Answering the Clinical Question of Mortality Benefit from Using the Sepsis Resuscitation Bundle Alone

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Clinical Significance of Sepsis

• Mortality rates 29-50% - higher than rates for myocardial infarction, stroke, or traumatic injury.   (Seymour et al., 2010)

• Treatment costs $17 billion annually, ~2.5% of all health care expenditure in the United States.

(IHI, 2012)

Research Background

Surviving Sepsis Campaign's international guidelines for presence of severe sepsis, septic shock, or lactic acid $\geq$ 4 mmol/l with confirmed or suspected infection:

- Sepsis Resuscitation Bundle (SRB) initiated in 6 hours

- Sepsis Management Bundle implementation within 24 hours

- Bundles are collectively known as early goal-directed therapy (EGDT)

(Dellinger et al., 2008; Rivers et al., 2012)

Purpose Appraise Clinical Guidelines

Research question

In adult patients over 18, does using the Sepsis Resuscitation Bundle (SRB) improve survival in the presence of severe sepsis/septic shock during hospital stay?

Clinical question looked to answer whether only the SRB's use could demonstrate a positive impact on mortality.

Theoretical Framework Change Model

A Model of Change to Evidence-Based Practice (EBP) guides nurses through a systematic process for change towards an evidence-based practice.

- Translates research into practice

- Uses research findings

- Applies standardized nomenclature

This model consists of 6 steps that:

1. Assess need for change in practice
2. Links problem intervention & outcomes
3. Synthesize best evidence
4. Design practice change
5. Implement & evaluate practice change
6. Integrate & maintain change in practice

(Rosswurm & Larrabee, 1999)

Research Methodology

- Rigour attempted at level of those who produced the sepsis clinical guidelines.

- Sepsis guidelines were peer-reviewed practice recommendations developed by experts from 27 professional international organizations. (SSC, 2008)

- SRB guideline recommendations used by the Surviving Sepsis Campaign (SSC) in 2008 were based on the Grades of Recommendation, Assessment, Development, & Evaluation (GRADE) methodology.

(Dellinger et al., 2008)

Research Method Used

Literature Search
- Identified all relevant published evidence
- Selected studies for inclusion
- Assessed quality of each study
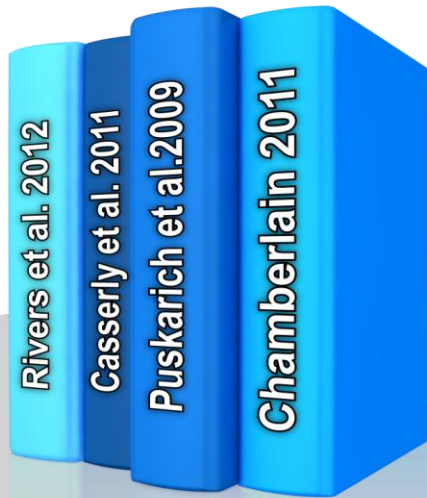
Critical Appraisal of the Evidence
- Examined all quantitative evidence
- Synthesized the research results from each study
- Summarized research findings in written paper

Systematic Review
- Compared each study to PICOT
- Used grid to record details of each study
- Noted gaps in research from PICOT
- Identified study weaknesses

Rivers et al. 2012

Casserly et al. 2011

Puskarich et al.2009

Chamberlain 2011
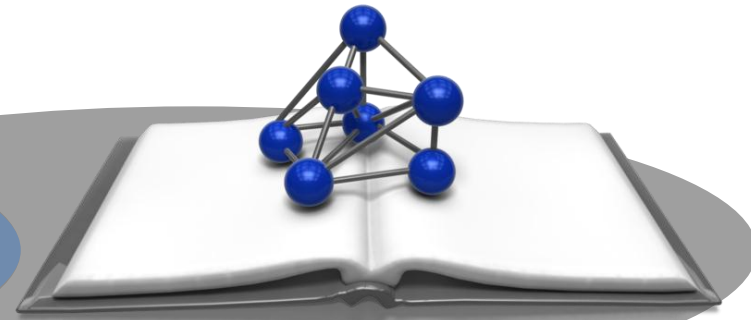
Literature Search

• Key words searched: Sepsis resuscitation bundle, severe sepsis, septic shock, sepsis treatment, early goal-directed therapy, EGDT

• Data bases searched: CINAHL Plus, PubMed, MEDLINE, & Scopus

• Search yielded 24 articles

• 8 research studies reviewed

• 1 practice guideline reviewed

• Levels & strengths of evidence guided credibility attributed to the research findings.

