") OR TS=((bacter* NEAR/2 arthriti*)) OR TS=((septic* NEAR/2 arthriti*)) OR TS=((suppurat* NEAR/2 arthriti*)) OR TS=((infect* NEAR/2 arthriti*)) OR TS=((staph* NEAR/2 arthriti*)) OR TS=(("S aureus"

NEAR/2 arthriti*)) OR TS=(("S.aureus" NEAR/2 arthriti*)) OR TS=(pneumoni*) OR TS=(((lung or lungs or pulmonary) NEAR/2 infection*)) OR TS=(((lung or lungs or pulmonary) NEAR/2 inflam*)) OR TS=(((lung or lungs or pulmonary) NEAR/2 (invasiv* or bacter* or staph*))) OR TS=(((lung or lungs or pulmonary) NEAR/2 "S aureus")) OR TS=(((lung or lungs or pulmonary) NEAR/2 "S.aureus")) OR TS=(((pulmonary or lung*) NEAR/2 necro*)) OR TS=(((Alveolar* or airway* or respiratory* or lung* or bronch*) NEAR/2 h$emorrhag*)) OR TS=(((Alveolar* or airway* or respiratory* or lung* or bronch*) NEAR/2 bleed*)) OR TS=(((Alveolar* or airway* or respiratory* or lung* or bronch*) NEAR/2 blood)) OR TS=(("multi lobar infiltrat*" or "multilobar infiltrat*")) OR TS=((respiratory NEAR/0 (collapse* or distress or insufficiency or failure))) OR TS=((lung* NEAR/0 (collapse* or distress or insufficiency or failure))) OR TS=((pulmonary NEAR/0 (collapse* or distress or insufficiency or failure))) OR TS=((influenza* or flu)) OR TS=(h$emoptys?s) OR TS=((leu?ocytop$eni* or leu?op$eni*))

OR

TS=(neutrop$eni*) OR TS=("oxygen saturation") OR TS=((blood NEAR/0 (oxygen or o2))) OR TS=(SPo2) OR TS=(((bacter* or "S.aureus" or "S aureus" or staph*) and blood*)) OR TS=(bacter$emi*) OR TS=(seps?s) OR TS=(septic*) OR TS=((infect* NEAR/2 (blood or bloodstream))) OR TS=((poison* NEAR/2 (blood or bloodstream))) OR TS=((bacter* NEAR/2 (blood or bloodstream))) OR TS=(("S aureus" NEAR/2 (blood or bloodstream))) OR ("S.aureus" NEAR/2 (blood or bloodstream)) OR TS=((Staph* NEAR/2 (blood or bloodstream))) OR TS=(septic$emi*) OR TS=(py$emi*) OR TS=(pyoh$emi*) OR TS=(abscess*) OR TS=((purpura NEAR/0 fulmina*)) OR TS=("h$emorrhagic vasculitis") OR TS=("henoch purpura*") OR TS=("henoch schoenlein purpura*") OR TS=("nonthrombocytopenic purpura*") OR TS=("non-thrombocytopenic purpura*") OR TS=("nonthrombopenic purpura*") OR TS=("non-thrombopenic purpura*") OR TS=("purpura h$emorrhagica") OR TS=("rheumatoid purpura*")

Results: 2,105

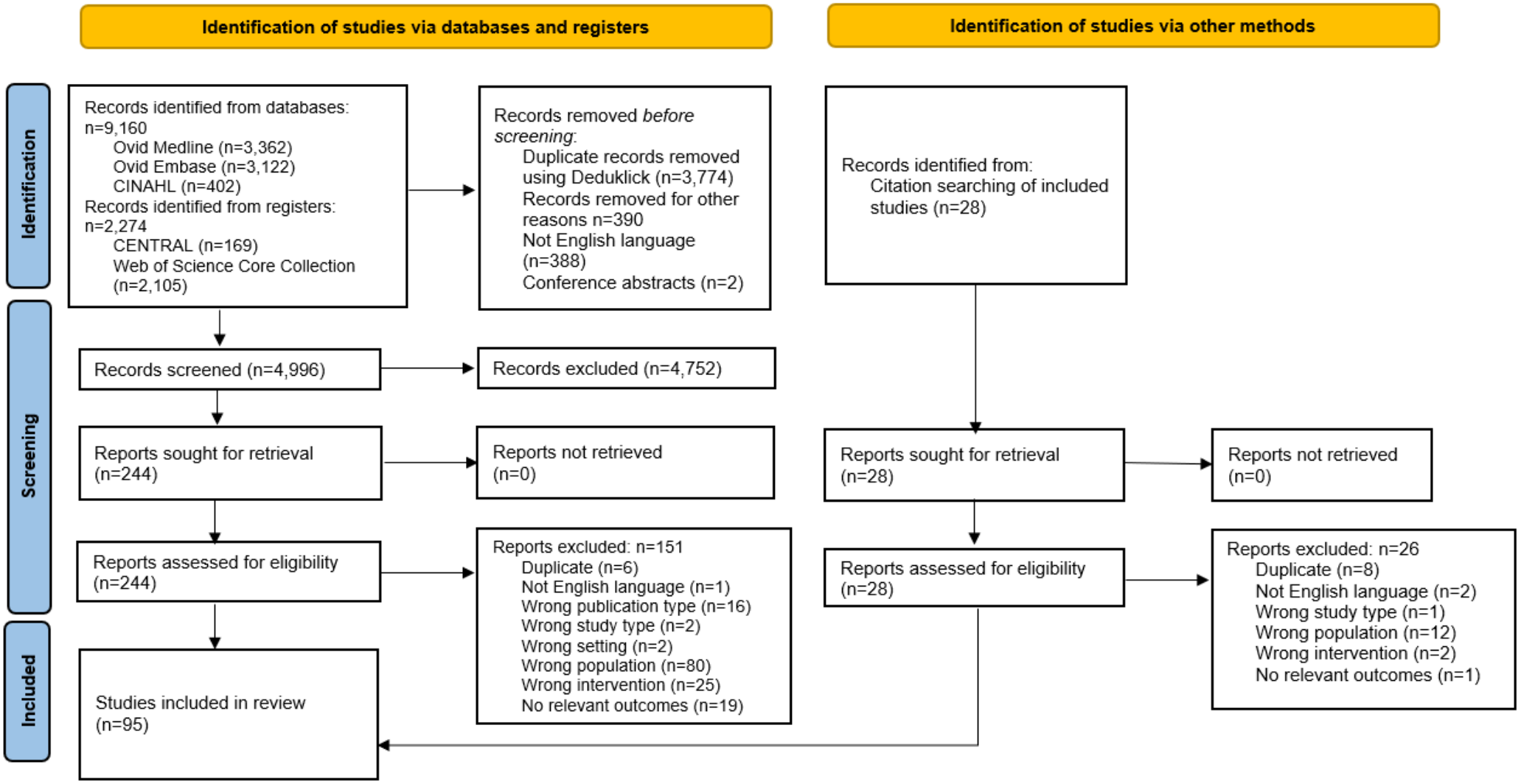
Annexe B. Agreed antibiotics

- amikacin
- amoxicillin-clavulanate / clavulanic acid
- ampicillin-sulbactam
- azithromycin
- benzylpenicillin
- cefaclor
- cefadroxil
- cefazolin
- cefdinir
- cefditoren
- cefepime
- cefixime
- cefoperazone
- cefotaxime
- cefotetan
- cefoxitin
- cefprozil
- ceftaroline
- ceftibuten
- ceftobiprole
- ceftriaxone
- cefuroxime
- cephalexin
- chloramphenicol
- ciprofloxacin
- clarithromycin
- clindamycin
- cloxacillin
- dalbavancin
- daptomycin
- delafloxacin
- dicloxacillin
- doxycycline
- eravacycline
- erythromycin
- flucloxacillin

- fusidic acid / fucidin
- gatifloxacin
- gemifloxacin
- gentamicin
- lefamulin
- levofloxacin
- linezolid
- minocycline
- moxifloxacin
- nafcillin
- omadacycline
- oritavancin
- oxacillin
- piperacillin-tazobactam
- pristinamycin
- quinupristin / dalfopristin
- rifampicin
- teicoplanin
- telavancin
- telithromycin
- tedizolid
- tetracycline
- tigecycline
- trimethoprim
- trimethoprim-sulphamethoxazole
- vancomycin

Annexe C. Study selection flowchart

Figure B.1. PRISMA diagram



Text version of Figure B.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 95 studies.

From identification of studies via databases and registers, n=9,160 records identified from databases:

- Ovid Medline (n=3,362)
- Ovid Embase (n=3,122)
- CINHAL (n=402)
- Cochrane CENTRAL (n=169)
- Web of Science Core Collection (n=2,105)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=3,774)
- records removed for other reasons (n=390)

n=4,996 records screened, of which n=4,752 were excluded, leaving n=244 papers sought for retrieval, of which n=0 were not retrieved.

n=28 studies were identified from citation searching of included studies identification of studies via other methods

Of the n=272 papers assessed for eligibility, n=177 reports were excluded:

- duplicate (n=14)
- not English language (n=3)
- wrong publication type (n=16)
- wrong study type (n=3)
- wrong setting (n=2)
- wrong population (n=92)
- wrong intervention (n=27)
- no relevant outcomes (n=20)

n=95 papers included in the review.

Annexe D. Excluded full texts

Duplicate (14 studies)

Ambrozova H and others. 'The first case of fatal pneumonia caused by Panton–Valentine leukocidin-producing *Staphylococcus aureus* in an infant in the Czech Republic' Folia microbiologica 2012: volume 58, issue 3, pages 225 to 228

Castellazzi ML and others. 'Panton-Valentine leukocidin *Staphylococcus aureus* severe infection in an infant: a case report and a review of the literature' Italian Journal of Pediatrics 2021: volume 47, issue 1

Fitzgerald F and others. 'Back pain in a previously healthy teenager' BMJ Case Reports 2013: volume 17, page 17

Garbo V and others. 'Severe Panton-Valentine-Leukocidin-Positive *Staphylococcus aureus* Infections in Pediatric Age: A Case Report and a Literature Review' Antibiotics 2024: volume 13, issue 12, page 7

Garbo V and others. 'Severe Panton-Valentine-Leukocidin-Positive *Staphylococcus aureus* Infections in Pediatric Age: A Case Report and a Literature Review' Antibiotics-Basel 2024: volume 13, issue 12

Karli A and others. 'Panton-Valentine leukocidin positive *Staphylococcus aureus* infection in childhood: a case report' Turkish Journal of Pediatrics 2015: volume 57, issue 6, pages 615 to 617

McAdams RM and others. 'Perinatal/neonatal case presentation. Necrotising Staphylococcal pneumonia in a neonate' Journal of Perinatology 2005: volume 25, issue 10, pages 677 to 679

Miller LG and others. 'Necrotising fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles' New England Journal of Medicine 2005: volume 352, issue 14, pages 1445 to 1453

Montagnani C and others. 'Severe infections caused by Panton–Valentine leukocidin-positive *Staphylococcus aureus* in infants: report of three cases and review of literature' Acta Paediatrica (Oslo, Norway: 1992) 2013: volume 102, issue 6, pages 284 to 287

Newell R and others. 'Panton-Valentine leucocidin *Staphylococcus aureus* necrotising pneumonia in a clinically well patient' British Journal of Hospital Medicine 2023: volume 29, issue 3, pages 1 to 4

Österlund A and others. 'Intrafamilial spread of highly virulent *Staphylococcus aureus* strains carrying the gene for Panton-Valentine leukocidin' Scandinavian Journal of Infectious Diseases 2002: volume 34, issue 10, pages 763 to 764

Sicot N and others. 'Methicillin resistance is not a predictor of severity in community-acquired *Staphylococcus aureus* necrotising pneumonia-results of a prospective observational study' Clinical Microbiology and Infection 2013: volume 19, issue 3, pages E142 to E148

Swaminathan A and others. 'Fulminant methicillin-sensitive *Staphylococcus aureus* infection in a healthy adolescent, highlighting 'Panton-Valentine leucocidin syndrome'' Internal Medicine Journal 2006: volume 36, issue 11, pages 744 to 747

Thomas B and others. 'Pleuropulmonary complications of PVL-positive *Staphylococcus aureus* infection in children' Acta Paediatrica 2009: volume 98, issue 8, pages 1,372 to 1,375

Not English language (3 studies)

Honda K and others. 'A Life-saving Case of Lung Abscess Caused by Panton-Valentine Leukocidin (PVL)-positive Methicillin-susceptible *Staphylococcus aureus* (MSSA) at the Sixth Day of Life' Iryo Yakugaku (Japanese Journal of Pharmaceutical Health Care and Sciences) 2021: volume 47, issue 12, pages 667 to 673

Sargın-Altunok E and others. 'Toplum Kökenli Metisiline Dirençli *Staphylococcus aureus*' un Neden Olduğu Bir Nekrotizan Fasiit Olgusu' Klimik Journal / Klimik Dergisi 2014: volume 27, issue 1, pages 26 to 29

Valentini P and others. 'Infezione invasiva grave da S. aureus meticillino-resistente (clone USA300) in un adolescente italiano' 2009

Wrong publication type (16 studies)

Arakawa S and others. 'The first case of necrotising fasciitis caused by Panton-Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* USA300 clone in Japan' Journal of Dermatology 2023: volume 50, issue 4, pages E131 to E132

Chini V and others. 'Methicillin-resistant *Staphylococcus aureus* producing Panton-Valentine leukocidin:: a cause of acute osteomyelitis in children' International Journal of Antimicrobial Agents 2007: volume 29, pages S55 to S55

Desachy A and others. 'Role of superantigenic strains in the prognosis of community-acquired methicillin-susceptible *Staphylococcus aureus* bacteraemia' Clinical Microbiology and Infection 2007: volume 13, pages 1,131 to 1,133

Duployez C and others. 'Panton-Valentine Leukocidin-Secreting *Staphylococcus aureus* Pneumonia Complicating COVID-19' Emerging Infectious Diseases 2020: volume 26, issue 8, pages 1,939 to 1,941

Ho H and others. 'COMMUNITY-ACQUIRED NECROTISING PNEUMONIA DUE TO METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* SECRETING PANTON-VALENTINE LEUKOCIDIN IN 4 PATIENTS ADMITTED TO CHILDREN'S HOSPITAL 1 IN NOVEMBER 2017: CASE SERIES REPORT' Respirology 2018: volume 23, pages 50 to 50

Imauven O and others. 'Community-acquired Panton-Valentine Leukocidin producing *Staphylococcus aureus* infections in adult ICU patients in New Caledonia Island: A cohort study' Anaesthesia Critical Care and Pain Medicine 2022: volume 41, issue 2, page 3

Ito T and others. 'Pediatric pneumonia death caused by community-acquired methicillin-resistant *Staphylococcus aureus*, Japan' Emerging Infectious Diseases 2008: volume 14, issue 8, pages 1,312 to 1,314

Jean M and others. 'BACT-04 - Reassessment of antibiotic therapy after identification of Panton-Valentine leukocidin in deep infections due to Staphylococcus spp' Medecine et Maladies Infectieuses 2016: volume 46, page 20

