Washington State Health Care Authority
Health Technology Assessment

Extracorporeal Membrane Oxygenation

Clinical Expert

Eileen Metzger Bulger, MD, FACS

Professor of Surgery, University of Washington

Chief of Trauma, Harborview Medical Center

Medical Director, Extracorporeal Life Support System Program,
Harborview Medical Center

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000.		X
2.	Equity interests such as stocks, stock options or other ownership interests.		X
3.	Status or position as an officer, board member, trustee, owner.		X
4.	Loan or intellectual property rights.		X
5.	Research funding.		X
6.	Any other relationship, including travel arrangements.		X

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		X

If yes to #7, provide name and funding Sources:

*If you believe that you do not have a conflict, but are concerned that it may appear that you do, you may **attach additional sheets** explaining why you believe that you should not be excluded.*

I certify that I have read and understand this Conflict of Interest form and that the information I have provided is true, complete, and correct as of this date.

X [redacted] 2/11/16

Signature *Date*

Eileen M. Bulger MD

Print Name

So we may contact you regarding this information, please provide the following:

Email Address: [redacted]

Phone Number: [redacted]

CURRICULUM VITAE

Eileen Metzger Bulger, M.D., F.A.C.S.

PERSONAL DATA:

Place of Birth:	Warwick, Rhode Island
Date of Birth:	February 17, 1966
Marital Status:	Married (Douglas)
Children:	Natalie Elizabeth (9/27/96) Kelsey Lynn (12/13/99)
Maiden Name:	Eileen Elizabeth Metzger
Citizenship:	U.S.A.
Home Address:	[redacted]
Home Phone:	
Work Address:	Box 359796, Dept of Surgery Harborview Medical Center 325 Ninth Ave. Seattle, WA 98104
Work Phone:	[redacted]
Fax:	
E-mail:	

EDUCATION:

The Johns Hopkins University Baltimore, Maryland	1984-1988	B.A.
Cornell University Medical College New York, New York	1988-1992	M.D.

POSTGRADUATE EDUCATION:

University of Washington Seattle, Washington	1992-1999	Residency General Surgery
University of Washington Seattle, Washington	1995-1997	NIH Trauma Research Fellowship
University of Washington Seattle, Washington	1999-2000	Surgical Critical Care Fellowship

ACADEMIC APPOINTMENTS:

Assistant Professor Department of Surgery University of Washington	2000
Associate Professor Department of Surgery University of Washington	2004

	Full Professor Department of Surgery University of Washington	2009

HOSPITAL APPOINTMENTS:

Attending Surgeon	University of Washington Hospitals Harborview Medical Center University Hospital Seattle Cancer Care Alliance	2000
Associate Medical Director	Harborview Medical Center	2009-2012
Chief of Trauma	Harborview Medical Center Trauma Medical Director for Adults and Pediatrics	2012-present
ECLS Program Medical Director	Harborview Medical Center	2015-present
Director of Emergency Services	Harborview Medical Center	2009-2012
Interim Director of Emergency Services	Harborview Medical Center	2008
Associate Director of Emergency Surgical Services	Harborview Medical Center	2000- 2008

BOARD CERTIFICATION:

National Board of Medical Examiners	1992
Advanced Trauma Life Support Instructor	2000
Diplomat, The American Board of Surgery	2000
Recertified	2008
Surgical Critical Care Certification,	
The American Board of Surgery	2001
Recertified	2009

LICENSURE TO PRACTICE:

Washington	1992

HONORS:

CURRENT

Outstanding Consultant Award, UW Medicine Emergency Medicine, 2013
Castle Connolly Top Doctor Recognition 2012, 2013
US News and World Report Top Doctors Recognition 2011
Seattle's Top Doctors Recognition, Seattle Magazine 2010, 2011
Mentor for Best Clinical Paper, State of Washington
Sam Mandell, MD, ACS Committee on Trauma, 2008
UW Medicine Service Excellence Award (HMC Cares), 2008
Mentor for Western Trauma Association Resident/Student
Best paper award Keir Warner, 2008
Mentor for Eastern Association for the Surgery of Trauma
Resident Research Scholarship, Sam Mandell, 2008-2009
Mentor for Seattle Surgical Best Clinical Paper
Keir Warner, 2007
Mentor for Region X Committee on Trauma Best Clinical Paper
Sharmilla Dissanake, 2006
University of Washington, Department of Surgery
Resident Teaching Award, 2005
Mentor for Henry Harkins Resident Paper Competition 1st Place
Daniel Anaya, MD, Washington State Chapter ACS, 2005
Mentor for Surgical Infection Society Best Resident Poster
Daniel Anaya, MD Surgical Infection Society, 2005
Peter C. Canizaro Award: American Association for the Surgery of Trauma, 2004
Mentor for Surgical Infection Society Best Resident Paper
Daniel Anaya, MD Surgical Infection Society 2004
Mentor for Young Investigator Award Winner,
David Gourlay, MD, Shock Society, 2002
American Association for the Surgery of Trauma
Wyeth-Ayert Research Scholarship Award, 2001
John H. Davis Research Scholarship Award, 2002

RESIDENCY/FELLOWSHIP

Henry Harkins Award- 2nd Place, Residents Paper Competition
ACS Washington State Chapter, 1994
Best Basic Science Paper- Regional resident paper competition,
ACS: Committee on Trauma, 1995
Seattle Surgical Society-Best Resident Paper 1996
Young Investigator Award Finalist-Shock Society 1996
Travel Award Grant- Shock Society 1996
Runner-up Best Basic Science Paper- Regional resident paper competition,
ACS: Committee on Trauma, 1996
Travel Award Grant- Shock Society, 1997
Travel Award Grant- Society for Leukocyte Biology, 1997

Pacific Northwest Vascular Society
Resident paper competition, 3rd place, 1998
Resident/Medical Student Teaching Award, 1999
Harborview Medical Center Resident of the Year, 1999
Best Basic Science Paper- Regional Resident paper competition, ACS-Committee on Trauma, 1999
First place for best paper presented at the Helen & John Schilling Research symposium, 2000

MEDICAL SCHOOL

Alpha Omega Alpha, Junior and Senior Year, 1991 &1992
NIH Summer research fellowship & Letter of Commendation, 1989
The John Metcalf Polk Prize, 1992
(Awarded to the 3 highest ranking graduates)
The Janet M. Glasgow Memorial Award, 1992
(Awarded to the highest ranking woman graduate)
The Clarence C. Coryell Prize in Surgery, 1992
Gate Pharmaceutical Award for Outstanding Achievement in General Surgery, 1992
The Ralph I. Poucher Prize for Proficiency in Obstetrics and Gynecology, 1992
The Elise Strang L'Esperance Prize in Public Health, 1992
Certificate of Commendation for Community Service
Veterans of Foreign Wars, 1989

UNDERGRADUATE

Phi Beta Kappa, 1988
Degree with Departmental and General Honors, 1988
Fight for Sight Student Fellowship, 1987

PROFESSIONAL SOCIETIES:

