WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

Worksheet author(s)

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Clinical question.

In hospital in-patients (adult) (P), does the presence of any specific factors (I) compared with no such factors (C), predict occurrence of cardiac arrest (or other outcome) (O)?

Is this question addressing an intervention/therapy, prognosis or diagnosis? Prognosis
State if this is a proposed new topic or revision of existing worksheet: New Topic

Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No

Search strategy (including electronic databases searched).

Databases searched: PubMed; Ovid/Medline.
PubMed ((("Heart Arrest" [MeSH] OR "Cardiopulmonary Resuscitation" [MeSH]) AND in hospital)) AND (incidence [MeSH:noexp] OR mortality [MeSH Terms] OR follow up studies [MeSH:noexp] OR prognos*[Text Word] OR predict*[Text Word] OR course*[Text Word])
AHA EndNote Master library, Cochrane database for systematic reviews. Search completed in November 2010
Revision of major review articles related to the issue with manual search of references

- **State inclusion and exclusion criteria**

The following articles were excluded: articles prior to 1980, pediatric patients, age < or =18, Outpatients, Long term risk prediction, Risk prediction among post cardiac arrest patients (in-hospital and out of hospital arrest), Risk prediction among patients with acute myocardial infarction, percutaneous coronary intervention, inotrope or pressor use, intraaortic balloon pump, ventricular assist devices, prior pulmonary embolism, prior cardiac surgery, unstable angina, malnutrition, Risk prediction among patients admitted to or in intensive care units.
Include
English language, hospitalized patients, adult, Pre-cardiac arrest risk prediction

- **Number of articles/sources meeting criteria for further review: 620**

Summary of evidence

Evidence Supporting Clinical Question

In hospital in-patients (adult) (P), does the presence of any specific factors (I) compared with no such factors (C), predict occurrence of **cardiac arrest (E1), unexpected ICU admission (E2) or death (E3)**?

Relevance	**Good**	Bell, 2006; 66 (E3) Buist, 2004; 137 (E3) Duckitt, 2007; 769 (E3) Fuhrmann, 2008; 325 (E3) Goldhill, 2004; 882 (E3) Goldhill, 2005; 547 (E3) Goodacre, 2006; 372 (E3) Harrison 2006; 327 (E3) Jacques, 2006; 175 (E1, E2, E3) Olsson, 2004; 579 (E3) Paterson, 2006; 281 (E3) Prytherch, 2003; 1300 (E3) Quarterman, 2005; 133 (E3) Smith, 2008; 170 (E3) Smith, 2008; 109 (E3) Smith, 2008; 11 (E3) Subbe 2001; 521 (E2, E3)	Gao, 2007; 667 (pooled E1, E2, E3) Kellett, 2006; 771 (E3) Prytherch, 2005; 203 (E3)	Cretikos, 2007; 62 (pooled E1, E2, E3) Fieselmann, 1993; 354 (E1) Hodgetts 2002; 125 (E1)		
	Fair	Gardner-Thorpe, 2006; 571 (E2) Neary 2007; 1300 (E3)	Jones, 2004; 410 (E3)	Asadollahi, 2007; 501 (E3) Cuthbertson, 2007; 402 (E2) Goldhill, 2004; 1908 (E3)		
	Poor	Barlow, 2007; 253 (E3) Goel, 2003; 824 (E3) Henry 2003; 37 (E3)	Alarcon, 1999; 429 (E3) Rowat, 2006; 340 (E3)	Sleiman, 2008; 1106 (E3)		
		P1	**P2**	**P3**	**P4**	**P5**
	Level of evidence					

A = Return of spontaneous circulation
C = Survival to hospital discharge
E1 = Cardiac Arrest
E2 = Unexpected ICU admission
E3= in-hospital mortality
B = Survival of event
D = Intact neurological survival

Evidence Neutral to Clinical question

In hospital in-patients (adult) (P), does the presence of any specific factors (I) compared with no such factors (C), predict occurrence of cardiac arrest (or other outcome) (O)?

Good					
Fair			Kause, 2004; 275 (E1, E2, E3)		
Poor					
	P1	**P2**	**P3**	**P4**	**P5**
Level of evidence					

A = Return of spontaneous circulation
C = Survival to hospital discharge
E1 = Cardiac Arrest
E2 = Unexpected ICU admission
E3= in-hospital mortality
B = Survival of event
D = Intact neurological survival

Evidence Opposing Clinical Question

In hospital in-patients (adult) (P), does the presence of any specific factors (I) compared with no such factors (C), predict occurrence of cardiac arrest (or other outcome) (O)?

Good			Cretikos, 2007; 62 (pooled E1, E2, E3)		
Fair			Cuthbertson, 2007; 402 (E2) Fieselmann, 1993; 354 (E1)		
Poor					
	P1	**P2**	**P3**	**P4**	**P5**
Level of evidence					

A = Return of spontaneous circulation
C = Survival to hospital discharge
E1 = Cardiac Arrest
E2 = Unexpected ICU admission
E3= in-hospital mortality
B = Survival of event
D = Intact neurological survival

REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

DISCUSSION

In hospital inpatients (adults), the effectiveness of specific factors in predicting outcome has been analyzed on the occurrence of cardiac arrest, unplanned ICU admission and mortality, alone or combined.

No systematic study of continuously acquired data on all inpatient populations to analyze the incidence of factors correlating with outcome has ever been undertaken; therefore data regarding risk prediction are inadequate. In addition, in hospitalized patients there may be a baseline rate of unpredictable events (for example medication errors) and undetected abnormalities that may confound findings of available studies. The rate of these events and their impact on prognostication is undetermined.