Levels of Evidence

Level 7 Evidence from the Opinion of Authorities or Expert Committees

Level 6 Single Descriptive or Qualitative Study

Level 5 Systematic Review of Descriptive or Qualitative Study

Level 4 Single Correlational/ Observational Study

Level 3 Systematic Review of Correlational/observational Studies

Level 2 Single RCT or non-randomized trial

Level 1 Systematic Review of RCTs or of Non-Randomized Trials

Level of evidence & grading the evidence proved valuable for comparison & weighing findings.

Level III was the highest level of evidence identified in comparing research on use of the SRB.

(Quantitative Pyramid, n.d .)

Levels of Evidence

• The original practice guideline relied heavily on one study, thus creating controversy in the recommendation despite the endorsement by 11 professional organizations. (Dellinger et al., 2008)

• Level of evidence found in compared studies ranged from Level III to Level IV

• Only 2 studies addressed the intervention of interest (levels of evidence III & IV)

USPSTF Scale Strength of Evidence Used

Level of Strength Description

A Strongly recommend; Good evidence that the benefits substantially outweigh harms

B Recommend; At least fair evidence that benefits outweigh harms

C U.S. Preventive Services Task Force (USPSTF) makes no recommendation; Recommend against routinely providing X service for Y population. There may be considerations supporting the provision of the service in an individual patient.

D Recommend against routine use; Ineffective or harms outweigh potential benefits

I Insufficient evidence to make a recommendation; No evidence or poor quality evidence

(U.S. Preventive Task Force Grade Definitions, 2008)

Systematic Review

Completion of Comparison of Sepsis Resuscitation Bundle Research Evidence to Research Question

Systematic Review Research Grid

IMPLEMENTATION OF SEVERE SEPSIS RESUSCITATION BUNDLE

1

DOCUMENTING EVIDENCE-BASED PRACTICE ASPECTS

Question to Consider within the Evidence-based Practice process:

P (Population of Interest): Adult (18+) in emergency and critical care settings

I (Intervention of Interest): Using the Institute for Healthcare Improvement's (IHI) Sepsis

Resuscitation Bundle in treatment of severe sepsis/septic shock

C (Comparison of Interest): Patient's who did not receive the IHI Sepsis Resuscitation

Bundle in treatment of severe sepsis/septic shock

O (Outcome of Interest): Reduced mortality

T (Time): During hospital stay

Comparison of Sepsis Resuscitation Bundle Research Evidence

Articles (level of evidence/evaluation of strength of the evidence)	Who Involved (sample size, sampling method, population)	What Occurred (qualitative, quantitative)	Where Completed (type of agency, state, country)	When (year research done)	Why (research question)	How (data collection, tool used with validity and reliability, statistical tests, qualitative control)	Consistencies (how addresses the PICOT question, how alike with other studies reviewed)	Gaps (how does it not address the PICOT question, what did the researchers state still needed to be studied)
Rivers, E P., Katranji, M., Jaehne, K. A., Brown, S., Abou Dagher, G., Cannon, C. & Coba, V. (2012). Early interventions in severe sepsis and septic shock: A review of the evidence one decade later. *Minerva Anestesiologica,78(6),* 712-	**Sample Size:** Over 18,000 adult patients were narrowed to 1,411 patients who received the resuscitation bundle (RB) or	**Quantitative** Meta-analysis included over 50 publications **Results:** The RB alone	Department of Emergency Medicine and Surgery, Henry Ford Hospital, Wayne State University, Detroit,	Published in 2012 Looked at evidence gathered from multiple studies on EGDT	This review examined one decade of evidence for the components of the sepsis RB examining	**Data Collection:** The mean age, baseline APACHE II scores, and mortality rate of the previous adult studies compiled for analysis are similar to the original EGDT study. Outcomes observed in	P (Met by study) I (Met by study with comparison of the RB to EGDT) C (Met by study through meta-analysis)	P: The population of interest was met I: The intervention of interest was met C: The comparison of interest was met O: The outcome of

(Boswell & Cannon, 2014)

PICOT Research Question

P (Population of Interest): Adult (18+) in emergency and critical care settings

I (Intervention of Interest): Using the SRB in treatment of severe sepsis/septic shock

