**Routine vs. on-demand blood sampling in critically ill patients:**

**a systematic review**

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**Supplemental digital content**

This supplement has been provided by the authors to give readers additional information about their work.

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# Supplemental Methods

## Search strategies

**EMBASE (Ovid) 1974 to date of search**

1. exp Critical care/
2. exp Intensive care/
3. exp Intensive care unit/
4. exp Critically ill patient/
5. exp Critical illness/
6. Intensive care.ab,ti.
7. Critical care.ab,ti.
8. Critically ill.ab,ti.
9. Critical illness.ab,ti.
10. ICU.ab,ti.
11. (1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10)
12. exp Diagnostic services/
13. exp Preventive health service/
14. exp Blood analysis/
15. exp Utilization review/ or Health care utilization/
16. exp Diagnostic test/
17. (12 or 13 or 14 or 15 or 16)
18. ((necessary or unnecessary or inappropriate or appropriat\* or routine or on-demand or routine or decreas\* or reduc\* or improv\* or optimi\*) adj7 (blood or hematolog\* or lab or laborator\*)).ab,ti.
19. (17 and 18)
20. ((necessary or unnecessary or inappropriate or appropriat\* or routine or on-demand or routine or decreas\* or reduc\* or improv\* or optimi\*) adj5 blood analysis).ab,ti.
21. ((necessary or unnecessary or inappropriate or appropriat\* or routine or on-demand or routine or decreas\* or reduc\* or improv\* or optimi\*) adj5 ((blood or hematolog\* or lab or laborator\*) adj3 (sampl\* or test\* or order\* or utili#ation))).ab,ti.
22. ((necessary or unnecessary or inappropriate or appropriate\* or routine or on-demand or routine or decreas\* or reduc\* or improv\* or optimi\*) adj5 ((blood or hematolog\* or lab or laborator\*) and (diagnostic services or diagnostic test or utilization review or health care utilization or preventive health service))).ab,ti.
23. (20 or 21 or 22)
24. (19 or 23)
25. (11 and 24)
26. animals/ not humans/
27. (25 not 26)

**MEDLINE (Ovid) 1946 to date of search**

1. exp Critical care/
2. exp Intensive care/
3. exp Intensive care unit/
4. exp Critical illness/
5. Intensive care.ab,ti.
6. Critical care.ab,ti.
7. Intensive care unit.ab,ti.
8. Critically ill.ab,ti.
9. Critical illness.ab,ti.
10. ICU.ab,ti.
11. (1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10)
12. exp Diagnostic services/
13. exp Preventive health service/
14. exp Hematologic tests/
15. exp Utilization review/ or health care utilization/
16. exp Diagnostic Tests, Routine/
17. exp Diagnostic Techniques and Procedures/
18. (12 or 13 or 14 or 15 or 16 or 17)
19. ((necessary or unnecessary or inappropriate or appropriat\* or routine or on-demand or decreas\* or reduc\* or improv\* or optim\*) adj7 (blood or hematolog\* or lab or laborator\*)).ab,ti.
20. (18 and 19)
21. ((necessary or unnecessary or inappropriate or appropriat\* or routine or on-demand or decreas\* or reduc\* or improv\* or optim\*) adj5 blood analysis).ab,ti.
22. ((necessary or unnecessary or inappropriate or appropriat\* or routine or on-demand or decreas\* or reduc\* or improv\* or optim\*) adj5 (blood or hematolog\* or lab or laborator\*) adj3 (sampl\* or test\* or order\* or utili#ation)).ab,ti.
23. ((necessary or unnecessary or inappropriate or appropriat\* or routine or on-demand or decreas\* or reduc\* or improv\* or optim\*) adj5 ((blood or hematolog\* or lab or laborator\*) and (diagnostic services or diagnostic test or utili\*ation review or health care utili\*ation or preventive health service))).ab,ti.
24. (21 or 22 or 23)
25. (20 or 24)
26. (11 and 25)
27. animals/ not humans/
28. (26 not 27)

**The Cochrane Library (Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews) from inception to latest issue**

1. Mesh Descriptor: [Critical Illness] explode all trees
2. Mesh Descriptor: [Critical Care] explode all trees
3. intensive care.ti,ab,kw
4. critical care.ti,ab,kw
5. critically ill.ti,ab,kw
6. critical illness.ti,ab,kw
7. ICU.ti,ab,kw
8. (#1 or #2 or #3 or #4 or #5 or #6 or #7)
9. Mesh Descriptor: [Hematologic Test] explode all trees
10. Mesh Descriptor: [Diagnostic Tests, Routine] explode all trees
11. Mesh Descriptor: [Diagnostic Services] explode all trees
12. Mesh Descriptor: [Diagnostic Technics and Procedures] explode all trees
13. Mesh Descriptor: [Utilization Review] explode all trees
14. Mesh Descriptor: [Preventive Health Services] explode all trees
15. (blood or hematologic or lab or laboratory) near/7 (test or sample or order or utilization).ti,ab,kw
16. (#9 or #10 or #11 or #12 or #13 or #14 or #15)
17. routine.ti,ab,kw
18. on-demand.ti,ab,kw
19. inappropriate.ti,ab,kw
20. appropriate.ti,ab,kw
21. necessary.ti,ab,kw
22. unnecessary.ti,ab,kw
23. reduce.ti,ab,kw
24. decrease.ti,ab,kw
25. optimize.ti,ab,kw
26. improve.ti,ab,kw
27. (#17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26)
28. (#16 and #27)
29. (#8 and #29)

## Data extraction template

**Trial identification**

|  |  |  |  |
| --- | --- | --- | --- |
| **Author** | **Year** | **Journal** | **Information sources** |
|  |  |  |  |

**Trial characteristics**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Design** | **Setting** | | | | |
| Country | Duration | Study period | No. of centers | Unit characteristics |
|  |  |  |  |  |  |

**Participants**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Inclusion criteria** | **Exclusion criteria** | **N patients** | **N patient days** | **Type of patients (Medical/surgical/mixed)** | **Age** |
|  |  |  |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Comorbidities/ disease severity score** | **No of pt with mechanical ventilation** | **No of pt with A-lines** | **No of patients with RRT** | **Severity of illness** |
|  |  |  |  |  |

**Comparison**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Intervention** | | | **Control** | | | **Co-interventions** |
| Description | Duration | N patient | Description | Duration | N patient |  |
|  |  |  |  |  |  |  |

**Outcomes evaluated in the trial**

|  |  |  |  |
| --- | --- | --- | --- |
| **Test-centred measures** | **Patient-centred outcomes** | **Resource utilisation-centred measures** | **Other measures** |
|  |  |  |  |

**Patient-centred outcomes**

|  |  |  |  |
| --- | --- | --- | --- |
| **All-cause mortality** | | | |
| ICU-mortality | | Hospital-mortality | |
| Intervention | Control | Intervention | Control |
|  |  |  |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Length of stay (days)** | | | | | |
| ICU length of stay | | Trauma centre length of stay | | Hospital length of stay | |
| Intervention | Control | Intervention | Control | Intervention | Control |
|  |  |  |  |  |  |

|  |  |  |
| --- | --- | --- |
| **Adverse events** | | |
| Outcome definition | Intervention | Control |
|  |  |  |

**Test-centred outcomes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Test characteristics** | | | |
| Characteristics of targeted test | Definition of routine/ unnecessary | Targeted laboratory tests | Targeted point-of-care tests |
|  |  |  |  |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Frequency of blood testing** | | | | | | | | | |
| Outcome definition | Control | | | Intervention | | | Post intervention | | |
| Total test | Lab tests | POCT | Total test | Lab tests | POCT | Total test | Lab tests | POCT |
|  |  |  |  |  |  |  |  |  |  |

|  |  |  |
| --- | --- | --- |
| **Reduction in blood testing** | | |
| Outcome definition | Reduction in tests in intervention | Theoretic reduction in tests (observational) |
|  |  |  |

|  |  |  |
| --- | --- | --- |
| **Exposure to daily testing** | | |
| Outcome definition | Intervention | Control | |
|  |  |  | |

|  |  |  |
| --- | --- | --- |
| **Abnormal values** | | |
| Outcome definition | Intervention | Control |
|  |  |  |

|  |  |  |
| --- | --- | --- |
| **Interventions per test** | | |
| Outcome definition | Intervention | Control |
|  |  |  |

**Resource utilisation-centred outcomes**

|  |  |  |
| --- | --- | --- |
| **Resource utilisation measures** | | |
| Reported estimated direct saving | Reported estimated indirect saving | Work hours freed |
|  |  |  |

**Other measures**

|  |  |  |
| --- | --- | --- |
| **Other measures** | | |
| Outcome definition | Intervention | Control | |
|  |  |  | |

## Deviations from study protocol

|  |  |  |
| --- | --- | --- |
| Protocol method | Deviation from protocol | Justification |
| We planned to include all study designs, including systematic reviews in our review. | Prior to commencing the record screening process, we restricted our eligibility criteria to include sources reporting original data only. | We sought to only include records reporting original data, thus minimizing the potential bias due to duplication of data.  We checked reference lists in all relevant systematic review articles identified. |
|  |  |  |

# Supplemental Results

## Supplemental Table 1: Author contact

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Author/ year | Author contacted | Author responded | Additional data provided | Did not respond |
| Agostini et al. 2017 | X |  |  | X |
| Bansal et al. 2001 | X | X |  |  |
| Bosque et al. 2019 | X |  |  | X |
| Chin et al. 2021 | X |  |  | X |
| Conroy et al. 2021 | X | X | X |  |
| Fresco et al. 2016 | X |  |  | X |
| Goddard et al. 2011 | X |  |  | X |
| Gray et al. 2014 | X |  |  | X |
| Hagg et al. 2015 | X |  |  | X |
| Hall et al. 2016 | X |  |  | X |
| Haney et al. 2022 | X |  |  | X |
| Hussey et al. 2011 | X |  |  | x |
| Jefferson et al. 2018 | X | X | X |  |
| Jones et al. 2019 | X |  |  | X |
| Khan et al. 2019 | X |  |  | X |
| Kotecha et la. 2017 | X |  |  | X |
| Laird et al. 2011 |  |  |  | X |
| Leydier et al. 2016 | X | X | X |  |
| Martínez-Balzano et al. 2017 | X |  |  | X |
| Marx et al. 1999 | X | X |  |  |
| Mian et al. 2019 | X | X |  |  |
| Mikhaeil et al. 2017 | X |  |  | X |
| Mukthar et al. 2011 | X | X | X |  |
| Murphy et al. 2016 | X | X | X |  |
| Packer et al. 2014 | X |  |  | X |
| Piexoto et al. 2013 |  |  |  | X |
| Rachankonda et al. 2017 | X | X | X |  |
| Rakes et al. 2016 | X | X |  |  |
| Rice et al. 2012 | X | X |  |  |
| Rutledge et al. 1991 | X |  |  | X |
| Raad et al. 2017 | X |  |  | X |
| Sasser et al. 2003 | X |  |  | X |
| Saxena et al. 2003 | X |  |  | X |
| Simvoulidids et al. 2020 | X |  |  | X |
| Sinitsky et al. 2017 | X | X | X |  |
| Smoller et al. 1986 | X | X |  |  |
| Venkatram et al. 2011 | X |  |  | X |
| Vezzani et al. 2013 | X |  |  | X |
| Viau-Lapointe et al. 2018 | X | X | X |  |
| Walsh et al. 2019 | X | X | X |  |