Korcheva VB and others. 'Study of Two Cases of Fatal Necrotising Pneumonia in Healthy Adults, Due to *Staphylococcus aureus* Infection. Is It Always Penton-Velentine Leukocidin?' Modern Pathology 2009: volume 22

Kudo K and others. 'Severe cervical abscess due to PVL-positive ST6562 MRSA-IVa, a presumptive variant of ST8-IVa USA300 clone in northern Japan' New Microbes and New Infections 2024: volume 58, 101230

Monaco M and others. 'Methicillin-resistant *Staphylococcus aureus* necrotising pneumonia' Emerging Infectious Diseases 2005: volume 11, issue 10, pages 1,647 to 1,648

O'Connor M and others. 'A CASE OF MRSA-PVL PNEUMONIA IN A 10-YEAR-OLD GIRL' Irish Journal of Medical Science 2010: volume 179, pages S268 to S268

Rasigade JP and others. 'Lethal necrotising pneumonia caused by an ST398 *Staphylococcus aureus* strain' 2010: volume 16, pages 1330 to 1330

Rein JL and others. 'Death of woman with peripartum influenza B virus infection and necrotising pneumonia' Emerging Infectious Diseases. Atlanta, Georgia, Centers for Disease Control and Prevention (CDC) 2014: volume 20, issue 89, pages 1,258 to 1,260

Sdougkos G and others. 'Methicillin-resistant *Staphylococcus aureus* producing Panton-Valentine leukocidin as a cause of acute osteomyelitis in children' Clinical Microbiology and Infection 2007: volume 13, issue 6, pages 651 to 654

Withers A and others. 'LONGER TERM OUTCOMES OF CHILDREN FOLLOWING PANTON-VALENTINE LEUKOCIDIN POSITIVE STAPHYLOCOCCAL PNEUMONIA' Internal Medicine Journal 2011: volume 41, pages 17 to 17

Wrong study type (3 studies)

Lopez-Aguilar C and others. 'Erratum: Association between the presence of the panton-valentine leukocidin-encoding gene and a lower rate of survival among hospitalized pulmonary patients with staphylococcal disease (Journal of Clinical Microbiology (2007) 45,1, (274-276))' Journal of Clinical Microbiology 2007: volume 45, page 3,150

Martin E and others. 'Clinical and microbiological characteristics of community acquired methicillin-resistant *Staphylococcus aureus* pneumonia' Chest Disease Reports 2012: volume 2:e7

Vardakas KS and others. 'Incidence, characteristics and outcomes of patients with severe community acquired-MRSA pneumonia' European Respiratory Journal 2009: volume 34, issue 5, pages 1,148 to 1,158

Wrong setting (2 studies)

Mosquera M and others. 'Pediatric case of fatal necrotising pneumonia due to Panton-Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* in Spain' Enfermedades Infecciosas y Microbiologia Clinica 2019: volume 37, page 63

Moussa I and others. 'Molecular characterization of methicillin-resistant *Staphylococcus aureus* recovered from outpatient clinics in Riyadh, Saudi Arabia' Saudi Medical Journal 2009: volume 30, issue 5, pages 611 to 617

Wrong population (92 studies)

Agarwal N and others. 'Pyomyositis: Are We Missing the Diagnosis?' Surgical Infections 2016: volume 17, issue 5, pages 615 to 621

Allou N and others. 'SARS-CoV-2 with Panton-Valentine leukocidin-producing *Staphylococcus aureus* healthcare-associated pneumonia in the Indian Ocean' Heliyon 2022: volume 8, issue 9, e10422

Almarzouqi F and others. 'Fatal Necrotising Fasciitis following Episiotomy' Case reports in surgery 2015: volume 2015, 562810

Al-Tawfiq JA and others. 'Community-acquired MRSA bacteremic necrotising pneumonia in a patient with scrotal ulceration' Journal of Infection 2005: volume 51, issue 4, pages e241 to 243

Baldwin LN and others. 'Panton-Valentine Leukocidin associated with community acquired methicillin resistant *Staphylococcus aureus*: a case report and review of interim guidelines' Anaesthesia 2008: volume 63, issue 7, pages 764 to 766

Barry PJ and others. 'Panton-Valentine Leukocidin-positive *Staphylococcus aureus*: a potentially significant pathogen in cystic fibrosis' Paediatric Respiratory Reviews 2014: volume 15, pages 22 to 25

Bhasin A and others. 'Resurgence of methicillin-sensitive *Staphylococcus aureus* in the community-associated, methicillin-resistant *Staphylococcus aureus* era: Four novel cases and review' Infectious Diseases in Clinical Practice 2014: volume 22, pages 1 to 7

Boan P and others. 'Epidemiological, clinical, outcome and antibiotic susceptibility differences between PVL positive and PVL negative *Staphylococcus aureus* infections in Western Australia: a case control study' BMC Infectious Diseases 2015: volume 15, page 10

Boussaud V and others. 'Life-threatening hemoptysis in adults with community-acquired pneumonia due to Panton-Valentine leukocidin-secreting *Staphylococcus aureus*' Intensive Care Medicine 2003: volume 29, issue 10, pages 1,840 to 1,843

Braga PRM and others. 'Necrotising Pneumonia and Conservative Treatment: A Case Report and Review of the Literature' Open Journal of Respiratory Diseases 2024: volume 14, issue 3, pages 69 to 76

Bruno GJ and others. 'Community-acquired methicillin-resistant *Staphylococcus aureus* infection with fatal necrotising pneumonia from lip abscess:: A case report' Journal of Oral and Maxillofacial Surgery 2007: volume 65, issue 11, pages 2,350 to 2,353

Camargo JF and others. 'Septic pulmonary embolism of unknown origin in patients with *Staphylococcus aureus* bacteremia; A case report and review of 18 cases' Infectious Diseases in Clinical Practice 2013: volume 21, pages 217 to 221

Capasso L and others. 'An unusual aggressive presentation of late onset sepsis due to *Staphylococcus aureus* MRSA producing Panton-Valentine Leukocidin in preterm neonate' Acta Bio-Medica de l Ateneo Parmense 2021: volume 92, e2021147

Carrillo-Marquez MA and others. '*Staphylococcus aureus* pneumonia in children in the era of community-acquired methicillin-resistance at Texas Children's Hospital' Pediatric Infectious Disease Journal 2011: volume 30, issue 7, pages 545 to 550

Chamseddine N and others. 'Polymicrobial necrotising fasciitis after a primary cesarean section in a low-risk patient: A case report and literature review' International journal of surgery case reports 2024: volume 124, page 110326

Choi SH and others. 'A Longitudinal Study of Adult Patients with *Staphylococcus aureus* Bacteremia over 11 Years in Korea' Journal of Korean Medical Science 2021: volume 36, issue 16, page e104

Christin L and others. 'Pyomyositis in North America: Case Reports and Review' Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 1992: volume 15, issue 4, pages 668 to 677

Consonni F and others. 'Severe necrotising staphylococcal pneumonia with late life-threatening tracheobronchial involvement in an infant' American Journal of Respiratory and Critical Care Medicine 2019: volume 199, pages 1,280 to 1,281

Cori MS and others. '*Staphylococcus aureus* Panton-Valentine Leukocidin causing hip osteomyelitis, thrombophlebitis and necrotising pneumonia in an immuocompetent child' Journal of Biological Regulators and Homeostatic Agents 2020: volume 34, issue 3, pages 53 to 56. ADVANCES IN MUSCULOSKELETAL DISEASES AND INFECTIONS - to SOTIMI 2019

Costa CA and others. 'Panton-Valentine Leukocidin in Necrotising Pneumonia: A Case Report' Cureus 2025: volume 17, issue 2, page e78774

Daneshvar C and others. 'Community-acquired pneumonia due to Panton-Valentine leukocidin-producing *Staphylococcus aureus* in an HIV-2-infected patient' International Journal of STD and AIDS 2011: volume 22, issue 10, pages 610 to 612

Dickson RP and others. 'Case of rapidly progressive necrotising pneumonia caused by community-acquired methicillin-resistant *Staphylococcus aureus*' Respiratory Care 2008: volume 53, issue 9, pages 1,223 to 1,226

Doudoulakakis AG and others. 'Community-associated *Staphylococcus aureus* pneumonia among Greek children: epidemiology, molecular characteristics, treatment, and outcome' European Journal of Clinical Microbiology and Infectious Diseases 2016: volume 35, issue 7, pages 1,177 to 1,185

Duarte FC and others. 'Phenotypic and genotypic characteristics of mecA - positive oxacillin-sensitive *Staphylococcus aureus* isolated from patients with bloodstream infection in a tertiary

hospital in Southern Brazil' Brazilian Journal of Microbiology 2024: volume 55, issue 3, pages 2,705 to 2,713

Dunlop RL and others. 'Idiopathic neonatal necrotising fasciitis caused by community-acquired MSSA encoding Panton-Valentine leukocidin genes' Journal of Plastic, Reconstructive and Aesthetic Surgery: JPRAS 2011: volume 64, issue 11, pages 1,522 to 1,524

Ebert MD and others. 'Necrotising pneumonia caused by community-acquired methicillin-resistant *Staphylococcus aureus*: an increasing cause of "mayhem in the lung"' Emergency Radiology 2009: volume 16, issue 2, pages 159 to 162

Erturan G and others. 'Successful use of daptomycin in Panton-Valentine leucocidin positive *Staphylococcus aureus* paediatric osteomyelitis' International Journal of Surgery Case Reports 2012: volume 3, issue 7, pages 238 to 241

Eshwara VK and others. '*Staphylococcus aureus* bacteremia in an Indian tertiary care hospital: observational study on clinical epidemiology, resistance characteristics, and carriage of the Panton-Valentine leukocidin gene' International Journal of Infectious Diseases 2013: volume 17, issue 11, pages e1051 to e1055

Feder HM and others. 'Occult methicillin-resistant *Staphylococcus aureus* abscesses in 2 pediatric patients' Clinical Pediatrics 2008: volume 47, issue 2, pages 176 to 179

Fortunov RM and others. 'Community-acquired *Staphylococcus aureus* infections in term and near-term previously healthy neonates' Pediatrics 2006: volume 118, issue 3, pages 874 to 881

Frantz M and others. 'Holocord spinal epidural abscess from community-acquired methicillin-resistant *Staphylococcus aureus*' Infectious Diseases in Clinical Practice 2011: volume 19, pages 61 to 63

Fröhlich EP and others. 'Necrotising fasciitis arising from Bartholin's abscess. Case report and review of the literature' Israel journal of medical sciences 1989: volume 25, issue 11, pages 644 to 647

Fujisaki N and others. 'Successful treatment of Panton-Valentine leukocidin-expressing *Staphylococcus aureus*-associated pneumonia co-infected with influenza using extracorporeal membrane oxygenation' In Vivo 2014: volume 28, issue 5, pages 961 to 965

Gelfand MS and others. 'Pathological fracture in acute osteomyelitis of long bones secondary to community-acquired methicillin-resistant *Staphylococcus aureus*: two cases and review of the literature' The American journal of the medical sciences 2006: volume 332, issue 6, pages 357 to 360

Gencpinar P and others. 'Nonketotic hyperglycinemia: novel mutation in the aminomethyl transferase gene. Case report' Archivos Argentinos de Pediatria 2016: volume 114, issue 3, pages e142 to e146

Gijon M and others. 'Factors associated with severity in invasive community-acquired *Staphylococcus aureus* infections in children: a prospective European multicentre study' Clinical Microbiology and Infection 2016: volume 22, issue 7, pages 643 e1 to 643

Gill SK and others. 'Multiple prostatic abscesses presenting with urethral discharge' Genitourinary medicine 1991, volume 67, issue 5, pages 411 to 412

Gonzalez BE and others. 'Panton-Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* necrotising pneumonia presenting as fever of unknown origin' Infectious Diseases in Clinical Practice 2009: volume 17, pages 55 to 57

Green K and others. 'Panton-Valentine Leukocidin Producing *Staphylococcus aureus* Facial Pyomyositis Causing Partial Cavernous Sinus Thrombosis' Pediatric Infectious Disease Journal 2017: volume 36, issue 11, pages 1,102 to 1,104

Groselj-Grenc M and others. 'Successful use of venovenous extracorporeal membranous oxygenation in a 22-month old boy with necrotising pneumonia, osteomyelitis and septic shock caused by Panton-Valentine leukocidin - producing *Staphylococcus aureus*' Signa Vitae 2011: volume 6, pages 82 to 85

Haider S and others. 'Panton-Valentine leukocidin Staphylococcus causing fatal necrotising pneumonia in a young boy' BMJ Case Reports 2013: volume 14, page 14

Hall MJ and others. 'Panton-Valentine leukocidin *Staphylococcus aureus* osteomyelitis of the adult tibia--a case report' Annals of the Royal College of Surgeons of England 2010: volume 92, issue 2, pages W17 to 19

Hardgrib N and others. 'Life-threatening MRSA sepsis with bilateral pneumonia, osteomyelitis, and septic arthritis of the knee in a previously healthy 13-year-old boy: a case report' Acta Radiologica Open 2016: volume 5, issue 10

Hardy C and others. 'Bone and joint infections with *Staphylococcus aureus* strains producing Panton-Valentine Leukocidin in French Guiana' Medicine 2019: volume 98, issue 27, page e16015

Have KLV and others. 'Community-associated Methicillin-resistant *Staphylococcus aureus* in Acute Musculoskeletal Infection in Children: A Game Changer' Journal of Pediatric Orthopaedics 2009: volume 29, issue 8, pages 927 to 931

Heelan K and others. 'Panton-Valentine leukocidin-producing Staphylococcal aureus: report of four siblings' Pediatric Dermatology 2012: volume 29, issue 5, pages 618 to 620

Hilton B and others. 'Necrotising pneumonia caused by non-PVL *Staphylococcus aureus* with 2-year follow-up' BMJ Case Reports 2017: volume 7, page 7

Ho PL and others. 'DNA typing of cytological samples for retrospective identification of an early case of Panton-Valentine leucocidin-positive, community-associated methicillin-resistant *Staphylococcus aureus* pneumonia' Journal of Clinical Microbiology 2008: volume 46, issue 7, pages 2,457 to 2,458

Hussain A and others. 'Purpura fulminans in a child secondary to Panton-Valentine leukocidin-producing *Staphylococcus aureus*' Journal of Medical Microbiology 2007: volume 56, pages 1,407 to 1,409

Hyvernat H and others. 'Fatal *Staphylococcus aureus* haemorrhagic pneumonia producing Panton-Valentine leucocidin' Scandinavian Journal of Infectious Diseases 2007: volume 39, issue 2, pages 183 to 185

Ionescu MD and others. 'Evolutionary Particularities in a Case of Severe Pneumonia in Children - Case Report' Medica 2018: volume 13, issue 1, pages 55 to 60

Jagernauth S and others. 'Subscapularis pyomyositis: a rare presentation of shoulder pain' BMJ Case Reports 2018: volume 16, page 16

Johnston JN and others. 'Characterization of *Staphylococcus aureus* infections in children with Down syndrome' Journal of Infection and Chemotherapy 2015: volume 21, issue 11, pages 790 to 794

Khalid M and others. 'Invasive Community Acquired Methicillin-Resistant Staphylococcal Aureus (CA-MRSA) Infections in Children' Jcpsp, Journal of the College of Physicians and Surgeons - Pakistan 2018: volume 28, issue 9, pages S174 to S177