C (Comparison of Interest): Patient's who did not receive the SRB in treatment of severe sepsis/septic shock

O (Outcome of Interest): Reduced mortality

T (Time): During hospital stay

Systematic Review Data Collection

Articles (level of evidence/evaluation of strength of the evidence)
Rivers, E.P., Katranji, M., Jaehne, K.A., Brown, S., Abou Dagher, G., Cannon, C. & Coba, V. (2012). Early interventions in severe sepsis and septic shock: A review of the evidence one decade later. Minerva Anestesiologica,78(6), 712-24. Level of Evidence: Level III Strength of Evidence: Level A

Systematic Review Data Collection

Who Involved

(sample size, sampling method, population)

Sample Size:

Over 18,000 adult patients were narrowed to 1,411 patients who received the resuscitation bundle (RB) or were in the control group compared to 263 patients in the original Early Goal Directed Therapy (EGDT) study by Rivers et al.

Sampling Method:

Meta-analysis of over 50 publications

Population:

18+ adult patients with severe sepsis or septic shock

Systematic Review Data Collection

What Occurred
(qualitative, quantitative)

Quantitative

Meta-analysis included over 50 publications

Results:

The RB alone demonstrated a relative risk reduction (RRR) of 0.37, absolute risk reduction (ARR) of 18.3%, number needed to treat (NNT) of 5.45, and a crude mortality reduction of 17.7%.

Systematic Review Data Collection

Where Completed
(type of agency, state, country)

Department of Emergency Medicine and Surgery, Henry Ford Hospital, Wayne State University, Detroit, Michigan, United States

Department of Medicine, Pulmonary and Critical Care Medicine, Pontiac Osteopathic Hospital, Pontiac, Michigan, United States

Department of Emergency Medicine, University of Kansas, Medical Center, Kansas City, Kansas, United States
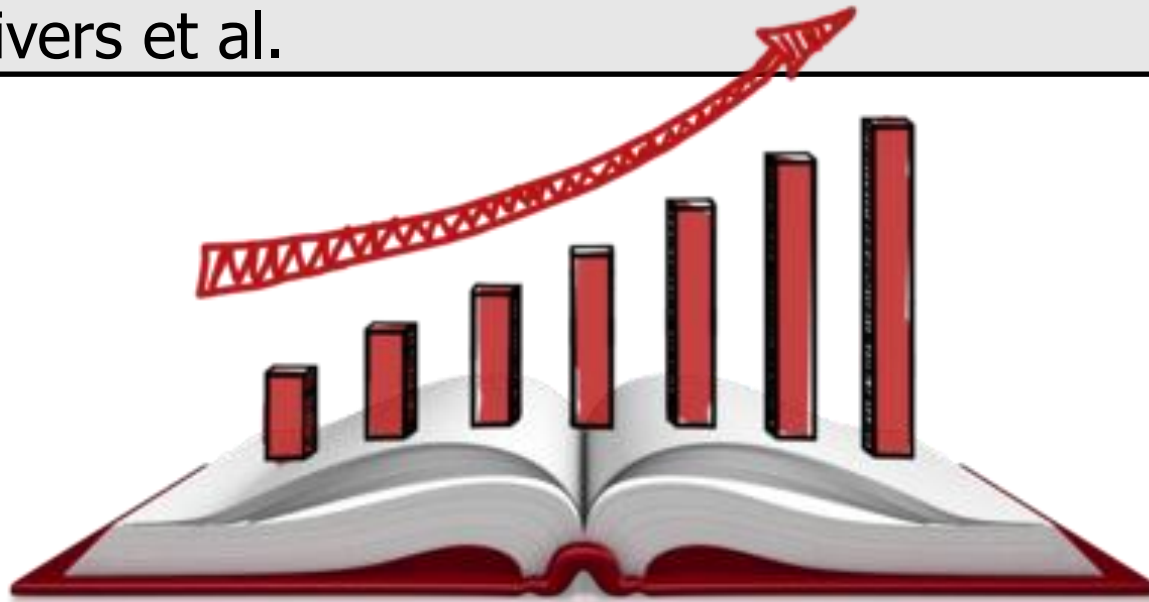
Systematic Review Data Collection

When

(year research done)