## Supplemental Table 2: Characteristics of non-randomised studies of interventions

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author/ year | Information source | Study type | Country | Setting | N Population | Intervention | Comparison | Duration | Outcome |
| Bansal et al. 20011 | Published paper | UTS, Retrospective | USA | Mixed ICU, teaching hospital | NR | Ordering process change | Usual care | 12 wks; C: 5 wks, I: 7 wks | **Test-centred measures:**  Number of ABGs |
| Barie et al. 19962 | Published paper and follow-up3 | UTS, Prospective | USA | Surgical ICU, teaching hospital | 1625; C: 502, I: 1123 | Education, feedback, financial incentives | Usual care | 34 mos; C: 4 mos, I: 30 mos | **Test-centred measures:**  Number of blood gasses and laboratory tests  **Patient-centred outcomes:**  ICU mortality, in-hospital mortality, ICU LOS, hospital LOS, RBC levels, RBF, FP and platelets transfusions  **Resource utilisation-centred measures:**  Cost reduction  **Other measures:**  Number of CXR and utilisation of pharmaceuticals |
| Bosque et al. 20194 | Two published abstracts4,5 | ITS, Prospective | Spain | Mixed ICU, teaching hospital | NR | Education | Usual care | 25 mos; C: 10 mos, I: 1 mos, PI: 3 mos | **Test-centred measures:**  Number of unnecessary blood tests |
| Chin et al. 20216 | Published paper and electronic supplementary material | UTS, Retrospective | USA | Mixed ICU, teaching hospital | 5685; C: 2852, I: 2833  (ICU sub-population) | Ordering process change | Usual care | 2 yrs; C: 1 yr, I: 1 yr | **Test-centred measures:**  Number of blood tests and number of labs completed per order  **Patient-centred outcomes:**  Adverse events and ICU LOS |
| Chu et al. 19967 | Published paper | NRCT | USA | Trauma setting, teaching hospital | 1155; C: 552; I:603 | Ordering process change | Usual care | 15 mos; C: 3 mos, I: 3mos | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  Hospital mortality, hospital LOS, adverse events, proportion of patients exposed to blood tests, number of test results outside the reference range, RBC levels. and medical interventions per blood test  **Resource utilisation-centred measures:**  Cost reduction |
| Clouzeau et al. 20198 | Published paper | CITS, Prospective | France | Medical ICU, teaching hospital | ICU A: 3315; C: 875, I: 1866, PI: 574  ICU B: 2392 | Education, feedback, supervision | Usual care | 4 yrs; C: 1 yr, I: 2 yrs, PI: 1yr | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  ICU mortality and adverse events  **Resource utilisation-centred measures:**  Cost reduction |
| Conroy et al. 20219 | Published paper and author contact | UTS, Prospective | USA | Medical ICU, teaching hospital | 3849; C: 2797, I: 1052 | Audit, education, ordering process change, review, visual reminders | Usual care | 3 yrs; C: 2 yrs; I: 9 mos | **Test-centred measures:**  Number of blood tests ordered and frequency of stat priority laboratory ordering  **Patient-centred outcomes:**  ICU mortality, RBC transfusions, RRT initiations, and CLABSI rate  **Resource utilisation-centred measures:**  Cost reduction |
| Dhanani et al. 201810 | Published paper | ITS, Retrospective | Australia | Mixed ICU, teaching hospital | 3250; C: 1141, I: 1067, PI: 1042 | Audit, education, guidelines, feedback, ordering process change, supervision | Usual care | 3 yrs; C: 6 mos, I: 6 mos, PI: 6 mos | **Test-centred measures:**  Number of blood test  **Patient-centred outcomes:**  ICU mortality, ICU LOS, mechanical ventilation, renal dialysis, transfusion rates, RBC levels, and proportion of test results outside the reference range  **Resource utilisation-centred measures:**  Cost reduction |
| Fresco et al. 201611 | Published abstract | CITS, Prospective | France | Surgical ICU, teaching hospital | 616; C: 274, I: 342 | Guidelines | Usual care | 1,5 yrs: C: 6 mos, I: 6 mos | **Test-centred measures:**  Number of routine blood tests  **Patient-centred outcomes:**  ICU LOS, ICU mortality, transfusion rates, and rate of nosocomial infections potentially related to blood sampling  **Resource utilisation-centred measures:**  Cost reduction |
| Goddard et al. 201112 | Published abstract | UTS, Prospective | UK | Critical care unit, teaching hospital | NR | Ordering process change | Usual care | 200 days; C: 100 days, I: 100 days | **Test-centred measures:**  Number of blood tests  **Resource utilisation-centred measures:**  Cost reduction |
| Hagg et al. 201513 | Published abstract | UTS, Prospective | USA | Medical ICU, non-teaching hospital | 1316; C: NR, I: NR | Education, checklists | Usual care | 4 mos; C: 1 mos, I: 3 mos | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  Adverse events |
| Hall et al. 201614 | Two published abstracts14,15 | ITS, Retrospective | UK | NR ICU, non-teaching hospital | 30; C: 20, I: 10 | Guidelines | Usual care | 4 mos; C: 2 mos, I: 2 mos | **Test-centred measures:**  Appropriateness of blood tests  **Patient-centred outcomes:**  Changes in haematocrit and haemoglobin, major change in overall condition, and volume of blood drawn for blood testing  **Resource utilisation-centred measures:**  Cost reduction |
| Haney et al. 202216 | Published abstract | ITS, Prospective | USA | Surgical ICU, teaching hospital | 1691; C: 827, I: 864 | Education | Usual care | 19 mos; C: 7 mos, I: 7 mos | **Test-centred measures:**  Number of laboratory tests |
| Hussey et al. 201117 | Published abstract | ITS, Retrospective | UK | Mixed ICU, non-teaching hospital | 125; C: 87, I: 58 | Guidelines | Usual care | 2 mos; C: 1 mos, I: 1 mos | **Test-centred measures:**  Number of coagulations tests  **Patient-centred outcomes:**  ICU LOS, adverse events, blood volume drawn for tests, and proportion of results outside reference range |
| Jacobs et al. 200018 | Published paper | NRCT, Prospective | USA | Trauma setting, teaching hospital | 235; C: 87, I:148 | Ordering process change | Usual care | 3 mos | **Test-centred measures:**  Number of blood tests ordered  **Patient-centred outcomes:**  Proportion of patients exposed to laboratory tests and adverse events  **Resource utilisation-centred measures:**  Cost reduction |
| Jefferson et al. 201819 | Published paper and author contact | ITS, Prospective | USA | Medical ICU, teaching hospital | 81; C: 41, I: 40 | Education, feedback guidelines | Usual care | 3 mos; C: 2 wks, I: 2 wks | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  ICU mortality, ICU LOS, adverse events and changes in RBC levels  **Resource utilisation-centred measures:**  Patient charges |
| Khan et al. 201920 | Published abstract | ITS, Prospective | USA | Medical ICU, teaching hospital | NR | Ordering process change | Usual care | NR | **Test-centred measures:**  Number of blood tests, percentage of patients on whom a lab-plan was discussed on rounds**,** andpercentage of labs deemed non-value added |
| Ko et al. 201621 | Published paper | UTS, Retrospective | USA | Surgical ICU, teaching hospital | C: 492, I: 1040 | Checklists, continuous capnography on ventilated patients, education | Usual care | 12 mos; C: 4 mos, I: 8 mos | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  ICU mortality, ICU LOS and volume blood drawn for blood testing  **Resource utilisation-centred measures:**  Cost reduction  **Other measures:**  Number of CXR |
| Kotecha et al. 201722 | Published abstract23 and published paper | ITS, Retrospective | USA | Medical ICU, teaching hospital | NR | Education, guidelines | Usual care | 11 mos; C: 3 wks, I: 2 mos, PI: NR | **Test-centred measures:**  Reduction in unnecessary tests and number of blood tests done without clinical indication  **Patient-centred outcomes:**  Adverse events and proportion of patients exposed to laboratory tests |
| Kumwilaisak et al. 200824 | Published paper | UTS, Prospective | USA | Surgical ICU, teaching hospital | 1117; C: 558, I: 559 | Education, guidelines | Usual care | 12 mos; C: 6 mos, I: 6 mos | **Test-centred measures:**  Number of laboratory tests and number of laboratory tests ordered through on demand  **Patient-centred outcomes:**  ICU mortality, ICU LOS, ICU readmission, laboratory values, duration of mechanical ventilation, RBC levels, RBC transfusion rates, proportion of test results outside the reference range, and adverse events |
| Le Maguet et al. 201525 | Published letter to the editor only | ITS, Prospective | France | Mixed ICU, teaching hospital | 1817; C: 886, I: 931 | Education, guidelines | Usual care | 16 mos; C: 2 mos, I: 4 mos | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  ICU mortality and ICU LOS  **Resource utilisation-centred measures:**  Cost reduction  **Other measures:**  Number of CXRs |
| Leydier et al. 201626 | Published abstract and unpublished paper | UTS, Retrospective | France | Medical ICU, teaching hospital | 3586; C: 746, I: 2822 | Guidelines | Usual care | 4 yrs; C: 1 yr, I: 3 yrs | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  ICU mortality, in-hospital mortality, transfusion rates, mechanical ventilation, RRT, invasive monitoring, vasoactive drugs and volume of blood drawn for testing  **Resource utilisation-centred measures:**  Cost reduction |
| Martínez-Balzano et al. 201727 | Published paper | UTS, Retrospective | USA | 7 ICUs; 3  medical, 2 trauma-surgery, 1 cardiovascular, and 1neurosurgical, teaching hospital | NR | Education, guidelines | Usual care | 2 yrs; C: 1 yrs, I: 1 yrs | **Test-centred measures:**  Number of ABG determinations, ABG determinations per patient per mechanical ventilation day, and appropriateness of ABG determinations  **Patient-centred outcomes:**  ICU mortality, ICU LOS, ICU readmission, days on mechanical ventilation, volume blood drawn for ABG determinations, and clinical interventions based on ABG determinations  **Resource utilisation-centred measures:**  Cost reduction and work time freed |
| Marx et al. 199928 | Published paper | ITS, Prospective | USA | Mixed ICU, teaching hospital | 157; C: 72, I: 85 | Education | Usual care | NR; C: NR, I: 6 mos | **Test-centred measures:**  Number of daily blood tests  **Patient-centred outcomes:**  ICU mortality, ICU LOS, rate of blood stream infections, rate of urinary tract infections, rate of nosocomial pneumonia, and mechanical ventilation  **Resource utilisation-centred measures:**  Cost reduction related to blood tests, CXRs, and neuromuscular blocking agents, and total reduction in annualized cost per patient day  **Other measures:**  Number CXRs |
| Mehari et al. 199729 | Published paper and published follow-up30 | ITS, Prospective | New Zealand | Mixed ICU and post-cardiac surgery ward, teaching hospital | 293; C: 99, I: 100, PI: 94 | Guidelines | Usual care | 5 mos; C: 1 mos, I: 1 mos, FU: NR | **Test-centred measures:**  Number of blood tests and number of blood tests pr ventilator time  **Patient-centred outcomes:**  Mean ventilator time  **Resource utilisation-centred measures:**  Cost reduction |
| Merkeley et al. 201631 | Published abstract32 and published paper | UTS, Prospective | Canada | Mixed ICU, teaching hospital | 1440; C: 709, I: 731 | Education, guidelines, ordering process change | Usual care | 24 mos; C: 12 mos, I: 12 mos | **Test-centred measures:**  Number of routine laboratory tests and number of non-routine laboratory tests  **Patient-centred outcomes:**  ICU mortality, in-hospital ICU, ICU LOS and RBC transfusion rates  **Resource utilisation-centred measures:**  Cost reduction |
| Merlani et al. 200133 | Published paper | UTS, Prospective | Switzerland | Surgical ICU, teaching hospital | 549; C: 189, pilot: 176, I: 184 | Education, feedback, guidelines | Usual care | 3 yrs: C: 10 mos, P: 10 mos, I: 10 mos | **Test-centred measures:**  Number of ABGs, number of non-targeted laboratory tests, and adherence to ABG guidelines  **Patient-centred outcomes:**  ICU mortality, ICU LOS, and volume blood drawn for ABG tests  **Resource utilisation-centred measures:**  Cost reduction and nurse work time reduction |
| Mian et al. 201934 | Published abstract and author contact | ITS, Prospective | UK | Mixed ICU, teaching hospital | 26; C: 10, I:16 | Ordering process change | Usual care | 16 days; C: 8 days, I: 8 days | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  Adverse events  **Resource utilisation-centred measures:**  Cost of unnecessary tests |
| Murphy et al. 201635 | Published paper and author contact | UTS, Prospective | USA | 7 ICUs; two cardiothoracic, two neurosciences, two medical, one surgical, teaching hospital | 22567; C: 7357, I: 7553, PI: 7657 | Audit, education, feedback, financial incentives | Usual care | 36 mos; C: 12 mos, I: 12 mos, FU: 12 mos | **Test-centred measures:**  Number of ABGs  **Patient-centred outcomes:**  ICU mortality, in-hospital mortality, ICU LOS, RBC transfusion rates and adverse events  **Resource utilisation-centred measures:**  Cost reduction  **Other measures:**  Number of CXRs |
| Musca et al. 201636 | Published paper | UTS, Prospective | Australia | Mixed ICU, teaching hospital | 253; C: 100, I: 153 | Education, guidelines, ordering process change | Usual care | 4 mos; C: 2 mos, I: 1 mos | **Test-centred measures:**  Number of coagulation tests and number of other pathology tests  **Patient-centred outcomes:**  ICU LOS, volume of blood drawn for testing and adverse events  **Resource utilisation-centred measures:**  Cost reduction |
| Pageler et al. 201337 | Published paper | UTS, Retrospective | USA | Paediatric ICU, teaching hospital | 1839; C: 818, I: 1021 | Audits, education, feedback, ordering process change | Usual care | 24 mos; C: 12 mos, I: 12 mos | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  ICU mortality, PICU LOS, and hospital LOS  **Resource utilisation-centred measures:**  Cost reduction |
| Pilon et al. 199738 | Published paper | ITS, Retrospective | Canada | Mixed ICU, teaching hospital | 150; C: 60, I: 90 | Education, guidelines | Usual care | 3 yrs; C: 2 yrs, I: 3 mos | **Test-centred measures:**  Number of ABGs and appropriateness of ABGs  **Patient-centred outcomes:**  ICU mortality, mechanical ventilation, and time to wean from mechanical ventilation  **Resource utilisation-centred measures:**  Cost reduction |
| Prat et al. 200939 | Published paper | UTS, Retrospective | France | Medical ICU, teaching hospital | 1175; C: 541, I: 634 | Education, feedback, guidelines | Usual care | 24 mos; C: 12 mos, I: 12 mos | **Test-centred measures:**  Number of blood tests  **Resource utilisation-centred measures:**  Cost reduction  **Other measures:**  Number of CXRs |
| Rachakonda et al. 201740 | Published paper and author contact | ITS, Prospective | Australia | Mixed ICU, teaching hospital | 2736; C: 1289, I: 1447 | Education, guidelines, ordering process change | Usual care | 18 mos; C: 6 mos, I: 6 mos | **Patient-centred outcomes:**  Adverse events and adverse patient outcomes  **Resource utilisation-centred measures:**  Cost reduction, cost of high-frequently ordered tests, expenses for individual blood tests  **Other measures:**  Protocol compliance |
| Rakes et al. 201641 | Two published abstracts41,42 | UTS, Prospective | USA | Paediatric ICU, teaching hospital | 2156; C: 1539, I: 617 | Checklists, education, feedback, ordering process change | Usual care | NR; C: NR, I: 12 mos | **Test-centred measures:**  Frequency of POC-testing, duplicate testing of BUN, creatinine and CBC, and number of non-POCT blood tests  **Patient-centred outcomes:**  ICU mortality  **Resource utilisation-centred measures:**  Cost reduction |
| Rice et al. 201243 | Published abstract | UTS, Prospective | UK | High dependency unit, non-teaching hospital | NR | Education | Usual care | 4 wks; C: 2 wks, I: 2 wks | **Test-centred measures:**  Frequency of coagulation tests, indication for coagulation test, and appropriateness of tests  **Patient-centred outcome measures:**  Proportion of test results outside the reference range  **Resource utilisation-centred measures:**  Cost reduction |
| Roberts et al. 199144 | Published paper and follow-up45 | UTS, Prospective | Canada | Mixed ICU, teaching hospital | 4232; C: 647, I:1236, PI:2349 | Guidelines | Usual care | 43 mos; C: 7 mos, I: 12 mos, PI: 24 mos | **Test-centred measures:**  Number of targeted blood tests and number of non-targeted blood tests  **Patient-centred outcomes:**  ICU mortality, ICU LOS, and adverse events  **Resource utilisation-centred measures:**  Cost reduction |
| Raad et al. 2017 46 | Published abstract47 and paper | UTS, Prospective | USA | Medical ICU, teaching hospital | NR | Education, guidelines, ordering process change | Usual care | 12 mos; C: 3 mos, I: 9 mos | **Test-centred measures:**  Number of laboratory tests, number of STAT-test, and number of duplicate testing  **Patient-centred outcomes:**  In-hospital mortality, hospital LOS, exposure to daily routine testing, RBC transfusion rate, central line utilisation, and CLABSI rate  **Resource utilisation-centred measures:**  Cost reduction and work hours freed  **Other measures:**  Number of CXR |
| Sachdeva et al. 199648 | Published paper | UTS, Prospective | USA | Paediatric ICU, teaching hospital | 598; C: 325, I: 273 | Education | Usual care | 4 mos; C: 2 mos, I: 2 mos | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  PICU mortality, PICU LOS, and quality assurance measures  **Other measures:**  Number of radiology tests, number CT images and drug consumption |
| Sasser et al. 201849 | Published abstract | UTS, Prospective | USA | Paediatric ICU, teaching hospital | 477; C: 271, I:206 | Guidelines | Usual care | NR | **Test-centred measures:**  Number of blood gas measures, proportion of blood gases ordered as part of ICU-panel, and proportion of blood gases ordered as individual tests  **Resource utilisation-centred measures:**  Cost reduction |
| Saxena et al. 200350 | Published paper | UTS, Prospective | USA | Surgical ICU, teaching hospital | NR | Ordering process change | Usual care | 8 mos; C: 3 mos, I: 5 mos | **Test-centred measures:**  Number of routine and STAT blood tests, number redundant and overlapping tests  **Patient-centred outcomes:**  RBC transfusion rates and volume blood drawn for tests |
| Seguin et al. 200251 | Published paper | UTS, Prospective | France | Surgical ICU, teaching hospital | 287; C: 128, I: 159 | Education, guidelines | Usual care | 4 mos; C: 2 mos, I: 2 mos | **Test-centred measures:**  Number of laboratory test  **Patient-centred outcomes:**  ICU LOS and ICU mortality  **Resource utilisation-centred measures:**  Cost reduction  **Other measures:**  Number of CXRs |
| Simvoulidis et al. 202052 | Published abstract | UTS, Retrospective | Brazil | NR ICU, non-teaching hospital | NR; C: NR, I: 1300 | NR | Usual care | NR | **Test-centred measures:**  Number of blood test requests  **Patient-centred outcomes:**  ICU mortality, ICU LOS, and use of invasive interventions  **Resource utilisation-centred measures:**  Cost reduction |
| Sinitsky et al. 201753 | Published paper, published abstract54 and author contact | ITS, Prospective | UK | Paediatric ICU, teaching hospital | 1365; C: 718, I: 647\* | Education, ordering process change | Usual care | 19 mos; C: 10 mos, I: 9 mos | **Test-centred measures:**  Number of routine blood tests  **Resource utilisation-centred measures:**  Cost reduction |
| Vezzani et al. 201355 | Published paper | ITS, Prospective | Italy | Mixed ICU, teaching hospital | NR | Guidelines | Usual care | 1 yrs; C: 1 mos, I: 2 mos | **Test-centred measures:**  Number of chemistry laboratory tests, number of routine tests, and number of non-routine tests  **Patient-centred outcomes:**  ICU mortality, ICU LOS, and adverse events  **Resource utilisation-centred measures:**  Cost reduction |
| Viau-Lapointe et al. 201856 | Published abstract and author contact | UTS, Prospective | Canada | Mixed ICU, teaching hospital | 87; C: 55, I: 32 | Education, guidelines, ordering process change | Usual care | 11 mos; C: 2 mos, I: 9 mos | **Test-centred measures:**  Number of routine tests per patient day in the first 28 days of ICU stay |
| Walsh et al. 202057 | Published abstract58, published paper, and author contact | ITS, Prospective | Australia | Two mixed ICUs, one cardiothoracic ICU, one neuroscience ICU, teaching hospital | 3750; C: 1891, I: 1859 | Education, guidelines | Usual care | 12 mos; C: 6 mos, I: 6 mos | **Test-centred measures:**  Number of ABG, appropriateness of ABG  **Patient-centred outcome measures:**  Volume of blood drawn for tests  **Resource utilisation-centred measures:**  Cost reduction |
| Wang et al. 200259 | Published paper | CITS, Prospective | USA | Coronary care unit, medical ICU, teaching hospital | 828; C: 438, I: 390 | Education, guidelines, ordering process change | Usual care | 15 mos; C: 3mos, I: 3mos | **Test-centred measures:**  Number of laboratory tests  **Patient-centred outcomes:**  ICU mortality, in-hospital mortality, ICU LOS, hospital LOS, ICU readmission rates and days on mechanical ventilation  **Resource utilisation-centred measures:**  Cost reduction  **Other measures:**  Number of CXRs |
| Welty et al 202260 | Published paper | UTS, Prospective | USA | Paediatric ICU, teaching hospital | 33; C: 14, I: 19 | Guidelines | Usual care | 2 yrs; C: 1yrs, I: 1 yrs | **Test-centred measures:**  Number of laboratory tests per ECMO day  **Patient-centred outcomes:**  Hospital LOS, hospital mortality, CLABSI rate, RBC transfusion rates while on ECMO and average time on ECMO  **Resource utilisation-centred measures:**  Cost reduction |
| Yorkgitis et al. 201861 | Published paper | UTS, Prospective | USA | Surgical ICU, teaching hospital | 307; C: 155, I: 152 | Ordering process change | Usual care | 7 mos; C: 3.5 mos, I: 3.5 mos | **Test-centred measures:**  Number of blood tests  **Patient-centred outcomes:**  In-hospital mortality, ICU LOS, days with mechanical ventilation, and RBC transfusions  **Other measures:**  Frequency of CXR ordered per day |