Outcome cardiac arrest

For the outcome cardiac arrest, four studies support the role of physiological derangements predicting cardiac arrest, of which three studies (discussed below) are most relevant. These studies report the predictive value of different physiological variables derangements.

1. *Hodgetts, 2002, 54: 125* Single center, case-control design of prevalence of risk factors for cardiac arrest (CA) in hospitalized pts. 118 consecutive patients with CA and 132 non-CA controlled for gender and age at a single hospital in UK. Multivariate analysis showed that risk factors for CA were abnormalities in:

Item	OR	(95% CI)	Item	OR	(95% CI)
RR	2.6	(1.2-5.6)	Breathing Indicator	2.7	(1.7-4.6)
Pulse	5.8	(3.3-10.3)	Low Systolic BP	17.7	(9.4-33.5)
Temperature	3.0	(1.6-5.5)	SpO2	4.1	(1.9-8.7)
Chest pain	24.6	(3.3-185.4)	Nurse/MD concern	7.5	(2.5-22.4)

ROC for scoring system score of 4 =sens 89% & spec 77% for CA. For score of 8 sens 52% & spec 99%.

2. *Jacques, 2006, 69: 275.* Cross-sectional survey of 3046 non-Do Not Attempt Resuscitation (nonDNAR) adult admissions in five Australian hospitals over 14 days to determine association between 26 early signs (ES) and 21 late signs (LS) of critical conditions and serious adverse events (SAE), including death, cardiac arrest, severe respiratory problems, or transfer to a critical care area.

The top 5 ES and LS and their association with cardiac arrest is:

Top 5 ES for CA	OR	(95% CI)	Top 5 LS for CA	OR	(95% CI)
Poor periph. circulation	94.8	(9.5-944.0)	pH < 7.2	433.9	(4.5-394.3)
Uncontrolled pain	22.8	(2.5-209.4)	Airway obstr./stridor	(0/4)	
Alteration in mentation	17.3	(2.9-104.4)	PaCO2 > 60	(0/8)	
Systolic BP 80-100	16.0	(1.8-143.3)	PaO2 < 50	58.2	(6.1-556.9)
Urine output <200/24H	14.7	(1.6-133.4)	Unresp. to V. command	42	(4.5-394.3)

3. *Cretikos, 2007; 73: 62*. Multicenter, retrospective, nested matched case control study in Australia with 450 cases and 520 controls matched for age, sex, hospital and ward. Utilizing a combined outcome including cardiac arrest, unexpected ICU admission and unexpected death, the combination of HR > 140, RR > 36, SPB < 90 and > 2 points GCS decrease predicted the occurrence of adverse events within 24 h with a sensitivity of 49.1% (44.4—53.8%), specificity of 93.7% (91.2—95.6%), and positive predictive value of 9.8%. (8.7—11.1%). The predictive value of the single variables, cut-off levels and

combinations has been analyzed in detail but with the best combinations, the overall predictive value remained below 16%.

The **neutral evidence**, provided by one study *(Kause, 2004; 275)* shows that 29.2% of cardiac arrests are preceded by physiologic variables' derangements.

The **opposing evidence** relates to the lack of evidence encountered in the ability of blood pressure and heart rate *(Fieselmann, 1993; 8: 354)* –a retrospective study—or derangements below certain cut-offs such as heart rate < 40, 45 or 50 *(Cretikos, 2007; 73: 62)*—a retrospective evaluation—to predict the occurrence of cardiac arrest.

The summary of supporting, neutral and opposing evidence supports the ability of physiologic variables' derangements in adult inpatients to predict the occurrence of cardiac arrest, although the best combination of variables and cut-off levels is still to be identified.

Outcome unplanned ICU admission
General Comment: Criteria for ICU admission may vary. Therefore using ICU admission as an outcome measure represents a 'soft' or undefined outcome for research purposes. Nevertheless, for the outcome "Unexpected ICU admission", supportive evidence is from four studies reporting the predicting value of different physiological variables' derangements. Two studies are in common with the outcome cardiac arrest. One (*Cretikos, 2007; 62)* is apropos because the outcome was pooled including cardiac arrest, unplanned ICU admission and death and the data are reported above. Another analyzed the effect of early and late signs in predicting each of the three outcomes considered (*Jacques, 2006, 69: 275).* The description of the study is reported above and the top 5 ES and LS for unplanned ICU admission are:

Top 5 ES for ICU	OR	(95%CI)	Top 5 LS for ICU	OR	(95%CI)
pH 7.2- 7.3	118.5	(19.5-729.3)	Cardiac arrest	51.3	(8.3-315.7)
RR 5-9 or 31-40	44.2	(18.5-105.1)	GCS $\leq$ 8	51.3	(3.9-49.3)
Base deficit -5 to -8	25.6	(5.0-131)	RR > 40 or < 5	47.4	(10.9-205.3)
Partial airway obstruction	25	(2.6-245.7)	Airway obstr./stridor	25	(2.6-245.7)
PaO2 50-60	24.4	(8.5-64.4)	PaO2	21.5	(5.8-80.1)

Other studies include:
3. *Cuthbertson 2007; 35:402.* Retrospective, observational study of 69 HDU and 67 HDU/ICU patients compared to identify VS differences. Logistic regression used to derive ROC for HR, RR, and SaO2. There were significant physiologic differences between groups with regard to heart rate (p < .001, area under the ROC curve [AUC] 0.7), respiratory rate (*p* < .001, AUROC 0.71), and oxygen saturation (*p* < .001, AUROC 0.78) across time points. This was not present for systolic blood pressure or temperature. Existing early warning scoring systems had good discriminatory power (AUROC 0.83– 0.86).
4. *Subbe 2001; 521*. Single center, prospective, cohort study. MEWS (BP, HR, RR, T, AVPU) were calculated in 709 medical emergency admissions: scores of 5 or more were associated with increased risk of ICU admission (OR 10.9, 95%CI 2.2-55.6). The analysis of predictive value of the single variables is reported for all events and not specifically for ICU admission.
5. *Gardner-Thorpe 2006; 571.* MEWS and its components had PPV of 11% to 50% (for MEWS >6), and NPV for all were >86%.