Published in 2012
Looked at evidence gathered from multiple studies on EGDT over the ten years since EGDT research was first published in 2001 by Rivers et al.
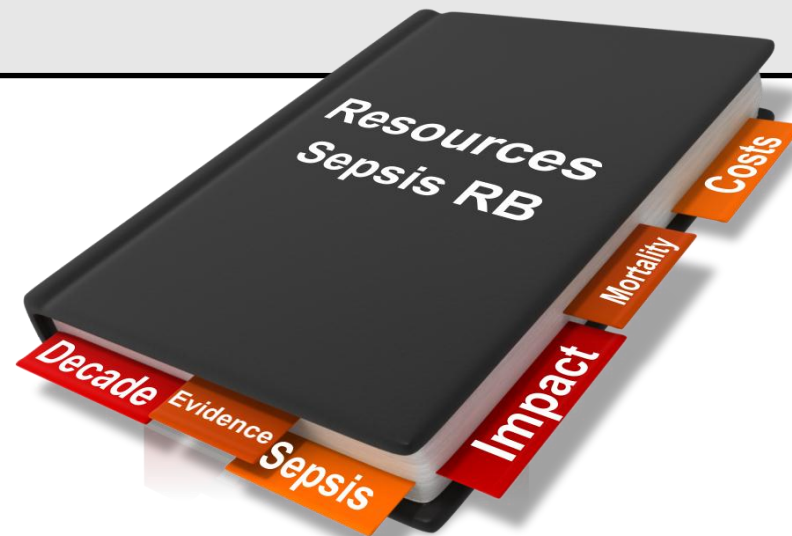
Systematic Review Data Collection

Why
(research question)

This review examined one decade of evidence for the components of the sepsis RB examining its impact on systemic inflammation, the progression of organ failure, health care resource consumption, and mortality in severe sepsis and septic shock

Systematic Review Data Collection

How

(data collection, tool used with validity and reliability, statistical tests, qualitative control)

Data Collection:

The mean age, baseline APACHE II scores, and mortality rate of the previous adult studies compiled for analysis are similar to the original EGDT study. Outcomes observed in community and tertiary care hospitals, Emergency Department (ED), Intensive Care Unit (ICU) settings, and medical and surgical patients. Compliance with the RB was assessed at 6, 18, and 24 hours after diagnosis of severe sepsis or septic shock.

Systematic Review Data Collection

Consistencies (how addresses the PICOT question, how alike with other studies reviewed)
P (Met by study)
I (Met by study with comparison of the RB to EGDT)
C (Met by study through meta-analysis)
O (Met by study; The outcome benefit of these studies combined equal or exceed the reduction in mortality found in the original Rivers et al. trials)
T (Because not specified, assumed to be during hospitalization)

Systematic Review Data Collection

Gaps

(how does it not address the PICOT question, what did the researchers state still needed to be studied)

P: The population of interest was met

I: The intervention of interest was met

C: The comparison of interest was met

O: The outcome of interest was met

T: Could be more clearly stated

Systematic Review Data Collection

Gaps (cont.)

(how does it not address the PICOT question, what did the researchers state still needed to be studied)

Noted Study Weaknesses:

No future research identified by the researchers. Notably, poor compliance demonstrated by not initiating the RB before the initial six hour window of recommendation or not extended use of the interventions past 18 hours of treatment. Poor compliance with the EGDT bundles still demonstrated a reduction in mortality.

Literature Systematic Review

Intervention applied in research findings

• 5 published research findings & the practice guideline used EGDT.

• All other 19 studies used either a modified version of the SRB or the EGDT bundles of care.

• Chamberlin et al. (2011) found that only 2 of 11 studies in their meta-analysis used an unmodified SRB.

• Coba et al. (2011) & Rivers et al. (2012) used the SRB, therefore standing out as most beneficial for answering the PICOT question.

Synthesis of Findings

Synthesis Critical Appraisal of the Evidence

**Variability in interventions applied found across reviewed studies**

• Despite intervention used, all studies demonstrated a positive effect on mortality except for Casserly et al. (2011) (did not address question of mortality).

• Since EGDT contains the SRB, mortality benefits seen in all studies that looked at mortality may be considered important findings.

Synthesis Critical Appraisal of the Evidence

Variability in timing of delivered intervention across reviewed studies

• Notable variability in timing of application of SRB & EGDT in entirety.