Abbreviations: Uninterrupted time series (UTS), Interrupted time series (ITS), Controlled interrupted time series (CITS), Non-randomised controlled trial (NRCT), Not reported (NR), Intensive care unit (ICU), High dependency unit (HDU), Critical care unit (CCU), Paediatric intensive care unit (PICU), Weeks (wks), Moths (mos), Years (yrs), Arterial blood gas (ABG), Length of stay (LOS), Central line-associated bloodstream infection (CLABSI), Red blood cell (RBC), Frozen plasma (FP), Chest x-ray (CXR), Computerised tomography (CT), Extracorporeal membrane oxygenation (ECMO)..

\*Calculated based on study duration and reported average number of monthly admissions

## Supplemental Table 3: Characteristics of observational studies

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author/ year | Information source | Study type | Country | Setting | Population | Exposure | Comparison | Duration | Outcome |
| Agostini et al. 201762 | Published abstract | Retrospective cohort | UK | CCU, non-teaching hospital | 44 | Usual care | NA | NR | **Test-centred measures:**  Number of laboratory tests and appropriateness of routine blood tests  **Patient-centred outcomes:**  Number of patients receiving transfusion  **Resource utilisation-centred measures:**  Cost of laboratory tests |
| Baigelman et al. 198563 | Published paper | Prospective cohort | USA | Mixed ICU, Respiratory care unit, teaching hospital | 145 | Usual care | NA | 2 mos | **Test-centred measures:**  Number of unnecessary serum electrolytes sets  **Resource utilisation-centred measures:**  Cost of unnecessary blood tests |
| Clark et al. 201164 | Published paper | Retrospective cohort | USA | Neuro ICU, teaching hospital | 93 | Usual care | NA | 7 mos | **Test-centred measures:**  Number of electrolyte measurements  **Patient-centred outcomes:**  Changes in haemoglobin, transfusion rates, number of electrolyte replacements, and medications affecting electrolytes  **Resource utilisation-centred measures:**  Cost of electrolyte panels |
| Gray et al. 201465 | Published abstract | Prospective cohort | UK | Mixed ICU, teaching hospital | NR | Routine blood test guidelines | NA | 28 days | **Test-centred measures:**  Number of inappropriate tests according to guideline  **Resource utilisation-centred measures:**  Cost of all blood tests, cost of inappropriate blood tests |
| Jones et al. 201966 | Published abstract | Retrospective cohort | UK | NR ICU, teaching hospital | NR | Usual care | NA | 6 wks | **Test-centred measures:**  Number of ABGs, and appropriateness of ABGs  **Patient-centred outcomes:**  Alterations in ventilation of oxygenation strategies, potential reduction in blood volume drawn for ABGs  **Resource utilisation-centred measures:**  Potential cost reduction |
| Keller et al. 200467 | Published paper | Retrospective cohort | USA | Trauma setting, teaching hospital | 240 | Usual care | NA | 2 yrs | **Patient-centred outcomes:**  ICU mortality, proportion of patients exposed to laboratory tests, Proportion of tests results outside reference range,  and interventions specific for laboratory abnormalities |
| Laird et al. 201168 | Published abstract | Prospective cohort | UK | Mixed ICU, non-teaching hospital | 42 | Usual care | NA | 3 wks | **Test-centred measures:**  Frequency and indication of blood sampling and proportion of tests labelled as routine  **Patient-centred outcomes:**  Days with organ support, ICU LOS, and volume blood drawn for tests  **Resource utilisation-centred measures:**  Cost of blood tests |
| Lennox et al. 202269 | Published paper | Prospective cohort | UK | Surgical ICU and HDU, teaching hospital | 39 | Usual care | NA | 4 wks | **Test-centred measures:**  Frequency of phlebotomy episodes and samples, reason for sampling, volume of blood discarded, and sample route  **Patient-centred outcomes:**  Volume blood drawn for tests, anaemia makers, intra operative blood loss, and transfusion requirements  **Resource utilisation-centred measures:**  Time consumed for sampling and documenting |
| Mikhaeil et al. 201770 | Published paper | Cross-sectional cohort | Canada | Mixed ICU, teaching hospital | 81 | Usual care | NA | 4 wks | **Test-centred measures:**  Number and appropriateness of blood tests  **Resource utilisation-centred measures:**  Cost of blood tests |
| Mukhtar et al. 201171 | Published abstract | Prospective cohort | UK | Mixed ICU, teaching hospital | 20 | Usual care | NA | 5 days | **Test-centred measures:**  Number of routine blood tests and indication for routine blood tests  **Patient-centred outcomes:**  Interventions based on routine blood tests  **Resource utilisation-centred measures:**  Cost and time consumed with obtaining blood tests |
| Namias et al. 199672 | Published paper | Prospective cohort | USA | Trauma setting, teaching hospital | 500 | Usual care | NA | 7,5 mos | **Patient-centred outcomes:**  Proportion of patients exposed to laboratory tests, number of test results outside the reference range, and medical interventions based on blood tests and |
| Oliveira et al. 201473 | Published paper | Cross-sectional cohort | Brazil | Mixed ICU, teaching hospital | 105 | Usual care | NA | 2 mos | **Test-centred measures:**  Number of blood tests and proportion of tests regarded as unnecessary  **Patient-centred outcomes:**  ICU LOS  **Resource utilisation-centred measures:**  Cost of unnecessary blood tests |
| Packer et al. 201474 | Published abstract | Prospective cohort | UK | ICU & HDU, teaching hospital | NR | Usual care | NA | 4 wks | **Test-centred measures:**  Amount of blood samples and reasons for clotting screens  **Patient-centred outcomes:**  Blood loss due to blood sampling and rate of blood transfusions |
| Peixoto et al. 201375 | Published abstract | Retrospective cohort | Brazil | Mixed ICU, teaching hospital | 48 | Usual care | NA | 2 mos | **Test-centred measures:**  Number of laboratory tests  **Patient-centred outcomes:**  ICU mortality, ICU LOS, proportion of test results inside reference range, and volume blood drawn for tests  **Resource utilisation-centred measures:**  Cost of blood test |
| Rutledge et al. 199176 | Published paper | Retrospective cohort | USA | Mixed ICU, teaching hospital | NR | Usual care | NA | 2 wks | **Test-centred measures:**  Most frequently blood tests performed, and factor associated with ABG utilization  **Resource utilisation-centred measures:**  Cost of all blood test and STAT |
| Smoller et al. 198677 | Published paper | Retrospective cohort | USA | Mixed ICU, teaching hospital | 50 | Usual care | NA | NR | **Test-centred measures:**  Frequency of laboratory tests and type of tubes used for blood sampling  **Patient-centred outcomes:**  Rate of transfusion and volume blood drawn for tests |
| Spence et al. 201378 | Published paper and electronic supplementary material | Retrospective cohort | Canada | 9 ICUs, teaching and non-teaching hospitals | 10262 | Usual care | NA | 58 mos | **Test-centred measures:**  Number of total testing: cumulative number of nine common laboratory tests, three radiologic tests, and electrocardiograms performed in each ICU, and factor associated with testing  **Patient-centred outcomes:**  ICU mortality, ICU LOS, and 30-day mortality |
| Ullman et al. 201679 | Published paper | Cross sectional cohort | Australia | Mixed ICU, teaching hospital | 66  (neonatal population excluded, N=30) | Usual care | NA | 1 wk | **Test-centred measures:**  Frequency and type of blood sampling and reason for blood samples  **Patient-centred outcomes:**  Volume blood drawn for blood tests and ICU outcome at study completion  **Resource utilisation-centred measures:**  Cost of laboratory tests |
| Venkatram et al. 201180 | Published abstract | Retrospective cohort | USA | Medical ICU, teaching hospital | 389 | Usual care | NA | 3 mos | **Test-centred measures:**  Number of routine blood test  **Patient-centred outcomes:**  ICU LOS, mechanical ventilation and percentage of routine blood panels associated with a medical intervention |
| Zimmerman et al. 199781 | Published article | Prospective cohort | USA | 42 ICUS, teaching and non-teaching hospitals | 17440 | Usual care | NA | Mean 9.7 mos per ICU | **Test-centred measures:**  Type and number of blood samples for laboratory testing were recorded on ICU days 1 to 7, factors associated with blood testing |

Abbreviations: Not reported (NR), Not applicable (NA), Intensive care unit (ICU), High dependency unit (HDU), Critical care unit (CCU), Paediatric intensive care unit (PICU), Weeks (wks), Months (mos), Years (yrs), Arterial blood gas (ABG), Spontaneous breathing trial (SBT), Length of stay (LOS), Red blood cell (RBC).