The **neutral evidence** is provided by two studies. *Kause 2004; 275* shows that 26,9% of unplanned ICU admissions are preceded by physiologic variables' derangements. Please note that ICU admission rate is higher in ANZ compared to the UK *(47.3% vs 24.2%)* which supports the notion that ICU admission rate may not be an objective measure.

The **opposing** evidence is provided by *Cuthbertson 2007; 402*. They showed the lack of ability of systolic blood pressure or temperature to predict the occurrence of unplanned ICU admission.

The summary of supporting, neutral, and opposing evidence suggests that for in-hospital patients, altered vital signs appear to be associated with unplanned ICU admission. The available data is not conclusive because 1) data from studies utilizing pooled outcome cannot be extracted, 2) the variables analyzed in the different studies are not comparable and yield different predictive ability of the single variables and 3) the comparability of criteria for ICU admission has not been demonstrated.

Outcome mortality
The stratification of risk death has been performed in two temporal clinical settings: 1) hospital admission (in both specific disease groups and among all admissions) and 2) during the hospital stay. These are not identical settings and predictive power may not be the same for both.

On admission to hospital
For specific subpopulations, six studies support the value of specific combinations of demographic, physiological and laboratory variables recorded on admission in predicting death in specific patient subpopulations such as geriatric *(Alarcon 1999, 429, Sleiman, 2008; 1106; Henry 2003; 37)*, COPD *(Goel 2003; 824)* , stroke *(Rowat 2006; 340*) and patients with community acquired pneumonia (*Barlow 2007; 253).* Being very specific, they provide poor relevance for the prediction in the general population.
For general populations, evidence from 14 studies supports the value of demographic, physiological and laboratory values derangements, recorded at admission to hospital in predicting death in a general hospital population. The studies tested the predictive value of laboratory altered values *(Asadollahi, 2007; 501*), EWS (BP, HR, O2sat, RR, AVPU score) (*Duckitt 2007; 769*), vital signs (HR, RR, BP, GCS, SpO2) and age to calculate RAPS and REMS score (*Goodacre 2006; 372*), hypotension (*Jones 2004; 410*), the simple clinical score (age, BP, HR, T, RR, O2 sat, breathlessness, abnormal ECG, diabetes, coma, altered mental state, new stroke, and limitation to motility) (*Kellett, 2006;771*), RAPS score (including BP, RR, HR and GCS) and REMS score (RAPS + age+O2 saturation) (*Olsson 2004; 579*), EWS (RR, O2Sat, T, BP, HR, LOC)(*Paterson 2006; 281*), different variables including laboratory, severity of surgery, age, gender and mode of admission in surgical patients (*Prytherch 2003; 1300 & Neary 2007; 1300*), routine lab values (*Prytherch 2005; 203*), aggregate weighted and single parameter trigger systems (*Smith 2008; 170*), 39 published vital signs trigger values (*Smith 2008; 109*) , 33 aggregate weighted trigger systems (*Smith, 2008; 11*) and MEWS (*Subbe 2001; 521*). The sensitivity and specificity of all are in the range of about .6 to .8. It is unclear whether this is sufficiently high to enable a good rule for prospective patient cohorting in higher levels of care.

During hospital stay on ordinary wards
Evidence from 8 studies supports the value of derangements in physiological variables, recorded during hospital stay on ordinary wards, in predicting death. The studies tested:

- Abnormal vital signs (two points GCS decrease, onset of coma, hypotension (<90 mmHg), respiratory rate <6 , oxygen saturation <90%, and bradycardia <30) and the presence of any one of the six events increased 6.8-fold (95% CI: 2.7–17.1) the risk of mortality (*Buist 2004; 137*).
- Abnormal physiological parameters (HR, RR, SBP) had a 30 days mortality higher than normal physiology (30 vs. 3, p<0.0001) (*Bell 2006; 66*).
- Abnormal vital signs (RR <6 or >30, O2 Sat <90%, HR <50 or >130, SBP <90 or >200mmHg) had a higher 30d mortality (13 v 5%) (*Fuhrmann 2008; 325*).

- Abnormal physiologic variables (HR, RR, SBP, T, SaO2, LOC, urine output, age, FiO2) were associated with mortality with OR in decreasing level of significance: LOC 4.63 (95% CI 1.79±12.00; P<0.05), HR 3.86 (1.49±9.97; P<0.05), age 1.04 (1.01±1.07;P<0.05), systolic pressure 3.16 (1.12±8.90; P<0.05) and respiratory rate 2.49 (0.92±6.72).This model had a sensitivity of 7.7%, specificity of 99.8% and a positive predictive value of 66.7%. (*Goldhill 2004; 882*).
- Abnormal physiologic variables (T, HR, SBP, RR, SatO2, LOC, urine output) the number of which increased hospital mortality (p<0.0001) from 4% with no abnormality to 51% with 5 abnormalities. (*Goldhill 2005; 547*).
- Abnormal physiological variables (Airway, RR, SBP, HR, AVPU, T, urine output): increasing age (p<0.001) and increasing MEWS score (p<0.01) were associated with death (*Quarterman 2005; 133*).
- In patients admitted to ICU, demographic, physiologic and pathologic variables, including LOS prior to ICU admission were all predictive of mortality (*Goldhill 2004; 1908*), but in a population of patients more severe than those on wards.