American College of Surgeons	
Associate member	1992-2002
Fellow	2002-present
ACS Washington State Chapter	
Councilor	2003 to 2006
Program Chair	2006
President	2010
The Henry N. Harkins Surgical Society	1998-present
Shock Society	2000-present
Scientific Program Committee	2003-2006
Clinical Science Councilor	2006-2009
Honors and Awards Committee	2010-2012
Chair	2012
Society of Critical Care Medicine	2000-2006
Reviewer: Critical Care Medicine	
Surgical Infection Society	2001-present
Membership committee	2002-2005

	Scientific Program Committee	2006-2009
	Association for Academic Surgery	2002-present
	Reviewer: Journal of Surgical Research	2003-present
	Editorial Board: J Surgical Research	2006-2010
	American Association for the Surgery of Trauma	2002-present
	Manager at Large	2012-2015
	Secretary-Treasurer Elect	2015
	Injury Assessment & Outcome Committee	2004-2008
	Program Committee	2008-2010
	Board of Managers	2012-present
	Seattle Surgical Society	2002-present
	Association for Surgical Education	2003-2006
	ACS Committee on Trauma	2003-present
	Disaster Preparedness Committee	2003-present
	Trauma System Committee	2006-present
	Emergency Medical Service Com	2003-present
	Chair	2011-2015
	Rural Trauma Committee	2003-present
	Resident Paper Competition Judge	2006-2009
	State Chair, Washington	2003-2006
	Region Chief, Region X	2006-2012
	Regional Committee on Trauma Board of Directors	2010-2012
	Chair, Membership Committee	2014-present
	Executive Committee	2014-present
	Society of University Surgeons	2004-present
	Surgical Biology Club III	2006-2015
	American Surgical Association	2013-present
UNIVERSITY ACTIVITIES	Surgical Education Committee University of Washington	2000-2005
	Assistant Program Director Univ. of Washington Surgical Residency	2002-2005
	Faculty Senator University of Washington	2002-2004
	Core Investigator Harborview Injury Prevention and Research Center	2003-present
	Dean's Committee on Women in Medicine University of Washington	2005-present

Grant Reviewer Medic One Foundation	2007-present
Member, Search Committee Division Chief, Emergency Medicine	2008
Member, Search Committee Dept of Hematology, Puget Sound Blood Ctr	2008
Grant Reviewer UW Royalty Research Fund	2008,2010
Team Stepps Master Trainer	2009-present
Member, Search Committee Division of Emergency Medicine	2009
Member, Search Committee Chair of Anesthesiology	2012
Member, Search Committee Orthopedic Trauma Division	2012
Department of Surgery Peer Support Leader	2014
Member, Search Committee Chair of Department of Surgery	2015

NATIONAL ACTIVITIES

Measurement of Quality & Outcomes Subcommittee Member Acute Care Research Agenda Centers for Disease Control	2004
Reviewer: Special Emphasis Panel NIH/NIGMS Trauma Program grants	2004
Reviewer: Special Emphasis Panel NIH/NIGMS Loan Repayment App	2005
Reviewer: Special Emphasis Panel NIH/NIGMS Multicenter clinical trial	2007

Reviewer: Surgery, Anesthesia, and Trauma
Study Section NIH 2008-2013

Reviewer: Special Emphasis Panel 2009 & 2010
NIH/NIGMS Trauma Program Project grant

Reviewer: Special Emphasis Panel 2012
NIH/NIGMS R34 Clinical trial planning grants

Reviewer: Special Emphasis Panel
NIGMS Clinical trial review 2012

Invited Reviewer

Journal Surgical Research (Associate Editor, 2006)	2004
Critical Care Medicine	2004
Intensive Care Medicine	2004
Journal of Trauma (Editorial Board, 2007)	2004
Injury Prevention	2004
Journal of the American Medical Association	2005
Surgical Infections (Editorial Board 2011)	2005
Archives of Surgery	2006
Journal of the American College of Surgeons	2006
Resuscitation	2006
Journal of Clinical Anesthesia	2006
Pediatrics	2007
Critical Care Forum	2008
Shock Journal (Editorial Board)	2008
Journal of Orthopedic Trauma	2009
Journal of Clinical Immunology	2011
Journal of Pediatric Surgery	2011
Critical Care Review	2011
Prehospital Emergency Care (Editorial Board)	2014
PLOS One	2014
British medical Journal	2015

Examination Consultant 2005- 2009
Clinical management Section
In-training/Surgical basic Science Examination
American Board of Surgery

Region Chief, Region X
ACS Committee on Trauma 2006-2012

Member, Data Safety Monitoring Board
RCT OF FISH OIL FOR ALI 2006

Participant CDC TIIDE grant
National Review of Mass Casualty
Triage Systems 2007

Editorial Boards
- J Trauma 2007
- Shock Journal 2008
- Surgical Infections 2011
- Prehospital Emergency Care 2014

Organizing Committee
US Critical Illness and Injury Trials Group
Funded: NIH U13 2007-2010

Associate Examiner: Oral Board Exam
American Board of Surgery 2008

CDC National Expert Panel on Field Triage 2011

CDC/NHTSA Expert Panel
National Guidelines for Helicopter EMS
use and availability 2012

Member
International Medical Surgical Response Team
(IMSURT- West), NDMS 2003-present
Acting Chief Medical Officer 2011-present

Strike Team Leader
Mobile Acute Care Teams
NDMS 2014-present

Member (AAST representative)
Trauma, Burns, Critical Care Component Board
American Board of Surgery 2012-2018

ACS COT representative

	NASEMSO Model Guidelines for EMS Committee	2013-2014
	ACS COT representative Stakeholder group for development of Evidence-based guidelines for EMS NHTSA/NAEMSP	2013-present
	Chair Committee for development of Prehospital Evidence-Based Guideline for Hemorrhage Control, ACS-COT	2013-2014
	Reviewer: Special Emphasis Panel NIGMS Clinical trial review: sepsis	2015
	Reviewer: Special Emphasis Panel NICHD Loan repayment program	2015
	Chair & Reviewer: Special Emphasis Panel NIGMS: Trauma Program Project grant	2015
	Trauma Center Verification Site reviewer ACS Committee on Trauma	2015-present
	Technical Expert Consultant AHRQ EPC program Field trauma triage guidelines: GCS score	2016
	National Trauma Research Repository Steering Committee, Vice Chair National trauma Institute	2015-present
	Reviewer: Special Emphasis Panel NICHD Loan Repayment Program	2016
INTERNATIONAL ACTIVITIES	Grant Reviewer: Burrough's Wellcome Fund United Kingdom	2004
	Data Safety Monitoring Board Member Prehosptial TXA study Australia	2013-present
STATE & REGIONAL ACTIVITIES	Advanced Trauma Life Support Course Director	2001-present