## Supplemental Table 4: Population characteristics of non-randomised studies of interventions

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author/ year | Country | Setting | Mortality | Length of stay | Severity of illness |
| Bansal et al. 2001 | USA | Mixed ICU, teaching hospital | NR | NR | NR |
| Barie et al. 1997 | USA | Surgical ICU, teaching hospital | Hospital, C: 10.5%, I: 7.2% | ICU, C: 5.9 days, I: 4.0 days | APACHE II: 13.9-14.4  APACHE III: 43.6-45.9 |
| Bosque et al. 2019 | Spain | Mixed ICU, teaching hospital | NR | NR | NR |
| Chin et al. 2021 | USA | Mixed ICU, teaching hospital | NR | ICU, C: 11.0 days, I: 10.9 days | NR |
| Chu et al. 1996 | USA | Trauma centre, teaching hospital | Hospital, C: 8%, I: 9% | Trauma: C: 6.9 days, I: 3.0 days | Injury severity score: C: 12.4, I: 12.3 |
| Clouzeau et al. 2019 | France | Medical ICU, teaching hospital | ICU, C: 22%, I: 20-21.5%, PI: 19% | NR | SAPS II; I:52.6, II: 53.2, III: 53.7, IV: 50.8 |
| Conroy et al. 2021 | USA | Medical ICU, teaching hospital | NR | NR | NR |
| Dhanani et al. 2018 | Australia | Mixed ICU, teaching hospital | ICU, C: 4.9%, I: 5.7%, PI: 5.5% | ICU, C: 1.92 days, I: 2.01 days, PI: 1.89 days | APACHE III mean: C: 47.7, I: 50.5, PI: 45.9 |
| Fresco et al. 2016 | France | Surgical ICU, teaching hospital | NR | NR | NR |
| Goddard et al. 2011 | UK | Critical care unit, teaching hospital | NR | NR | NR |
| Hagg et al. 2015 | USA | Medical ICU, non-teaching hospital | NR | NR | NR |
| Hall et al. 2016 | UK | NR ICU, non-teaching hospital | NR | NR | NR |
| Haney et al. 2022 | USA | Surgical ICU, teaching hospital | NR | NR | NR |
| Hussey et al. 2011 | UK | Mixed ICU, non-teaching hospital | NR | NR | NR |
| Jacobs et al. 2000 | USA | Trauma centre, teaching hospital | NR | NR | Injury severity score: C: 11.6, I: 10.3 |
| Jefferson et al. 2018 | USA | Medical ICU, teaching hospital | ICU, C: 6 deaths, I: 4 deaths | ICU, C: 5.2 days, I: 6.2 days | APACHE IV: C: 82.4, I: 68.6  SOFA-score C: 9.6, I: 10.7 |
| Khan et al. 2019 | USA | Medical ICU, teaching hospital | NR | NR | NR |
| Ko et al. 2016 | USA | Surgical ICU, teaching hospital | ICU, C: 7.1%, I: 5.1% | ICU, C: 4.48 days, I: 4.82 days | APR severity of illness: C: 3.20, I: 3.20 |
| Kotecha et al. 2017 | USA | Medical ICU, teaching hospital | NR | NR | NR |
| Kumwilaisak et al. 2008 | USA | Surgical ICU, teaching hospital | ICU, C: 6.8%, I: 6.3% | ICU, C: 2 days, I: 2 days | ASA physical status: C: 3, I: 3 |
| La Maguet et al. 2015 | France | Mixed ICU, teaching hospital | ICU, C: 18%, I: 16% | ICU, C: 9 days, I: 8 days | SAPS II: 39 (C: 39, I: 40) |
| Leydier et al. 2016 | France | Medical ICU, teaching hospital | NR | NR | NR |
| Martínez-Balzano et al. 2017 | USA | 7 ICUs; 3  medical, 2 trauma-surgery, 1 cardiovascular, and 1neurosurgical, teaching hospital | NR | NR | NR |
| Marx et al. 1999 | USA | Mixed ICU, teaching hospital | NR | NR | NR |
| Mehari et al. 1997 | New Zealand | Mixed ICU and post-cardiac surgery ward, teaching hospital | NR | NR | C,I: APACHE II: no diff  FU: APACHE II: general ICU: 10.1, cardiac ICU: 9.15 |
| Merkeley et al. 2016 | Canada | Mixed ICU, teaching hospital | ICU, C: 18%, I: 17%  Hospital, C: 25%, I: 24% | ICU, C: 4 days, I: 4 days | APACHE II: C: 21, I: 20 |
| Merlani et al. 2001 | Switzerland | Surgical ICU, teaching hospital | ICU, C: 7.1, P: 7.2, I: 6.6 | ICU, C: 4.6 days, P: 4.3 days, I: 4.3 days | SAPS II: C: 29, P: 30, I: 30 |
| Mian et al. 2019 | UK | Mixed ICU, teaching hospital | NR | NR | NR |
| Murphy et al. 2016 | USA | 7 ICUs; two cardiothoracic, two neurosciences, two medical, one surgical, teaching hospital | ICU, C: 6.3%, I: 4.6%, PI: 5.1%  Hospital, C: 7.0%, I: 5.2%, PI: 5.5% | ICU, C: 4.0 days, I: 3.9 days, PI: 4.0 days | SOFA-score: 3.7 vs 5.3 vs 5.7, CCI: 3.1 vs 3.1 vs 3.1 |
| Musca et al. 2016 | Australia | Mixed ICU, teaching hospital | NR | ICU, C: 4 days, I: 3 days | APACHE II: C: 17, I: 15 |
| Pageler et al. 2013 | USA | Paediatric ICU, teaching hospital | Hospital, C: 3.9%, I: 3.0% | ICU, C: 5.1 days, I: 4.2 days  Hospital, C: 16.2 days, I: 11.6 days | Case mix index: C: 3.7, I: 3.0 |
| Pilon et al. 1997 | Canada | Mixed ICU, teaching hospital | ICU, C1: 21%, C2: 19%, I1: 20%, I2: 18%, I3: 13% | NR | APACHE II: 16.5 |
| Prat et al. 2009 | France | Medical ICU, teaching hospital | ICU, C: 25.3%, I: 24.8% | ICU, C: 9.2 days, I: 7.3 days | SAPS II: C: 45.9, I: 44.3 |
| Rachakonda et al. 2017 | Australia | Mixed ICU, teaching hospital | NR | ICU, C: 2.2 days, I: 2.3 days | NR |
| Rakes et al. 2016 | NR | Paediatric ICU, teaching hospital | ICU, C and I: 1-2% | NR | APACHE II: MICU: C: 22.9, I: 21.5; SICU: C: 18.1, I: 17.6 |
| Rice et al. 2012 | UK | High dependency unit, non-teaching hospital | NR | NR | NR |
| Roberts et al. 1993 | Canada | Mixed ICU, teaching hospital | MICU: C: 19.7%, I: 22.6%,  SICU: C: 12.7%, I: 8.9% | MICU: C: 4.3 days, I: 4.1 days;  SICU: C: 3.5 days, I: 3.1 days | NR |
| Raad et al. 2017 | USA | Medical ICU, teaching hospital | NR | NR | APACHE III: C: 53, I: 51 |
| Sachdeva et al. 1996 | USA | Paediatric ICU, teaching hospital | ICU, C: 5.2, I: 7.3 | ICU, C: 5.5 days, I: 5.2 days | PRISM: C: 9.7, I: 8.6 |
| Sasser et al. 2018 | USA | Paediatric ICU, teaching hospital | NR | NR | NR |
| Saxena et al. 2003 | USA | Surgical ICU, teaching hospital | NR | NR | NR |
| Seguin et al. 2002 | France | Surgical ICU, teaching hospital | ICU, C: 14%, I: 15% | ICU, C: 10 days, I:7 days | SAPS II: C: 34, I: 33.0 |
| Simvoulidis et al. 2020 | Brazil | NR ICU, non-teaching hospital | NR | NR | NR |
| Sinitsky et al. 2017 | UK | Paediatric ICU, teaching hospital | NR | NR | NR |
| Vezzani et al. 2013 | Italy | Mixed ICU, teaching hospital | ICU, C: 14%, I1: 18.5%, I2: 34% | ICU, C: 5.4 days, I1: 7.4 days, I2: 5.5 days | SAPS II: C: 34.8, I1: 42.2, I2: 43.9 |
| Viau-Lapointe et al. 2018 | Canada | Mixed ICU, teaching hospital | NR | NR | NR |
| Walsh et al. 2020 | Australia | Two mixed ICUs, one cardiothoracic ICU, one neurosciences ICU, teaching hospital | NR | NR | APACHE III |
| Wang et al. 2002 | USA | Coronary care unit, medical ICU, teaching hospital | CCU, C: 8.9%, I: 10.7%  Hospital, C:12.2%, I: 14.7% | CCU, C: 4.2 days, I: 4.0 days  Hospital, C: 12.3 days, I: 11.6 days | NR |
| Welty et al. 2022 | USA | Paediatric ICU (ECMO program) | C: 20%, I: 10.5% | Hospital, C:86.1, I: 78.1 | NR |
| Yorkgitis et al. 2018 | USA | Surgical ICU, teaching hospital | Hospital, C: 13/155, I: 15/152 | ICU, C: 5.60 days, I: 5.64 days | CCI: C: 2.3, I: 1.89  SOFA-score: C 4.06, I: 3.66, |

Abbreviations: Intensive care unit (ICU), Coronary care unit (CCU), Medical intensive care unit (MICU), Surgical intensive care unit (SICU), Not reported (NR), Control period (C), Intervention period (I), Post-intervention period (PI), Acute Physiology and Chronic Health Evaluation (APACHE), implified Acute Physiology Score (SAPS), All Patients Refined (APR), American Society of Anesthesiology (ASA), Sequential Organ Failure Asessment (SOFA), Charlson Comorbidity Index (CCI), Pediatric Risk of Mortality (PRISM).

## Supplemental Table 5: Population characteristics of observational studies

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author/ year | Country | Setting | Mortality | Length of stay | Severty of illness |
| Agostini et al. 2017 | UK | CCU, non-teaching hospital | NR | NR | NR |
| Baigelman et al. 1985 | USA | Mixed ICU, Respiratory care unit, teaching hospital | NR | NR | NR |
| Clark et al. 2011 | USA | Neuro ICU, teaching hospital | NR | ICU, 10.4 days | NR |
| Gray et al. 2014 | UK | Mixed ICU, teaching hospital | NR | NR | NR |
| Jones et al. 2019 | UK | NR ICU, teaching hospital | NR | NR | NR |
| Keller et al. 2004 | USA | Trauma centre, teaching hospital | Hospital, 6% | NR | Adult: Injury severity score: 7.2  Paediatric:  Paediatric Trauma Score: 9.1 |
| Laird et al. 2011 | UK | Mixed ICU, non-teaching hospital | NR | NR | NR |
| Lennox et al. 2022 | UK | Surgical ICU and HDU, teaching hospital | NR | NR | NR |
| Mikhaeil et al. 2017 | Canada | Mixed ICU, teaching hospital | NR | NR | NR |
| Mukhtar et al. 2011 | UK | Mixed ICU, teaching hospital | NR | NR | NR |
| Namias et al. 1996 | USA | Trauma centre, teaching hospital | NR | NR | NR |
| Oliveira et al. 2014 | Brazil | Mixed ICU, teaching hospital | NR | ICU, 8.6 days | NR |
| Packer et al. 2014 | UK | ICU & HDU, teaching hospital | NR | NR | NR |
| Peixoto et al. 2013 | Brazil | Mixed ICU, teaching hospital | ICU, 33% | ICU, 11.5 days | APACHE II: C1: 26, C2: 26.5, I1: 25, I2: 28, I3: 26.5 |
| Rutledge et al. 1991 | USA | Mixed ICU, teaching hospital | NR | NR | NR |
| Smoller et al. 1986 | USA | Mixed ICU, teaching hospital | NR | NR | NR |
| Spence et al. 2013 | Canada | 9 ICUs, teaching and non-teaching hospitals | ICU, T: 10.6%, nT: 10.2% | ICU: T: 2.6 days, nT: 2.7 days | APACHE II: T:14.9, nT 15.6 |
| Ullman et al. 2016 | Australia | Mixed ICU, teaching hospital | ICU, Adult: 2% ICU, Paediatric: 0% | NR | Adult: APACHE II: 16.1,  Paediatric: PELOD2: 3.5 |
| Venkatram et al. 2011 | USA | Medical ICU, teaching hospital | NR | NR | APACHE IV: 66.7±28.3 vs 73.8±28 |
| Zimmerman et al. 1997 | USA | 42 ICUS, teaching and non-teaching hospitals | Hospital, T:19.4%, nT: 15.8% | ICU, T: 5.4 days, nT: 4.5 days | APACHE III at ICU day 1: T: 52.1, nT: 48.4 |

Abbreviations: Intensive care unit (ICU), Critical care unit (CCU), High dependency unit (HDU), Not reported (NR), Acute Physiology and Chronic Health Evaluation (APACHE), Paediatric Logistic Organ Dysfunction (PELOD), teaching (T), non-teaching (nT), Extracorporeal Membran Oxygenation (ECMO).

## Supplemental Table 6: Reported outcome measures categorised

|  |  |
| --- | --- |
| Category | Specific outcome measures within the category |
| Patient-centred outcome measures | ICU LOS, hospital LOS, ICU readmissions, RBC transfusion rate, RRT initiations, time on mechanical ventilation, nosocomial infections potentially related to phlebotomies, CLABSIs, nosocomial pneumonia, UTIs, bloodstream infections, anaemia makers, adverse events, blood volume drawn for tests, proportion of patients exposed to blood testing, proportion of test results outside the reference range, clinical interventions based on a blood test, intra operative blood loss, transfusion requirements, time on ECMO ICU mortality in-hospital mortality, 30-day mortality |
| Blood test-centred outcome measures | Number of blood tests, number of routine tests, number of non-routine tests, number of POC tests, number of unnecessary blood tests, number of individual tests, number of ABGs, number of electrolytes, number of coagulation screens, number of duplicative tests, number of non-targeted tests, number of ABG determinations per MV time, appropriateness of blood tests, factors associated with the frequency of testing, types of tubes used for phlebotomy, reason for blood tests, sampling route |
| Resource utilisation-centred outcome measures | Net cost reduction, cost of blood tests, workload reduction |
| Other outcome measures | CXRs, CT scans, medication, protocol compliance |

Abbreviations: Intensive care unit (ICU), Length of stay (LOS), red blood cell (RBC), renal replacement therapy (RRT), Central line-associated bloodstream infection (CLABSI), Urinary tract infections (UTIs), point of care (POC), arterial blood gas (ABG), mechanical ventilation (MV), Chest radiography (CXR), Computerised tomography (CT), Extracorporeal Membran Oxygenation (ECMO).