Two studies are in common with the outcomes cardiac arrest and unplanned ICU admission, one (*Cretikos 2007; 62)* because the outcome was pooled including cardiac arrest, unplanned ICU admission and death and the data are reported above, the other because it analyzed the effect of early and late signs in predicting each of the three outcomes considered (*Jacques 2006; 275).* The description of the study is reported above and the top 5 ES and LS for death are:

Top 5 ES death	**OR**	**(95%CI)**	**Top 5 LS death**	**OR**	**(95%CI)**
Base deficit -5 to -8	40.2	(7.7—208.8)	Cardiac Arrest	524.9	(56.5-4878.2)
Partial airway obstr.	38.7	(3.9—64.4),	Urine output < 200/24H	188.6	(30.1—1179.8)
Poor periph. circulation	34.4	(6.8—174.0)	pH <7.2	116.1	(7.1—1906.1)
>expected drain fluid loss	30.1	(6.1—148.9)	unresponsive to voice	34.8	(10.7—113.0)
pH <7.3 >7.2	29.0	(3.1—268.3)	anuric	29.0	(3.1—268.3)

One study, based on the SOCCER data, analyzed the association of ES alone, ES+LS and LS alone with death and concluded that ES+LS and LS were better than ES alone and that a scoring system adapted from MEWS showed a significant direct relationship between increasing score and mortality (*Harrison 2006; 327).*

The **neutral evidence**, provided by one study, analyzing antecedents of cardiac arrest, unplanned ICU admission and deaths (*Kause 2004; 275)* shows that 43.9% of deaths are preceded by physiologic variables' derangements.

The summary of evidence supports the ability of physiological derangements measured in adult patients on wards to predict death. The higher the number of abnormalities the higher the risk of death is, with a positive predictive value ranging from 11 to 70%.

Best variables to predict outcome

1. One systematic review article searching (*Gao 2007; 667*) the track and trigger (TT) systems in use identified 13 single parameters systems and 10 aggregate scoring systems, including a variety of physiologic variables and utilizing a variety of cut-offs for abnormality. When tested in a cohort study of existing datasets against outcome defined by a composite of death, admission to critical care, "do not attempt resuscitation" or cardiopulmonary resuscitation the TT systems showed low sensitivities and positive predictive values, with median (quartiles) of 43.3 (25.4–69.2) and 36.7 (29.3–43.8), respectively.
2. One single center study (*Smith 2008; 11*) tested 39 published single parameter track and trigger systems in 9987 single hospital consecutive patients on hospital mortality. Marked variation in sensitivity (7.3-52.8%), specificity (69.1-98.1%), positive predictive values (13.5-26.1%) and negative

predictive values (92.1-94.2%) were reported. The best performing system (26.1 PPV) had cut-off point of HR < 35 and > 140, RR < 6 and > 32 and SBP < 80.
3. One single center study (*Smith 2008; 170*) tested 33 aggregate weighted trigger systems in 9987 consecutive patients on hospital mortality. 33 AWTTS were identified with AUROC (± 95%CI) ranging from 0.657 (0.638-0.678) to 0.782 (0.767-0.797). The best AWATTS (AUROC 0.782 95%CI 0.767-0.797) included HR, RR, SBP, AVPU, T, age, and O2Sat, the last being absent in the second best system (AUROC 0.761 95%CI 0.745-0.777).
4. One single center study (*Smith 2008; 109*) tested the valued of age added to aggregate weighted (MEWS) and single parameter (MET criteria) trigger systems in 9987 consecutive patients on mortality. In the MET criteria mortality varied significantly with age for RR> 36, SBP < 90, and decreased LOC. At all MEWS scores, increasing age was associated with higher mortality. Age adds 7-9% of predictive power to the scoring systems.

KNOWLEDGE GAPS:

1. There is no assessment of these factors among continuously monitored patients. Therefore there is a knowledge gap regarding the true rate of abnormalities and any relationship to outcome (mortality, cardiac arrest).
2. There is a knowledge gap regarding which scoring system (multi-parameter or single parameter) is better in clinical practice for reliably triggering a response.
3. Which combination of physiologic variables best predicts the occurrence of cardiac arrest.
4. Which cutoff levels for physiologic abnormality best predicts the occurrence of cardiac arrest.

Acknowledgements: Nil

Citation List

Alarcon T. Barcena A. Gonzalez-Montalvo JI. Penalosa C. Salgado A. Factors predictive of outcome on admission to an acute geriatric ward. Age & Ageing. 28(5):429-32, 1999 Sep.

Level P2 Study, evidence in favour, relevance poor.
Single hospital analysis of 353 patients admitted to a geriatric ward after acute illness: on admission variables were recorded including polipharmacy, severe previous functional disability and moderate to devere disability on admission and all three predicted mortality.

Asadollahi K, Hastings IM, Beeching NJ, Gill GV. Laboratory risk factors for hospital mortality in acutely admitted patients. QJM 2007; 100(8):501-507.

Level P3 (retrospective cohort) Study, evidence in favour, relevance fair.
Retrospective case-control (1:2) study of 16219 consecutive admissions (mortality 7.6%) to a single hospital during 1 year. Abnormal admission labs were evaluated between deaths (cases) and survivors (controls). OR for death was between 2 and 4 for abnormalities of glu, Na, WBC.

Barlow G, Nathwani D, Davey P. The CURB65 pneumonia severity score outperforms generic sepsis and early warning scores in predicting mortality in community-acquired pneumonia. Thorax. 62(3):253-9, 2007 Mar.

