

Supplemental table 1: QUADAS-2 results

| Study     | Risk of bias      |            |   | Applicability concerns |                   |            |                    |
|-----------|-------------------|------------|---|------------------------|-------------------|------------|--------------------|
|           | Patient selection | Index test | Reference standard  | Flow and timing        | Patient selection | Index test | Reference standard |
| Ávila     | +                 | -          | -Positive culture and two SIRS criteria or<br><br>-cytobiochemical suspicion (hypoglycorrhachia less than 45 mg/dL and neutrophilic pleocytosis higher than 100 per mL) and SIRS-symptoms.<br><br>The clinicians determines whether culture- or SIRS symptoms could be attributed to another cause. | -                      | +                 | +          | +                  |
| Berger    | +                 | -          | Positive gram, antigen test or culture  | +                      | +                 | -          | -                  |
| Boer 2008 | -                 | -          | Positive gram or culture  | -                      | -                 | -          | -                  |
| Boer 2011 | +                 | -          | Two positive cultures   | +                      | +                 | +          | -                  |
| Bota      | +                 | +          | Criteria Lozier et al.  | +                      | +                 | +          | +                  |
| Coen      | -                 | +          | Positive culture $\geq$ 24 hours after drain insertion, pleocytosis, fever and/or headache, meningeal signs and altered mental status   | -                      | -                 | +          | +                  |

|             |   |   |  |   |   |   |   |
|-------------|---|---|--|---|---|---|---|
| Gordon      | + | - | Criteria Lozier et al.   | + | + | + | + |
| Grille      | + | + | Criteria Lozier et al.   | - | + | + | + |
| Hader       | + | - | Positive Gram stain or culture on consecutive days   | + | + | - | - |
| Hariri      | + | + | Criteria Lozier et al.   | - | + | + | + |
| Hong        | - | + | Pyogenic ventriculitis on MRI  | - | - | + | - |
| Hopkins     | - | - | Definite: positive culture with a clinical picture of infection or commencement of intrathecal AB Probable: raised CSF WCC: red cell count ratio (>1:7900) in the absence of positive culture or starting intrathecal AB with a clinical picture of infection. | ? | + | + | + |
| Jost        | - | ? | CDC-criteria   | - | + | - | + |
| Khalil      | - | ? | Positive CSF culture   | - | + | + | - |
| Lackner     | - | - | Positive CSF culture   | - | + | - | - |
| Lenski 2017 | + | + | Modified CDC criteria  | + | + | + | + |
| Lenski 2018 | + | - | Modified CDC criteria  | + | + | + | + |
| Liu         | + | ? | Positive CSF culture   | - | - | + | - |

|                        |   |   |   |   |   |   |   |
|------------------------|---|---|---|---|---|---|---|
| Lukaszewicz            | - | ? | positive for bacterial infection upon direct examination or in culture and contained > 100 leukocytes/mm <sup>3</sup>   | + | + | + | + |
| Lunardi                | - | + | CDC criteria  | - | + | + | + |
| Martínez 1994          | ? | ? | ?   | + | ? | ? | ? |
| Martínez 2002          | - | + | compatible clinical findings and either<br>(1) a positive CSF culture or<br>(2) negative culture but identification of bacteria on CSF Gram stain or<br>(3) negative CSF culture accompanied by a CSF pleocytosis of less than 500 neutrophils/mm <sup>3</sup> with a predominance of 50% or more of polymorphonuclear cells. | - | - | - | + |
| Mayhall                | + | - | Positive culture  | - | + | + | - |
| Mounier 2015           | - | + | Positive culture and start antibiotics  | + | + | + | - |
| <i>Acta Neurochir.</i> |   |   |   |   |   |   |   |
| Mounier 2015           | + | + | Positive CSF culture obtained from the ventricular catheter except for commensals, where the same strain had to be isolated in two or more CSF samples.   | + | + | + | - |
| <i>PLoS One</i>        |   |   |   |   |   |   |   |
| Munoz-Gomez            | ? | - | marked CSF pleocytosis >50 WBC/mm <sup>3</sup> in high lactic acid levels (>6mmol/L), positive Gram stain and positive CSF  | - | ? | - | + |

|           |   |   | culture of a neuropathogen.  |   |   |   |   |
|-----------|---|---|--|---|---|---|---|
| Muttaiyah | + | ? | Positive CSF culture, CSF leukocytosis >5x10 <sup>6</sup> /L, clinical diagnosis of ventriculitis by an infectious diseases physician. | - | + | - | + |
| Omar      | - | - | CDC criteria   | + | - | + | + |
| Passer    | + | - | IDSA guideline   | + | + | + | + |
| Pfausler  | + | + | ?  | + | + | + | ? |
| Pfisterer | + | + | ?  | + | - | + | - |
| Ramírez   | + | ? | A positive CSF culture accompanied by abnormal CSF findings and appropriate clinical signs and symptoms.                               | ? | + | + | + |
| Rath      | - | - | Positive culture on two consecutive days   | - | + | - | + |
| Ruiz-Mesa | - | ? | ?  | ? | - | ? | ? |
| Schoch    | - | - | At least two of the following three criteria:  | - | + | + | + |
|           |   |   | 1. One or more new clinical signs such as nuchal rigidity, headache, fever or neurological deterioration                               |   |   |   |   |
|           |   |   | 2. CSF cell count increased by more than 100% over   |   |   |   |   |

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the previous day

3. bacteria detected in CSF Gram staining and/or culture. Repeated evidence in two different samples was required to prove CSF infection in skin commensals.