Instructor Course Director	2003-present
Vice Chair ACS Washington State Committee on Trauma	2002-2003
Chairman ACS Washington State Committee on Trauma	2003-2006
Trauma Center Designation Site Reviewer Department of Health State of Washington	2002-present
Member Prehospital Technical Advisory Committee Department of Health, Washington State	2003-present
Chair, Trauma Medical Directors Technical Advisory Committee Department of Health, Washington State	2003-2010
Chair Emergency Medical Services/Trauma Care Govenor's Steering Committee Washington State (member)	2010-2015 2003-present
Program Chair Washington State Chapter ACS meeting Sunriver, OR	2006
Rural Trauma Team Development Course Director American College of Surgeons	2007-present
Grant Reviewer Medic One Foundation	2007- present
President Washington State Chapter, American College of Surgeons	2010-2011
Disaster Management & Emergency Preparedness Course American College of Surgeons Course Director & Instructor	 2013-present

Chair
COST Technical Advisory Committee 2010-2016
Department of Health, Washington State

Clinical Expert, ECMO
WA Health Technology Assessment Program
WA State Health Care Authority 2015-2016

HOSPITAL ACTIVITIES

Medical Director
Emergency Services
Harborview Medical Center 2008-2012

Associate Director
Emergency Surgical Services
Harborview Medical Center 2000-2008

Clinical Nutrition Committee 2001-2008
Harborview Medical Center

Chair, Enteral Feeding
Guideline Subcommittee 2001-2002
Harborview Medical Center

Trauma Council 2000-present
Interim Chair 2003
Chair 2012

Emergency Department
Bond Planning Committee 2003-2007

Medical Executive Board
Elected member at large 2005-2008

Chair, Search Committee
for Chief of Oral Maxillofacial Surgery 2006-2007

President of the Medical Staff
Harborview Medical Center 2007-2008

Associate Medical Director 2008-2012
Harborview Medical Center

Credentialing Committee 2008-present

Harborview Medical Center

Co-Chair, Department of Surgery
Peer Support Program 2014-preset

Director
HMC ECLS Program 2015-present

Chair, Search Committee
for Chief of Oral Maxillofacial Surgery 2015

Member
OR TeamStepps Oversight Committee 2016

RESEARCH TRAINING:

Wilmer Eye Institute 1985-1987
Johns Hopkins Hospital
Fight for Sight Student Fellowship
Mentor: Judith Whittum-Hudson, PhD

National Institutes of Health 1989
Neuroimmunology Branch

University of Washington 1995-1997
NIH Trauma Research Fellowship
Mentor: Ronald V. Maier, MD

RESEARCH FUNDING:

"Pre-Hospital Management of the Difficult Airway" (PI: Bulger)
Medic One Foundation, Seattle, WA
10/1/99-10/1/02, $10,000

"The Advantages of Oxandrolone Use in the Chronic Surgical ICU Patient"
Pilot & Feasibility Award- Clinical Nutrition Research Unit, University of Washington, Seattle, WA (PI: Bulger)
12/1/00-12/1/02, $50,000 for 2 years

"The Cytokine Profile of Burn Patients Undergoing Plasmapheresis"
Washington State Council of Firefighters, Seattle, WA (PI: Bulger)
9/1/00-9/1/02, $25,978

" The Role of Platelet Activating Factor in ARDS" (PI: Bulger)
American Association for the Surgery of Trauma/
Wyeth-Ayerst Research Scholarship
Awarded 7/1/01-7/1/02, $35,000

"Immunomodulation of Macrophages Following Trauma" (PI:Maier)
NIH RO1 GM45873 4/1/99-3/31/03
Co-investigator 10% NIH, NIGMS $266,704

"Postdoctoral Training" (PI:Maier)
NIH, NIGMS T32 GM07037 7/1/00-6/30/05
Mentor $192,330 per annum

"Modulation of Alveolar Macrophage Activation in ARDS"(PI: Bulger)
John H. Davis Scholarship Award, American Association for the Surgery of Trauma, Awarded 7/1/02-7/1/03, $35,000

"The Impact of Prehospital Intervention on Outcome following Traumatic Brain Injury" (PI: Bulger)
Brain Trauma Foundation, Center of Excellence for Prehospital Research
11/1/02-11/1/08, $25,000 per annum

"National Variability in Pre-hospital Care for Trauma Patients: Impact on Outcome" (PI: Bulger)
Medic One Foundation, 11/7/02-11/6/03, $35,000

"The Effect of Hypertonic Resuscitation for Blunt Trauma" (PI: Bulger)
NIH, R01 HL073233 4/1/03-3/31/07 $1,054,661

" Videoendoscopic drainage of infected pancreatic collections" (PI Horvath)
NIDDKD Site coordinator, Harborview Medical Center

"Biofunctional Polymers for Intracellular Drug Delivery" (PI: Stayton)
NIH, R01 EB 002991-01 9/19/2003 - 07/31/2007
Co-investigator 10% $259,005

"The Impact of Hypertonic Resuscitation on the Inflammatory Response" (PI: Bulger)
Medic One Foundation, 11/1/03-8/31/05 $50,000

"HL-04-001 Clinical Research Consortium to Improve Resuscitation Outcomes" (PI: Kudenchek)
NIH, NHLBI, 9/1/04-6/30/16 Co-Principal Investigator 20%

HL-04-001 Data Coordinating Center, Resuscitation Consortium (PI: van Belle)
NIH, NHLBI, 9/1/04-6/30/16 Co-Principal Investigator 10%

"Crash Injury Research & Engineering Network (CIREN)"
NHTSA, 4/1/06-5/31/16 Principal Investigator 15%

" Hypertonic Modulation of Inflammation after Injury"
(PI: Bulger) 1R01GM76101-01A1 6/11/2007-5/31/2012
Principal Investigator 10% $395,929/annum

Prehospital Management of the Pediatric Airway
(co-PI Bulger/Warner)
Medic One Foundation 11/1/07-11/1/09 $20,000

Prospective Observational Multi-center Massive Transfusion Study
Department of Defense
(Site PI: Bulger 10%) 3/15-09-9/15/10 $443,307

Prospective Validation and Cost Analysis of the National Guidelines for Field Triage, Centers for Disease Control (PI: Newgard)
Co-investigator 9/1/10-8/31/12 $299,732

Muscle Oxygenation for Noninvasive Stratification of Shock Severity
Coulter Foundation UW Bioengineering Grant &
Life Science Discovery Fund (PI: Schenkman) $150,000
Co-investigator

Multicenter Phase 2a trial of a Novel drug for Patients with Necrotizing Soft Tissue Infections, AtoxBio Ltd (PI: Bulger) 2012-2013

Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR)
NIH/DOD
Site PI

Pacific Northwest Clinical Center for the NHLBI PETAL Network
UO1 , NHLBI $2,281,259
Co-PI

Prehospital Tranexamic Acid Use for Traumatic Brain injury
W81XWH-13-2-0090 MODP01 (May) 07/01/14-17
Co-investigator DOD $2,583,506 (overall)

Prehospital Resuscitation on Helicopter
HL-077863-11, NIH NHLBI (May)
Co-Investigator 01/01/15-12/31/15 $190,066/yr

The Value of Emergency Care For Injured Older Adults
NIH AHRQ (Newgard) (Bulger, Site PI) 01/01/15-12/31/18
(Subcontract from Oregon Health Sciences) $9,539 (Yr 1)

Multicenter Phase 3 trial of a novel drug for patients with Necrotizing Soft Tissue Infections, AtoxBio Ltd (PI: Bulger) 2015-present (site PI and national PI)

PUBLICATIONS:

Peer Reviewed

1**. Metzger EE*** and Whittum-Hudson JA. The dichotomy between Herpes Simplex Virus Type 1 induced ocular pathology and systemic immunity. Invest Ophthalmol Vis Sci. 28:1533, 1987.