Khattak SG and others. 'Unusual presentation of late-onset disseminated staphylococcal sepsis in a preterm infant' BMJ Case Reports 2019: volume 12, issue 3, page 15

Kreienbuehl L and others. 'Community-acquired necrotising pneumonia due to methicillin-sensitive *Staphylococcus aureus* secreting Panton-Valentine leukocidin: a review of case reports' Annals of Intensive Care 2011: volume 1, issue 1, page 52

Lemaitre C and others. 'Necrotising pneumonia in children: report of 41 cases between 2006 and 2011 in a French tertiary care center' Pediatric Infectious Disease Journal 2013: volume 32, issue 10, pages 1,146 to 1,149

Low TB and others. 'Panton-Valentine leukocidin MSSA leading to multi-organ failure' Irish Medical Journal 2009: volume 102, issue 6

Matsumoto CT and others. 'Rapidly fatal tropical pyomyositis in an elderly diabetic woman' International Journal of Infectious Diseases 2021: volume 104, pages 677 to 679

McDonald JE and others. 'Upper-Extremity Deep Venous Thrombosis Associated with Proximal Humeral Osteomyelitis in a Child A Case Report' Journal of Bone and Joint Surgery-American Volume 2010: volume 92, issue 11, pages 2,121 to 2,124

Melendez J and others. 'MRSA bacteraemia after caesarean section wound infection: When screening is missed and things go wrong' Archives of Gynecology and Obstetrics 2012: volume 285, pages 663 to 665

Mercieri N and others. 'Critical pneumonia complicating early-stage pregnancy' Anesthesia and Analgesia 2010: volume 110, issue 3, pages 852 to 854

Mitchell PD and others. 'Panton-Valentine leukocidin-secreting *Staphylococcus aureus* causing severe musculoskeletal sepsis in children. A new threat' Journal of Bone and Joint Surgery - British Volume 2007: volume 89, issue 9, pages 1,239 to 1,242

Mutale W and others. 'Community acquired Panton-Valentine Leukocidin (PVL) positive Methicilin Resistant Staphylococcal aureus cerebral abscess in an 11-month old boy: a case study' BMC Research Notes 2014: volume 7, page 862

Noguchi Y and others. 'An infant with necrotising pneumonia caused by methicillin-resistant *Staphylococcus aureus* strain USA300' Pediatrics International 2022: volume 64, issue 1, page e14658

Noor M and others. 'Panton-valentine leukocidin staphylococcus causing necrotising pneumonia in a young male' Journal of Anesthesia and Critical Care: Open access 2021: volume 13, issue 3, pages 124 to 127

Obando I and others. 'Necrotising pneumonia due to influenza A (H1N1) and community-acquired methicillin-resistant *Staphylococcus aureus* clone USA300: successful management of the first documented paediatric case' Archives of Disease in Childhood 2010: volume 95, issue 4, pages 305 to 306

Ono R and others. '*Staphylococcus aureus* Bacteremia With Disseminated Multiple Foci and Pyomyositis in an Immunocompetent Patient: A Case Report' Cureus 2024: volume 16, issue 2, page e53483

Patel K and others. 'Subscapular Abscess Caused by Panton-Valentine Leukocidin-Positive *Staphylococcus aureus*: An Atypical Presentation' Case Reports in Orthopedics 2018: volume 2018, page 8256428

Paul M and others. 'Panton-valentine leukocidin producing *Staphylococcus aureus* pneumonia with pneumatocele, formation: A fatal complication after influenza in an immunocompetent patient' Chest 2007: volume 132, issue 4, pages 709S to 710S

Penn-Barwell JG and others. 'PVL *Staphylococcus aureus* osteomyelitis complicating septic arthritis in a UK soldier serving in Iraq' Journal of the Royal Army Medical Corps 2009: volume 155, issue 3, pages 208 to 209

Poli EC and others. 'Clindamycin clearance during hemoadsorption: A case report and pharmacokinetic study' International Journal of Artificial Organs 2019: volume 42, issue 5, pages 258 to 262

Puthiyaveetil SA. 'Osteomyelitis A case report' Australian Family Physician 2009: volume 38, issue 7, pages 521 to 523

Rafai M and others. 'Evolution of a fatal septic arthritis caused by a Panton-Valentine leukocidin (PVL)-producing *Staphylococcus aureus* strain' Joint, Bone, Spine: Revue du Rhumatisme 2013: volume 80, issue 5, pages 525 to 527

Raghavan S and others. 'Intracranial thrombosis associated with MSSA bacteraemia in the setting of influenza A' BMJ Case Reports 2021: volume 14, issue 4, page 22

Rouzic N and others. 'Prompt and successful toxin-targeting treatment of three patients with necrotising pneumonia due to *Staphylococcus aureus* strains carrying the Panton-Valentine leukocidin genes' Journal of Clinical Microbiology 2010: volume 48, issue 5, pages 1,952 to 1,955

Rubinacci V and others. 'Necrotising pneumonia in a preterm baby' Pediatric Pulmonology 2025, volume 60, issue 1, page e27350

Shedek BK and others. 'Community-associated methicillin-resistant *Staphylococcus aureus* pyomyositis complicated by compartment syndrome in an immunocompetent young woman' American Journal of Emergency Medicine 2008: volume 26, issue 6, pages 737.e733 to 737.e34

Shiiba R and others. 'A case of community-acquired Panton-Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* (MRSA) necrotising pneumonia successfully treated with two anti-MRSA drugs' Respiratory Medicine Case Reports 2024: volume 49, 102023

Sohoni A and others. 'A cluster of fulminant, fatal necrotising community-associated methicillin-resistant *Staphylococcus aureus* pneumonias' American Journal of Critical Care 2013: volume 22, issue 4, pages 364 to 367

Takadama S and others. 'A case of acute septic arthritis of the hip joint caused by Panton-Valentine leukocidin-positive ST772 community-acquired methicillin-resistant *Staphylococcus aureus*' Journal of Infection and Chemotherapy 2019: volume 25, issue 3, pages 212 to 214

Takemori T and others. 'A rare case of acute osteomyelitis due to Panton-Valentine leukocidin-positive community-acquired methicillin-resistant *Staphylococcus aureus* in a young healthy adult' International Journal of Surgery Case Reports 2017, volume 33, pages 4 to 7

Terata K and others. 'Multidisciplinary treatment for infective endocarditis complicated with systemic multiple abscess due to Panton-Valentine leukocidin producing community-acquired methicillin-resistant *Staphylococcus aureus* and Candida albicans: a case report' General Thoracic and Cardiovascular Surgery Cases 2023: volume 2, issue 1, page 36

Thapaliya D and others. 'Epidemiology of necrotising infection caused by *Staphylococcus aureus* and Streptococcus pyogenes at an Iowa hospital' Journal of Infection and Public Health 2015: volume 8, issue 6, pages 634 to 641

Thomas B and others. 'Pleuropulmonary complications of PVL-positive *Staphylococcus aureus* infection in children' Acta paediatrica (Oslo, Norway: 1992) 2009: volume 98, issue 8, pages 1,372 to 1,375

Trieu TV and others. 'Sudden death caused by *Staphylococcus aureus* carrying Panton-Valentine leukocidin gene in a young girl' BMJ Case Reports 2009

Tseng MH and others. 'Fatal sepsis and necrotising pneumonia in a child due to community-acquired methicillin-resistant *Staphylococcus aureus*: case report and literature review' Scandinavian Journal of Infectious Diseases 2005: volume 37, issue 6, pages 504 to 507

Ünal A and others. 'Septic pulmonary embolism associated with *Staphylococcus aureus*: case series and review of the literature' Journal of tropical pediatrics 2025: volume 71, issue 2

Vamsidhar V and others. 'Bilateral subretinal abscess in community-acquired meticillin-susceptible *Staphylococcus aureus* infection' Journal of the Royal College of Physicians of Edinburgh 2020: volume 50, issue 1, pages 42 to 45

van Eck J and others. 'Necrotising pneumonia after COVID-19 infection due to Panton-Valentine Leucocidin-producing, methicillin-susceptible *Staphylococcus aureus*' Clinical Infection in Practice 2023: volume 20, 100241

Van Gasse N and others. 'Recurrent Skin Abscesses Caused by Panton-Valentine Leukocidin-Producing Methicillin-Susceptible *Staphylococcus aureus*' Clinical Microbiology Newsletter 2009: volume 31, pages 172 to 174

Venkatesh J and others. 'Panton-valentine Leucocidin (PVL) Pneumonia: Case report' Scottish Medical Journal 2010: volume 55, issue 2

Wrong intervention (27 studies)

Alawad MJ and others. 'Catastrophic complications of PVL-MRSA necrotising pneumonia presenting as respiratory failure and rhabdomyolysis, case report and review of the literature' Clinical Case Reports 2023: volume 11, issue 5, page e6809

Baba-Moussa L and others. 'Nosocomial Pneumonia Associated to PVL-Producing *Staphylococcus aureus* in Children in Benin' ISRN Infectious Diseases 2013: volume 2013, page 45839

Banthia S and others. 'A fatal case of necrotising pneumonia caused by community-associated methicillin-resistant *Staphylococcus aureus*' Infectious Diseases in Clinical Practice 2005: volume 13, pages 132 to 138

Broadfield E and others. 'Cunning and community-acquired pneumonia' The Lancet 2009: volume 373, page 270

Catena V and others. 'Necrotising pneumonia caused by Panton-Valentine leukocidin-producing methicillin-susceptible *Staphylococcus aureus* (MSSA)' Infezioni in Medicina 2012: volume 20, issue 3, pages 205 to 210

Cuddihy J and others. 'Near-fatal Panton-Valentine leukocidin-positive *Staphylococcus aureus* pneumonia, shock and complicated extracorporeal membrane oxygenation cannulation: A case report' World Journal of Critical Care Medicine 2021: volume 10, issue 5, pages 301 to 309

Fitzgerald F and others. 'Back pain in a previously healthy teenager' BMJ Case Reports 2013: pages 1 to 2

Hoehn K and others. 'Lemierre-like syndrome caused by community-associated methicillin-resistant *Staphylococcus aureus* complicated by hemorrhagic pericarditis' Pediatric Critical Care Medicine 2010: volume 11, issue 3, pages e32 to e35

Hoppe PA and others. 'Severe infections of Panton-Valentine leukocidin positive *Staphylococcus aureus in children*' Medicine 2019: volume 98, issue 38, page e17185

Imauven O and others. 'Paediatric and adult patients from New Caledonia Island admitted to the ICU for community-acquired Panton-Valentine leucocidin-producing *Staphylococcus aureus* infections' Scientific Reports 2022: volume 12, issue 1, article number 11024

Jorda Gomez P and others. 'Osteomyelitis, Venous Thrombosis, and Septic Emboli in a Pediatric Patient: A Case Report' Plastic Surgical Nursing 2020: volume 40, issue 4, pages 197 to 201

Lorenz U and others. 'Severe pyomyositis caused by Panton-Valentine leucocidin-positive methicillin-sensitive *Staphylococcus aureus* complicating a pilonidal cyst' Langenbecks Archives of Surgery 2007: volume 392, issue 6, pages 761 to 765

McAdams RM and others. 'Necrotising staphylococcal pneumonia in a neonate' Journal of Perinatology 2005: volume 25, issue 10, pages 677 to 679

McGuire E and others. 'Is Panton-Valentine leucocidin (PVL) toxin associated with poor clinical outcomes in patients with community-acquired *Staphylococcus aureus* bacteraemia?' Journal of Medical Microbiology 2023: volume 72, issue 4

Miller LG and others. 'Necrotising fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles' New England Journal of Medicine 2005: volume 352, issue 14, pages 1,445 to 1,453

Nguyen E and others. 'Community-acquired methicillin-resistant *Staphylococcus aureus* pneumonia radiographic and computed tomography findings' Journal of Thoracic Imaging 2008: volume 23, pages 13 to 19

Noah MA and others. 'Panton-Valentine leukocidin expressing *Staphylococcus aureus* pneumonia managed with extracorporeal membrane oxygenation: experience and outcome' Critical Care Medicine 2010: volume 38, issue 11, pages 2,250 to 2,253

Ogata H and others. 'Psoitis and multiple venous thromboses caused by Panton-Valentine Leukocidin-positive methicillin-sensitive *Staphylococcus aureus* in a 12-year-old girl: A case report' Journal of Infection and Chemotherapy 2019: volume 25, issue 8, pages 630 to 634

Peyrani P and others. 'Severity of disease and clinical outcomes in patients with hospital-acquired pneumonia due to methicillin-resistant *Staphylococcus aureus* strains not influenced by the presence of the Panton-Valentine leukocidin gene' Clinical Infectious Diseases 2011: volume 53, issue 8, pages 766 to 771

Prabha N and others. 'PVL PRODUCING MRSA OSTEOMYELITIS IN NEONATE - A RARE' 2014

Qu T and others. 'Whole genome analysis of a community-associated methicillin-resistant *Staphylococcus aureus* ST59 isolate from a case of human sepsis and severe pneumonia in China' PLoS ONE [Electronic Resource] 2014: volume 9, issue 2, e89235

Rasigade J-P and others. 'A history of Panton-Valentine leukocidin (PVL)-associated infection protects against death in PVL-associated pneumonia' Vaccine 2011: volume 29, issue 25, pages 4,185 to 4,186

Sicot N and others. 'Methicillin resistance is not a predictor of severity in community-acquired *Staphylococcus aureus* necrotising pneumonia--results of a prospective observational study' Clinical Microbiology and Infection 2013: volume 19, issue 3, pages E142 to E148

Vanhecke C and others. 'Retrospective study of pneumonia due to Panton-Valentine leukocidin-producing *Staphylococcus aureus* in Reunion' Medecine et Maladies Infectieuses 2019: volume 49, issue 7, pages 534 to 539

Van Nieuwenhuyse B and others. 'Case report: Personalized triple phage-antibiotic combination therapy to rescue necrotising fasciitis caused by Panton-Valentine leukocidin-producing MRSA in a 12-year-old boy' Frontiers in Cellular and Infection Microbiology 2024: volume 14, 1354681

Vayalumkal JV and others. 'Necrotising pneumonia and septic shock: suspecting CA-MRSA in patients presenting to Canadian emergency departments' CJEM Canadian Journal of Emergency Medical Care 2007: volume 9, issue 4, pages 300 to 303

Zhang L and others. 'A fatal case of pneumonia and sepsis caused by sequence type 398 methicillin-susceptible *Staphylococcus aureus* carrying Pantone-Valentine leukocidin in China' Journal of Infection and Chemotherapy 2022: volume 28, issue 9, pages 1,329 to 1,331

No relevant outcomes (20 studies)

Adeyemi OA and others. 'Invasive infections with community-associated methicillin-resistant *Staphylococcus aureus* after kidney transplantation' Journal of Clinical Microbiology 2008: volume 46, issue 8, pages 2,809 to 2,813

Albinski MK and others. 'Paediatric musculoskeletal infections with Panton-Valentine leucocidin' Swiss Medical Weekly 2018: volume 148, page w14669

Antonelou M and others. 'Recurrent cutaneous abscesses caused by PVL-MRSA' BMJ Case Reports 2011: volume 29, page 29