Level P1 (retrospective cohort) Study, evidence in favour, relevance poor.
Relevance limited to specific population of CAP patients: retrospective analysis of prospectively collected data from 2 hospitals on 419 pts with CAP, comparing relationship of different scoring methods(calculated on variables recorded at admission to hospital) with outcome (not tested single physiological variables). CURB 65 performs better than generic MEWS in predicting death in this subcategory of patients.

Bell MB. Konrad D. Granath F. Ekbom A. Martling CR. Prevalence and sensitivity of MET-criteria in a Scandinavian University Hospital. Resuscitation. 70(1):66-73, 2006 Jul.

Level P1 Study, evidence in favour, relevance good.
Single institution, cross sectional prevalence. Physiological parameters recorded (HR, RR, SBP) and associated with mortality. Mortality with criteria for derangement in study higher first 30 days than normal physiology (30 vs 3, $p<0.0001$) but not confirmed at 2-6 months.

Buist M. Bernard S. Nguyen TV. Moore G. Anderson J. Association between clinically abnormal observations and subsequent in-hospital mortality: a prospective study. Resuscitation. 62(2):137-41, 2004 Aug.

Level P1 Study, evidence in favour, relevance good.
Prospective, multicenter (5 Australian hospitals), 5 wards (investigator checked medical records daily) tested relationship between presence of abnormal vital signs and mortality: six clinical observations were significant predictors of mortality. These were: a decrease in Glasgow Coma Score by two points, onset of coma, hypotension (<90 mmHg), respiratory rate <6 min−1, oxygen saturation <90%, and bradycardia >30 min−1. The presence of any one of the six events was associated with a 6.8-fold (95% CI: 2.7–17.1) increase in the risk of mortality.

Cretikos M, Chen J, Hillman K, Bellomo R, Finfer S, Flabouris A. MERIT study investigators. The objective medical emergency team activation criteria: a case control study. Resusciation 2007; 73(1): 62-72.

Level P3 Study, evidence in favour, relevance good.

Multicenter, nested matched case control study in Australia with 450 cases and 520 controls matched for age, sex, hospital and ward (control cases assessed retrospectively). Utilizing a combined outcome including cardiac arrest, unexpected ICU admission and unexpected death. the combination of HR > 140, RR > 36, SPB < 90 and > 2 points GCS decrease predicted the occurrence of adverse events within 24 h with a sensitivity of 49.1% (44.4—53.8%), specificity of 93.7% (91.2—95.6%), and positive predictive value of 9.8%. (8.7—11.1%). The detailed predictive value of the single variables, cutoff levels and combinations have been analyzed in detail but with the best combinations the overall predictive value remained below 16%.

Cuthbertson BH, Boroujerdi M, McKie L, Aucott L, Prescott G. Can physiological variables and early warning scoring systems allow early recognition of the deteriorating surgical patient? Crit Care Med 2007; 35(2):402-409.

Level P3 (retrospective cohort)Study, evidence in favour, relevance fair .
Retrospective, observational study of 69 HDU and 67 HDU/ICU patients compared to identify VS differences. Logistic regression used to derive ROC for HR, RR, SaO2. AUC =.90. Groups diverged 8-7-8 hours before ICU admission.

Duckitt RW, Buxton-Thomas R, Walker J et al. Worthing physiological scoring system: derivation and validation of a physiological early-warning system for medical admissions. An observational, population-based single-centre study. Br J Anaesth 2007; 98(6):769-774.

Level P1 Study, evidence in favour, relevance good (Validation of a clinical Decisione Rule) .
Observational, derivation (n=3184) and validation (n=1102) of physiological EWS, single center study. RR>19, HR>101, SBP <100, T<35.3, SpO2 <97, altered MS assoc with hospital mortality. EWS derived with AUROCC .74 and if age included 0.81 (for WPSS=3: sens 0.63, spec: 0.72).

Fieselmann JF, Hendryx MS, Helms CM, Wakefield DS. Respiratory rate predicts cardiopulmonary arrest for internal medicine inpatients. J Gen Intern Med 1993; 8(7): 354-60.

Level P3 Study, evidence in favour, relevance good .
Retrospective case-control study 72 hours of consecutive VS measurements from patients who did (59)or did not (91) have a subsequent cardiac arrest at a single institution 1989-1990. RR>27 (sens .54 spec .83, OR 5.6); for low incidence units (sens range .69-1.0; spec range .86-.87). Pulse and BP not predictive.

Fuhrmann L, Lippert A, Perner A, Ostergaard D. Incidence, staff awareness and mortality of patients at risk on general wards. Resuscitation 2008: 77, 325-330

Level P1 Study, evidence in favour, relevance good .
Prospective, observational, single center study, 877 consecutive patients. Abnormal vital signs (Respiratory rate <6 or >30 , Oxygen saturation <90% with or without supplementary oxygen therapy, Pulse rate <50 or >130, Systolic blood pressure <90 or >200mmHg) were found in 155 patients who had higher 30d mortality than patients with normal vital signs (13 v 5%).

Gao H, McDonnell A, Harrison DA, et al: Systematic review and evaluation of physiological track and trigger warning systems for identifying at-risk patients on the ward Intensive Care Med (2007) 33:667–679

LOE P2 Metanalysis of datasets without controls

Systematic Review and Cohort study of 15 datasets from hospitals in England andWales
The Systematic review identified 13 single parameters systems incorporating between 4 and 11 physiological parameters all including some measure of BP and LOC and most including HR and RR and 10 aggregate scoring systems, all including HR, RR, SBP, AVPU, most including urine output and temperature and only four including oxygen saturation and three evaluation of pain.
For the cohort study, track and trigger (TT) systems in use were tested against outcome defined by a composite of death, admission to critical care,'do not attempt resuscitation' or cardiopulmonary resuscitation. Sensitivities and positive predictive values were low, with median (quartiles) of 43.3 (25.4–69.2) and 36.7 (29.3–43.8), respectively. Available data were insufficient to identify the best TT.