2. Hoyt DB, **Bulger EM**, Knudson MM et al. Death in the Operating Room: An analysis of a multi-center experience. J Trauma 37: 426-432, 1994.

3. Jurkovich GJ, Hoyt DB, Moore FA, Ney AL, Morris JA, Scalea TM, Patcher HL, **Bulger E**, Simmons RK, Moore EE, McGill JW, Miles WS. Portal Triad Injuries. J Trauma 39: 426-434,1995.

4. **Bulger EM**, Garcia I, Maier RV. The differential effects of the membrane antioxidant, vitamin E on macrophage activation. Surgical Forum. 47:92-95, 1996.

5. **Bulger EM**, Smith DG, Maier RV, Jurkovich GJ. Fat embolism syndrome: A ten year review. Archives of Surgery 132:435-439, 1997.
.

6. **Bulger E**, Garcia I, Maier R. The role of Vitamin E as a modulator of macrophage activation. *in* 4th International Congress on the Immune Consequences of Trauma, Shock, and Sepsis: Mechanisms and Therapeutic Approaches. ed E. Faist, Monduzzi Editore, Bologna, Italy, 1997. p.349-353

5. **Bulger EM**, Helton WS, Clinton CM, Roque RP, Garcia I, Maier RV. Enteral vitamin E supplementation inhibits the cytokine response to endotoxin. Archives of Surgery 132:1337-1341, 1997.

6. **Bulger EM**, Garcia I, Maier RV. Dithiocarbamates enhance tumor necrosis factor-α production by rabbit alveolar macrophages, despite inhibition of NF-κB. Shock 9 (6): 397-405,1998.

7. **Bulger EM**, Arneson MA, Mock CM, Jurkovich GJ. Rib Fractures in the Elderly , J Trauma 48(6): 1040-1046, 2000.

8**. Bulger EM**, Nathens AB, Rivara FP, Grossman DC, Moore M, Jurkovich GJ. Variations in the Care of the Head Injured Patient, Surgical Forum 51:506-508, 2000.

9. Carter Y, Meissner M, **Bulger EM**, Demirer S, Brundage S, Jurkovich GJ, Borsa J, Mulligan M, Karmy-Jones R, Anatomical Considerations in the Surgical Management of Blunt Aortic Injury, J Vasc Surg 34: 628-33, 2001.

10. **Bulger EM**, Arbabi S, Garcia I, Maier RV: The macrophage response to endotoxin requires platelet activating factor. Shock, 17 (3): 173-179, 2002.

11. **Bulger EM**, Garcia I, Maier RV: Intracellular antioxidant activity is necessary to modulate the macrophage response to endotoxin. Shock 18 (1):58-63, 2002.

12. Guerrero A, Gibson K, Kralovich K, Pipinos I, Agnostopolous P, Carter Y, **Bulger E**, Meissner M, Karmey-Jones R. Limb loss following lower extremity trauma arterial trauma: What can be done proactively? Injury, 33:765-769, 2002.

13. **Bulger EM** & Foy H. Myodesis: A novel approach to the repair of complex traumatic hernias. J Trauma 52: 756-758, 2002.

14. **Bulger EM**, Nathens AB, Rivara FP, Moore M, MacKenzie EJ, Jurkovich GJ. Management of Severe Head Injury: Institutional Variations in Care and Effect on Outcome. Critical Care Medicine 30 (8): 1870-1876, 2002.

15. **Bulger EM,** McMahon K, Jurkovich GJ. The morbidity of penetrating colon injury. Injury, Int J Care Injured 34:41-46, 2003.

16. **Bulger EM**, Copass MK, Maier RV, Larsen J, Knowles J, Jurkovich GJ. An analysis of advanced prehospital airway management. J Emerg Med 23:183- , 2002.

17. Cuschieri J, Gourlay D, **Bulger EM**, Garcia I, Jelacic S, Maier RV. Platelet Activating Factor (PAF) priming of inflammatory cell activity requires cellular adherence. Surgery 132:157-66, 2002.

18. **Bulger EM**, Gourlay D, Cuschieri J, Jelacic S, Staudenmeyer K, Garcia I, Maier RV. Platelet Activating Factor Acetylhydrolase inhibits alveolar macrophage activation, *in vivo*. Shock 20:17-22, 2003.

19. **Bulger EM**, Garcia I, Maier RV. Induction of heme-oxygenase 1 inhibits the proinflammatory response of endothelial cells. Surgery 134:146-52, 2003.

20. Kao L, **Bulger EM**, Parks D, Byrd G, Jurkovich GJ. Predictors of morbidity following traumatic pancreatic injury. J Trauma 55(5): 898-905, 2003.

21.**Bulger EM**, Edwards T, Klotz P, Jurkovich GJ. Epidural analgesia improves outcome following multiple rib fractures. Surgery 136(2): 426-30, 2004.

22. Cuschieri J, Gourlay D, **Bulger E**, Garcia I, Jelacic S, and Maier R. Calcium/Calmodulin-dependent kinase II is required for platelet activating factor (PAF) priming of inflammatory cells. Shock 23 (2): 99-106, 2005.

23. **Bulger EM**, Jurkovich GJ, Farver CL, Klotz P, Maier RV. Oxandrolone dose not improve outcome for chronically ventilated surgical patients. Annals of Surgery 240(3):472-8, 2004.

24. Anaya D, McMahon K, Nathens AB, Sullivan S, Foy H, **Bulger EM**. Predictors of Mortality and Limb Loss in Necrotizing Soft Tissue Infections. Archives of Surgery 140:151-157, 2005.

25. **Bulger EM**, Copass MK, Sabath D, Maier RV, Jurkovich GJ. The use of Neuromuscular Blocking Agents to Facilitate Prehospital Intubation does not Impair Outcome following Traumatic Brain Injury, J. Trauma, 58 (4):718-724, 2005.

26. Pickens J, Copass MK, **Bulger EM**. Trauma Patients Receiving CPR: Predictors of Survival. J Trauma, 58(5):951-958, 2005.

27.Staudenmeyer K, Maier RV, Jelacic S, **Bulger EM**. Hypertonic saline modulates innate immunity in a model of systemic inflammation. Shock 23 (5): 459-463, 2005.

28. Cuschieri J, **Bulger EM**, Garcia I, Maier RV. Oxidative Induced Calcium Mobilization is Dependant on Annexin IV release from Lipid Rafts. Surgery, 138: 158-64, 2005.

29. Gourlay D, Hoffer R, Routt,M, **Bulger EM.** Pelvic angiography for recurrent pelvic arterial hemorrhage. J Trauma 59:1168-1173, 2005.