Blaine KP and others. 'Progression to bacteremia in critical care patients colonized with methicillin-resistant *Staphylococcus aureus* expressing Panton-Valentine leukocidin' Diagnostic Microbiology and Infectious Disease 2010: volume 68, issue 1, pages 28 to 33

Brust T and others. 'Hospital-associated methicillin-resistant *Staphylococcus aureus* carrying the PVL gene outbreak in a Public Hospital in Rio de Janeiro, Brazil' Brazilian journal of microbiology : [publication of the Brazilian Society for Microbiology] 2014: volume 44, issue 3, pages 865 to 868

Clerc A and others. 'Hematogenous osteomyelitis in childhood can relapse many years later into adulthood: A retrospective multicentric cohort study in France' Medicine 2020: volume 99, issue 20, e19617

Cocchi P and others. 'Evidence of transmission of a Panton-Valentine leukocidin-positive community-acquired methicillin-resistant *Staphylococcus aureus* clone: a family affair' Clinical Microbiology and Infection 2013: volume 19, issue 12, pages 1,158 to 1,162

Cupane L and others. 'Patients with Panton-Valentine leukocidin positive *Staphylococcus aureus* infections run an increased risk of longer hospitalisation' International Journal of Molecular Epidemiology and Genetics 2012: volume 3, issue 1, pages 48 to 55

Dohin B and others. 'Pediatric bone and joint infections caused by Panton-Valentine leukocidin-positive *Staphylococcus aureus*' Pediatric Infectious Disease Journal 2007: volume 26, issue 11, pages 1,042 to 1,048

Gilbert M and others. 'Outbreak in Alberta of community-acquired (USA300) methicillin-resistant *Staphylococcus aureus* in people with a history of drug use, homelessness or incarceration' CMAJ Canadian Medical Association Journal 2006: volume 175, issue 2, pages 149 to 154

Gillet Y and others. 'Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients' Lancet 2002: volume 359, issue 9308, pages 753 to 759

Gillet Y and others. 'Prognostic factors of severe community-acquired staphylococcal pneumonia in France' European Respiratory Journal 2021: volume 58, issue 5, page 11

Le Thomas I and others. 'Breast milk transmission of a Panton-Valentine leukocidin-producing *Staphylococcus aureus* strain causing infantile pneumonia' Journal of Clinical Microbiology 2001: volume 39, issue 2, pages 728 to 729

Lee T-M and others. 'Molecular Characterization of Community- and Healthcare-Associated Methicillin-Resistant *Staphylococcus aureus* Isolates in Southern Taiwan' Microbial Drug

Resistance-Mechanisms Epidemiology and Disease 2015: volume 21, issue 6, pages 610 to 621

Nickerson EK and others. 'Factors predicting and reducing mortality in patients with invasive *Staphylococcus aureus* disease in a developing country' PLoS ONE [Electronic Resource] 2009: volume 4, issue 8, e6512

Pardo L and others. 'Community-associated methicillin-resistant *Staphylococcus aureus* in children treated in Uruguay' Journal of Infection in Developing Countries 2013: volume 7, issue 1, pages 10 to 16

Rose HR and others. 'Cytotoxic Virulence Predicts Mortality in Nosocomial Pneumonia Due to Methicillin-Resistant *Staphylococcus aureus*' Journal of Infectious Diseases 2015: volume 211, issue 12, pages 1,862 to 1,874

Tadros M and others. 'Epidemiology and outcome of pneumonia caused by methicillin-resistant *Staphylococcus aureus* (MRSA) in Canadian hospitals' PLoS ONE [Electronic Resource] 2013: volume 8, issue 9, e75171

Trobisch A and others. 'Osteoarticular Infections in Pediatric Hospitals in Europe: A Prospective Cohort Study From the EUCLIDS Consortium' Frontiers in Pediatrics 2022: volume 10, 744182

Zhang C and others. 'Presence of the Panton-Valentine Leukocidin Genes in Methicillin-Resistant *Staphylococcus aureus* Is Associated with Severity and Clinical Outcome of Hospital-Acquired Pneumonia in a Single Center Study in China' PLoS ONE [Electronic Resource] 2016: volume 11, issue 6, e0156704

Annexe E. Data extraction tables

Table E.1. Data extraction table of observational studies in adults

Abbreviations: ICU: intensive care unit, PVL-SA: Panton-Valentine leukocidin *Staphylococcus aureus,* UK: United Kingdom

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Beaumont 2024 (1)	UK, July 2018 to July 2022	Case 1: Age and sex not reported (age range: 33 to 51 years) History of drug use Medical history: previous infective endocarditis, hepatitis C, pulmonary embolus	Bacteraemia	Initial treatment: • rifampicin, daptomycin and benzylpenicillin Switched to: • rifampicin and cotrimoxazole Total duration of antibiotic treatment: 6 weeks (dosage not reported)		Case recovered
		Case 2: Age and sex not reported (age range: 33 to 51 years) History of drug use Medical history: previous infective endocarditis and empyema	• bacteraemia • groin abscess • sepsis	Clindamycin and teicoplanin (dosage not reported)	ICU admission	Case died
		Case 3: Age and sex not reported (age range: 33 to 51 years) History of drug use	• osteomyelitis • spinal abscess	Initial treatment: • teicoplanin and rifampicin Switched to: • fusidic acid and linezolid Total duration of antibiotic treatment: 6 weeks (dosage not reported)		Case recovered
		Case 4: Age and sex not reported (age range: 33 to 51 years) History of drug use Medical history: asthma, previous septic arthritis	Pneumonia	Initial treatment: • linezolid Switched to: • teicoplanin and rifampicin Switched to: • daptomycin, rifampicin • clindamycin (dosage not reported)	• ICU admission • intubation and ventilation • vasopressor support • multi-organ failure	Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Case 5: Age and sex not reported (age range: 33 to 51 years) History of drug use Medical history: groin abscess	Pneumonia	Initial treatment: • vancomycin, rifampicin and linezolid Switched to: • daptomycin, rifampicin and linezolid (dosage not reported)		Case recovered

Table E.2. Data extraction table of case series in adults

Abbreviations: ECMO: extracorporeal membrane oxygenation, HIV: human immunodeficiency virus, ICU: intensive care unit, gm: gram, IV: intravenous, mg: milligram, MRSA: methicillin-resistant *Staphylococcus aureus*, PVL-SA: Panton-Valentine leukocidin *Staphylococcus aureus*, UK: United Kingdom, USA: United States of America

Study	Country, time period	Population (query separate)	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Hanratty 2015 (7)	UK, 2013	Case 1: Age: 44 years Sex: female Ethnicity not reported Medical history: alcohol abuse and suicidal attempts, admitted to hospital for septic shock and cellulitis	Lung abscess	Initial empiric treatment: • clindamycin IV 600mg every 6 hours • flucloxacillin 2,000mg every 6 hours • metronidazole 500mg every 8 hours On day 5: • clindamycin switched to linezolid IV 600mg every 12 hours • rifampicin 450mg every 12 hours (added to treatment regimen) On day 7: • metronidazole stopped On day 11: • moxifloxacin IV 500mg once daily added to flucloxacillin and linezolid	• ICU admission • multi-organ failure • dialysis	Case died
		Case 2: Age: 32 years	• abscess	Initial empiric treatment:	• ICU admission	Case recovered

Study	Country, time period	Population (query separate)	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Sex: female Ethnicity not reported Medical history: hepatitis C, self-harm and alcohol and IV drug dependence	• ventilator-associated pneumonia	• benzyl penicillin IV 1.2gm every 6 hours • metronidazole 500mg every 8 hours • later, flucloxacillin IV 2gm every 6 hours and clindamycin 1,200mg every 6 hours added to treatment regimen Switched to: • piperacillin-tazobactam 4.5gm every 8 hours • gentamicin 280mg once daily • vancomycin IV 1gm twice daily • vancomycin changed to linezolid IV 600mg every 12 hours (for better lung penetration)	• mechanical ventilation	
Hayakawa 2020 (8)	Japan, time period not reported	Case 1: Age: 20 years Sex: male Ethnicity: Nepalese Medical history: no significant medical history	Necrotising pneumonia	Initial empiric treatment: • tazobactam-piperacillin IV 4.5gm 4 times daily • azithromycin IV 500mg once daily Switched to: • tazobactam-piperacillin IV 4.5gm 4 times a day • azithromycin IV 500mg once daily • linezolid IV 600mg twice daily	• mechanical ventilation • vasopressors (noradrenaline) administered • veno-venous ECMO	Case died
		Case 2: Age: 61 years Sex: female Ethnicity: Nepalese	Necrotising pneumonia	Initial treatment: • ceftriaxone IV 1gm twice a day • linezolid IV 600mg twice a day		Case recovered

Study	Country, time period	Population (query separate)	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: no significant medical history		On day 2 of hospital admission, linezolid was replaced with vancomycin IV (1gm twice a day) due to allergy complications		
Kravitz 2005 (9)	USA, 2000 to 2004	Case 1: Age: 40 years Sex: female Ethnicity not reported Medical history: chronic back pain	Purpura fulminans	Initial empiric treatment: • ceftriaxone IV 2gm (frequency not reported) Switched to: • nafcillin IV 2gm every 4 hours • evofloxacin 250mg once daily	• ICU admission • intubation • vasopressors (dopamine) administered	Case died
		Case 2: Age: 34 years Sex: female Ethnicity not reported Medical history: More than 20 years history of juvenile rheumatoid arthritis	Purpura fulminans	• vancomycin • gentamicin • gatifloxacin • fluconazole (dosage not reported)	• hemodialysis • renal failure	Case died
		Case 3 (Patient 4 as reported by case series): Age: 21 years Sex: male Ethnicity not reported Medical history: no significant medical history	• purpura fulminans • necrotising pneumonia	• cefotaxime • azithromycin • gatifloxacin (dosage not reported)	• ICU admission • intubation	Case died
Lin 2008 (10)	USA, December 2005 to February 2007	Case 1: Age: 36 years Sex: male Ethnicity not reported Medical history: obesity, type 2 diabetes	• pyomyositis • bacteraemia	Vancomycin for 6 weeks (dosage not reported)		Case recovered
		Case 2:	• prostatic abscess	Vancomycin for 4 weeks		Case recovered

Study	Country, time period	Population (query separate)	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Age: 55 years Sex: male Ethnicity not reported Medical history: hypertension, benign prostatic hypertrophy and chronic rectal haemorrhoids	• bacteraemia	(dosage not reported)		
		Case 3: Age: 46 years Sex: male Ethnicity not reported Medical history: no significant medical history	• pyomyositis • osteomyelitis • bacteraemia	Initial empiric treatment: vancomycin for 5 days Switched to: trimethoprim-sulfamethoxazole IV due to suspected drug fever for 6 weeks (dosage not reported)		Case recovered
		Case 4: Age: 65 years Sex: male Ethnicity not reported Medical history: history of alcoholism, homelessness and assault	• pyomyositis • bacteraemia	Vancomycin for 6 weeks (dosage not reported)		Case recovered
Micek 2005 (12)	USA, November 2004 to February 2005	Case 1: Age: 21 years Sex: male Ethnicity not reported Medical history: no significant medical history	• purpura fulminans • necrotising pneumonia	• cefotaxime • azithromycin • gatifloxacin (dosage not reported)	• ICU admission • intubation	Case died
		Case 2: Age: 34 years Sex: male Ethnicity not reported Medical history: history of cocaine and heroin use	Pneumonia	Initial empiric treatment: • ceftriaxone and azithromycin (dosage not reported) Switched to (after ICU admission): • vancomycin 1g twice daily Switched to:	• ICU admission • tracheal intubation and mechanical ventilation	Case recovered

Study	Country, time period	Population (query separate)	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				• linezolid 600mg twice daily for 4 days Moved back to vancomycin with the addition of clindamycin 900mg every 8 hours Total antibiotic course: 14 days		
		Case 3: Age: 40 years Sex: male Ethnicity not reported Medical history: 6 years history of insulin dependent diabetes mellitus and abuse of alcohol and cocaine	Pneumonia	Initial empiric treatment (for pancreatitis): • imipenem (dosage not reported) • on day 3 after intubation: vancomycin 1.5gm twice daily Switched to: • linezolid 600mg twice daily for 14 days • rifampicin 300mg every 8 hours for 14 days	• ICU admission • intubation and mechanical ventilation • haemodialysis for acute renal failure	Case recovered
Osterlund 2002 (13)	Sweden, March 2001 and March 2002	Case 1: Age: 32 years Sex: female Ethnicity not reported Medical history: influenza-like symptoms one week before admission	• pneumonia • septicaemia	Clindamycin (dosage not reported)	• ICU admission • mechanical ventilation	Case recovered
Toro 2014 (16)	Canada, May 2004 to October 2011	Case 1: Age: 34 years Sex: female Ethnicity: not reported Medical history: MRSA risk factors (illicit drug use)	• necrotising pneumonia • bacteraemia	• vancomycin • clindamycin • linezolid (dosage not reported)	• ICU admission • chest tube placement • multi-organ failure	Case died
		Case 2: Age: 38 years Sex: male Ethnicity: not reported	Necrotising pneumonia	Vancomycin and linezolid (dosage not reported)	Chest tube placement	Case recovered

Study	Country, time period	Population (query separate)	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: MRSA risk factors (illicit drug use)				
		Case 3: Age: 68 years Sex: male Ethnicity: not reported Medical history: cardiac disease, diabetes mellitus, hypertension and MRSA risk factors (illicit drug use)	• necrotising pneumonia • bacteraemia	Vancomycin and linezolid (dosage not reported)	Chest tube placement	Case recovered
		Case 4: Age: 36 years Sex: male Ethnicity: not reported Medical history: hepatitis C and MRSA risk factors (illicit drug use)	• necrotising pneumonia • lung abscess	Vancomycin (dosage not reported)	• ICU admission • chest tube placement • multi-organ failure	Case died
		Case 5: Age: 48 years Sex: female Ethnicity: not reported Medical history: hepatitis C and MRSA risk factors (illicit drug use)	• necrotising pneumonia • bacteraemia • lung abscess	Vancomycin and linezolid (dosage not reported)	• ICU admission • chest tube placement	Case recovered
		Case 6: Age: 37 years Sex: male Ethnicity: not reported Medical history: hepatitis C and HIV	Necrotising pneumonia	Trimethoprim-sulfamethoxazole (dosage not reported)		Case recovered
		Case 7: Age: 41 years Sex: female Ethnicity: not reported	• necrotising pneumonia • bacteraemia	Vancomycin and trimethoprim sulfamethoxazole (dosage not reported)		Case recovered