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|         |   |   |   |   |   |   |   |
|---------|---|---|---|---|---|---|---|
| Schultz | + | ? | 1. No other detectable source of CNS infection. | ? | + | ? | + |
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2. Negative CSF cultures obtained at the time of ventriculostomy placement.
3. Ventricular catheterization  $\geq 24$  hours.
4. Two positive CSF-cultures with the same organism taken on different days.
5. CSF white blood cell count  $\geq 11 \times 10^6/L$  and CSF polymorphnuclear leukocytes  $\geq 50$ .

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|       |   |   |  |   |   |   |   |
|-------|---|---|--|---|---|---|---|
| Shang | - | ? | 1. CSF cell count was $> 1000 \times 10^6/L$ , and CSF | - | - | ? | - |
|-------|---|---|--|---|---|---|---|

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- sugar was  $< 1.9$  mmol/l.
  2. Bacteria were found on the CSF smear, or bacterial cultures were positive more than twice consecutively.
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3. Intracranial CT or MRI confirmed intraventricular debris and pus.

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|          |   |   |   |   |   |   |   |
|----------|---|---|---|---|---|---|---|
| Stubljar | ? | - | Gold standard was constructed on the basis of clinical grounds, culture, and molecular results of bacterial identification from CSF and the results of response to antibiotic treatment | - | ? | - | - |
| Walti    | ? | - | Modified CDC criteria   | + | + | - | + |
| Wiegand  | + | - | NHSN/CDC criteria   | - | + | + | + |
| Wong     | + | + | ?   | ? | + | + | ? |
| Wostrack | - | - | Positive microbial CSF culture with a clinical picture of infection or elevated CSF cell count, red cell/white cell ratio > 1: 700, increased lactate and/or decreased glucose.         | - | - | + | + |

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Supplementary table 2: Direction of evidence in studies reporting on a parameter

|                            | Studies reporting on parameter (n) | Total patients (n) | Direction of evidence in studies where patients with DAV were compared to patients without ventriculitis |
|----------------------------|------------------------------------|--------------------|--|
| Clinical parameters        |                                    |                    |  |
| Fever                      | 17                                 | 701                | 8 of 12 studies higher frequency of fever in DAV   |
| Headache                   | 2                                  | 58                 | -  |
| Meningeal signs            | 4                                  | 82                 |  |
| Increased heart rate       | 2                                  | 50                 | Symptom present in 52% of patients with DAV  |
| Increased respiratory rate | 2                                  | 50                 | Symptom present in 46% of patients with DAV  |
| SIRS                       | 2                                  | 248                | 86% (15/22) of patients with DAV met SIRS criteria   |

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AUC 0.575 (95% CI 0.5-0.6)

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CSF parameters

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|                          |    |      |  |
|--------------------------|----|------|--|
| CSF cell count           | 21 | 1    | 13 of 17 studies found higher cell count in DAV, one article AUC 0.644 |
| %Polymorphnuclear cells  | 6  | 162  | 3 of 5 studies sign. increased proportion PMN in DAV                   |
| Cell index               | 6  | 425  | 4 of 6 studies sign. Higher cell index in DAV                          |
| Protein concentration    | 19 | 1705 | 6 of 11 studies sign. Higher protein conc. In DAV                      |
| Glucose concentration    | 10 | 1054 | 6 of 10 studies sign. Lower glucose in CSF in DAV                      |
| Glucose ratio CSF:plasma | 8  | 468  | 5 of 8 studies sign. Lower ratio in DAV                                |
| Lactate concentration    | 8  | 872  | 4 of 6 studies sign. Higher lactate conc. in DAV                       |
| IL-1 $\beta$             | 3  | 97   | 2 studies sign. Higher IL-1 $\beta$ in DAV                             |

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|  |    |      |   |
|--|----|------|---|
| IL-8                                   | 2  | 76   | 2 studies sign. higher IL-8 in DAV  |
| TNF- $\alpha$                          | 2  | 53   | 1 of 2 studies higher TNF- $\alpha$ in DAV  |
| Blood parameters                       |    |      |   |
| Leukocyte count<br>( $\times 10^9/L$ ) | 14 | 1428 | 4 of 14 studies higher leukocyte count in DAV   |
| CRP                                    | 11 | 656  | 2 of 6 studies sign. Higher CRP in DAV  |
| Glucose                                | 2  | 668  | 2 studies no sign. Difference in glucose concentration in DAV   |
| Procalcitonin                          | 6  | 203  | 2 of 6 studies sign. higher procalcitonin concentration in DAV  |
| % Neutrophils                          | 2  | 129  | Stubjar et al: no sign. difference<br><br>Lenski et al: AUC=0.900, sensitivity 70%, spec. 100%<br><br>Symptom present in 66% of patients with DAV and 61% of patients without DAV |