• Despite delayed implementation, mortality benefit was demonstrated.
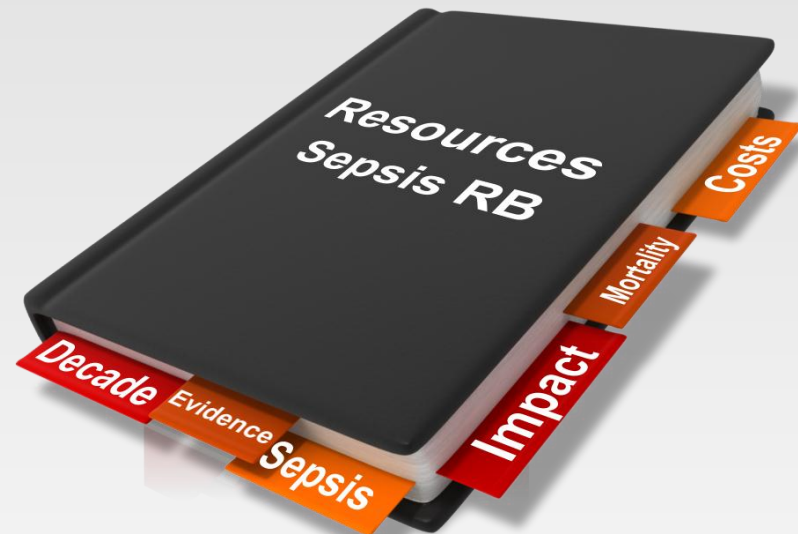
Synthesis Critical Appraisal of the Evidence

Rivers et al. (2012) addressed the PICOT without any gaps in the research & question being asked

• Correlation was strengthened by study design's meta-analysis of over 50 publications & large sample size of > 18,000 adults.

• The strongest evidence supporting the use of the SRB was noted in this meta-analysis.

Rivers et al. (2012) Comparison of Sepsis Intervention Studies Using the Resuscitation Bundle Compared to the Original EGDT Study

	Summary of implementation study		Rivers et al.	
	Before or Control	After	Control	EGDT
Number of patients	9527	9884	133	130
APACHE II score	24.2	24.2	20.4	21.4
Sex, % Males	58.15	57.3	50.4	50.8
Age (years)	63.8	62.9	64.4	67.1
Mortality before (SD)**	46.8 (26)%	29.1 (12)%	46.5%	30.5%
Relative risk reduction		0.37	0.34	
Absolute risk reduction		18.3%	16.0%	
NNT		5.45	6.25	

Note. Includes before and after concurrent implementation studies. **The average mortality of each study. NNT=number needed to treat. Adapted from "Early Interventions in Severe Sepsis and Septic Shock: A Review of the Evidence One Decade Later", by E.P. Rivers, M. Katranji, K.A. Jaehne, S. Brown, G. Abou Dagher, C. Cannon, and V. Coba, 2012, *Mirnerva Anestesiologica 78(6),* 712-24. Copyright 2012 by Edizioni Minerva Medica.

Synthesis

Critical Appraisal of the Evidence (cont)

One Level IV study examined intervention of interest included an 18 month prospective cohort study of patients & the impact of the SRB on patient outcomes when completed after the 6 hour recommendation period.

(Coba et al., 2011)