Study	Country, time period	Population (query separate)	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: MRSA risk factors (illicit drug use)				
		Case 8: Age: 71 years Sex: female Ethnicity: not reported Medical history: hypertension	• necrotising pneumonia • bacteraemia • lung abscess	Vancomycin and linezolid (dosage not reported)	ICU admission	Case recovered
		Case 9: Age: 44 years Sex: male Ethnicity: not reported Medical history: no significant medical history	• necrotising pneumonia • bacteraemia	Vancomycin and linezolid (dosage not reported)	• ICU admission • chest tube placement	Case recovered
		Case 10: Age: 34 years Sex: male Ethnicity: not reported Medical history: hepatitis C and MRSA risk factors (illicit drug use)	• necrotising pneumonia • bacteraemia	• vancomycin • clindamycin • linezolid (dosage not reported)	Chest tube placement	Case recovered
Young 2008 (17)	USA, January 1 2004 to February 28 2006	Case 1: Age: 32 years Sex: male Ethnicity: white Medical history: no significant medical history	• necrotising fasciitis • bacteraemia	• initial empiric treatment: nafcillin • vancomycin added to treatment regimen after 12 hours (dosage not reported)		Case recovered
		Case 2: Age: 55 years Sex: Female Ethnicity: African American	Necrotising fasciitis	Empiric treatment: penicillin G, nafcillin, and clindamycin (dosage not reported)		Case recovered

Study	Country, time period	Population (query separate)	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: diabetes mellitus, hypertension and coronary artery disease				
		Case 3: Age: 29 years Sex: male Ethnicity: white Medical history: nephrolithiasis and depression	Necrotising fasciitis	Initial empiric treatment: • cefazolin and clindamycin Switched to: • vancomycin and clindamycin (dosage not reported)		Case recovered

Table E.3. Data extraction table of case reports in adults

Abbreviations: CVVH: continuous veno-venous hemofiltration, DIC: disseminated intravascular coagulation, ECMO: extracorporeal membrane oxygenation, HIV: human immunodeficiency virus, ICU: intensive care unit, gm: gram, IV: intravenous, kg: kilogram, mg: milligram, min: minute, MRSA: methicillin-resistant *Staphylococcus aureus*, PVL-SA : Panton-Valentine leukocidin *Staphylococcus aureus*, RICU: respiratory intensive care unit, UK: United Kingdom, USA: United States of America

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Alonso-Tarres 2005 (19)	Spain, time period not reported	Sample size: 1 Age: 28 years Sex: male Ethnicity not reported Medical history: no significant medical history	Necrotising pneumonia	Initial treatment in ICU: • cloxacillin IV 2gm every 4 hours • gentamicin 240gm every 24 hours On day 6: • levofloxacin 500mg every 12 hours for 6 days and then every 24 hours added to treatment On day 19: • oral linezolid 600mg every 12 hours substituted for cloxacillin and levofloxacin	ICU admission	Case recovered
Al- Talib 2011 (20)	Malaysia, August 2009	Sample size: 1 Age range: 29 years Sex: male Ethnicity not reported	Necrotising pneumonia	Ceftriaxone IV 1gm twice daily for 12 days	• ICU admission • mechanical ventilation	Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history not reported, no pulmonary or systemic signs of infection upon hospital admission				
Carroll 2017 (25)	Australia, time period not reported	Sample size: 1 Age: 53 years Sex: male Ethnicity: Indigenous Australian Medical history: history of type 2 diabetes, chronic hepatitis B infection, recurrent skin and soft tissue infections, long-term kava use	Prostatic abscess	Initial treatment: • vancomycin iv Later: • oral clindamycin added to treatment regimen Total duration of antibiotic therapy: 4 weeks (dosage not reported)		Case recovered
Chen 2024 (27)	China, time period not reported	Sample size: 1 Age: 39 years Sex: female Ethnicity not reported Medical history: no significant medical history	• necrotising pneumonia • sepsis	Initial empiric treatment: • imipenem and moxifloxacin Switched to: • imipenem and linezolid (dosage not reported)	• ICU admission • tracheal intubation and mechanical ventilation • multiple organ dysfunction syndrome • renal replacement therapy	Case died
Chetchotisakd 2007 (29)	Thailand, August 2004	Sample size: 1 Age: 38 years Sex: male Ethnicity: Thai Medical history: history of HIV, tuberculous colitis, candida esophagitis, cryptococcus lymphadenitis and pulmonary rhodococcosis	Necrotising pneumonia	Ceftriaxone and metronidazole iv (dosage not reported)	Intubation	Case died
Conan 2021 (30)	France, time period not reported	Sample size: 1 Age: 20 years Sex: female	Renal abscess	Initial treatment: • cefotaxime IV 1gm 3 times daily		Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Ethnicity not reported Medical history: no significant medical history except for left bifid ureter and urinary symptoms with fever 2 months previously		Switched to: • cefazoline IV 80 mg/kg/day (continuous infusion after a loading dose of 2gm) Switched to (2 days later): • oral clindamycin 600mg 3 times daily for 21 days		
Dhanoa 2012 (32)	Malaysia, time period not reported	Sample size: 1 Age: 28 years Sex: male Ethnicity not reported Medical history: no significant medical history, patient reported prolonged exposure to deer carcass, regular smoker	• osteomyelitis • pyomyositis • septic arthritis • deep-seated tissue abscess • bacteraemia	Initial empiric treatment: • vancomycin IV 1gm twice daily until discharge • fusidic acid (added later) On discharge: • fusidic acid oral 500mg 3 times daily • rifampicin oral 300mg 3 times daily		Case recovered
Dubos 2014 (33)	France, time period not reported	Sample size: 1 Age: 20 years Sex: male Ethnicity not reported Medical history: history of allergic asthma and recurrent furuncles for 1.5 years	• prostatic abscess • sepsis	Initial treatment: • oral ofloxacin Switched to (after 2 days): • ceftriaxone and amikacin iv • ciprofloxacin (added to treatment regimen 6 days later, just before ICU admission) Treatment at ICU: • fosfomycin and ofloxacin IV Switched to (on day 16): • oral rifampicin and ofloxacin Total antibiotic duration: 6 weeks (dosage not reported)	ICU admission	Case recovered
Enany 2007 (35)	Egypt, April 2007	Sample size: 1 Age: 50 years Sex: male Ethnicity: Egyptian	• brain abscess • pneumonia	Vancomycin IV 1gm every 12 hours for 6 weeks	ICU admission	Case died (initially recovered, discharged twice, died after cerebral infarction)

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: history of chronic hepatitis and diabetes				
Enayet 2006 (36)	USA, time period not reported	Sample size: 1 Age: 27 years Sex: female Ethnicity: African-American Medical history: no significant medical history, cared for a patient with history of MRSA one month prior to the development of her symptoms	Pneumonia	• vancomycin IV for 3 days (dosage not reported) On discharge: • high-dose trimethoprim-sulfamethoxazole oral (2 tablets twice daily) for 6 weeks		Case recovered
Fahmy 2008 (38)	USA, time period not reported	Sample size: 1 Age: 39 years Sex: male Ethnicity not reported Medical history: no significant medical history	Pyomyositis	Vancomycin IV for 6 weeks (dosage not reported)		Case recovered
Fernandez 2015 (39)	Argentina, February 2013	Sample size: 1 Age: 50 years Sex: male Ethnicity not reported Medical history: hypertension (on enalapril), overweight	Necrotising pneumonia	Initial empiric treatment: • ceftrixone and clarithromycin Switched to: • vancomycin • piperacillin / tazobactam • clarithromycin (continued) (dosage not reported)	• ICU admission • mechanical ventilation	Case died
Fica 2023 (40)	Chile, 202	Sample size: 1 Age: 37 years Sex: female Ethnicity not reported Medical history: history of hypothyroidism, pregnant female	Bacteraemia	Initial empiric treatment: • ceftriaxone 1gm every 12 hours Switched to: • vancomycin 1.5gm loading dose and then 1gm every 12 hours • continuous infusion of vancomycin (3.5gm in 24 hours) prescribed after 4 days		Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				Switched to: • daptomycin IV 500mg daily (6 mg/kg/day) cefazolin IV 2gm every 8 hours		
Fogo 2011 (41)	UK, time period not reported	Sample size: 1 Age: 39 years old Sex: female Ethnicity: not reported Medical history: no significant medical history	Deep painful abscess	Initial empiric treatment: • flucloxacillin and erythromycin (ineffective) • switched to: rifampicin and clindamycin for 4 weeks (dosage not reported)		Case recovered
Frazee 2005 (42)	USA, February 2005	Sample size: 1 Age: 31 years Sex: male Ethnicity not reported Medical history: no significant medical history, occasionally used alcohol and cocaine	• necrotising pneumonia • sepsis	• piperacillin / tazobactam • levofloxacin • vancomycin (dosage not reported)	Intubation and mechanical ventilation	Case died
Govindan 2012 (45)	India, time period not reported	Sample size: 1 Age: 48 years Sex: Male Ethnicity not reported Medical history: no significant medical history	Necrotising fasciitis	Initial empiric treatment: • augmentin and metronidazole iv Switched to (on day 7): • oral linezolid Switched to (on day 21): • amikacin and ceftazidime IV Switched to (on day 30): • netilmycin IV Switched to (on day 60): • amikacin and clindamycin IV On discharge (day 90): • cotrimoxazole, oral (dosage not reported)		Case recovered
Higashiyama 2010 (47)	Japan, June 2008	Sample size: 1 Age: 25 years Sex: Female	Epidural abscess	Vancomycin and ceftriaxone (dosage not reported)		Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Ethnicity: Caucasian Medical history: no significant medical history				
Honarpour 2007 (48)	USA, time period not reported	Sample size: 1 Age range: 48 years old Sex: female Ethnicity not reported Medical history: no significant medical history	• necrotising pneumonia • sepsis	• piperacillin / tazobactam • vancomycin (dosage not reported)	• intubation • vasopressor support • DIC	Case died
Iwanaga 2013 (51)	Japan, time period not reported	Sample size: 1 Age: 31 years Sex: male Ethnicity: African-American Medical history: no significant medical history	• necrotising pneumonia • osteomyelitis	Initial treatment: • imipenem / cilastatin IV 0.5gm every 6 hours • clindamycin IV 600mg every 12 hours Vancomycin IV 2gm added to treatment on day 3 of hospital admission (frequency not reported)	DIC	Case recovered
Jung 2008 (52)	Germany, October 2006	Sample size: 1 Age: 23 years Sex: female Ethnicity: not reported Medical history: no significant medical history	• necrotising pneumonia • sepsis • muscle abscesses	Initial empiric treatment: • piperacillin / tazobactam and levofloxacin IV for 1 day (dosage and frequency not reported) Switched to (on day 2): • flucloxacillin IV 4gm 3 times daily Switched to (on day 4): • flucloxacillin IV 4gm 3 times daily • rifampicin 600mg for 2 days Main treatment (on day 7): • flucloxacillin IV 4gm 3 times daily for 8 weeks • rifampicin 600mg for 5 weeks	ICU admission	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				• clindamycin 600mg 3 times daily for 5 weeks		
Kuo 2016 (57)	Taiwan, time period not reported	Sample size: 1 Age: 23 years Sex: male Ethnicity: not reported Medical history: no significant medical history	• necrotising pneumonia • pyomyositis	Initial treatment: • teicoplanin, imipenem, and clarithromycin (dosage not reported) Switched to: • oxacillin IV 2gm every 4 hours • linezolid IV 600mg every 12 hours On discharge: • oxacillin for 6 weeks • linezolid for 7 days	• ICU admission • intubation and mechanical ventilation • Vasopressor support	Case recovered
Larsen 2021 (58)	Faroe Islands, time period not reported	Sample size: 1 Age: 47 years Sex: male Ethnicity not reported Medical history: co-infection with Influenza B	Necrotising pneumonia	Initial treatment (on day of hospital admission): • benzylpenicillin IV 1.2gm 4 times daily • ciprofloxacin IV 400mg twice a day Switched to: • meropenem IV 2gm 3 times daily and Ciprofloxacin IV 400mg twice a day Switched to (on day 2): • meropenem IV 2gm 3 times daily • moxifloxacin IV 400mg 3 daily Switched to (on day 4): • meropenem IV 2gm 3 times daily • moxifloxacin IV 400mg once daily • clindamycin IV 600mg 3 times daily Switched to (on day 10):	• ICU admission • intubation and mechanical ventilation • Haemodialysis	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				• meropenem IV 2gm 3 times daily • clindamycin IV 600mg 3 times daily Switched to (on day 13): • clindamycin IV 900mg 3 times daily		
Leung 2024 (61)	Hong Kong, January 2023	Sample size: 1 Age: 38 years Sex: male Ethnicity: Southeast Asian Medical history: chronic smoking and alcohol use, history of asthma, history of lung abscess	Lung abscess	Initial treatment: • metronidazole and ceftriaxone iv Switched to: • vancomycin IV for 4 weeks On discharge: • linezolid oral for 2 weeks (dosage not reported)		Case recovered
Magira 2007 (62)	Greece, time period not reported	Sample size: 1 Age: 61 years Sex: female Ethnicity: Caucasian Medical history: pulmonary tuberculosis (in her teens), hypothyroidism, total hysterectomy 10 years back.	Necrotising pneumonia	• vancomycin • clindamycin • moxifloxacin • ceftriaxone (dosage not reported)	• ICU admission • intubation and mechanical ventilation • vasopressors administered: norepinephrine (0.1 to 0.2 mg/kg/min) and vasopressin (0.02 U/min)	Case died
Mattu 2024 (63)	Canada, time period not reported	Sample size: 1 Age: 29 years Sex: female Ethnicity not reported Medical history: one week previously had a surgical incision of a Bartholin gland abscess (discharged without antimicrobial therapy), no systemic signs of infection	• necrotising pneumonia • abscesses	• dexamethasone • ceftriaxone • azithromycin (dosage not reported)	• ICU admission • intubation • continuous renal replacement therapy • multi-organ failure	Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Morimoto 2024 (66)	Japan, time period not reported	Sample size: 1 Age range: 60 years Sex: male Ethnicity not reported Medical history: hypertension and Stroke	Pneumonia	• sulbactam / ampicillin 3gm every 6 hours • vancomycin 1gm every 12 hours On day 2, switched to: • linezolid 600mg every 12 hours On day 5, antibiotic switched to: • teicoplanin, initially at 400mg every 12 hours and later adjusted to 400mg every 24 hours along with clindamycin 600mg every 6 hours On day 15: • clindamycin discontinued and concomitant tedizolid initiated 200mg every 24 hours	• ventilation • ECMO	Case died
Newell 2023 (68)	UK, time period not reported	Sample size: 1 Age: 35 years Sex: male Ethnicity not reported Medical history: no significant medical history, history of smoking and a fracture to the distal phalanx of hallux	Necrotising pneumonia	Initial empiric treatment: • benzylpenicillin IV and clarithromycin oral Switched to: • co-amoxiclav IV and then switched again to flucloxacillin iv • linezolid added to treatment regimen Later: • flucloxacillin stopped and teicoplanin and rifampicin initiated alongside linezolid (dosage not reported)		Case recovered
Obed 2006 (70)	Germany, time period not reported	Sample size: 1 Age: 51 years Sex: female Ethnicity: not reported	Necrotising pneumonia	Initial treatment: • ceftriaxone and fluconazole Peri-operative prophylaxis: • ceftriaxone for 48 hours Switched to:	• ICU admission • intubation and mechanical ventilation • vasopressor support	Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: decompensated liver cirrhosis due to hepatitis C infection, past medical history not reported		• meropenem and vancomycin (dosage not reported)		
Ote 2023 (73)	Japan, time period not reported	Sample size: 1 Age: 25 years Sex: male Ethnicity not reported Medical history: skin lesions on buttocks since 2020 (self-limiting and healed 3 days prior to Emergency department visit)	• pyomyositis • necrotising pneumonia • bacteraemia	Initial treatment: • cefmetazole 1gm every 8 hours Switched to: • vancomycin 1gm every 12 hours along with continuous IV infusion of heparin Main treatment: • linezolid 600mg every 12 hours • daptomycin 700mg (12 mg/kg) every 24 hours	• ICU admission • intubation and ventilation	Case died
Ramos 2009 (75)	Spain, time period not reported	Sample size: 1 Age: 34 years Sex: male Ethnicity not reported Medical history: recurrent furuncles over last 15 years and history of head trauma at age 16	• parietal osteomyelitis • brain abscess	Initial treatment: • vancomycin 1gm every 12 hours • cefotaxime 2gm every 8 hours • metronidazole 500mg every 8 hours Switched to: • cloxacillin IV 2gm every 4 hours for 4 weeks		Case recovered
Riedweg-Moreno 2014 (78)	France, November 2012	Sample size: 1 Age: 26 years Sex: female Ethnicity not reported Medical history: no significant medical history, coinfection with A/H1N12009 influenza virus	Necrotising pneumonia	• amoxyclavulanate (autoprescribed) • treatment in hospital: oxacillin (during 1 month) clindamycin (during 10 days) (dosage not reported)	• ICU admission • mechanical ventilation	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Roberts 2008 (79)	USA, April 2007	Sample size: 1 Age: 30 years Sex: female Ethnicity: Black Medical history: no significant medical history	Necrotising pneumonia	• ceftriaxone • moxifloxacin • gentamycin • ciprofloxacin • piperacillin-tazobactam (dosage not reported)	• intubation • admission to ICU • vasopressor support	Case died
Schefold 2007 (82)	Germany, time period not reported	Sample size: 1 Age: 51 years Sex: male Ethnicity: Caucasian Medical history: no significant medical history, diagnosed with ARDS	• necrotising pneumonia • sepsis • metastatic soft tissue abscesses	Initial treatment at local hospital: • azithromycin and ciprofloxacin After transfer to tertiary care hospital: • linezolid, imipenem and clindamycin Switched to: • daptomycin and clindamycin (after 2 weeks) On discharge: • oral moxifloxacin for 45 days (dosage not reported)	• mechanical ventilation • vasopressor support	Case recovered
Sifri 2007 (83)	USA, time period not reported	Sample size: 1 Age: 37 years Sex: female Ethnicity not reported History of injection drug use and incarceration	Brain abscess	• vancomycin iv • cefepime (dosage not reported)	• ICU admission • intubation	Case died
Soavi 2011 (84)	Italy, January 2008	Sample size: 1 Age: 49 years Sex: female Ethnicity: Caucasian Medical history: no significant medical history	• necrotising pneumonia • septic shock	Initial treatment: • ampicillin-sulbactam Switched to: • linezolid and levofloxacin Switched to: • vancomycin, rifampicin and caspofungin Later: • linezolid and clindamycin replaced vancomycin and	• ICU admission • intubation and mechanical ventilation • multi-organ failure requiring CVVH	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				rifampicin. Caspofungin was continued (dosage not reported)		
Takigawa 2019 (87)	Japan, February 2017	Sample size: 1 Age: 66 years Sex: male Ethnicity not reported Medical history: heavy smoker (96 pack years), history of pneumonia and acute renal failure in his teens and twenties	Necrotising pneumonia	Initial treatment (before hospital admission): • sulbactam / ampicillin • levofloxacin (dosage not reported) After hospital admission: • vancomycin 1,000 mg/day, later increased to 1,500 mg/day (route of administration not reported) Switched to: • linezolid (MIC 2 µg/mL) on day 27	Clinical support with oxygen (nasal canula)	Case recovered
Torell 2005 (88)	Sweden, March 2005	Sample size: 1 Age: 24 years Sex: female Ethnicity not reported Medical history: no significant medical history apart from recent furunculosis	Pneumonia	First hospital admission: • penicillin G IV 1gm • oral phenoxymethylpenicillin Second admission: • clindamycin iv • oral rifampicin Antibiotics continued after discharge for 3 weeks (dosage not reported)	Clinical support with oxygen (mechanical ventilation not required)	Case recovered
Venugopal 2007 (92)	USA, time period not reported	Sample size: 1 Age: 46 years Sex: female Ethnicity not reported Medical history: chronic hepatitis C, history of injection drug use (heroin)	Psoas abscess	Empirical treatment: • ceftriaxone and azithromycin (dosage not reported) Switched to: • vancomycin IV 750mg every 12 hours for 6 weeks		Case recovered
Wan 2016 (93)	Country and time period not reported	Sample size: 1 Age: 92 years Sex: male	Pneumonia	Initial empiric treatment: • piperacillin (drip infusion) 2gm every 12 hours		Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Ethnicity not reported Medical history: cerebral infarction, diagnosed with Influenza A 2 days before hospital admission		Day 5: • levofloxacin oral 500mg every 24 hours initiated on day 5 of hospital admission		
Xia 2020 (94)	China, time period not reported	Sample size: 1 Age: 68 years Sex: male Ethnicity not reported Medical history: appendectomy, history of 15-pack-year smoking history and long-term alcohol intake 100g/day	Pneumonia	• mezlocillin sodium / sulbactam sodium • linezolid (dosage not reported)	• RICU admission • intubation and mechanical ventilation • vasopressor • (noradrenaline) administered iv	Case died