30. . Coates BM, Vavilala MS, Mack C, Muangmun S, Sharar S, **Bulger EM**, Lam AM. The Influence of Definition and Timing of Hypotension on Outcome Following Severe Pediatric Traumatic Brain Injury. Crit Care Med 33:2645-50, 2005.

31. Muangman N, Stern EJ, **Bulger EM**, Jurkovich GJ, Mann FA. Chest Radiographic Evolution in Fat Embolism Syndrome. J Med Assoc Thai 88: 1854-1860, 2005.

32. Kozar R, Moore FA, Cothren CC, Moore EE, Sena M, **Bulger EM**, Miller CC, Eastridge B, Acheson E, Brundage SI, Tataria M, McCarthy M, Holcomb JB, Risk factors for hepatic morbidity following non-operative management: a multicenter study. Arch Surg 141: 451-8, 2006.

33. Bulger EM, Nathens AB, Rivara FP, MacKensie E, Copass MK, Sabbath D, Jurkovich GJ. National variability in out-of-hospital treatment after traumatic injury. Ann Emerg Med 49:293-301, 2007.

34. Cuschieri J, **Bulger E**, Biligrin J, Garcia I, Maier RV. Acid Sphingomyelinase is required for lipid raft TLR4 complex formation. Sugical Infections 8, 91-106, 2007.

35**. Bulger EM**, Jurkovich GJ, Nathens AB, Copass MK, Hanson H, Cooper C, Liu PY, Warner K, Maier RV. Hypertonic resuscitation of hypovolemic shock after blunt trauma: a randomized controlled trial. Arch Surg 143:139-148, 2008

36. **Bulger EM**, Cuschieri J, Warner K, Maier RV Hypertonic Resuscitation modulates the inflammatory response in patients with traumatic hemorrhagic shock. Ann Surg 245 (4), 635-641, 2007.

37. . Warner KJ, Cuschieri JC, Copass MK, Jurkovich GJ**, Bulger EM**. The Impact of Prehospital Ventilation on Outcome Following Severe Traumatic Brain Injury J Trauma 62 (6) 1330-6, 2007.

38. Sullivan SR, Engrav L, Anaya DA, **Bulger EM**, Foy HM. Bilateral anterior abdominal bipedicle flap with permanent prosthesis for the massive abdominal skin grafted hernia. Am J Surg 193(5), 651-655, 2007.

39. Cuschieri J, **Bulger E**, Biligrin J, Garcia I, Maier RV. Vitamin E inhibits Endotoxin Mediated Transport of Phosphatases to Lipid Rafts. Shock 27: 19-24, 2007.

40. Kuan JK, Kaufman R, Wright JL, Mock C, Nathens AB, Wessells H, **Bulger EM**. Renal Injury Mechanisms in Motor Vehicle Collisions: analysis of the Crash Injury Research and Engineering (CIREN) dataset. J Urology 178 (3pt1), 935-40, 2007.

41. Schaeffer V, Cuschieri J, Garcia I, Knoll M, Billgren J, Jelacic S, **Bulger E**, Maier R. The priming effect of C5a on monocytes is predominantly mediated by the p38 MAPK pathway. Shock 27 (6): 623-30, 2007 .

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PRESENTATIONS:

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2. Death in the Operating Room: A trauma center review. Washington State Chapter, American College of Surgeons, Second Place Henry Harkins Paper Competition, 1994.

3. Ischemic Necrosis of the Lesser Curve: A complication of highly selective vagotomy. Washington State Chapter, American College of Surgeons, 1995

4**.** Dithiocarbamates enhance alveolar macrophage TNF production in response to endotoxin despite inhibition of NF-kB, Region X Resident Paper Competition- ACS Committee on Trauma, Winner Best Basic Science Paper, 1995.

5. Fat Embolism Syndrome: A Ten Year Review. Seattle Surgical Society - Winner Best Resident Paper, 1996

6. The effect of dithiocarbamates on macrophage activation. Society of University Surgeons, Residents' Section, 1996.

7. The effect of dithiocarbamates on macrophage activation Shock Society - Young Investigator Award Finalist, 1996.

8. Fat Embolism Syndrome: A Ten Year Review American Association for the Surgery of Trauma, 1996

9. The differential effects of the membrane antioxidant, vitamin E on macrophage activation. American College of Surgeons: Surgical Forum, 1996

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11. Enteral vitamin E supplementation inhibits the cytokine response to endotoxin Runner up Best Basic Science Paper Region X Resident Paper Competition- ACS Committee on Trauma, 1996

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19. The evaluation of thoracic aortic injury in the community hospital. Pacific Northwest Vascular Society, 1998. 3rd place, Resident paper competition

20.Rib fractures in the elderly trauma patient. Regional Resident Paper Competition- American College of Surgeons Committee on Trauma, 1998

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27. Variations in the Care of the Head Injured Patient. American College of Surgeons- Surgical Forum, Chicago, IL, 2000.

28. The morbidity of a Colostomy following Penetrating Colon Injury. Western Trauma Association, Big Sky, MT, 2001.

29. Rib fractures in the elderly trauma patient. WAMI 2001: Current Practices in Adult and Pediatric Trauma Conference, Tukwilla, WA, 2001.

30. Differential modulation of macrophage signaling pathways by phenolic antioxidants. Shock Society, Marco Island, FL, 2001.

31. Colon Injury: The Current Standard. The Annual Harkins Surgical Symposium: What's New in General Surgery 2001, Seattle, WA 2001.

32. The use of Anabolic Agents in Critical Illness. What's New in Nutrition Lecture Series, University of Washington, Seattle, WA 2002.

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37. Induction of heme-oxygenase 1 inhibits the proinflammatory response of endothelial cells, Society of University Surgeons, Houston, TX, 2003.

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39. National Controversies in Prehospital Trauma Care. Department of Surgery Grand Rounds, University of Washington, Seattle, WA 2003

40. Resuscitation Immunology. Surgical Infection Society Plenary Session, San Antonio, TX 2003.

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45. Oxandrolone does not Improve Outcome for Ventilator Dependent Surgical Patients. American Surgical Association, San Francisco, CA 2004.

46. The Use of Neuromuscular Blocking Agents to Facilitate Prehospital Intubation does not Impair Outcome following Traumatic Brain Injury, American Association for the Surgery of Trauma, Maui Hawaii 2004

47. Predictors of Survival for Trauma Patients Requiring CPR. American Association for the Surgery of Trauma, Maui Hawaii 2004.

48. Choosing the Optimal Resuscitation Fluid, American College of Surgeons, New Orleans, LA 2004

49. EMS Data: Prehospital Research & Quality Assurance, EMS for Children Symposium, Seattle, WA 2005.

50. The Evolution of Resuscitation Science. Department of Surgery Grand Rounds, University of Washington, Seattle, WA 2005

51. Management of Necrotizing Soft Tissue Infections, Surgical Infection Society, Miami, FL 2005.

51. The Use of Neuromuscular Blocking Agents to facilitate Prehospital Intubation: Impact on Outcome. WAMI 2005: Current Practices in Adult and Pediatric Trauma Conference, Seattle, WA 2005

52. Prehospital Airway and Ventilation Issues for Trauma Patients, Resuscitation Rounds, University of Washington, Seattle, WA, 2005.