Gardner-Thorpe J. Love N. Wrightson J. Walsh S. Keeling N. The value of Modified Early Warning Score (MEWS) in surgical in-patients: a prospective observational study. Annals of the Royal College of Surgeons of England. 88(6):571-5, 2006 Oct.

Level P1 Study, evidence in favour, relevance fair.
Prospective, single center, observational study of 334 surgical patients. MEWS calculated and risk assessed. MEWS and its components had PPV of 11% to 50% (for MEWS >6), and NPV for all were >86%.

Goel A. Pinckney RG. Littenberg B. APACHE II predicts long-term survival in COPD patients admitted to a general medical ward. Journal of General Internal Medicine. 18(10):824-30, 2003 Oct.

Level P1 Study, evidence in favour, relevance poor.
Relevance poor. Retrospective cohort study of 92 patients in single center admitted to hospital with COPD and long term mortality. ICU excluded.

Goldhill DR. McNarry AF. Physiological abnormalities in early warning scores are related to mortality in adult inpatients. British Journal of Anaesthesia. 92(6): 882-4, 2004 Jun.

Level P1 Study, evidence in favour, relevance good .
Single day, single institution, variables (HR, RR, SBP, T, SaO2, LOC, urine output, age, FiO2), were recorded on all 433 pts on ward. Among the varibles tested, the odds ratio for mortality for the most significant variables were, in decreasing level of significance: LOC 4.63 (95% CI 1.79±12.00; P<0.05), HR 3.86 (1.49±9.97; P<0.05), age 1.04 (1.01±1.07;P<0.05), systolic pressure 3.16 (1.12±8.90; P<0.05) and respiratory rate 2.49 (0.92±6.72).This model had a sensitivity of 7.7%, specificity of 99.8% and a positive predictive value of 66.7%. Mortality increased with the number of physiological variables deranged (p<0.001) and with level of care lower than required (p<0.01).

Goldhill DR. McNarry AF. Hadjianastassiou VG. Tekkis PP. The longer patients are in hospital before Intensive Care admission the higher their mortality. Intensive Care Medicine. 30(10):1908-13, 2004 Oct.

Level P3 (retrospective cohort) Study, evidence in favour, relevance fair.
Observational study of prospectively collected data multicenter, 24 hospitals 7190 pts admitted to ICU. LOS on ward before ICU adm, age, APS, CPR, GCS and chronic health were independent predictors of hospital mortality.

Goldhill DR. McNarry AF. Mandersloot G. McGinley A. A physiologically-based early warning score for ward patients: the association between score and outcome. Anaesthesia. 60(6):547-53, 2005 Jun.

Level P1 (retrospective cohort) Study, evidence in favour, relevance good .
Single hospital, analysis of database of physiologic variables (T, HR, SBP, RR, SatO2, LOC, urine output) on 1047 pts on wards assessed by outreach. Examining the PAR score binary logistic regression showed all

variables except T and HR contributed to the model predicting hospital mortality. Increasing number of physiological abnormalities increased hospital mortality (p<0.0001) from 4% with no abnormality to 51% with 5 abnormalities.

Goodacre S, Turner J, Nicholl J. Prediction of mortality among emergency medical admissions. Emerg Med J 2006; 23(5):372-375.

Level P1 Study, evidence in favour, relevance good .
Single center, secondary analysis of database of emergency room admissions of patients brought in by ambulance for unconsciousness, chest pain, or apnea. Vital sign database (age, HR, RR, BP, GCS, SpO2) was recorded, and RAPS and REMS scores were analyzed as predictors for hospital mortality. AROCC for RAPS 0.64, REMS 0.74. New score using independent predictors in multivariate analysis (GCS, age, SpO2), AROCC 0.84. Score calculation not shown.

Harrison GA, Jacques T, McLaws ML, Kilborn G. Combinations of early signs of critical illness predict in-hospital death—the SOCCER study (signs of critical conditions and emergency responses). Resuscitation 2006; 71: 327-334.

Level P1 Study, evidence in favour, relevance good .
Cross-sectional survey of 3046 non Do Not Attempt Resuscitation (nonDNAR) adult admissions in five hospitals over 14 days to determine association between 26 early signs (ES) and 21 late signs (LS) of critical conditions and death searched by retrospective chart review. Late signs (LS) or LS+ES (early signs) had higher OR for mortality than ES alone (range 418-17:1.) In no LS group did more than 30% of LS patients die. Sens low as well best was 13/27 deaths.

Henry OF. Blacher J. Verdavaine J. Duviquet M. Safar ME. Alpha 1-acid glycoprotein is an independent predictor of in-hospital death in the elderly. Age & Ageing. 32(1):37-42, 2003 Jan.

Level P1 Study, evidence in favour, relevance poor.
Single hospital, 433 elderly patients admitted to hospital after acute events were followed prospectively: (Mortality=81) alfa 1 acid glycoprotein, previous stroke and previous congestive heart failure were the only parameters significantly and independently correlated with all cause mortality.

Hodgetts TJ, Kenward G, Vlachonikolis IG, Payne S, Castle N. The identification of risk factors for cardiac arrest and formulation o factivation criteria to alert a medical emergency team. Resuscitation 2002; 54 (2): 125-31.

Level P3 (retrospective cohort) Study, evidence in favour, relevance good .
"quasi experimental" [case-control] design of prevalence of risk factors for cardiac arrest (CA) in hospitalized pts. 118 consecutive patients with CA and 132 non-CA controlled for gender and age at a single hospital in UKl. Multivariate analysis showed risk factors for CA abnormal breathing (RR or Shortness of breath), abnormal pulse, low BP.ROC for scoring system score of 4 =sens 89% & spec 77% for CA. for score of 8 sens 52% & spec 99%.