## Supplemental Table 7: Summary of results for each outcome category

|  |  |  |  |
| --- | --- | --- | --- |
| Outcome category | Specific outcome measure | Total no. of studies | Summary of results |
| Patient-centered outcome measures | ICU mortality | 24 studies | Twenty-two studies found no significant differences in ICU mortality between groups3,8-11,19,21,24-28,31,33,37,38,41,48,51,52,55,59  One study found OR for ICU mortality of 0.41 (95% CI: 0.35–0.48) associated with an intervention targeting reduced use of routine blood tests35  One study found a statistically significant decrease in ICU mortality in their surgical ICU but not in their medical ICU in the intervention group44 |
| Hospital mortality | 8 studies | Six studies found no significant differences in in-hospital mortality between groups3,7,26,46,59,61  One study found OR for in-hospital mortality of 0.43 (95% CI: 0.37–0.51) associated with an intervention targeting reduced use of routine blood tests35  One study reported a reduction in mortality rates from 20% to 10.5% after implementing an intervention targeting reduced use of routine blood tests60 |
| ICU LOS | 23 studies | Five studies reported a statistically significant reduction in ICU LOS associated with an intervention targeting reduced use of routine blood tests3,11,28,36,37  Eighteen studies found no significant differences in ICU LOS between groups6,10,17,19,21,24,25,27,31,33,35,44,48,51,52,55,59,61 |
| Hospital LOS | 6 studies | Three studies reported a reduction in hospital LOS associated with an intervention targeting reduced use of routine blood tests3,37,60  Three studies found no significant differences in hospital LOS between groups7,46,59 |
| ICU readmissions | 3 studies | All studies reported no differences in ICU readmission rates between groups24,27,59 |
| Transfusions | 12 studies | Five studies found no difference in transfusions between groups3,9,46,50,61  Three studies found a non-significant reduction in transfusions associated with an intervention targeting reduced use of routine blood tests10,24,26  Three studies reported a significant reduction in RBC transfusion rates associated with an intervention targeting reduced use of routine blood tests11,35,60  One study found a non-significant increase in weekly RBC units transfused associated with an intervention targeting reduced use of routine blood tests31 |
| Blood test results outside the reference range | 8 studies | One study found a decrease in the proportion of blood test results outside the reference range associated with an intervention targeting reduced use of routine blood tests10  Two studies found an increase in the proportion of blood test results outside the reference range associated with an intervention targeting reduced use of routine blood tests7,43  Two studies found no difference in the proportion of blood test results outside the reference range associated with an intervention targeting reduced use of routine blood tests17,24  One study found that 51% of blood test results in an ICU setting were outside the reference range75  One study found that 91% of patients in a trauma setting had blood test results outside the reference range67  One study reported that the proportion of test results outside the reference range in a trauma setting ranged from 8%-55%, depending on the specific test72 |
| Exposure to daily routine blood tests | 6 studies | Two studies reported that 100% of patients in medical ICU were routine blood tested daily22,46  One study reported that 52% of patients in a trauma setting were routine blood tested67  Two studies reported that 91% of patients in a trauma setting were routine blood tested18,72  One study reported that 97% of patients in a trauma setting were routine blood tested7 |
| Adverse events | 19 studies | Sixteen studies reported none or no differences in adverse events between groups7-9,11,13,17-19,22,24,34-36,44,46,55  One study found a decrease in adverse events associated with an intervention targeting reduced use of routine blood tests6  One study reported two minor adverse effects resulting in delayed testing with no adverse patient outcomes associated with an intervention targeting reduced use of routine blood tests40  One study reported a reduction in infections related to blood sampling associated with an intervention targeting reduced use of routine blood tests28 |
| Blood drawn for blood testing | 15 studies | Eight studies reported a reduction in daily mL phlebotomies with an intervention targeting reduced use of routine blood testing17,21,26,27,33,36,57  One study reported that the volume phlebotomized was lower in children compared to the adults (5 mL vs. 22 mL)79  Seven observational studies reported the volume phlebotomized to 13 to 74 mL per day per patient14,50,68,69,75,77,79 |
| Changes in anemia makers | 7 studies | Three studies found no differences in red blood cell levels between groups7,10,19  One study found increased levels of red blood cells with an intervention targeting reduced use of routine blood testing24  One study found decreasing red blood cell levels with an intervention to reduce routine blood testing3  One study found an association between a higher frequency of blood testing and lower hemoglobin64  One study attributed changes in anemia makers during ICU stay to intra-operative blood loss rather than blood sampling69 |
| Routine blood tests leading to medical interventions | 8 studies | Two studies reported that 15% to 16% of blood test panels were associated with medical interventions or changes in therapy71,80  Two studies reported that routine blood test results led to medical interventions in 3 to 10% of trauma patients67,72  One study reported that 65% of arterial gasses led to ventilation interventions post-sample66  One study reported that appropriately indicated tests led to changes in patient management more often than inappropriately indicated tests27  Two studies found no differences in the proportion of blood tests leading to a medical intervention before and after an intervention targeting reduced use of routine blood testing7,17 |
| Blood test-centered outcome measures | Reduction in blood tests | 47 studies | Forty-two studies reported a statistically significant reduction in routine blood sampling associated with an intervention targeting reduced routine blood tests3,4,6-13,17,18,20-22,24-29,31,33-39,41,44,46,48-53,55,57,59,60  Three studies reported a non-significant reduction in routine blood sampling with an intervention targeted reduced use of routine blood tests3,16,61  One study found no significant difference in routine blood sampling between groups56  One study reported an increase in routine blood sampling associated with an intervention targeted reduced use of routine blood tests19 |
| Appropriateness of blood tests | 11 studies | Five studies found an increase in appropriateness associated with an intervention targeting reduced use of routine blood testing14,27,38,43,57  Six studies reported that 12% to 75% of routine blood tests were excessive or non-essential depending on the specific test62,63,65,66,70,71 |
| The proportion of tests recorded as routine | 6 studies | One study reported that 80% of all phlebotomies and 86% of all ABGs were recorded as routine69  One study reported that 27-85% of specific laboratory tests were carried out per routine68  One study reported that 64% of all laboratory tests were carried out per routine50  One study reported that 72% of complete blood counts and 75% of chemistry panels were performed as routine tests31  One study reported that up to 80% of all tests were carried out per routine55  One study reported that 39% of clotting screens were assessed per routine74 |
| Number of duplicate blood tests | 2 studies | One study reported a 96% reduction in duplicate testing with the first hour associated with an intervention targeting reduced use of routine blood tests46  One study found no significant differences in duplicate testing between groups41 |
| Factors associated with more frequent routine blood testing | 5 studies | Two studies reported that the frequency of routine blood testing was significantly higher in teaching hospitals compared with non-teaching hospitals78,81  Four studies reported the presence of an arterial line as a risk factor associated with more frequent laboratory and ABG testing76-78,81  Three studies reported the use of mechanical ventilation as a risk factor associated with increased laboratory and ABG testing76,78,81  One study reported emergency surgery as a risk factor associated with more frequent blood testing78  One study reported gender as a risk factor associated with more frequent blood testing78  One study found that routine blood testing was significantly more frequent on Mondays compared to the rest of the week27 |
| Resource utilization-centered outcome measures | Changes in cost related to laboratory tests | 35 studies | Thirty-five studies reported a cost reduction associated with an intervention targeting reduced use of routine blood tests3,8-12,17,18,21,25-29,31,33-41,43,44,46,49,51-53,55,57,59,60 |
| Changes in patient charges | 2 studies | One study reported an increase in patient charges associated with an intervention targeting reduced use of routine blood tests19  One study reported a reduction in laboratory-related patient charges associated with an intervention targeted reduced use of routine blood tests in a trauma setting7 |
| Cost of redundant blood tests | 13 studies | Thirteen studies reported potential savings related to reducing unnecessary routine blood tests14,62-66,68,70,71,73,75,76,79 |
| Workload reduction | 4 studies | Four studies reported an estimated workload reduction associated with an intervention targeting reduced use of routine blood tests ranging from 36 to 373 work hours annually27,33,46,71 |

Abbreviations: intensive care unit (ICU), Odds ratio (OR), Confidence interval (CI), Length of stay (LOS), Red blood cell (RBC), Arterial blood gas (ABG), Versus (vs), milliliters (mL).