53. Best Practices in Prolonged Mechanical Ventilation after Injury, American College of Surgeons, San Francisco, CA, 2005

54. Hypertonic Resuscitation following Traumatic Injury. Resuscitation Science Symposium, American Heart Association, Dallas, TX 2005.

55. The Development of Clinical trials of Hypertonic Resuscitation. Resuscitation Science Symposium, American Heart Association, Dallas, TX 2005.

56. Evaluation of Blunt Cervical Injury. Grand Rounds, Kadlec Medical Center, Pasco, WA 2005

57. Evaluation of Cervical Spine Injury and Mild Traumatic Brain Injury, Trauma Conference, Kadlec Medical Center, Pasco, WA, 2005.

58. Indications and contraindications for Epidural Analgesia in Multiply Injured Patients. American Society Regional Anesthesia and Pain Medicine, 2005 (poster)

59. Development of Clinical Trials of Hypertonic Resuscitation 1980-2005. Society of Critical Care Medicine, San Francisco, CA, 2006.

60. Hypertonic Resuscitation modulates the inflammatory response in patients with traumatic hemorrhagic shock . Surgical Infection Society, San Diego, CA 2006

61. Community Acquired MRSA: (Invited moderator) Surgical Infection Society, San Diego, CA 2006.

62, Hypertonic Saline Resuscitation in Trauma. WAMI 2006: Current Practices in Adult and Pediatric Trauma Conference, Seattle, WA 2006.

63. Management of Necrotizing Soft Tissue Infections. Northwestern University Trauma Conference, Chicago, IL, 2006.

64. Hypertonic Resuscitation of Hypovolemic Shock after Blunt Trauma: A Randomized Controlled Trial. Shock Society, Broomfield, CO 2006.

65. Management of Necrotizing Soft Tissue Infections. Auburn Regional Medical Center Grand Rounds, Auburn, WA 2006.

66. Geriatric Trauma: Challenges and Opportunities. Sacred Heart Medical Center Grand Rounds, Spokane, WA 2006.

67. Childhood Crash Injury Patterns Associated with Restraint Misuse. CIREN network conference. Milwaukee, WI 2006.

68. Targeted Prehospital Ventilation is Associated with Improved Outcome after Severe TBI. American Association for the Surgery of Trauma, New Orleans, LA 2006.

69. Hypertonic Resuscitation Modulates the Inflammatory Response in Patients with Traumatic Hemorrhagic Shock, Surgical Biology Club, American College of Surgeons, Chicago, IL 2006.

70. Prehospital Intubation Saves Lives (Debate vs. D Hoyt) American College of Surgeons, Chicago, IL 2006.

71. Prehospital End Tidal CO2 Monitoring of Ventilation: Not Ready for Prime Time (Debate vs. D Davis) Resuscitation Science Symposium, American Heart Association, Chicago, IL 2006.

72. The ABCs of Traumatic Brain Injury. Seattle Medic One Tuesday Series, Seattle, WA 2007

73. The ABCs of Thoracic Trauma. West Region EMS Conference, Ocean Shores, WA 2007

74. Important Aspects of Managing the Trauma Patient: Trauma Resuscitation, Society of Interventional Radiology, Seattle, WA 2007.

75. Differential Leukocyte Gene Expression after Hypertonic Resuscitation. Shock Society, Baltimore, MD 2007.

76. Prehospital Management of Traumatic Brain Injury. Kitsap County EMS Continuing Education Meeting, Silverdale, WA 2007.

77. Rural Trauma: Unique Injuries, Unique Solutions. Combined Idaho, Wyoming, Montana Chapter Meeting, American College of Surgeons, Coeur de Lane Idaho, 2007.

78. Prehospital Management following Injury. Combined Idaho, Wyoming, Montana Chapter Meeting, American College of Surgeons, Coeur de Lane Idaho, 2007.

79. Challenging Trauma Cases. Combined Idaho, Wyoming, Montana Chapter Meeting, American College of Surgeons, Coeur de Lane Idaho, 2007.

80. The Effect of Reclined Seats on Mortality in Motor Vehicle Collisions, American Association for the Surgery of Trauma, Las Vegas, 2007.

81. The Advantages of Drug-Assisted Prehospital Intubation. (Debate vs. D. Hoyt) American College of Surgeons, New Orleans, LA 2007.

82. Clinical Trials of Hypertonic Resuscitation: What's gone wrong?. Resuscitation Science Symposium, American Heart Association, Orlando, FL 2007.

83. Telemedicine in the Treatment of Traumatic Brain Injury. American College of Surgeons, Committee on Trauma, Washington DC, 2008.

84. Management of Thoracic Trauma. Medic One Tuesday Series, Seattle, WA 2008.

85. Management of Necrotizing Soft Tissue Infections. Naval Hospital Grand Rounds, Bremerton, WA 2008

86. End Tidal Capnography in Trauma. American Association for the Surgery of Trauma, Maui, Hawaii, 2008.

87. End Tidal Capnography in Trauma. Medic One Tuesday Series, Seattle, WA 2008

88. Exception from Informed Consent: Practical Implications of Research in the Emergency Setting, American Heart Association, New Orleans, 2008

89. Clinical Trials of Hypertonic Resuscitation: Where are we now? Society of Critical Care Medicine, Nashville, TN, 2009.

90. Clinical Trials of Hypertonic Resuscitation. Invited lecture, Visiting Professor, University of Michigan, Ann Arbor, MI 2009.

91. Issues in the Surgical Management of Abscesses and Deep Tissue Infections. 49th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA 2009.

92. Meet the Expert: Management of Necrotizing Skin and Soft Tissue Infections. 49th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA 2009.

93. Hypertonic Resuscitation following Severe Trauma and Cardiac Arrest. Resuscitation Science Symposium, American Heart Association, Orlando, FL 2009.

94: Prehospital Hypertonic Resuscitation following Traumatic Hypovolemic Shock: A Randomized, placebo-controlled trial. Resuscitation Science Symposium, American Heart Association, Orlando, FL 2009.

95. Hypertonic Resuscitation: Where are we now? Prehospital Fluid Resuscitation Conference, Department of Defense, Dallas, TX 2010.

96. The Disaster Response to the Earthquake in Haiti. Medic One Tuesday Series, Seattle, WA 2010.

97. The Disaster Response to the Earthquake in Haiti. Washington State Govenor's Steering Committee for EMS and Trauma, Olympia, WA 2010.

98. Geriatric Trauma: Challenges and Opportunities. Oregon Trauma Conference, Sunriver , OR 2010.

99. Early Management of Traumatic Brain Injury. Oregon Trauma Conference, Sunriver , OR 2010.

100. Geriatric Trauma: Challenges and Opportunities. WWAMI 2010: Current Practices in Adult and Pediatric Trauma Conference, Seattle, WA 2010.

101. Why doesn't Hyperosmolar therapy improve outcome after TBI? National Trauma Institute Conference, San Antonio, TX 2010.