Jacques T, Harrison GA, McLaws ML, Kilborn G. Signs of critical conditions and emergency responses (SOCCER): a model for predicting adverse events in the inpatient setting. Resuscitation 2006; 69: 175-183.

Level P1 (retrospective cohort)Study, evidence in favour, relevance good .
Cross-sectional survey of 3046 non Do Not Attempt Resuscitation (nonDNAR) adult admissions in five hospitals over 14 days to determine association between 26 early signs (ES) and 21 late signs (LS) of critical conditions and serious adverse events (SAE), including death, cardiac arrest, severe respiratory

problems, or transfer to a critical care area. 12384 ES and 1410 LS were recorded . Among LS, urine output (OR 188) had highest and low BP (OR 7) had lowest OR for death. For Cardiac arrest, PaO2<50 (OR 58) had highest and SpO2 <90% (OR 2.3) had lowest OR. Sens and spec Very low. Best was 2/8 deaths.

Jones AE, Aborn LS, Kline JA. Severity of emergency department hypotension predicts adverse hospital outcome. Shock 2004; 22(5):410-414.

Level P2 Study, evidence in favour, relevance fair.
Retrospective observational study of consecutive hypotensive admits from ED at a single hospital. 190 patients BP<100, 81 had adverse outcome (death, ICU>3d, vasopressor>2d, Mech vent, ARF +HD). Mortality associated with BP 72 (81 in no AE), BP<80: sens 65, spec 62 for adverse events.

Kause J, Smith G. Prytherch D. Parr M. Flabouris A. Hillman K. Intensive Care Society (UK). Australian and New Zealand Intensive Care Society Clinical Trials Group. A comparison of antecedents to cardiac arrests, deaths and emergency intensive care admissions in Australia and New Zealand, and the United Kingdom--the ACADEMIA study. Resuscitation. 62(3):275-82, 2004

Level P3 (retrospective cohort) Study, evidence neutral, relevance fair
Multicenter, prospective, observational, UK and Australian study, measured incidence of cardiac arrests, death and unplanned ICU admissions preceeded or not by antecedents. There were differences in the pattern of primary events netween the UK and ANZ (p<0.01) with proportionally more deaths in the UK (52.3% vs 35.3%) and a higher numebr of unplanned ICU admissions (47.3% vs 24.2%). 60% of primary events (29.2% of cardiac arrests, 43.9% of deaths and 26.9% of ICU admissions) had antecedents, the more frequent beeing SBP and GCS decrease.

Kellett J, Deane B. The Simple Clinical Score predicts mortality for 30 days after admission to an acute medical unit. QJM 2006; 99(11):771-781.

Level P2 Study, evidence in favour, relevance good (validation of clinical decision rule) .
Single center, 9964 patients: 6736 derivation, 3228 validation. 316 (4.7%) died within 30d. Clinical score stratifies into 5 risk classes. 5% of patients met highest risk, 1/3 died; 1/3 were lowest risk, 2(<1%) died. Independent predictors: abnormal ECG, temp., dyspnea, BP, Coma, O2 sat, prior illness, inability to stand, age. Area under the curve (AUC=88.9%)

Neary WD. Prytherch D. Foy C. Heather BP. Earnshaw JJ. Comparison of different methods of risk stratification in urgent and emergency surgery. British Journal of Surgery. 94(10):1300-5, 2007 Oct.

Level P1 Study, evidence in favour, relevance fair .
Single center, 2349 consecutive emergent surgical patients. Evaluation of P-POSSUM, revised Goldman cardiac risk (RGCRI), Surgical Risk Score (SRS), Biochem and Heme outcome models (BHOM) were assessed for variation between expected and predicted. 30d Mortality risk was assessed. 141(6%) died. ROC for P-POSSUM .90, SRS .85, BHOM .84, RGCRI .73.

Olsson T, Terent A, Lind L. Rapid Emergency Medicine score: a new prognostic tool for in-hospital mortality in nonsurgical emergency department patients. J Intern Med 2004; 255: 579—87.

Level P1 Study, evidence in favour, relevance good (validation of clinical decision rule).
Single hospital, prospective cohort study. 12006 nonsurgical patients on admission. RAPS score (including BP, RR, HR and GCS) and REMS score (RAPS + age+O2 saturation) were calculated. The REMS (validated by split sample) was superior to RAPS in predicting in-hospital mortality ROC curve 0.852 ± 0.014 SEM for

REMS compared with 0.652 ± 0.019 for RAPS, P < 0.05]. An increase of 1-point in the 26-point REMS scale was associated with an OR of 1.40 for in-hospital death (95% CI: 1.36–1.45, P < 0.0001).

Paterson R, MacLeod DC, Thetford D, et al. Prediction of inhospital mortality and length of stay using an early warning scoring system: clinical audit. Clin Med 2006; 6:281—4.

Level P1 Prospective cohort study, evidence in favour, relevance good .
Single center, prospective. In 848 pastients on admission to combined medical ad surgical unit, standardised EWS (RR, O2Sat, T, BP, HR, LOC) (collected from charts), in-hospital mortality, transferr to ICU and LOS were documented. The admission EWS score correlated both with in-hospital mortality (p<0.001) and LOS (p=0.001)

Prytherch DR, Sirl JS, Weaver PC, Schmidt P, Higgins B, Sutton GL. Towards a national clinical minimum data set for general surgery. Brit J Surg 2003; 90: 1300-1305.