## Supplemental Table 8: Results of the individual non-randomised studies of interventions

|  |  |
| --- | --- |
| Author/ year | Outcome results |
| Bansal et al. 2001 | **Test-centred measures:**   * Non-significant trend towards reduction of ABGs per week (p=0.310) |
| Barie et al. 1997 | **Test-centred measures:**   * 46% reduction in ABG determination (p<0.0001) * 29% reduction in nonarterial blood gas laboratory tests (p<0.0001)   **Patient-centred outcomes:**   * No significant difference in ICU mortality * Trend towards decreased hospital mortality (p=0.07) * Significant reduction in ICU LOS (p<0.05) * Significant reduction in hospital LOS (p<0.05) * Significant reduction in lowest daily hematocrit * Significant reduction in number of transfused patientes * No difference in units of RBC transfused per patient * Significant reduction in units of frozen plasma and platelets transfused per patient   **Resource utilisation-centred measures:**   * Cost reduction of US$ 47.00 per patient day   **Other measures:**   * 34% reduction in CXR * 73% reduction in pharmaceutical costs |
| Bosque et al. 2019 | **Test-centred measures:**   * Significant reduction in unnecessary tests in critical patient (p=0.02) * No significant difference in unnecessary tests in semi-critical patients |
| Chin et al. 2021 | **Test-centred measures:**   * 21 % reduction in mean number of CDC w DIFF performed per patient day (p=0.002) * No difference in all other blood tests * Significant decrease in completed labs per order (p<0.02)   **Patient-centred outcomes:**   * Significant decrease in number of rapid responses (p<0.001) * No significant difference in number of code blues * No significant difference in ICU LOS |
| Chu et al. 1996 | **Test-centred measures:**   * Blood test per patient were reduced by 5.6 tests * Increase in proportion of results outside reference range (p<0.0001)   **Patient-centred outcomes:**   * Significant reduction in proportion of patients exposed in blood tests (p<0.0001) * No significant difference in patients receiving medical interventions base on blood tests * No adverse effects on patient care related to the intervention * No significant difference in LOS * No significant difference in mortality   **Resource utilisation-centred measures:**   * Estimated annual cost reduction in trauma centre laboratory charges of US$ 1.5 million |
| Clouzeau et al. 2019 | **Test-centred measures:**   * 59% reduction in the overall number of tests per patient day (p<0.0001)   **Patient-centred outcomes:**   * No significant adverse events related to the intervention * No significant difference in mortality between periods   **Resource utilisation-centred measures:**   * Estimated annual cost reduction of € 502,254 |
| Conroy et al. 2021 | **Test-centred measures:**   * 20% reduction in overall number of laboratory tests per patient day * No significant difference in STAT labs per patient day   **Patient-centred outcomes:**   * No significant difference in mortality * No significant difference in RRT initiations * No significant difference in CLABSI rate per 1000-line days * Not enough data to discern a trend regarding RBC transfusions   **Resource utilisation-centred measures:**   * Weekly cost reduction of US$ 29,800 during intervention phase |
| Dhanani et al. 2018 | **Test-centred measures:**   * 28% reduction in blood tests performed in the intervention period compared to baseline (*P* <0.0001) * 26% reduction in blood tests performed in the post intervention period compared to baseline (p<0.001) * Reduction in proportion of test results outside reference range in intervention and post-intervention period compared to baseline (statistical significance depended on specific test)   **Patient-centred outcomes:**   * Non-significant reduction in utilization of packed red blood cells, fresh frozen plasma, and platelets transfusion * No significant difference in median ICU LOS * No significant difference in ICU mortality rates * No significant difference in number of patients with mechanical ventilation * No significant difference in number of patients with renal dialysis * No significant difference in haemoglobin changes during hospitalisation   **Resource utilisation-centred measures:**   * Net cost reduction of A$213,326 in the intervention period and A$175,267 in the post-intervention period, compared to the pre-intervention period |
| Fresco et al. 2016 | **Test-centred measures:**   * 27.21% relative reduction in routine laboratory tests per patient day * Significantly greater reduction in surgical ICU compared to medical ICU (27.21% vs 15.13%; p=0.008)   **Patient-centred outcomes:**   * 27.45% relative reduction in blood transfusions * No significant difference in mortality * Significantly reduced ICU LOS * No significant difference in nosocomial infections potentially related to blood sampling   **Resource utilisation-centred measures:**   * Cost reduction of € 124,000 related to laboratory expenses during study period * Cost reduction of € 53,000 related to transfusion expenses during study period |
| Goddard et al. 2011 | **Test-centred measures:**   * 33% net reduction in number of blood tests between periods   **Resource utilisation-centred measures:**   * Overall estimated annual cost reduction of £ 17,914 |
| Hagg et al. 2015 | **Test-centred measures:**   * 50% reduction in overall laboratory tests ordered per patient day * 40% reduction in laboratory tests ordered daily per patient day   **Patient-centred outcomes:**   * No adverse patient effects related to the intervention |
| Hall et al. 2016 | **Test-centred measures:**   * Reduction in proportion of unnecessary tests (46% vs 41%)   **Patient-centred outcomes:**   * Average volume of unnecessary blood taken from a patient per week was 73 ml pre-intervention   **Resource utilisation-centred measures:**   * The cost of carrying out unnecessary blood tests added up to £842 in pre-intervention period |
| Haney et al. 2022 | **Test-centred measures:**   * Non-significant reduction in mean number of blood tests per patient day (13.91vs 13.43; p=0.087) |
| Hussey et al. 2011 | **Test-centred measures:**   * 27% reduction in coagulation tests per patient day   **Patient-centred outcomes:**   * No changes in detection rate of abnormal clotting * No changes in proportion of blood tests leading to a medical intervention * No significant difference in ICU LOS * Reduction in average blood taken for coagulation tests per patient (15.1 ml vs 9.6 ml) * No adverse effects on patient care related to the intervention   **Resource utilisation-centred measures:**   * Estimated annual cost reduction of £ 7,500 |
| Jacobs et al. 2000 | **Test-centred measures:**   * 21% reduction in tests being sent to blood bank * 27 % reduction in the amount of non-protocol tests ordered * 24% increase in ABGs   **Patient-centred outcomes:**   * 91% of patient were exposed to routine blood testing * No adverse events related to the intervention   **Resource utilisation-centred measures:**   * Estimated annual cost reduction of US$ 20,000 |
| Jefferson et al. 2018 | **Test-centred measures:**   * 25.5% increase in overall blood testing (p=0.36) * 35% increase in individual lab tests (p=0.64) * 7.2% increase in panel lab tests (p=0.22)   **Patient-centred outcomes:**   * No significant difference in reported adverse event * No significant difference in ICU mortality * No significant difference in ICU LOS * No significant difference in changes in haemoglobin during ICU stay   **Resource utilisation-centred measures:**   * 13.2% increase in patient charges |
| Khan et al. 2019 | **Test-centred measures:**   * 20% reduction in number of blood tests per patient day * Percentage of patients on whom a lab-plan was discussed on rounds increased from 30-95% * At baseline 34% of blood tests were ‘non-value added’ |
| Ko et al. 2016 | **Test-centred measures:**   * 51.4% reduction in arterial blood gasses per patient (p=0.004) * 30.2% reduction in coagulation profiles per patient (p=0.011) * 17.8% reduction in basic metabolic panels per patient (p=0.007) * 12% reduction in complete blood counts per patient (p=0.066) * 4 L reduction in blood used for laboratory testing per month   **Patient-centred outcomes:**   * No significant difference in ICU LOS * No significant difference in ICU mortality   **Resource utilisation-centred measures:**   * Estimated monthly cost reduction of $59,137   **Other measures:**   * 20.3% reduction in CXR ordered per month (p=0.010) |
| Kotecha et al. 2017 | **Test-centred measures:**   * Significant reduction in all tests performed (p<0.01) * 22% reduction in unnecessary blood tests * 56% of blood tests were done without indication at baseline   **Patient-centred outcomes:**   * No reported adverse events or delays related to the intervention |
| Kumwilaisak et al. 2008 | **Test-centred measures:**   * 37% reduction in total number of blood tests performed * 22.8% reduction in blood tests performed per patient day (p<0.001) * Significant increase in proportion of blood tests with a physician order (p<0.001) * No difference in the rate of laboratory results outside of reference range   **Patient-centred outcomes:**   * No significant difference in ICU mortality * No significant difference in days on mechanical ventilation * No significant difference in ICU LOS * No significant difference in ICU readmission rates * Trend towards a lower number of red blood cells transfused per patient (p=0.08) * No differences in laboratory values, except an increase in haemoglobin from baseline to intervention period(p=0.03) * No significant difference in reported adverse event |
| La Maguet et al. 2015 | **Test-centred measures:**   * 7.48% reduction in total number of laboratory tests per patient day (95% CI: -9.17; -5.79)   **Patient-centred outcomes:**   * No significant difference in ICU LOS * No significant difference in ICU mortality   **Resource utilisation-centred measures:**   * Estimated annual cost reduction of € 157,000   **Other measures:**   * 10.09% reduction in CXR orderings (95% CI: -15.32; -4.86) |
| Leydier et al. 2016 | **Test-centred measures:**   * Reduction in total number of laboratory tests per patient day from 18.1 to 6.4   **Patient-centred outcomes:**   * Average daily blood volume drawn decreased from 29.2 ± 13 ml/day to 22.4 ± 10.1 ml/day (*p* < 0.001) * Trend towards reduction in red blood cell transfusion * Increase in need for vasoactive drugs * No significant difference in ICU mortality * No significant difference in in-hospital mortality * No significant difference in vital organ support   **Resource utilisation-centred measures:**   * Annual cost reduction of € 318,000 |
| Martínez-Balzano et al. 2017 | **Test-centred measures:**   * 41.5% reduction in monthly ABG determinations (p<0.001) * 43.1% reduction in ABG determinations per patient MV day (p<0.001) * Proportion of appropriately indicated tests increased from 67.5% to 83.4% (p<0.002)   **Patient-centred outcomes:**   * 49 L blood saved per month related to the intervention * Appropriately indicated tests more often led to medical interventions compared to inappropriately indicated tests (Pre-intervention: 70.8% vs 7.8%; Intervention: 56% vs 4.3%) * No significant difference in MV days * No significant difference in ICU mortality * No significant difference in ICU LOS * No significant difference in ICU readmission rates   **Resource utilisation-centred measures:**   * Direct cost reduction of US$ 39,432 * Indirect cost reduction of US$ 98,580 * 1,643 staff work hours freed annually |
| Marx et al. 1999 | **Test-centred measures:**   * 65% reduction in daily blood tests   **Patient-centred outcomes:**   * Average ICU LOS was reduced from 5.0 to 3.5 days * Rates of blood stream infections, urinary tracts infections and nosocomial pneumonia were reduced * No significant difference in ICU mortality   **Resource utilisation-centred measures:**   * Annual cost reduction of US$ 21,593 related to reduction in blood tests * Annual cost reduction of US$ 3,941 related to reduction in CXRs * 4% decrease in annualized cost per patient day * 75% reduction in cost of neuromuscular blocking agents   **Other measures:**   * 56% reduction in daily CXRs * 35% reduction in ventilator hours |
| Mehari et al. 1997 | **Test-centred measures:**   * 16.6 % reduction in all blood tests for general ICU patients in intervention period compared to baseline * 2.1% increase in all blood tests for general ICU patients in follow-up period compared to intervention period (p=0.24) * 5.6% decrease in all blood tests performed per ventilator time for general ICU patients in post-intervention period compared to intervention period * 25.9% reduction in all blood tests for post-cardiac surgery patients in intervention period compared to baseline * 4.7% decrease in all blood tests for post-cardiac surgery patients in follow-up period compared to intervention period (p=0.94) * 4% decrease in all blood tests performed per ventilator time for post-cardiac surgery patients in post-intervention period compared to intervention period   **Patient-centred outcomes:**   * No significant differences in mean ventilator time tests for general ICU patients in intervention period compared to baseline * Significant reduction in mean ventilator time tests for post-cardiac surgery patients in intervention period compared to baseline (p=0.0093)   **Resource utilisation-centred measures:**   * Estimated annual cost reduction of NZ$ 81,636 |
| Merkeley et al. 2016 | **Test-centred measures:**   * 15% reduction in routine complete blood count * 13% reduction in routine electrolyte/renal panel * 7% increase in non-routine complete blood count * 8% increase in non-routine electrolyte/renal panel   **Patient-centred outcomes:**   * No significant difference in LOS * No significant difference in ICU mortality * No significant difference in in-hospital mortality * Non-significant increase in weekly RBC units transfused   **Resource utilisation-centred measures:**   * Estimated annual cost reduction of $ 11,200 |
| Merlani et al. 2001 | **Test-centred measures:**   * Reduction in arterial blood gasses per patient from 8.2 to 4.8 (p<0.0001) * Increased adherence to ABG guidelines from 53% to 80% (p<0.0001) * No difference in non-targeted blood tests during intervention   **Patient-centred outcomes:**   * 17 ml reduction in blood used for laboratory tests per patient day * No significant difference in ICU mortality * No significant difference in ICU LOS   **Resource utilisation-centred measures:**   * Estimated annual cost reduction was SFr 271.560 * Estimated work time reduction of 187 nurse working days |
| Mian et al. 2019 | **Test-centred measures:**   * 38.5% reduction in routine blood tests per patient   **Patient-centred outcomes:**   * No reported adverse events related to the intervention   **Resource utilisation-centred measures:**   * Cost of unnecessary blood tests reduced by 50% |
| Murphy et al. 2016 | **Test-centred measures:**   * 42% reduction in unadjusted ABGs per patient in intervention period compared to baseline (95% CI: -48; -38) * 42% reduction in unadjusted ABGs per patient in follow-up period compared to baseline (95% CI: -48; -35)   **Patient-centred outcomes:**   * 17% reduction in unadjusted RBC transfusion per patient in intervention period compared to baseline (95% CI: -22; -12) * 9% reduction in unadjusted RBC transfusions per patient in follow-up period compared to baseline (95% CI: -17; -0.3) * No significant difference in ICU LOS between baseline, intervention period and follow-up period * Significant decrease in ICU mortality in intervention and follow-up period compared to baseline (p<0.01) * Significant decrease in in-hospital mortality in intervention and follow-up period compared to baseline (p<0.01) * No reported adverse events related to the intervention   **Resource utilisation-centred measures:**   * Average annual cost reduction of US$ 772,048   **Other measures:**   * 26% reduction in unadjusted CXRs per patient intervention period compared to baseline (95% CI: -29; -22) * 32% reduction in unadjusted CXRs per patient in follow-up period compared to baseline (95% CI: -37; -27) |
| Musca et al. 2016 | **Test-centred measures:**   * 63.68% reduction in number of coagulation profiles per patient day (p<0.001) * 14.97% reduction in number of FBC, UEC and LTF bundles per patient day (p=0.003)   **Patient-centred outcomes:**   * 1.79 ml reduction in blood taken for coagulation tests per patient day * No reported adverse events related to the intervention * Significant reduction in ICU LOS (p=0.013)   **Resource utilisation-centred measures:**   * Estimated annual cost reduction of US$ 98,349 |
| Pageler et al. 2013 | **Test-centred measures:**   * Significant reduction in tests per patient day (complete blood cell counts: 1.5 ± 0.1 to 1.0 ± 0.1; chemistry: 10.6 ± 0.9 to 6.9 ± 0.6; coagulation: 3.3 ± 0.4 to 1.7 ± 0.2; p<0.01)   **Patient-centred outcomes:**   * Significant decrease in PICU LOS (5.1 ± 0.7 vs. 4.2 ± 0.6 days; p<0.050) * Significant decrease in hospital LOS (16.2 ± 2.1 vs. 11.6 ± 1.6 days; p<0.001) * No significant difference in mortality rate   **Resource utilisation-centred measures:**   * Estimated annual saving was US$ 600,000 |
| Pilon et al. 1997 | **Test-centred measures:**   * Number of ABGs decreased from 4.9 +/- 1.6 to 3.1 +/- 1.8 (SD) tests/patient/day at 2 to 3 months and to 2.4 +/- 1.2 tests/patient/day at 12 to 13 months * Appropriateness increased from a mean of 44% at baseline to 78% at 2 to 3 months and 79% at 12 to 13 months   **Patient-centred outcomes:**   * No significant difference in number of ventilator days * No significant differences in in time to wean from ventilator * No significant difference in ICU mortality   **Resource utilisation-centred measures:**   * Estimated annual cost reduction was US$ 40,175 * Estimated cost reduction per patient day was US$ 19.18 |
| Prat et al. 2009 | **Test-centred measures:**   * 38 to 71.5% relative reduction of routine laboratory tests per patient day depending on the type of tests (P<0.001 in all cases)   **Resource utilisation-centred measures:**   * Estimated annual cost reduction €297,000 * 59% cost reduction in cost per ICU stay * 51% cost reduction in cost per ICU day   **Other measures:**   * For chest radiographs, a 40.8% relative reduction was observed between the two periods (P<0.001). |
| Rachakonda et al. 2017 | **Patient-centred outcomes:**   * Two reported minor protocol-related adverse events * No reported adverse patient outcomes   **Resource utilisation-centred measures:**   * Overall ICU laboratory test costs decreased by 12.3% (US$ 161,754.66) over the six months (*P*=0.0022) * The costs of frequently ordered tests (classified as high-volume) decreased by 20% (*P*=0.0022 versus historical control) * Blood gas analyses contributed most to the overall cost (17%) followed by simple chemistry (14%), coagulation tests (12%) and full blood counts (11%)   **Other measures:**   * Mean compliance with the test authorisation protocol was 51% |
| Rakes et al. 2016 | **Test-centred measures:**   * Number of POC cartridges utilized per patient day decreased from 0.98 to 0.4 * Number of POC blood gasses performed per patient day decreased from 0.7 to 0.3 * No significant difference in duplicate rate * 12% reduction in non-POCT blood testing   **Patient-centred outcomes:**   * No significant difference in mortality   **Resource utilisation-centred measures:**   * Estimated annual cost reduction was US$ 30,000-60,000 |
| Rice et al. 2012 | **Test-centred measures:**   * Appropriateness of coagulation tests increase from 37% to 50%   **Patient-centred outcomes:**   * Detection rate for results outside the reference range increased from 81% to 100%   **Resource utilisation-centred measures:**   * Estimated annual cost reduction was £10,000 |
| Roberts et al. 1993 | **Test-centred measures:**   * 25 % reduction in total number of tests per admission between control and intervention period * 30% reduction in targeted tests per admission between control and intervention period * 18% reduction in non-targeted tests per admission between control and intervention period   **Patient-centred outcomes:**   * No significant difference in medical ICU mortality between control and intervention period * Significant decreased surgical ICU mortality (p<0.05) between control and intervention period * No significant difference in LOS between control and intervention period * No adverse events related to the intervention   **Resource utilisation-centred measures:**   * Estimated annual cost reduction was CA$ 150,594 * No difference in medication expenses |
| Raad et al. 2017 | **Test-centred measures:**   * 32.7% reduction in total number of laboratory tests per patient day (p<0.001) * 85.1% reduction in number of iSTAT laboratory tests per patient day (p<0.001) * 95.6% reduction in number of iSTAT/central processing duplicates within 1 hour per patient day (p<0.001)   **Patient-centred outcomes:**   * Proportion of patients subjected to daily laboratory tests orders decreased on 100% to 11.94% (p<0.001) * No significant difference in RBC transfusion rate * No significant difference in CLABSI rate * No significant difference in in-hospital mortality * No significant difference in hospital LOS * Trend towards decreased central line utilisation   **Resource utilisation-centred measures:**   * Estimated annual direct cost reduction US$ 123,436 * Estimated annual indirect cost reduction US$ 258,035   **Other measures:**   * Non-significant reduction in CXR from 0.47 to 0.41 per patient day (p=0.14) |
| Sachdeva et al. 1996 | **Test-centred measures:**   * 16.7% reduction in average daily blood tests (p=0.002)   **Patient-centred outcomes:**   * No significant difference in PICU LOS * Non-significant increase in PICU mortality * No significant differences in measures of quality assurance   **Other measures:**   * 9.1% reduction in radiology (p=0.36) * 8.5% reduction in CT imaging (p=0.635) * 25.1% reduction in pharmacy (p=0.0001) |
| Sasser et al. 2018 | **Test-centred measures:**   * 19% reduction in total ABGs performed * Proportion of ABGs ordered as part of panel decreased from 79% to 58% * Proportion of ABGs ordered as individual tests increased from 17% to 35%   **Resource utilisation-centred measures:**   * Estimated annual cost reduction was US$ 637,608 |
| Saxena et al. 2003 | **Test-centred measures:**   * 50% reduction in blood test requests   **Patient-centred outcomes:**   * 33-46% reduction in blood volume drawn for blood tests * No significant difference in RBC transfusion rates |
| Seguin et al. 2002 | **Test-centred measures:**   * Total number of blood tests and CXR per admission decreased from 13.64 ±20.50 to 11.06±14.95   **Patient-centred outcomes:**   * No significant difference in ICU LOS * No significant difference in ICU mortality   **Resource utilisation-centred measures:**   * 22% decrease in expenditure |
| Simvoulidis et al. 2020 | **Test-centred measures:**   * >50% reduction in requests for laboratory test   **Patient-centred outcomes:**   * No significant difference in mortality * No significant difference in mean LOS * No significant difference in use of invasive resources   **Resource utilisation-centred measures:**   * Estimated annual cost reduction was US$ 150,000 |
| Sinitsky et al. 2017 | **Test-centred measures:**   * Significant reduction in number of liver function tests, full blood counts, CRP tests and coagulation screens per PICU bed day   **Resource utilisation-centred measures:**   * Estimated cost reduction was £ 36,000 during intervention period |
| Vezzani et al. 2013 | **Test-centred measures:**   * Total number of biochemical tests per patient decreased from 73.20 to 40.2 * Number of routine biochemical tests per patient decreased from 42.23 to 28.7 * Number of non-routine biochemical tests per patient decreased from 30.97 to 11.5 (p<0.001)   **Patient-centred outcomes:**   * No significant difference in ICU LOS * Non-significant increase in ICU mortality * No reported adverse events related to the intervention   **Resource utilisation-centred measures:**   * Cost of routine and non-routine biochemical tests per patient decreased from € 168.33 to € 98.30 |
| Viau-Lapointe et al. 2018 | **Test-centred measures:**   * No significant difference in the overall number of blood tests per patient day in the first 28 days in ICU * Significant decrease in liver function tests from 0.65 to 0.25 per patient day (p<0.001) |
| Walsh et al. 2020 | **Test-centred measures:**   * 31.3% reduction in ABGs per patient day * Inappropriateness of ABGs decreased from 54.2% to 28.6%   **Patient-centred outcomes:**   * 100L in annual reduction in blood drawn for blood tests   **Resource utilisation-centred measures:**   * Estimated annual cost reduction was A$ 750,000 |
| Wang et al. 2002 | **Test-centred measures:**   * Significant reductions for all chemistry tests per patient day * Non-significant reductions in complete blood counts and ABGs per patient day   **Patient-centred outcomes:**   * No significant difference in mean hospital or ICU LOS * No significant difference in mean number of days on mechanical ventilation * No significant difference in readmission rates * No significant difference in in-hospital or ICU mortality   **Resource utilisation-centred measures:**   * 17% reduction in expenses related to routine blood tests and CXRs per patient day   **Other measures:**   * Non-significant reductions in CXRs per patient day |
| Welty et al. 2022 | **Test-centred measures:**   * 52% reduction in laboratory tests per ECMO day   **Patient-centred outcomes:**   * 9.3% reduction in hospital length of stay * 9.5% reduction in hospital mortality * No difference in CLABSI rates between groups * 15% reduction in packed RBC transfusion rates   **Resource utilisation-centred measures:**   * 14.7% reduction in direct cost per ECMO case |
| Yorkgitis et al. 2018 | **Test-centred measures:**   * Non-significant decrease in mean number of coagulation tests ordered per day (0.62 [0.062] vs 0.60 [0.061]; p=0.75) * Non-significant increase in mean number of complete blood count (1.36 [0.67] vs 1.37 [0.69]; p=0.86), chemistry panel (1.27 [0.62] vs 1.31 [0.61]; p= 0.60), and ABG (0.58 [0.76] vs 0.61 [0.77]; p=0.74) ordered per day   **Patient-centred outcomes:**   * No significant difference in ICU LOS * No significant difference in in-hospital mortality * No significant difference in days of mechanical ventilation * No significant difference in RBC transfusions ordered per day   **Other measures:**   * Non-significant decrease in mean number of CXR ordered per day (0.56 [0.42] vs 0.52 [0.41]; p=0.39) |