102. Management of Necrotizing Soft Tissue Infections. American Association for the Surgery of Trauma, Maintenance of Certification Session, Boston, MA 2010

103. Lessons learned from the Disaster Response to the Haiti Earthquake. American Association for the Surgery of Trauma, Panel Moderator, Boston, MA 2010

104. The Results of the ROC Trials of Prehospital Resuscitation with Hypertonic Fluids. Combat Casualty Resuscitation: Diagnosis and Intervention Conference, Toronto, Canada, 2010.

105. Fluid resuscitation after severe injury. Resuscitation Rounds, University of Washington, Seattle, WA 2011.

106. Massive Transfusion: What's the Right Ratio? Seattle Surgical Society, Seattle, WA 2011.

107. Increased Neutrophil Adenosine A3 Receptor Expression is Associated with Hemorrhagic Shock and Injury Severity in Trauma Patients, Shock Society, Norfolk VA 2011.

108. Geriatric Trauma: Challenges and Opportunities, Hawaiian Islands Trauma Symposium, Honolulu, HI 2011.

109. Ventilation Management & End Tidal Capnography, Hawaiian Islands Trauma Symposium, Honolulu, HI 2011.

110. The Disaster Response to the 2010 Haiti Earthquake. Hawaiian Islands Trauma Symposium, Honolulu, HI 2011.

111. Update on Thoracic Trauma Management, Hawaiian Islands Trauma Symposium, Honolulu, HI 2011.

112. Rural Trauma: Unique Injuries, Unique Solutions, Hawaiian Islands Trauma Symposium, Honolulu, HI 2011.

113. Predictive Modeling of Injury Severity utilizing Pre-hospital Trauma Triage and Mechanism of Injury Criteria for Advanced Automatic Crash Notification (AACN) Systems. Annual CIREN Conference, NHTSA, Washington DC 2011.

114. Impact of Prehospital Mode of Transport after Severe Injury: A multicenter evaluation from the Resuscitation Outcomes Consortium. American Association for the Surgery of Trauma, Chicago, IL 2011.

115. Meet the Expert Luncheon: Necrotizing Soft Tissue Infections. American College of Surgeons Clinical Congress, San Francisco, CA 2011.

116. Necrotizing Soft Tissue Infections: You Have to Operate! American College of Surgeons Clinical Congress, San Francisco, CA 2011.

117. Fluid Resuscitation after Severe Injury: What's New? Detroit Trauma Symposium, Detroit, MI 2011.

118. Management of Necrotizing Soft Tissue Infections, Detroit Trauma Symposium, Detroit, MI 2011.

119. The Hospital Response to a Terrorist Bombing Event in King County, WA, Tale of Our Cities Conference, Seattle, WA 2011.

120. Trauma Systems and Disaster Planning. Washington State Society of Anesthesiologists, Seattle, WA 2011.

121. Cardiac and Major Thoracic Injuries: From Field to ED Thoracotomy. Medic One Tuesday Series, Seattle WA, 2011.

122. Management of Necrotizing Soft Tissue Infections. Tacoma Joint Trauma Program Grand Rounds, Tacoma, WA 2012.

123. The Local Response to a 9.0 Earthquake and Tsunami, Disaster Planning Symposium, American Burn Association, Seattle, WA 2012.

124.Optimizing Resuscitation after Hemorrhagic Shock. Resuscitation and Critical Interventions Conference, Anchorage, AK 2012.

125. Optimizing Initial Management of Severe Traumatic Brain Injury. Resuscitation and Critical Interventions Conference, Anchorage, AK 2012.

126. Trauma System Adoption of Advanced Automatic Collision Notification (AACN), CIREN Research Conference, NHTSA, Washington DC, 2012.

127. Surviving ED Thoracotomy: It Takes a Team. UW Medicine EMS and Trauma Conference, Seattle, WA, 2012.

128. Resuscitation of Traumatic Hemorrhagic Shock. Bellevue Medic One CME conference, Bellevue, WA, 2012.

129. Optimizing Resuscitation after Severe Injury: What is the Evidence? Air Medical Transport Conference, Seattle, WA 2012.

130. Management of Necrotizing Soft Tissue Infections. Meet the Expert Luncheon, American College of Surgeons, Chicago, IL 2012.

131. Geriatric Trauma: Challenges and Opportunities. Highline Medical Center Grand Rounds, Burien, WA 2012

132. Mechanism of Injury in Motor Vehicle Crashes: What you need to know! Seattle Surgical Society Annual Meeting, Seattle, WA 2013.

133. Geriatric Trauma: Challenges and Opportunities. St Mary's Medical Center Trauma Conference, Walla Walla, WA 2013.

134. Geriatric Trauma: Challenges and Opportunities. Medic One Trauma Symposium, Seattle WA, 2013.

135. Damage Control Resuscitation. Southeast Regional Alaskan EMS Conference, Sitka AK 2013

136. Resuscitation of Shock in the Trauma Patient. Southeast Regional Alaskan EMS Conference, Sitka AK 2013

137. Geriatric Trauma: Challenges and Opportunities. Southeast Regional Alaskan EMS Conference, Sitka AK 2013

138. Geriatric Trauma: Challenges and Opportunities. Western Montana Trauma Conference, Misoula, MT 2013

139. Massive Transfusion: What's the right ratio? Western Montana Trauma Conference, Misoula, MT 2013

140. Rural Trauma: Unique Injuries/Unique Solutions Western Montana Regional Quality Improvement Conference. Misoula, MT 2013

141. Massive Transfusion: What's the Right Ratio? Washington State Trauma Nurse Network meeting, Seattle WA 2013.

142. Management of Necrotizing Soft Tissue Infections, A QI Review. Kadlec Medical Center, Richland, WA 2013.

143. What do Trauma Surgeons want from Radiology, Emergency Radiology Symposium, Seattle, WA 2013.

144. Lessons Learned from the Crash Injury Research and Engineering Network. Department of Surgery Grand Rounds, University of Washington, Seattle, WA 2013.

145. Management of Earthquake Injuries. UW Medicine EMS and Trauma Conference, Seattle, WA 2013.

146. Geriatric Trauma: Challenges and Opportunities. Mason County Regional Medic meeting, Shelton, WA 2013.

147. The New Field Trauma triage Guidelines. Mason County Regional Medic meeting, Shelton, WA 2013.

148. Geriatric Trauma: Challenges and Opportunities. Northwest Region EMS meeting, Bremerton, WA 2013.

149. Evaluating the Benefits of Advanced Automatic Crash Notification. CIREN National research Conference, Washington DC, 2013.

150. Pediatric Penetrating Trauma. Medic One Tuesday Series (Paramedic CME). Seattle, WA 2014.

151. Development of an Evidence-based Guideline for External Hemorrhage Control. NAEMSP National Evidenced-based Guideline Development Stakeholder meeting, Tuscon, AZ 2014.

152. Development of an Evidence-based Guideline for External Hemorrhage Control. DHS Federal stakeholder meeting to improve outcome from mass shootings and IED explosions, Washington DC, 2014.