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Microbiology results

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Culture                    6                                    246

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Gram stain                6                                    114

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PCR analysis on 16S    2                                    59                                    sensitivity of 100%, specificity of 78.6%

rRNA

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DAV=Drain Associated Ventriculitis

Supplementary table 3: results of parameters researched in one study

|  | Studies | Total patients | Proportion infected | Symptom present or mean concentration in DAV | Symptom present in non-ventriculitis patients | Direction of evidence in studies where patients with DAV were compared to patients without DAV |
|--|---------|----------------|---------------------|--|---|--|
| <b>Clinical parameters</b>                                   |         |                |                     |  |   |  |
| SIRS <sup>1,2</sup>  | 2       | 248            | 27%                 | 86%, 15/22 patients                          |   | AUC 0.575 (95% CI 0.5-0.6)   |
| Number of neurological pathological signs <sup>a1</sup>      | 1       | 226            | 20%                 |  |   | AUC 0.542 (0.5-0.6)  |
| <b>CSF parameters</b>  |         |                |                     |  |   |  |
| Visual inspection <sup>3</sup>                               | 1       | 7              | 100%                | 14% (1)                                      |   |  |
| WBC:RBC ratio <sup>1</sup>                                   | 1       | 226            | 20%                 |  |   | AUC 0.690 (95% CI 0.6-0.8)   |
| Correction of protein conc. for blood admixture <sup>4</sup> | 1       | 187 samples    | 0%                  | -  | 139 (74%)                                     |  |
| Procalcitonin concentration <sup>5</sup>                     | 1       | 32             | 25% (8)             |  |   | No significant difference  |

|                                      |   |     |          |         |         |   |
|--------------------------------------|---|-----|----------|---------|---------|---|
| Radical oxygen species <sup>6</sup>  | 1 | 30  | 23% (7)  |         |         | Significant difference  |
| TGF- $\beta^5$                       | 1 | 32  | 25% (8)  |         |         | No significant difference   |
| sCD14-st <sup>7</sup>                | 1 | 18  | 100%     |         |         | Significant difference  |
| CD62L <sup>8</sup>                   | 1 | 45  | 22% (10) |         |         | Significant difference  |
| sCD62L <sup>8</sup>                  | 1 | 44  | 20% (9)  |         |         | No significant difference   |
| sCD62L/TP ratio <sup>8</sup>         | 1 | 44  | 20% (9)  |         |         | No significant difference   |
| sTREM-1 <sup>9</sup>                 | 1 | 73  | 8% (6)   |         |         | Significant difference  |
| Blood parameters                     |   |     |          |         |         |   |
| % Neutrophils <sup>7,10</sup>        | 2 | 129 | 57% (74) | 66%     | 61%     | Stubljär et al: no significant difference<br><br>Lenski et al: AUC=0.900, sensitivity 70%, spec. 100% |
| Protein concentration <sup>11</sup>  | 1 | 638 | 9% (58)  | 71 mg/L | 68 mg/L | No difference   |
| $\alpha$ 1 antitrypsin <sup>12</sup> | 1 | 130 | 21 (16%) |         |         | No significant difference   |
| fibronectin <sup>12</sup>            | 1 | 130 | 21 (16%) |         |         | No significant difference   |

|                                  |   |     |           |      |     |  |
|----------------------------------|---|-----|-----------|------|-----|--|
| haptoglobin <sup>12</sup>        | 1 | 130 | 21 (16%)  |      |     | No significant difference  |
| Band forms on WBC <sup>13</sup>  | 1 | 39  | 39 (100%) |      |     | No significant difference  |
| <i>Microbiology results</i>      |   |     |           |      |     |  |
| Biofilm formation <sup>14</sup>  | 1 | 32  | 6 (19%)   | 100% | 64% | 75% (8/12) of colonized drains positive, 64% (9/14) of ventriculitis negative patients positive for biofilm formation  |
| Sonication <sup>15</sup>         | 1 | 14  | 5 (36%)   | 80%  | 56% | 5 false positive results   |
| <i>Other parameters</i>          |   |     |           |      |     |  |
| Metabonomics <sup>16</sup>       | 1 | 15  | 5 (33%)   |      |     | Good discriminatory effect   |
| <i>Radiological findings</i>     |   |     |           |      |     |  |
| Changes in MRI DWI <sup>17</sup> | 1 | 4   | 4 (100%)  |      |     | Strong correlation between ADC count and leukocytes and protein concentration in CSF ( $r^2 = -0.84$ , $r^2 = -0.62$ ) |
| Intraventricular debris          | 1 | 11  | 11 (100%) | 100% |     |  |

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on CT or MRI<sup>18</sup>

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<sup>a</sup>Meningeal irritation, altered consciousness, headache

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