Abbreviations: Interrupted time series (ITS), Controlled interrupted time series (CITS), Non-randomised controlled trial (NRCT), Not reported (NR), Intensive care unit (ICU), High dependency unit (HDU), Critical care unit (CCU), Paediatric intensive care unit (PICU), Arterial blood gas (ABG), Length of stay (LOS), Central line-associated bloodstream infection (CLABSI), Red blood cell (RBC), Chest x-ray (CXR), Computed tomography (CT), Extracorporeal Membran Oxygenation (ECMO).

## Supplemental Table 9: Results of the individual observational studies

|  |  |
| --- | --- |
| Author/ year | Results |
| Agostini et al. 2017 | **Test-centred measures:**   * Average number of samples per patient was 33 * Appropriateness of coagulation samples (33%), Group and Saves (17%), Magnesium (17%), Full Blood Count (13%), Liver Function Tests (12%) and Urea and electrolytes (12%)   **Patient-centred outcomes:**   * 29% of patients received a transfusion during study period   **Resource utilisation-centred measures:**   * Average cost of blood samples £3,156 per patient |
| Baigelman et al. 1985 | **Test-centred measures:**   * Of 924 sets of complete electrolytes and 24 individual electrolytes measured in 145 patients 10% were considered unnecessary and 65% were considered only one electrolyte was considered necessary respectively   **Resource utilisation-centred measures:**   * The calculated unnecessary cost to the hospital was US$ 2,396 |
| Clark et al. 2011 | **Test-centred measures:**   * Total phlebotomies: Average 67.3 per patient (range 1-372) * Potassium: Average of 13.1 draws per patient (range 1–104) * Sodium: Average of 14.1 draws per patient (range 1-104) * Magnesium: Average of 7.6 draws per patient (range 0–35) * Ionized calcium: average of 4 draws per patient, (range 0–26) * Phosphorus: average of 4.3 draws per patient (range 0–23)   **Patient-centred outcomes:**   * Haemoglobin concentration decreases on average -2.5 g/ dl (median -2.1, range -7.8 to 0 g/dl) * There was a significant correlation between frequency of phlebotomies and drop in haemoglobin concentration (P <0.0001) * 26.9% of patients required blood transfusion during their stay * Average of replacement orders per patient based on electrolyte measures potassium 4.6 (range 0-23), sodium not reported, magnesium 1.4 (range 0.11), ionized calcium 0.1 (range 0-3) and phosphorus 0.6 (range 0-6) * Use of diuretics was associated with more potassium (P <0.0001) and magnesium (P <0.001) measurements, and with hypokalaemia (P <0.0001) * Average ICU LOS was 10.4 days   **Resource utilisation-centred measures:**   * Average cost for electrolyte panels during this study period exceeded $2200 per patient |
| Gray et al. 2014 | **Test-centred measures:**   * Number of inappropriate full blood count were 4, urea and electrolytes were 6, liver function tests were 95, coagulation screen were 117, CRP were 45, bone profile were 112, magnesium were 88   **Resource utilisation-centred measures:**   * €12,849.96 was spent on all blood tests * €2,914.96 was spent on inappropriate tests (€37,998.63 per year) |
| Jones et al. 2019 | **Test-centred measures:**   * Total of 1,393 arterial blood gases were taken during audit   **Patient-centred outcomes:**   * 492 arterial blood gases were taken with no ventilation intervention post sample |
| Keller et al. 2004 | **Test-centred measures:**   * Complete trauma laboratory panels, including all 17 tests, were obtained in 52% of the children * Specific tests were obtained in 92% for cell counts, 90% for electrolytes, 85% for transaminase, 85% for AMY, 77% for coagulation profiles * Test results outside the reference range was reported for 91% of patients, correlating with injury severity score and GCS (*P <*0.05)   **Patient-centred outcomes:**   * 10% of patients had interventions based on abnormal test results * ICU mortality was 6% |
| Laird et al. 2011 | **Test-centred measures:**   * Average of 8ABGs per patient per 24 h day were performed in ventilated patients and 5.6 in non-ventilated patients. * >70% of FBP were ‘Routine’, 74% coagulation screen were ‘Routine’ and 59% U + Es were ‘Routine’ with 27% U + Es performed after replacement. 61% of bone profile bloods were ‘Routine’ and 85% LFTS ‘Routine’   **Patient-centred outcomes:**   * Approximately 49.8 ml of blood per patient per day was drawn for blood tests   **Resource utilisation-centred measures:**   * Average cost of blood samples was £56.32 per patient per day. |
| Lennox et al. 2022 | **Test-centred measures:**   * Mean number of phlebotomies per patient were 3.7 per day (range 1-7) * 94% of phlebotomies were taken form an arterial line, 6% of phlebotomies were taken from a central line * 86% of ABGs were recorded as routine, 80% of all phlebotomies were recorded as routine * Mean 8.5 ml blood per patient were discarded during phlebotomies   **Patient-centred outcomes:**   * 7.4 ml blood were drawn for ABGs per patient per day * 21.7 ml blood were drawn for tests other than ABG per patient per day * Blood loss and transfusion requirements were attributed to intra operative blood loss rather than blood sampling   **Resource utilisation-centred measures:**   * Nurses spend 14 min per patient per day for phlebotomies and 16 min per patient per day for documenting |
| Mikhaeil et al. 2017 | **Test-centred measures:**   * 51% of blood tests were deemed non-essential * In 80% of patient days at least one test was considered non-essential   **Resource utilisation-centred measures:**   * Average cost of unnecessary tests was $27.70 per patient day |
| Mukhtar et al. 2011 | **Test-centred measures:**   * 58% of routine blood tests were not indicated   **Patient-centred measures:**   * 15% of routine blood tests were associated with a medical intervention   **Resource utilisation-centred measures:**   * Average cost of inappropriate routine blood tests was € 8.23 per patient day * Average time consumed obtaining one set of routine blood samples was 10 min and 56 s |
| Namias et al. 1996 | **Test-centred measures:**   * Mixed biochemistry panel was performed in 456 of 500 patients, amylase in 429 of 500 patients, coagulation profile in 413 of 500 patients * Proportion of test results outside the reference range: Na: 8%, K: 12%, CO2: 44%, BUN: 38%, Cr: 41%, Glu: 64%, Amylase: 7%, PT: 55%, PTT: 10%   **Patient-centred outcomes:**   * Five of 456 patients received a medical intervention based on a biochemistry panel testing * None of 429 patients received a medical intervention based on amylase measures * 11 of 413 patients received a medical intervention based on coagulation testing |
| Oliveira et al. 2014 | **Test-centred measures:**   * Average number of blood test were 13.4 tests/patient day * Grouped by age children had 16.2 tests/patient day, adults 14.4 tests/patient day and elderly 15.6 tests/patient day (ns) * 41% of blood tests were considered unnecessary (range 7.9% – 95.3%) * Most requested test was complete blood count * More tests recorded on Mondays compared to other weekdays (P <0.05) * ICU LOS > 5 days was not related with a higher number of laboratory test requests * ICU LOS > 10 was related to higher number of unnecessary tests (P <0.05)   **Patient-centred outcomes:**   * Average ICU LOS was 8.6 days   **Resource utilisation-centred measures:**   * Cost of unnecessary tests during study period was US$ 638.21 |
| Packer et al. 2014 | **Test-centred measures:**   * Average number of blood tests were 8.08 tests/patient day * 39% of clotting screens were routine   **Patient-centred outcomes:**   * 13.5 ml blood was drawn per patient per day * Seven patients received blood transfusion during study period (four for acute bleeding) |
| Peixoto et al. 2013 | **Test-centred measures:**   * 3622 tests recorded during study period (67.1/surviving patient, 90.6/deceased patient) * Predominance of potassium (13.5%), sodium (13.3%), and creatinine (13.3%) levels, and complete blood count (13.2%) * 48.8% of test results were inside the reference range (43.9 tests/surviving patient × 44.9 tests/deceased patient)   **Patient-centred outcomes:**   * Average volume of blood drawn were 84.2 ml per hospitalisation for surviving patients and 103.5 ml per hospitalisation for deceased patients * ICU motility was 33% * Average ICU LOS was 11.5 days   **Resource utilisation-centred measures:**   * Approximately US$ 65,000 was spent on test with normal results during study per**iod** |
| Rutledge et al. 1991 | **Test-centred measures:**   * Arterial blood gases were the most ordered test in ICU * Presence of arterial line, mechanical ventilation, severity of illness, PaO2, PCO2 were associated with ABG utilization.   **Resource utilisation-centred measures:**   * STAT requests constituted 14.6% of total laboratory costs in surgical ICU and 10% of total laboratory costs in medical ICU |
| Smoller et al. 1986 | **Test-centred measures:**   * Average phlebotomies per day in ICU was 5.2 phlebotomies pr day * Average phlebotomies per day in ICU for patients without an arterial line was 2.6 and 6.3 for patients with an arterial line   **Patient-centred outcomes:**   * Volume of blood drawn per day in ICU was 41.5 ml per patient * Volume of blood drawn per day in ICU was 33.5 ml for patients without an arterial line and 73.9 ml for patients with an arterial line * 47 % of transfused patients had large blood losses from phlebotomies deemed to contribute to transfusion requirements |
| Spence et al. 2013 | **Test-centred measures:**   * Median tests per day was 11.0 (IQR 7.7–16.2) in teaching ICUs and 7.5 (IQR 5.5-10.6) in nonteaching units * Median tests er day was higher among men, age <50 years, those admitted at night, trauma patients, those who had emergency surgery, patients who died in the ICU, and those who on the first ICU day had an arterial catheter, pulmonary artery catheter, mechanical ventilation, or vasoactive drugs   **Patient-centred outcomes:**   * Mean ICU LOS was 4.0 ± 4.5 days for teaching units vs 4.1 ± 4.6 days for nonteaching units * ICU mortality was 10.6% in teaching units vs 10.2% in nonteaching units * 30-day mortality was 16.4% in teaching units vs 16.8% in nonteaching units |
| Ullman et al. 2016 | **Test-centred measures:**   * Median samples per patient day was 5.0 (IQR 2.4) for adult and 2.3 (IQR 2.9) for paediatrics * ABG were the major reason for blood sampling in each ICU (82% of samples in adults; 80% of samples in paediatrics) * The main reason for blood sampling across ICU settings was routine (adults 47.5%; paediatrics 45.4%) (52.1% missing data for reason for blood sampling)   **Patient-centred outcomes:**   * Volume drawn for blood testing was 22.3 ml/day for adult and 5.0 ml/day for paediatrics * For paediatric ICU 62% were discharged, 37% still in ICU and 0% died during cohort * For adult ICU 64% were discharged, 34% still in ICU and 2% died during cohort   **Resource utilisation-centred measures:**   * Cost of total blood sampling per patient day was AU$ 41.55 for paediatrics and AU$ 101.11 for adults * Cost of ABG per patient day was AU$ 19.96 for paediatrics and AU$ 51.51 for adults |
| Venkatram et al. 2011 | **Test-centred measures:**   * Patients with ICU LOS of 5 days or less had 9.18 test pr admission * Patients with ICU LOS of 6 days or more had 51.91 tests pr admission * Routine laboratory tests with high interventional rates (19.8-97.2%): BMP, INR, ABG, drug levels * Routine laboratory tests with low interventional rates (0.4-9.6%): Mg, Po, CBC, LFT   **Patient-centred outcomes:**   * 15.7% of routine laboratory panels were associated with a medical intervention * Mechanical ventilation requirements were higher for patient with ICU LOS of 6 days or more |
| Zimmerman et al. 1997 | **Test-centred measures:**   * Significantly more samples performed in teaching compared to nonteaching ICUs (Day 1: 12.8, Day 2: 7.6 Day2-7: 23.0 vs Day 1: 6.4, Day 2: 3.7, Day 2-7: 9.9) * 37% of all samples are drawn on ICU day 1 * Significantly more samples performed in patients with a-canula on day 1 or mechanical ventilation on day 1 * Exposure to lab testing correlates with severity of illness at admission and LOS * Chemistry test were most frequent type of test (day 1: 4.3, day 2: 2.6, day 2-7: 7.8), followed by blood gas analysis (day 1: 2.3, day 2: 1.4, day 2-7: 4.3), haematology (day 1: 2.0, day 2: 1.1, day 2-7: 3.0), and coagulation tests (day 1: 0.9, day 2: 0.4, day 2-7: 1.1) |