Level 1 Study, evidence in favour, relevance fair .
Observational study of 11263 consecutive non-op emergencies, operative emergencies, and elective operative admissions. SPECIFIC FACTORS=urea, hgb, WBC Na, K, age, gender, Operative severity score, and mode of admission. Risks stratified into 5 "bands" of predicted mortality.

Prytherch DR, Sirl JS, Schmidt P, Featherstone PI, Weaver PC, Smith GB. The use of routine laboratory data to predict in-hospital death in medical admissions. Resuscitation 2005; 66:203-207.

Level P2 Study, evidence in favour, relevance good (Validation of clinical decision rule) .
Tested relevance of routine lab values in predicting mortality on 9497 single hospital consecutive patients. C indices were 0.757-0.779. But for risk stratification only. At highest risk, 12 patients, 8 predicted, 6 died. At lowest, 1279 patients, 29 predicted and 35 died.

Quarterman CP. Thomas AN. McKenna M. McNamee R. Use of a patient information system to audit the introduction of modified early warning scoring. Journal of Evaluation in Clinical Practice. 11(2):133-8, 2005 Apr.

Level P1 Study, evidence in favour, relevance good .
Single hospital retrospective analysis of data on 619 trigger scores utilized for activating RRS (corresponding to derangements of physiological variables Airway, RR, SBP, HR, AVPU, T, urine output) in 365 patients and outcome (death from all causes): multivariant analysis showed that increasing age (p<0.001) and increasing MEWS score (p<0.01) are associated with death.

Rowat AM. Dennis MS. Wardlaw JM. Central periodic breathing observed on hospital admission is associated with an adverse prognosis in conscious acute stroke patients. Cerebrovascular Diseases. 21(5-6):340-7, 2006.

Level P2 Study, evidence in favour, relevance poor.
Single institution, measured presence of central periodic breathing and Sat O2 on admission in 156 stroke pts: CPB independently associated with poor outcome after stroke but not due to hypoxia : 91% of patients with CPB were dead or dependent (MRS>or=3) compared with 53% of those without (OR 8.8; 95% CI 2.5-30.5); the association remained statistically significant after adjusting for covariates (OR 5.9; 95% CI 1.4-25.4).

Sleiman I. Morandi A. Sabatini T. Ranhoff A. Ricci A. Rozzini R. Trabucchi M. Hyperglycemia as a predictor of in-hospital mortality in elderly patients without diabetes mellitus admitted to a sub-intensive care unit. Journal of the American Geriatrics Society. 56(6):1106-10, 2008 Jun.

Level P3 Retrospective cohort study, evidence in favour, relevance fair.

Retrospective cohort single center study of 1229 patients without and with DM admitted outside ICU. Overall Mortality 14%. Mortality without and with DM for Glu normal (11 & 8%); Glu 127-180 (17 & 11%); and Glu >180 (34 & 13%). OR in hospital mortality 2.7.

Smith GB, Prytherch DR, Schmidt PE, Featherstone PI, Kellett J, Deane B, Higgins B. Should age be included as a component of track and trigger systems used to identify sick adult patients? Resuscitation 2008; 78: 109-115.

Level P1 Study, evidence in favour, relevance good .
Tested the value of the addition of age to aggregate weighted (MEWS) and single parameter (MET cirteria) trigger systems on 9987 consecutive patients on admission to single hospital. Where groups of patients had triggered a certain MET criterion, mortality was higher as patient age increased. At all MEWS scores increasing age associated with higher mortality. Max mortality was 75% (>80y+>6EWS); all others save 1 were <40%. Age adds 7-9% of predictive power of the scoring systems.

Smith GB, Prytherch DR, Schmidt PE, Featherstone PI, Higgins B. A review, and performance evaluation of single-parameter "track and trigger" systems. Resuscitation 2008; 79: 11-21.

Level P1 Study, evidence in favour, relevance good .
Tested 39 published vital signs trigger values on 9987 single hospital consecutive patients in single hospital on hospital mortality. Marked variation in sensitivity (7.3-52.8%), specificity (69.1-98.1%), positive predictive values (13.5-26.1%) and negative predicitve values (92.1-94.2%). The best performing system (26.1 PPV) had cutoff point of HR < 35 and > 140, RR < 6 and > 32 and SBP < 80.

Smith GV, Prytherch DR, Schmidt PE, Featherstone PI. Review and performance evaluation of aggregate weighted 'track and trigger' systems. Resuscitation 2008; 77: 170-179.

Level P1 Study, evidence in favour, relevance good .
Tested 33 aggregate weighted trigger systems on 9987 single hospital consecutive patients and hospital mortality. 33 AWTTS were identified with AUROC (± 95%CI) ranging from 0.657 (0.638-0.678) to 0.782 (0.767-0.797) . The best AWATTS (AUROC 0.782 95%CI 0.767-0.797) included HR, RR, SBP, AVPU, T, age and O2Sat, the latter being absent in the second best (AUROC 0.761 95%CI 0.745-0.777).

Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified Early Warning Score in medical admissions. QJM 2001;94:521—6.

Level P1 Study, evidence in favour, relevance good . (Validation of clinical decisione rule)
Single center, prospective, cohort study. MEWS (BP, HR, RR, T, AVPU) were calculated in 709 medical emergency admissions and correlated with outcome, including death, ICU admission, HDU admission, cardiac arrest and hospital discharge at 60 days. Scores of 5 or more were associated with increased risk of death (OR 5.4, 95%CI 2.8-10.7), ICU admission (OR 10.9, 95%CI 2.2-55.6) and HDU admission (OR 3.3 95%CI 1.2-9.2). Patients who achieved predefined endpoints were significantly older, and on admission had lower systolic blood pressure, higher pulse rate and higher respiratory rate.