Table E.4. Data extraction table of observational studies in children

Abbreviations: PVL-SA: Panton-Valentine leukocidin *Staphylococcus aureus*, SARS-CoV2: severe acute respiratory syndrome coronavirus 2, UK: United Kingdom, USA: United States of America

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Nygaard 2022 (2)	Denmark, 1 January 2016 to 1 November 2021	Case 1: Age: 2 years Sex: female Ethnicity not reported Medical history: no significant medical history, exposed to SARS-CoV-2, parainfluenza and rhinovirus Case 2: Age: 15 years Sex: male Ethnicity not reported	• Case 1: necrotising pneumonia and septic shock • Case 2: necrotising pneumonia complicated by pulmonary necrotising abscess and septic shock	• Case 1 - amoxicillin • Case 2 - meropenem (dosage not reported)	Case 2: mechanical ventilation, fluid resuscitation and ionotropic support	Both cases died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: no significant medical history, exposed to Influenza A				
Tang 2007 (3)	Vietnam, April to May 2006	Case 1: Age: 17 months Sex: male Ethnicity not reported Medical history: no significant medical history apart from minor trauma in left heel (few days before admission)	• necrotising fasciitis • necrotic abscess	Vancomycin and imipenem (dosage not reported)	Vasopressor support	Case recovered

Table E.5. Data extraction table of case series in children

Abbreviations: CVVH: continuous veno-venous hemofiltration, DIC: disseminated intravascular coagulation, ECMO: extracorporeal membrane oxygenation, ICU: intensive care unit, gm: gram, IV: intravenous, kg: kilogram, mg: milligram, min: minute, MRSA: Methicillin-resistant *Staphylococcus aureus*, NICU: neonatal intensive care unit, PICU: paediatric intensive care unit, PVL-SA: Panton-Valentine leukocidin *Staphylococcus aureus*, UK: United Kingdom, USA: United States of America

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Adem 2005 (4)	USA, July 2000 to April 2004	Case 1: (July 2000) Age: 15 months Sex: female Ethnicity not reported Medical history not reported	• necrotising pneumonia • sepsis • bacteraemia	Vancomycin and ceftriaxone (dosage not reported)	Multi-organ system failure	Case died
		Case 2: (April 2003) Age: 9 months Sex: female Ethnicity not reported Medical history not reported	• necrotising pneumonia • sepsis	Vancomycin and ceftriaxone (dosage not reported)	• ICU admission • intubation • ECMO • multi-organ system failure	Case died
		Case 3: (April 2004) Age: 17 months Sex: male	• necrotising pneumonia • sepsis	Vancomycin and ceftriaxone (dosage not reported)	• intubation • ECMO	Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Ethnicity not reported Medical history: reactive airway disease and pharyngitis	• purpura fulminans		• multi-organ system failure	
Bybeck Nielsen 2020 (5)	Denmark, 2013	Case 1: Age: 10 years Sex: not reported Ethnicity not reported Medical history: not reported	• osteomyelitis • bacteraemia • multiple abscesses	Clindamycin (dosage not reported)		Case recovered
		Case 8 (as reported by study): Age: 14 years Sex: not reported Ethnicity not reported Medical history: not reported	• necrotising fasciitis • bacteraemia	Clindamycin (dosage not reported)	• mechanical ventilation • DIC • dialysis	Case recovered
Cunnington 2009 (6)	UK, January 2004 and May 2008	Case 1: Age: 10 years Sex: male Ethnicity: white Medical history: no significant medical history reported	Necrotising pneumonia	Initial empiric treatment in hospital: • cephalosporin iv, penicillin and macrolides Main treatment in hospital: • flucloxacillin and clindamycin (dosage not reported)	PICU admission	Case recovered
		Case 2: Age: 3 years Sex: female Ethnicity: non-white Medical history: no significant medical history reported	• septic arthritis • nosocomial sepsis	Initial treatment: • cephalosporin IV and flucloxacillin (dosage not reported) Main treatment regimen not reported, frequent changes due to nosocomial sepsis	• PICU admission • renal failure leading to CVVH	Case died
		Case 3: Age: 6 years Sex: female Ethnicity: non-white	Osteomyelitis	Initial treatment: • flucloxacillin and fusidic acid Main treatment: • flucloxacillin, clindamycin and rifampicin (dosage not reported)	PICU admission	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: no significant medical history reported				
		Case 4: Age: 10 years Sex: male Ethnicity: non-white Medical history: no significant medical history	Septic arthritis	Initial empiric treatment: • cephalosporin iv, clindamycin and gentamicin Main treatment: • cephalosporin iv and clindamycin (dosage not reported)		Case recovered
		Case 5: Age: 13 years Sex: male Ethnicity: non-white Medical history: no significant medical history	Septic arthritis	Initial treatment: • cephalosporin iv Main treatment: • cephalosporin iv and clindamycin (dosage not reported)		Case recovered
		Case 6: Age: 7 months Sex: female Ethnicity: non-white Medical history: no significant medical history	Retropharyngeal abscess	Initial treatment: • cephalosporin iv and macrolides Main treatment: • cephalosporin iv and clindamycin (dosage not reported)	PICU admission	Case recovered
		Case 7: Age: 5 years Sex: male Ethnicity: non-white Medical history: no significant medical history	Pyomyositis	Initial treatment: • flucloxacillin and fusidic acid Main treatment: • clindamycin, rifampicin and linezolid (dosage not reported)		Case recovered
Hanratty 2015 (7)	UK, 2013	Case 1: Age: 13 years Sex: male Ethnicity not reported Medical history: latent tuberculosis	Submandibular abscess	Amoxicillin and flucloxacillin iv (dosage not reported)	• ventilation • high dependency unit admission	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
McAdams 2008 (11)	USA, January 1, 2004 to June 30, 2005	Case 1: Age: 26 weeks Sex: female Medical history: prematurity, central venous line	Bacteraemia	• vancomycin • amikacin • clindamycin (dosage not reported)	NICU admission	Case recovered
		Case 2: Age: 25 weeks Sex: male Medical history: prematurity, central venous line	• bacteraemia • necrotising pneumonia	• vancomycin • amikacin • piperacillin-tazobactam (dosage not reported)	NICU admission	Case died
Osterlund 2002 (13)	Sweden, March 2001 and March 2002	Sample size: 1 Age: 13 years Sex: female Ethnicity not reported Medical history: no significant medical history	Pneumonia	Cefuroxime and clindamycin (dosage not reported)	• ICU admission • mechanical ventilation	Case recovered
Peleg 2005 (14)	Australia, March 2000 to December 2003	Case 1 (as reported by the study): Age: 9 years Sex: male Ethnicity: Pacific Islander Medical history not reported	• septicaemia • septic arthritis	Initial treatment: • not reported Main treatment: • vancomycin IV for 4 weeks Followed by: • clindamycin oral or combination therapy with rifampicin and fusidic acid for 2 weeks (dosage not reported)		Case recovered
		Case 2 (as reported by the study) Age: 16 years Sex: male Ethnicity: Caucasian Medical history not reported	• septicaemia • osteomyelitis	Initial treatment: • not reported Main treatment: • vancomycin IV for 4 weeks Followed by: • clindamycin oral or combination therapy with		Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				rifampicin and fusidic acid for 2 weeks (dosage not reported)		
		Case 4 (as reported by the study) Age: 45 years Sex: female Ethnicity: Aboriginal Medical history: diabetes mellitus	Septicaemia	Initial treatment: • not reported Main treatment: • vancomycin IV for 4 weeks Followed by: • clindamycin oral or combination therapy with rifampicin and fusidic acid for 2 weeks (dosage not reported)		Case recovered
		Case 5 (as reported by the study) Age: 21 years Sex: male Ethnicity: Aboriginal Medical history: no significant medical history	• septicaemia • necrotising pneumonia	• ceftriaxone • erythromycin • gentamicin • rifampicin (dosage not reported)	• intubation and mechanical ventilation • no other morbidity indicators reported	Case died
		Case 6 (as reported by the study) Age: 34 years Sex: female Ethnicity: Caucasian Medical history: IV drug use	• septicaemia • necrotising pneumonia • psoas abscess • iliacus abscess	• initial treatment not reported • main treatment: vancomycin IV for 4 weeks • followed by clindamycin oral or combination therapy with rifampicin and fusidic acid for 2 weeks (dosage not reported)	Intubation and mechanical ventilation	Case recovered
		Case 7 (as reported by the study) Age: 4 years Sex: female Ethnicity: Aboriginal Medical history not reported	• septicaemia • osteomyelitis	• initial treatment not reported • main treatment: vancomycin IV for 4 weeks • followed by clindamycin oral or combination therapy with rifampicin and fusidic acid for 2 weeks (dosage not reported)		Case recovered
		Case 8 (as reported by the study)	• septicaemia	Initial treatment:		Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Age: 12 years Sex: male Ethnicity: Aboriginal Medical history not reported	• paraspinal abscess	• not reported Main treatment: • vancomycin IV for 4 weeks Followed by: • clindamycin oral or combination therapy with rifampicin and fusidic acid for 2 weeks (dosage not reported)		
Schwartz 2012 (15)	Australia, time period not reported	Sample size: 1 Age: 8 months Sex: female Ethnicity: Caucasian Medical history: no significant medical history	Necrotising pneumonia	Initial empiric treatment: • cefotaxime IV Later: • flucloxacillin IV and vancomycin added to treatment regimen • linezolid, rifampicin and gentamicin added 14 hours after hospital admission Main treatment: • flucloxacillin and rifampicin (continued) (dosage not reported)	• intubation • ECMO	Case died
		Sample size: 1 Age: 8 months Sex: female Ethnicity: Caucasian Medical history: no significant medical history	Necrotising pneumonia	Initial empiric treatment: • clindamycin and cefotaxime IV (dosage and frequency not reported) Later: • vancomycin added to treatment regimen (dosage, route of administration and frequency not reported) Switched to: • clindamycin, linezolid and rifampicin (dosage, route of administration and frequency not reported) On discharge:	Intubation and mechanical ventilation	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				• oral antibiotics for 6 weeks		
		Sample size: 1 Age: 5 months Sex: male Ethnicity: Caucasian Medical history: no significant medical history	• necrotising pneumonia • bacteraemia	Initial empiric treatment (2 days after symptom onset): • cefotaxime, flucloxacillin and vancomycin Switched to: • linezolid, lincomycin and rifampicin Main treatment: • clindamycin (dosage not reported)	Mechanical ventilation	Case recovered