Synthesis Critical Appraisal of the Evidence

Chamberlin et al. (2011) used a meta-analysis of non-RCTs

• Level III evidence

• Only 2 of the 21 studies used the complete SRB

• The highest identified level of evidence found through systematic review

• Applicability to answering the PICOT question is lacking

Conclusions Systematic Review

Despite the inconsistency in applied treatment bundles & timing of interventions identified through literature review, all studies that measured mortality demonstrated a clinically significant reduction in mortality.
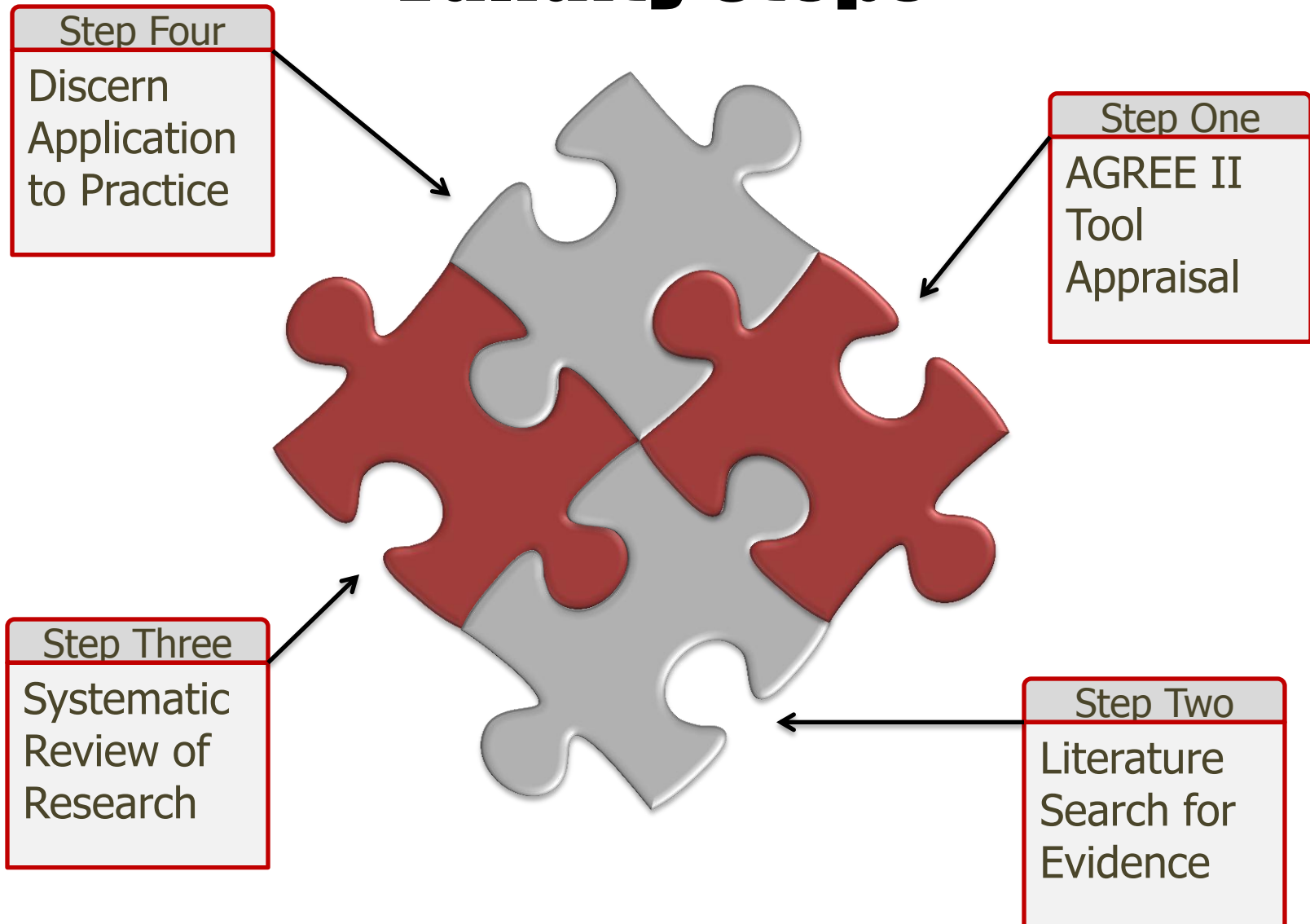
Conclusions Systematic Review

• EGDT, the complete SRB, & modified SRB each demonstrated clinically significant decreases in mortality when implemented up to 24 hours after clinical presentation of severe sepsis or septic shock.

• Other positive effects were measured & reported by some of the research.

• No identified harm was associated with the initiation of goal directed sepsis management through the use of the SRB.

Sepsis Resuscitation Bundle Guideline

Validity Steps

Step Four
Discern Application to Practice

Step One
AGREE II Tool Appraisal

Step Three
Systematic Review of Research

Step Two
Literature Search for Evidence

Appraisal of Guidelines for Research & Evaluation II (AGREE II)

Validity AGREE II Tool

- Allowed for analysis of the rigorous development methodology used to create clinical guidelines for treating severe sepsis & septic shock.

- Allowed for assessment of SSC guideline prior to recommending adoption into practice.

- Led to a better understanding of the development of the clinical recommendations within the practice guideline.

- Allowed for scoring of the SSC SRB by 4 clinicians using a 7-point Likert scale.