Abbreviations: Interrupted time series (ITS), Controlled interrupted time series (CITS), Non-randomised controlled trial (NRCT), Not reported (NR), Intensive care unit (ICU), High dependency unit (HDU), Critical care unit (CCU), Paediatric intensive care unit (PICU), Arterial blood gas (ABG), Length of stay (LOS), Red blood cell (RBC), Chest x-ray (CXR), Computed tomography (CT).

## Supplemental Table 10: Overall quality of evidence (GRADE)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Overall quality of evidence (GRADE) | | | | | | | |
| Outcome | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Publication bias** | **Overall quality of evidence** |
| Exposure to routine blood testing-centred outcome measures  (n=6) | 4 NRSI | Serious (a) | Not serious | Serious (c) | Serious (d) | Undetected | Very low |
| 2 Observational | Serious (b) | Not serious | Serious (c) | Serious (d) | Undetected | Very low |
| Most frequent routine blood test-centred outcome measures (n=22 studies) | 19 NRSI | Serious (a) | Serious (e) | Serious (c) | Not serious | Undetected | Very low |
| 3 Observational | Serious (b) | Serious (e) | Serious (c) | Not serious | Undetected | Very low |
| Factors associated with blood tests-centred outcomes  (n=27) | 20 NRSI | Serious (a) | Serious (e) | Serious (c) | Not serious | Undetected | Very low |
| 7 Observational | Serious (b) | Serious (e) | Serious (c) | Not serious | Undetected | Very low |
| Patient-centred outcome measures  (n= 56 studies) | 41 NRSI | Serious (a) | Not serious | Serious (f) | Not serious | Undetected | Low |
| 15 Observational | Serious (b) | Not serious | Not serious | Not serious | Undetected | Very low |
| Resource utilisation-centred outcome measures (n=40 studies) | 37 NRSI | Serious (a) | Serious (e) | Serious (g) | Not serious | Undetected | Very low |
| 13 Observational | Serious (b) | Serious (e) | Serious (g) | Not serious | Undetected | Very low |
| *Abbreviations: Grading of Recommendations Assessment, Development, and Evaluation (GRADE), Non-Randomised Study of Interventions (NRSI)* | | | | | | | |

1. NRSIs were overall judged to be of high risk of bias, due to lack of randomisation and blinding, risk of bias due to confounding, and selective outcome reporting, which potentially could have a substantial effect on the results.
2. Observational studies were overall judged to be of high risk of bias due to a lack of contemporaneous comparison groups which potentially could have an effect on reported results.
3. Measurement of surrogate endpoints.
4. Only a small proportion of the included studies reported on exposure to routine blood sampling
5. Inconsistencies in outcome measures were partly explained due to differences in trial settings and interventions. Despite adjusting for these factors, we still observed large variations in reported results.
6. A not insubstantial part of NRSIs (12/39) investigated interventions targeting reduced use of routine chest radiographs and medications simultaneous with routine blood sampling, which could have an effect on the reported results.
7. Measurement of surrogate endpoints, as well as the presence of concurrent interventions targeting reduced use of chest radiographs and medications simultaneous with routine blood sampling, which could have an effect on the reported results.

GRADE Working Group grades of evidence

* **High quality:** We are very confident that the true effect lies close to that of the estimate of the effect
* **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
* **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
* **Very Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

## Supplemental Table 11: Variations in blood test frequency measures

|  |  |
| --- | --- |
| Study characteristics | No. of studies, n (%) |
| Total studies reporting on test frequencies | 63 (100) |
| Counting measure |  |
| Mean number of tests per admission | 11 (17.5) |
| Mean number of tests per patient day | 34 (54.0) |
| Mean number of tests per patient MV-day | 1 (1.6) |
| Mean number of tests per day | 1 (1.6) |
| Mean number of tests per week | 2 (3.2) |
| Mean number of tests per month | 2 (3.2) |
| Total number of tests during the study period | 3 (4.8) |
| The median number of tests per patient day | 1 (1.6) |
| Mean number of phlebotomies per patient day | 1 (1.6) |
| Mean number of tests per ECMO day | 1 (1.6) |
| Not reported | 6 (9.5) |
| Type of tests measured |  |
| Blood gasses | 8 (12.7) |
| Blood gasses, chest x-rays | 1 (1.6) |
| Coagulation screen | 3 (4.8) |
| Mixed biochemistry | 1 (1.6) |
| Mixed biochemistry, blood gasses | 1 (1.6) |
| Mixed biochemistry, coagulation screens | 2 (3.2) |
| Mixed biochemistry, haematology | 3 (4.8) |
| Mixed biochemistry, haematology, blood gasses, chest x-rays | 1 (1.6) |
| Mixed biochemistry, haematology, coagulation screens | 11 (17.5) |
| Mixed biochemistry, haematology, coagulation screens, blood gasses | 21 (33.3) |
| Mixed biochemistry, haematology, coagulation screens, blood gasses, blood cultures | 1 (1.6) |
| Mixed biochemistry, haematology, coagulation screens, blood gasses, chest x-rays | 6 (9.5) |
| Non-specified routine tests | 4 (6.5) |

Abbreviations: Intensive care unit (ICU), Extracorporeal Membrane Oxygenation (ECMO).

## Supplemental Table 12: Adjusted estimated annual cost reduction

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Author/ year | Country | Setting | N beds | Test targeted for reduction | Reported estimated annual cost reduction | Reported estimated annual cost reduction adjusted for inflation and currency (€) | Adjusted estimated annual cost reduction per ICU bed (€) |
| Clouzeau et al. 2019 | France | Medical ICU | 12 | Mixed biochemistry, haematology, coagulation | GBP 502 254 | € 616 706  $ 697 495 | € 51 392  $ 58 125 |
| Conroy et al. 2021 | USA | Medical ICU | 24 | Mixed biochemistry, haematology, coagulation | USD 1 549 600 | € 1 370 115  $ 1 549 600 | € 57 088  $ 64 567 |
| Dhanani et al. 2018 | Australia | Mixed ICU | 22 | Mixed biochemistry, haematology, coagulation | AUD 213 000 | € 149 112  $ 168 646 | € 6 778  $ 7 666 |
| Goddard et al. 2011 | UK | Mixed ICU | 6 | Mixed biochemistry | GBP 17 914 | € 25 683  $ 29 048 | € 4 281  $ 4841 |
| Ko et al. 2016 | USA | Surgical ICU | 24 | Mixed biochemistry, haematology, coagulation, blood gasses | USD 710 000 | € 702 751  $ 794 812 | € 29 281  $ 33 117 |
| Le Maguet et al. 2015 | France | Mixed ICU | 65 | Mixed biochemistry, haematology, coagulation, blood gasses and CXR | Euro 157 000 | € 167 737  $ 189 711 | € 2 581  $ 2 919 |
| Martínez-Balzano et al. 2017 | USA | Mixed ICU | 98 | Blood gasses | USD 138 012 | € 136 603  $ 154 498 | € 1 394  $ 1 577 |
| Marx et al. 1999 | USA | Mixed ICU | 8 | Mixed biochemistry, haematology, coagulation and CXR | USD 21 593 | € 29 621  $ 33 501 | € 3 703  $ 4 188 |
| Mehari et al. 1997 | New Zealand | Mixed ICU | 11 | Mixed biochemistry, haematology, coagulation, blood gasses | NZD 81 636 | € 86 151  $ 97 437 | € 7 832  $ 8 858 |
| Merkeley et al. 2016 | Canada | Medical ICU | 15 | Mixed biochemistry, haematology | CAD 11 200 | € 14 685  $ 16 609 | € 979  $ 1 197 |
| Merlani et al. 2001 | Switzerland | Surgical ICU | 20 | Blood gasses | CHF 271 560 | € 218 225  $ 246 812 | € 10 911  $ 12 341 |
| Musca et al. 2016 | Australia | Mixed ICU | 23 | Mixed biochemistry, coagulation | AUD 98 349 | € 72 946  $ 82 502 | € 3 172  $ 3 587 |
| Pageler et al. 2013 | USA | Paediatric ICU | 20 | Mixed biochemistry, haematology, coagulation | USD 600 000 | € 617 156  $ 698 004 | € 30 858  $ 34 900 |
| Pilon et al. 1997 | USA | Mixed ICU | 10 | Blood gasses | USD 40 175 | € 56 516  $ 63 920 | € 5 652  $ 6 392 |
| Prat et al. 2009 | France | Medical ICU | 15 | Mixed biochemistry, haematology, coagulation and CXR | Euro 207 000 | € 234 044  $ 264 704 | € 15 603  $17 647 |
| Rachakonda et al. 2017 | Australia | Mixed ICU | 30 | Mixed biochemistry, haematology, coagulation, blood gasses | AUD 323 509 | € 231 576  $ 261 913 | € 7 719  $ 8 730 |
| Rakes et al. 2019 | USA | Paediatric ICU | 32 | Mixed biochemistry, haematology, coagulation, blood gasses | USD 60 000 | € 55 921  $ 63 247 | € 1 748  $ 1 976 |
| Roberts et al. 1993 | Canada | Surgical ICU | 10 | Mixed biochemistry, haematology, coagulation, blood gasses and CXR | CAD 150 594 | € 303 269  $ 342 997 | € 30 327  $ 34 300 |
| Raad et al. 2017 | USA | Medical ICU | 18 | Mixed biochemistry, haematology, coagulation, blood gasses and CXR | USD 381 471 | € 370 543  $ 419 085 | € 20 586  $ 23 282 |
| Sasser et al. 2018 | USA | Mixed ICU | 22 | Blood gasses | USD 637 608 | € 604 893  $ 684 134 | € 27 495  $ 31 097 |
| Seguin et al. 2002 | France | Surgical ICU | 21 | Mixed biochemistry, haematology, coagulation, blood gasses and CXR | Euro 73 500 | € 94 142  $ 106 475 | € 4 483  $ 5 070 |
| Walsh et al. 2020 | Australia | Medical ICU | 58 | Blood gasses | AUD 750 000 | € 504 684  $ 570 798 | € 8 701  $ 9 841 |

Only showing studies were size of the unit were obtained (n beds).

Abbreviations: Intensive care unit (ICU), Respiratory care unit (RCU), Chest radiography (CXR), U.S. dollar (USD), British pound (GBP), Australian dollar (AUD), New Zealand dollar (NZD), Canadian dollar (CAD), Swizz franc (CHF).

# PRISMA 2020 checklist

Completed PRISMA82 checklist

**Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Checklist**

| **Section and Topic** | **Item #** | **Checklist item** | **Location where item is reported** |
| --- | --- | --- | --- |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review. | p. 1 |
| **ABSTRACT** | | |  |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | p. 4 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | p. 6 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | p. 6 |
| **METHODS** | | |  |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | pp. 7-8 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | p. 8 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Supplemental methods |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | p. 9 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | p. 9 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Supplemental methods |
| 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Supplemental methods |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | NA\* |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | NA |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | p. 10 |
| 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | p. 10 |
| 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | p. 10 |
| 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | p. 10 |
| 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | p. 10 |
| 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | NA\* |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | NA\* |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | p. 9 |
| **RESULTS** | | |  |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Figure 1 |
| 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Figure 1 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Supplemental tables 2 and 3 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | NA\* |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Supplemental tables 8 and 9 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Characteristics: p. 11  Risk of bias: NA |
| 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | pp. 12-15 |
| 20c | Present results of all investigations of possible causes of heterogeneity among study results. | pp. 12-15 |
| 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | NA\* |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | NA\* |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | pp. 12-15 |
| **DISCUSSION** | | |  |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | pp. 16-17 |
| 23b | Discuss any limitations of the evidence included in the review. | p. 19 |
| 23c | Discuss any limitations of the review processes used. | p. 19 |
| 23d | Discuss implications of the results for practice, policy, and future research. | pp. 17-18 |
| **OTHER INFORMATION** | | |  |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | p. 7 |
| 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | p. 7 |
| 24c | Describe and explain any amendments to information provided at registration or in the protocol. | p. 19 |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | p. 1 |
| Competing interests | 26 | Declare any competing interests of review authors. | p. 1 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Data extraction form |

Abbreviations: page: p, pages: pp, not applicable: NA

\*Meta-analysis and risk of bias assessment were not protocolized.

*From:*  Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: <http://www.prisma-statement.org/>

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