Table E.6. Data extraction table of case reports in children

Abbreviations: CVVH: continuous veno-venous hemofiltration, DIC: disseminated intravascular coagulation, ECMO: extracorporeal membrane oxygenation, ICU: intensive care unit, ITU: intensive therapy unit, gm: gram, IV: intravenous, kg: kilogram, mg: milligram, min: minute, MRSA: Methicillin-resistant *Staphylococcus aureus,* NICU: neonatal intensive care unit, PICU: paediatric intensive care unit, PVL-SA: Panton-Valentine leukocidin *Staphylococcus aureus*, UK: United Kingdom, USA: United States of America

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Akpaka 2011 (18)	Trinidad and Tobago, time period not reported	Sample size: 1 Age: 13 years Sex: male Ethnicity: African Medical history: no significant medical history	• septic arthritis • necrotising fasciitis • septicaemia	• clindamycin • ceftriaxone • vancomycin • cloxacillin (dosage not reported)	• ICU admission • intubation and mechanical ventilation	Case died
Ambrozova 2013 (21)	Czech Republic, December 2008	Sample size: 1 Age: 10 months Sex: male Ethnicity not reported Medical history: no significant medical history	Pneumonia	Initial treatment: • cotrimoxazole (empiric for suspected UTI) Antibiotic treatment: • after deterioration: cefotaxime IV (on 3rd day of hospital admission) Upon PICU admission for next 6 days: • cefotaxime • clindamycin • gentamicin • fluconazole	• PICU admission • intubation and mechanical ventilation • vasopressors (IV noradrenaline) administered	Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				Switched to: • oxacillin • clindamycin • gentamicin (dosage not reported)		
Ballis 2007 (22)	Greece, time period not reported	Sample size: 1 Age: 17 years Sex: male Ethnicity not reported Medical history: no significant medical history	• pneumonia • bacteraemia	• moxifloxacin and linezolid On discharge: • moxifloxacin continued for 2 weeks (dosage not reported)	• ICU admission • intubation and mechanical ventilation • vasopressors administered (noradrenaline 100 µg/min)	Case recovered
Bukhari 2012 (23)	Saudi Arabia, time period not reported	Sample size: 1 Age range: 9 months Sex: female Ethnicity not reported Medical history not reported	• osteomyelitis • femur abscess	Initial empiric treatment: • ceftriaxone IV 75 mg/kg/day every 12 hours • cloxacillin IV 150 mg/kg/day every 6 hours Switched to: • clindamycin IV 40 mg/kg/day every 8 hours • cloxacillin IV 150 mg/kg/day every 6 hours (continued) Follow-up: • additional 4 weeks of cloxacillin and clindamycin		Case recovered
Camargo 2013 (24)	Brazil, December 2010	Sample size: 1 Age: 16 years Sex: male Ethnicity not reported Medical history: no significant medical history, reported local trauma (a hit with another player) during a soccer match approximately one month prior to hospital admission	Pneumonia	Initial treatment: • vancomycin 15 mg/kg twice daily and cefepime Switched to: • vancomycin and imipenem On discharge: • trimethoprim / sulfamethoxazole for 30 days (dosage not reported)	• ICU admission • mechanical ventilation	Case recovered
Castellazzi 2021 (26)	Italy, time period not reported	Sample size: 1	• osteomyelitis	Initial treatment upon PICU admission:	PICU admission	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Age: 6 months Sex: male Ethnicity not reported Medical history: history of recurrent respiratory infections and 4 hospitalisations in first 5 months of life	• multiple muscle abscesses	• cefotaxime IV 100mg/kg/day Switched to: • ceftaroline IV 24 mg/kg/day • daptomycin IV 12 mg/kg/day • clindamycin IV 30 mg/kg/day Antibiotic regimen continued for 2 weeks followed by ceftaroline IV for another 4 weeks On discharge: • oral linezolid 30 mg/kg/day divided in 3 doses for 2 weeks		
Chen 2014 (28)	China, time period not reported	Sample size: 1 Age: 15 years Sex: female Ethnicity not reported Medical history: no significant medical history	Necrotising pneumonia	Initial treatment at local hospital: • azithromycin IV for 4 days (dosage not reported) Upon hospital admission: • tigecycline (dosage, route of administration and frequency not reported) Switched to: • linezolid IV 600mg every 12 hours for 20 days • fosfomycin IV 4gm every 8 hours for 20 days Switched to: • teicoplanin and fosfomycin for 6 more weeks (dosage not reported)	Clinical support with oxygen	Case recovered
Cupane 2010 (31)	Latvia, November 2009	Sample size: 1 Age: 15 years Sex: male Ethnicity not reported Medical history: no significant medical history Coinfected with influenza A (H1N1)	Pneumonia	Initial treatment at local hospital: • ceftriaxone and metronidazole (dosage and frequency not reported) After admission to regional hospital: • ceftriaxone (continued) • oxacillin • clindamycin added one day later Main treatment: • ceftriaxone for 14 days iv • oxacillin for 14 days iv • clindamycin for 21 days	• ICU admission • mechanical ventilation	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
				(dosage not reported)		
Elledge 2014 (34)	UK, time period not reported	Sample size: 1 Age range: 10 years Sex: male Ethnicity not reported Medical history: recent history of travel to Indian subcontinent, insect bites and boils over buttocks and thighs	Osteomyelitis	Initial empiric treatment: • flucloxacillin IV and benzyl penicillin Later: • benzyl penicillin switched to rifampicin (due to poor clinical response) Main treatment: • high dose IV flucloxacillin, rifampicin and linezolid for 2 weeks On discharge: • flucloxacillin oral for 6 weeks • rifampicin oral for 6 weeks • linezolid oral for 2 weeks (dosage not reported)		Case recovered
Esteves 2010 (37)	Portugal, time period not reported	Sample size: 1 Age: 14 years Sex: male Ethnicity not reported Medical history: not reported	• pneumonia • septic arthritis	Initial treatment: • piperacillin-tazobactam IV Switched to: • flucloxacillin IV for 4 weeks (dosage not reported)	PICU admission	Case recovered
Garbo 2024 (43)	Italy, June 2023	Sample size: 1 Age: 10 years Sex: male Ethnicity not reported Medical history: no significant medical history	• necrotising pneumonia • osteomyelitis	Initial treatment: • linezolid and ceftaroline (dosage, route of administration and frequency not reported) Main treatment for 8 weeks: • clindamycin • daptomycin • fosfomycin (dosage not reported) On discharge: • dalbavancin 18 mg/kg, single dose		Case recovered
Goemanne 2022 (44)	Belgium, February 2021	Sample size: 1 Age: 21 months Sex: female Ethnicity: African	Abscess	Initial treatment: • ceftriaxone IV 100 mg/kg/day • clindamycin IV 30 mg/kg/day for 1 day Switched to:	PICU admission	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: no significant medical history		• flucloxacillin IV 200 mg/kg/day for 10 days and oral for 5 day		
Harada 2023 (46)	Japan, time period not reported	Sample size: 1 Age: 10 years Sex: male Ethnicity not reported Medical history: no significant medical history	• osteomyelitis • septic arthritis	• initial treatment: linezolid • switched to: vancomycin • clindamycin added to treatment regimen • on discharge: clindamycin oral for 6 months (dosage not reported)		Case recovered
Irenji 2018 (49)	UK, time period not reported	Sample size: 1 Age: 13 years Sex: male Ethnicity not reported Medical history: no significant medical history	• pneumonia • osteomyelitis • sepsis • psoas abscess	Initial empiric treatment: • flucloxacillin and cefotaxime Switched to: • linezolid and clindamycin (dosage not reported)		Case recovered
Isobe 2013 (50)	Japan, October 2004	Sample size: 1 Age: 17 years Sex: Female Ethnicity not reported Medical history: no significant medical history	• osteomyelitis • multifocal pelvic abscesses	First episode (October to November 2004): • vancomycin IV 2gm/day (drip infusion) • pazufloxacin IV 1gm/day (after vancomycin) • minocycline oral 300 mg/day (post-discharge, until February 2005) Second episode (March to April 2005): • vancomycin IV 2gm/day • fosfomycin IV 4gm/day • minocycline oral 400 mg/day (post-discharge until June 2005)		Case recovered
Karli 2016 (53)	Turkey, time period not reported	Sample size: 1 Age: 12 years Sex: male Ethnicity: not reported Medical history: no significant medical history	• osteomyelitis • psoas abscess	Initial treatment (upon hospital admission): • ceftriaxone: 100 mg/kg/day • vancomycin: 40 mg/kg/day Switched to (on day 6): • linezolid IV 30 mg/kg/day for 15 days Switched to (on day 21): • clindamycin oral 30 mg/kg/day for 9 days		Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Karli 2016 (54)	Turkey, time period not reported	Sample size: 1 Age: 13 years Sex: male Ethnicity: not reported Medical history: No significant medical history	Gluteal abscess	Initial treatment: • cefotaxime 200 mg/kg/day Switched to (on day 8): • cefazolin IV 100 mg/kg/day • clindamycin IV 40 mg/kg/day Switched to (on day 18): • linezolid 30 mg/kg/day • clindamycin 40 mg/kg/day (continued) On discharge (day 28): • amoxicillin clavulanate oral for 10 days		Case recovered
Kefala-Agoropoulou 2010 (55)	Greece, 2007	Sample size: 1 Age: 10 years Sex: female Ethnicity: not reported Medical history: no significant medical history	• osteomyelitis • pyomyositis	Initial treatment: • cloxacillin 200 mg/kg/day Switched to (on day 3): • vancomycin IV 15 mg/kg/day • clindamycin IV 35 mg/kg/day for 8 weeks • gentamicin IV 5.5 mg/kg/day for 10 days Switched to: • teicoplanin iv • clindamycin oral for 5 months	Clinical support with oxygen	Case recovered
Kim 2023 (56)	South Korea, time period not reported	Sample size: 1 Age: 7 days Sex: female Ethnicity not reported Medical history: no significant medical history	Necrotising fasciitis	Initial empiric treatment: • vancomycin, meropenem, and ampicillin Switched to: • vancomycin for 4 weeks (dosage not reported)		Case recovered
Laurens 2008 (59)	USA, time period not reported	Sample size: 1 Age: 10 years Sex: male Ethnicity: African-American Medical history: no significant medical history	Osteomyelitis	Initial treatment: • ceftriaxone and vancomycin iv Switched to (on day 3): • clindamycin and gentamycin IV for 8 weeks Main treatment: • clindamycin and vancomycin IV for 8 weeks (dosage not reported)		Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Lehman 2010 (60)	USA, time period not reported	Sample size 1 Age: 6 years Sex: male Ethnicity not reported Medical history: no significant medical history Family history: patient's father had recurrent skin pustules of unknown aetiology but no other infections or autoimmune conditions	• septic arthritis • osteomyelitis • necrotising fasciitis • myositis	Initial treatment: • amoxicillin-clavulanate oral for 2 days Switched to: • vancomycin and cefotaxime iv Switched to: • oxacillin and gentamicin Main treatment: • oxacillin IV for 6 weeks (dosage not reported)	Intubation and mechanical ventilation	Case recovered
Miyashita 2002 (64)	Japan, time period not reported	Sample size: 1 Age: 17 years Sex: male Ethnicity not reported Medical history: no significant medical history	Bacteraemia	• cefazolin 3.0gm/day		Case recovered
Montagnani 2013 (65)	Italy, time period not reported	Case 1: Age: 3 months Sex: male Ethnicity not reported Medical history: no significant medical history	Necrotising pneumonia	Initial treatment: • ampicillin / sulbactam 50 mg/kg every 8 hours • gentamicin 6 mg/kg daily for 5 days Switched to: • vancomycin iv • clindamycin (dosage not reported) On discharge: • linezolid orally for 3 weeks	Clinical support with oxygen	Case recovered
Mushtaq 2008 (67)	UK, time period not reported	Sample size: 1 Age: 14 years Sex: male Ethnicity not reported	• necrotising pneumonia • purpura fulminans	• cefotaxime IV and gentamycin (dosage not reported)	• intubation and mechanical ventilation • admission to ITU • vasopressors (noradrenaline and adrenaline) administered	Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: no significant medical history			• multiple organ failure	
Ng 2018 (69)	Malaysia, time period not reported	Sample size: 1 Age: 19 months Sex: female Ethnicity not reported Medical history: no significant medical history	Bacteraemia	Initial treatment: • cloxacillin IV for 2 weeks • gentamicin IV for the first 5 days (dosage and frequency not reported) On discharge: • oral cefuroxime for 4 weeks • oral clindamycin for 4 weeks (dosage not reported)		Case recovered
Ogawa 2022 (71)	Japan, 2017	Sample size: 1 Age: 1 year Sex: female Ethnicity not reported Medical history: no significant medical history	Retropharyngeal and parapharyngeal abscess	Initial treatment: • ampicillin sulbactum • vancomycin (dosage not reported) Switched to: • clindamycin monotherapy on day 5 • continued for 21 days (dosage not reported)	• ICU admission • intubation	Case recovered
Oshima 2021 (72)	Japan, time period not reported	Sample size: 1 Age: 1 month Sex: male Ethnicity: Vietnamese Medical history: no significant medical history Note: patient had meningitis complicated by necrotising pneumonia and cerebral infarction	• necrotising pneumonia • deep-seated abscess	Initial treatment: • meropenem IV 40 mg/kg 3 times daily • cefotaxime IV 75 mg/kg 4 times daily Later: • cefotaxime replaced with vancomycin 15 mg/kg 4 times daily Switched to: • linezolid IV 10 mg/kg 3 times daily On discharge: • oral linezolid over 6 weeks		Case recovered
Perbet 2010 (74)	France, time period not reported	Sample size: 1 Age: 16 years Sex: female Ethnicity not reported	• necrotising fasciitis • sepsis	• amoxicillin 2gm and clavulanic acid 200mg Switched to: • piperacillin-tazobactam 4gm/500mg every 8 hours Switched to:	ICU admission	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: no significant medical history		• gentamicin IV 300mg over 30 minutes Switched to: • oxacillin 2gm every 6 hours • clindamycin 600mg every 6 hours		
Ravishankar 2016 (76)	USA, time period not reported	Sample size: 1 Age: 10 years Sex: female Ethnicity not reported Medical history: no significant medical history	Necrotising pneumonia	• vancomycin IV 1gm • ceftriaxone IV 2gm	• oxygen support by nonbreather face mask • vasopressors administered (dopamine and epinephrine infusions) • PICU admission • intubation and mechanical ventilation	Case died
Reichert 2005 (77)	UK, time period not reported	Sample size: 1 Age: 15 years Sex: male Ethnicity not reported Medical history: insulin dependent diabetes mellitus	Deep soft tissue abscess	Initial treatment: • flucloxacillin IV (dosage and frequency not reported) Switched to: • clindamycin IV 300mg 6 hourly **Adjustments** • returned to flucloxacillin IV 2gm every 6 hours) after 3 days of clindamycin • on day 10, switched to: teicoplanin IV 6 mg/kg/day with oral fucidic acid (500mg, 8 hourly) added 2 days later • on day 14: teicoplanin dosage increased to 10 mg/kg/day • on day 19: fucidic acid stopped and replaced with oral rifampicin (450mg twice daily) • on day 21: teicoplanin was changed to oral flucloxacillin 1gm 6 hourly • on discharge: oral flucloxacillin and rifampicin or 4 weeks	• oxygen support • admission to local high dependency unit • renal failure (mild, but clinically significant)	Case recovered
Rovira 2015 (80)	Africa, time period not reported	Sample size: 1 Age: 6 years Sex: male Ethnicity not reported	• necrotising pneumonia • osteomyelitis	Initial treatment: • penicillin and gentamycin (dosage not reported) Switched to:	Oxygen support	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: no significant medical history		• ceftriaxone (dosage, route of administration and frequency not reported) • cotrimoxazole IV added to treatment (dosage not reported) Main treatment: • vancomycin and gentamycin IV for 10 days (dosage not reported) Switched to: • oral flucloxacilin after significant improvement (dosage not reported)		
Rozenbaum 2009 (81)	Brazil, January, 2007	Sample size: 1 Age: 10 years Sex: female Ethnicity not reported Medical history: no significant medical history	• osteomyelitis • septic shock	Empirical parenteral antibiotic therapy: • oxacillin, ampicillin and gentamicin (dosage not reported) Parenteral antimicrobial therapy switched to: • vancomycin 40 mg/kg per day in 4 doses • clindamycin 30 mg/kg per day in 3 or 4 doses (for 8 weeks) • ciprofloxacin (discontinued soon after) After 3 weeks, vancomycin replaced with teicoplanin (dosage not reported) On discharge: • clindamycin 300mg orally every 8 hours	• admission to PICU • tracheal intubation and mechanical ventilation • insertion of a chest tube to drain a right pleural empyema	Case recovered
Swaminathan 2006 (85)	Australia, time period not reported	Sample size: 1 Age: 14 years Sex: male Ethnicity: Samoan background Medical history: mild asthma controlled with inhalers, recurrent skin furunculosis (prior to admission)	• osteomyelitis • septic arthritis • deep tissue abscesses	Initial empirical antibiotic therapy: • flucloxacillin IV 2gm every 6 hours • gentamicin IV 240mg daily Later: • flucloxacillin IV increased to 2gm every 4 hours continued for 6 weeks On discharge: • dicloxacillin (dosage not reported)		Case recovered
Székely 2010 (86)	Romania, March 2007	Sample size: 1 Age: 4 years Sex: female Ethnicity not reported	Necrotising pneumonia	Empirical treatment: • meropenem iv • ciprofloxacin iv • teicoplanin iv	Orotracheal intubation mechanical ventilation	Case died