Recommendations

In adult patients with severe sepsis, septic shock, or lactic acid ≥ 4 mmol/l with confirmed or suspected infection admitted to acute care facilities:

• Systematic review of current research supported use of the SRB alone to reduce mortality

• A decade of evidence showed a significant decrease in mortality rates with the use of the SRB

• Implementation of the SRB into clinical practice is recommended based on findings

References Bibliography

Boswell, C.A., & Cannon, S.B., (2014). Introduction to nursing research: Incorporating evidence-based practice. (3rd ed.). Sudbury, MA: Jones and Bartlett Publishers.

Casserly, B., Baram, M., Walsh, P., Sucov, A., Ward, N.S., & Levy, M.M. (2011). Implementing a collaborative protocol in a sepsis intervention program: Lessons learned. *Lung*, *189(1),* 11-19. doi:10.1007/s00408-010-9266-z

Chamberlain, D. J., Willis, E. M., Bersten, A. B. (2011). The severe sepsis bundles as processes of care: A meta-analysis. *Australian Critical Care,* 24: 229-243.

Coba, V., Whitmill, M., Mooney, R., Horst, H., Brandt, M., Digiovine, B., & ... Jordan, J. (2011). Resuscitation bundle compliance in severe sepsis and septic shock: Improves survival, is better late than never. *Journal of Intensive Care Medicine (Sage Publications Inc.)*, *26*(5), 304-313. doi:10.1177/0885066610392499

References Bibliography

Dellinger, R. P., Levy, M. M., Schorr, C. A., Townsend, S. R. (2008). Surviving Sepsis Campaign. Retrieved from: http://www.survivingsepsis.org/About_the_Campaign/Pages/Committees.aspx

Dellinger, R., Levy, M., Carlet, J., Bion, J., Parker, M., Jaeschke, R., & ... Vincent, J. (2008). Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. *Critical Care Medicine*, *36*(1), 296-327.

Institute for Healthcare Improvement (2012). *Implement the Sepsis Resuscitation Bundle*. Retrieved from http://www.ihi.org/knowledge/Pages/Changes/ImplementheSepsisResuscitationBundle.aspx

References Bibliography

Jones, A., Brown, M., Trzeciak, S., Shapiro, N., Garrett, J., Heffner, A., & Kline, J. (2008). The effect of a quantitative resuscitation strategy on mortality in patients with sepsis: A meta-analysis. *Critical Care Medicine*, *36*(10), 2734-2739.

Melnyk, B. & Fineout-Overhold, E. (2011). *Evidence-based practice in nursing & healthcare: A guide to best practice*. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins.

Nguyen, H. B., Corbett, S. W., Steele, R., Banta, J., Clark, R. T., Hayes, S. R., Edwards, J., Cho, T. W., Wittlake, W. A. (2007). Implementation of a bundle of quality indicators for the early management of severe sepsis and septic shock is associated with decreased mortality. *Critical Care Medicine, 35*(4), 1105-1112.

References Bibliography

Puskarich, M., Marchick, M., Kline, J., Steuerwald, M., & Jones, A. (2009). One year mortality of patients treated with an emergency department based early goal directed therapy protocol for severe sepsis and septic shock: A before and after study. *Critical Care*, *13*(5), R167. doi:10.1186/cc8138

Quantitative Pyramid. (n.d.). In *Alaska Medical Library*. Retrieved from http://consortiumlibrary.org/aml/researchaids/ebp/ebp_pyramid_quantitative.pdf

Rivers, E.P., Katranji, M., Jaehne, K.A., Brown, S., Abou Dagher, G., Cannon, C. & Coba, V. (2012). Early interventions in severe sepsis and septic shock: A review of the evidence one decade later. *Minerva Anestesiologica,78*(6), 712-24.

References Bibliography

Roswurm, M.A. & Larrabee, J.H. (1999). A model for change to evidence-based practice. *Journal for Nursing Scholarship,31*(4), 317-22)

Seymour, C. W., Cooke, C. R., Mikkelsen, M. E., Hylton, J., Rea, T. D., Goss, C. H., & … Band, R. A. (2010). Out-of-hospital fluid in severe sepsis: Effect on early resuscitation in the emergency department. *Prehospital Emergency Care, 14*(2), 145-152. doi:10.3109/10903120903524997

U. S. Preventive Services Task Force. (2008). What the grades mean and suggestions for practice. *U. S. Preventive Services Task Force Grade Definitions.* Retrieved from http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm

Questions?

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