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
		Medical history: no significant medical history apart from minor trauma in left heel (few days before admission)		(dosage not reported)		
Uda 2020 (89)	Japan, time period not reported	Sample size: 1 Age: 3 years Sex: female Ethnicity not reported Medical history: no significant medical history	Septic arthritis	Vancomycin IV for 3 weeks (dosage not reported)		Case recovered
Valentini 2008 (90)	Italy, time period not reported	Sample size: 1 Age: 15 years Sex: male Ethnicity not reported Medical history: mild asthma during childhood	• necrotising pneumonia • lung abscess • bacteraemia	• clarithromycin and ceftriaxone Switched to: • ampicillin, doxycycline and ceftriaxone Later: • ampicillin discontinued and vancomycin added (dosage not reported) On day 5, antibiotic therapy switched to: • teicoplanin IV 400mg twice a day • linezolid IV 600mg twice a day • rifampicin IV 600mg once a day	PICU admission (for 18 hours)	Case recovered
Vanbiervliet 2022 (91)	Belgium, time period not reported	Sample size: 1 Age: 12 years Sex: male Ethnicity: Congolese Medical history: no significant medical history	• osteomyelitis • pyomyositis	Initial treatment at emergency department: • ceftriaxone IV 2gm Empirical treatment after PICU admission: • piperacillin-tazobactam • vancomycin Switched to (on day 2): • flucloxacillin and clindamycin Later: • linezolid and levofloxacin added to treatment (continued for 6 weeks) (dosage not reported)	• PICU admission • intubation and mechanical ventilation • vasopressor (noradrenalin) and inotropic (adrenalin) support • continuous veno-venous hemodialysis later replaced by intermittent dialysis • multiple organ failure	Case recovered

Study	Country, time period	Population	Invasive PVL-SA infection (laboratory confirmed)	Intervention	Outcome: Morbidity	Outcome: Mortality
Yonezawa 2015 (95)	Japan, time period not reported	Sample size: 1 Age: 23 months old Sex: female Ethnicity: Japanese Medical history: no significant medical history	• osteomyelitis • necrotising fasciitis • necrotising pneumonia • bacteraemia • sepsis	Initial treatment: • cefotaxime 100 mg/kg/day Switched to: • vancomycin 55 mg/kg/day (on day 2) and meropenem (on day 3) On hospital admission to tertiary emergency department: • linezolid IV 10 mg/kg/day every 8 hours for 3 weeks • meropenem IV 40 mg/kg 3 times daily for 3 weeks		Case recovered

Annexe F. Risk of bias assessment

Table F.1. Risk of bias assessment for case series

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Comments
Adem, 2005 (4)	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	NA	Q1: No explicit inclusion criteria reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No explicit clinic or hospital demographic information reported Q10: Statistical analysis not performed
Beaumont, 2024 (1)	No	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	NA	Q1: No explicit inclusion criteria reported Q6: Exact age of participants not reported Q10: Statistical analysis not performed
Bybeck, 2020 (5)	Yes	Yes	Yes	Yes	Yes	No	Unclear	Yes	No	NA	Q6: Sex and ethnicity not reported Q7: Antibiotic regime specified for 2 cases only Q9: No explicit clinic or hospital demographic information reported Q10: Statistical analysis not performed
Cunnington, 2009 (6)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	NA	Q9: No hospital demographic information reportedQ10: Statistical analysis not performed
Hanratty, 2015 (7)	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	NA	Q1: No explicit inclusion criteria reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No hospital demographic information reported Q10: Statistical analysis not performed
Hayakawa, 2020 (8)	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	NA	Q1: No explicit inclusion criteria reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No hospital demographic information reported Q10: Statistical analysis not performed
Kravitz, 2005 (9)	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	NA	Q1: No explicit inclusion criteria reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No hospital demographic information reported Q10: Statistical analysis not performed

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Comments
Lin, 2008 (10)	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	NA	Q1: No explicit inclusion criteria reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No hospital demographic information reported Q10: Statistical analysis not performed
Micek, 2005 (12)	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	NA	Q1: No explicit inclusion criteria reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No hospital demographic information reported Q10: Statistical analysis not performed
McAdams, 2008 (11)	Unclear	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	NA	Q1: No explicit inclusion criteria reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No hospital demographic information reported Q10: Statistical analysis not performed
Nygaard, 2022 (2)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	NA	Q9: Demographics not reported Q10: Statistical analysis not performed
Osterlund, 2002 (13)	No	Unclear	Yes	Unclear	Unclear	Yes	Yes	Yes	No	NA	Q1: No explicit inclusion criteria reported Q2: Diagnostic methods for invasive infections not reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No hospital demographic information reported Q10: Statistical analysis not performed
Peleg, 2005 (14)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Q10: Statistical analysis not performed
Schwartz, 2012 (15)	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	NA	Q1: No explicit inclusion criteria reported Q4: Unclear if the case series had consecutive inclusion of participants Q5: The case series does not describe whether all eligible patients were included or if any were excluded Q9: No hospital demographic information reported Q10: Statistical analysis not performed
Tang, 2007 (3)	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	NA	Q1: No explicit inclusion criteria reported Q9: No hospital demographic information reported Q10: Statistical analysis not performed

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Comments
Toro, 2014 (16)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	NA	Q9: No hospital demographic information reported Q10: Statistical analysis not performed
Young, 2008 (17)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	NA	Q9: No hospital demographic information reported Q10: Statistical analysis not performed

Note: The data presented in the observational studies (1 to 3) was descriptive in nature and resembled a case series format without any comparison groups, therefore, the JBI tool for case series was used for risk of bias assessment of these studies.

Critical appraisal was done using the JBI checklist for case series (96)

List of questions:
Q1: Were there clear criteria for inclusion in the case series?
Q2: Was the condition measured in a standard, reliable way for all participants included in the case series?
Q3: Were valid methods used for identification of the condition for all participants included in the case series?
Q4: Did the case series have consecutive inclusion of participants?
Q5: Did the case series have complete inclusion of participants?
Q6: Was there clear reporting of the demographics of the participants in the study?
Q7: Was there clear reporting of clinical information of the participants?
Q8: Were the outcomes or follow up results of cases clearly reported?
Q9: Was there clear reporting of the presenting site(s)/clinic(s) demographic information?
Q10: Was statistical analysis appropriate?

Table F.2. Risk of bias assessment for case reports

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Comments
Akpaka, 2011 (18)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Alonso-Tarres, 2005 (19)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Al-Talib, 2011 (20)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Ambrozova, 2013 (21)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Balis, 2007 (22)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Bukhari, 2012 (23)	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Q2: Medical history not reported

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Comments
									Q7: Adverse or unanticipated events were not reported
Camargo, 2013 (24)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Carroll, 2017 (25)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Castellazzi, 2021 (26)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Chen, 2024 (27)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Chen, 2014 (28)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Chetchotisakd, 2007 (29)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Conan, 2021 (30)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Cupane, 2010 (31)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Dhanoa, 2012 (32)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Dubos 2014 (33)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Elledge, 2014 (34)	Yes	No	Yes	Yes	Unclear	Yes	No	Yes	Q2: Unclear medical and family history – clinical events were reported in sequence, but no formal or structured timeline, some gaps in past medical and family history Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Enany, 2007 (35)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Enayet, 2006 (36)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Comments
									Q7: Adverse or unanticipated events were not reported
Esteves, 2010 (37)	Yes	No	Yes	Yes	Unclear	Yes	No	Yes	Q2: Medical history not reported Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Honarpour, 2007 (48)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Fahmy, 2008 (38)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Fernandez, 2015 (39)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Fica, 2023 (40)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Fogo, 2011 (41)	Yes	Yes	No	Yes	Unclear	Yes	No	Yes	Q3: Patient's clinical condition not described in sufficient detail – no lab results included Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Frazee, 2005 (42)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Garbo, 2024 (43)	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	No	Q5: Dosage of intervention not reported Q7: Unclear if adverse event was due to intervention Q8: Case report provided no takeaway lessons relevant to outcomes
Goemanne, 2022 (44)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse events not reported
Govindan, 2012 (45)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Harada, 2023 (46)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Q5: Dosage of intervention not reported

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Comments
									Q7: Adverse or unanticipated events were not reported Q8: Case report provided no takeaway lessons relevant to outcomes
Higashiyama, 2010 (47)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Irenji, 2018 (49)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Isobe, 2013 (50)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Iwanaga, 2013 (51)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Jung, 2008 (52)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Karli, 2016 (53)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Karli, 2016 (54)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Q7: Unclear if adverse event was due to intervention
Kefala-Agoropoulou, 2010 (55)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Kim, 2023 (56)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Kuo, 2016 (57)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Larsen, 2021 (58)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Laurens, 2008 (59)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Lehman, 2010 (60)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Leung, 2024 (61)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Comments
Mattu, 2024 #120 (63)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Magira, 2007 (62)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Miyashita, 2002 (64)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Montagnani, 2013 (65)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Morimoto, 2024 (66)	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Q1: Age not reported
Mushtaq, 2008 (67)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Newell, 2023 (68)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Ng, 2018 (69)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Obed, 2006 (70)	Yes	No	Yes	Yes	Unclear	Yes	No	Yes	Q2: Medical history not reported Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Ogawa, 2022 (71)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Oshima, 2021 (72)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Ote, 2023 (73)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Perbet, 2010 (74)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Ramos, 2009 (75)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Q7: Adverse or unanticipated events were not reported

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Comments
									Q8: Case report provided no takeaway lessons relevant to outcomes
Ravishankar, 2016 (76)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Reichert, 2005 (77)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Riedweg-Moreno, 2014 (78)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Roberts, 2008 (79)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported Q8: Case report provided no takeaway lessons relevant to outcomes
Rovira, 2015 (80)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported Q8: Case report provided no takeaway lessons relevant to outcomes
Rozenbaum, 2009 (81)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Schefold, 2007 (82)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Sifri, 2007 (83)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Soavi, 2011 (84)	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Q5: Dosage of intervention not reported
Swaminathan, 2006 (85)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Q7: Adverse or unanticipated events were not reported Q8: Case report provided no takeaway lessons relevant to outcomes
Székely, 2010 (86)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Takigawa, 2019 (87)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Torell, 2005 (88)	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	No	Q5: Dosage of intervention not reported

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Comments
									Q8: Case report provided no takeaway lessons relevant to outcomes
Uda, 2020 (89)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Q5: Dosage of intervention not reported Q7: Adverse events or unanticipated events were reported Q8: Case report provided no takeaway lessons relevant to outcomes
Valentini, 2008 (90)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Vanbiervliet, 2022 (91)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported Q8: Case report provided no takeaway lessons relevant to outcomes
Venugopal, 2007 (92)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Q7: Adverse or unanticipated events were not reported
Wan, 2016 (93)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Q7: Adverse or unanticipated events were not reported Q8: Case report provided no takeaway lessons relevant to outcomes
Xia, 2020 (94)	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Q5: Dosage of intervention not reported Q7: Adverse or unanticipated events were not reported
Yonezawa, 2015 (95)	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Q7: Adverse or unanticipated events were not reported Q8: Case report provided no takeaway lessons relevant to outcomes

Critical appraisal was done using the JBI Checklist for case reports (96).

List of questions:

Q1: Were patient's demographic characteristics clearly described?
Q2: Was the patient's history clearly described and presented as a timeline?
Q3: Was the current clinical condition of the patient on presentation clearly described?
Q4: Were diagnostic tests or assessment methods and the results clearly described?
Q5: Were the interventions or treatment procedures clearly described?
Q6: Was the post-intervention clinical condition clearly described?
Q7: Were adverse events (harms) or unanticipated events identified and described?
Q8: Does the case report provide takeaway lessons?

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation heath secure.

UKHSA is an executive agency, sponsored by the Department of Health and Social Care.

Prepared by Aishwarya Bhatia, Jennifer Hill, Maheen Qureshi, Susannah Brown and Serena Carville

For queries relating to this document, please contact: enquiries@ukhsa.gov.uk

Published: September 2025
Publication reference: GOV-19079 (CPHR029e)

Suggested citation: Bhatia A, Hill J, Qureshi M, Brown S, Carville S. Morbidity and mortality in hospital inpatients with invasive Panton-Valentine leukocidin *Staphylococcus aureus* (PVL-SA) infections receiving antibiotic treatment: a rapid systematic review. UKHSA; 2025.