153. Massive transfusion: What's the Right Ratio, Yakima Memorial Valley Hospital and Yakima Regional Medical Center, Yakima WA, 2014

154. Trauma Systems and Regionalized Care, Russo CME Conference, Yakima WA 2014.

155. Infections at Sea: The Cruise from Hell, Medical Disaster Response Symposium, Las Vegas, NV 2014

156. Early Control of Shock: Limited EMS/ER Crystalloids: Trauma, Critical Care, and Acute Care Surgery Conference, Las Vegas, NV 2014.

157. Trauma and Acute Care Surgery Case Management panel, Trauma, Critical Care, and Acute Care Surgery Conference, Las Vegas, NV 2014.

158. Geriatric trauma: Challenges and Opportunities: Rimrock Trauma Conference, Billings, MT 2014.

159. Shock Resuscitation and Massive Transfusion: Rimrock Trauma Conference, Billings, MT 2014

160. Management of Earthquake related Injuries. NDMS Disaster team training, Anniston, AL 2014.

161. Massive Transfusion: What's the Right Ratio? Skagit Valley Hospital CME program, Monroe, WA 2014

162. Management of Necrotizing Soft Tissue Infections. Meet the Expert Luncheon, American College of Surgeons, San Francisco, CA 2014.

163. Hypertonic Resuscitation: Lessons Learned. Pacific Northwest PETAL conference, Seattle, WA, 2014.

164. Mass Casualty Management and Disaster Preparedness. Mini-Med School Lecture, University of Washington, Seattle, WA 2015

165. Management of Exsanguinating Hemorrhage, Medic One Tuesday Series, Seattle, WA 2015

166. Massive transfusion: What's the Right Ratio? Providence Centralia & Providence St. Peter's Hospital Grand Rounds, Centralia, WA 2015.

167. The Impact and Progression of Organ Dysfunction in Patients with Necrotizing Soft Tissue Infections. Surgical Infection Society, Los Angeles, CA, 2015.

168. Massive Transfusion: What's the Right Ratio? Highline Medical Center Trauma Grand Rounds. Burien, WA 2015.

169. Massive Transfusion and the Role of Tranexamic Acid following Injury, South Central Region Trauma Quality Improvement meeting, Richland, WA 2015.

170. Necrotizing Soft Tissue Infections: What's New? Oregon-Washington State Chapters of the American College of Surgeons meeting, Suncadia, WA 2015.

171. Resuscitation of the Multisystem trauma patient with severe TBI. AO Neuro TBI CME course, Bellevue, WA , 2015.

172. Management of Exsanguinating Hemorrhage, Mason County Paramedic CME, Shelton, WA, 2015.

173. Massive Transfusion and the Role of Tranexamic acid for Trauma Patients, Fairbanks Medical Center Grand Rounds, Fairbanks, AK 2015.

174. Geriatric Trauma Challenges and Opportunities, Rocky Mountain Rural Trauma Symposium, Billings MT 2015

175. Motor Vehicle Crashes: Mechanism of injury, What you need to know. Rocky Mountain Rural Trauma Symposium, Billings, MT 2015

176. Management of Exsanguinating Hemorrhage, UW Medicine EMS and Trauma Conference, SeaTac, WA 2015.

177. Integration of Automatic Crash Notification into Trauma Systems. UW Medicine EMS and Trauma Conference, SeaTac, WA 2015.

178. Necrotizing Soft Tissue infections: Delay in Diagnosis. NSTI Time Matters Panel session, Speaker and Co-Moderator, American College of Surgeons Clinical Congress, Chicago, IL 2015

179. Necrotizing Soft Tissue infections: Emerging bacterial resistance, American College of Surgeons Clinical Congress, Chicago, IL 2015

180. Meet the Expert Luncheon: Necrotizing Soft Tissue Infections. American College of Surgeons Clinical Congress, Chicago, IL 2015

181. Challenging Trauma Case Panel. American College of Surgeons Clinical Congress, Chicago, IL 2015

182. Massive Transfusion Protocols and the Role of Tranexamic Acid. Olympic Memorial Trauma Symposium, Port Angeles, WA 2015

183. Massive Transfusion Protocols and the Role of Tranexamic Acid, Whidbey General Hospital. Coupeville, WA 2015.

184. The role of Hypothermia in Trauma, American Heart Association, Resuscitation Science Symposium, Orlando FL, 2015

185. Trauma: A Year in Review, American Heart Association, Resuscitation Science Symposium, Orlando FL, 2015

186. Pain Management following Chest Wall Injury. ACS Trauma Quality Improvement Project meeting, Nashville, TN 2015

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Agency Medical Director Comments

Extracorporeal Membrane Oxygenation (ECMO)

G. Steven Hammond, PhD, MD, MHA
Chief Medical Officer
WA - Department of Corrections

March 18, 2016

Background

- Extracorporeal membrane oxygenation (ECMO) is a life support technology that provides respiratory and/or circulatory assistance through devices outside the body
- ECMO may be used for extracorporeal gas exchange with or without circulatory support
  - Sometimes it is used primarily to oxygenate blood
  - Sometimes it is used primarily to clear carbon dioxide from the blood
  - Heat exchange/warming may also provide significant clinical benefit
- ECMO takes blood from the venous system and returns it to the venous system when only gas exchange is done, but returns blood to the arterial system when circulatory support is required

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ECMO

Background, cont'd

- ECMO is a highly invasive procedure that can sustain life to allow recovery from acute illness or intervention (such as lung or heart/lung transplant) to address respiratory and/or circulatory failure
  - It is typically used only when mortality risk is deemed to be extremely high (≥ 50%)
  - It is used when there is judged to be reasonable chance of recovery or intervention to restore adequate cardiorespiratory function without ECMO

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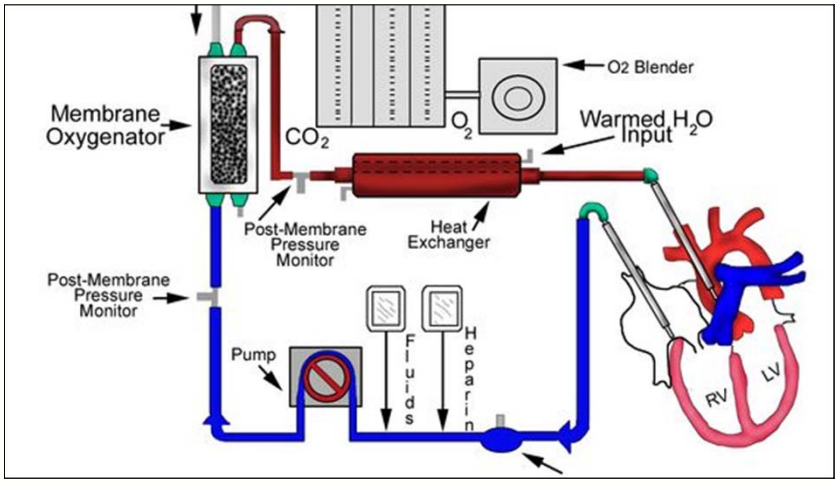
ECMO



ECMO Circuit – Complex Technology

Medscape, **Extracorporeal Membrane Oxygenation**
Author: Edwin Rodriguez-Cruz, MD; Chief Editor: Stuart Berger. Accessed 2/23/16

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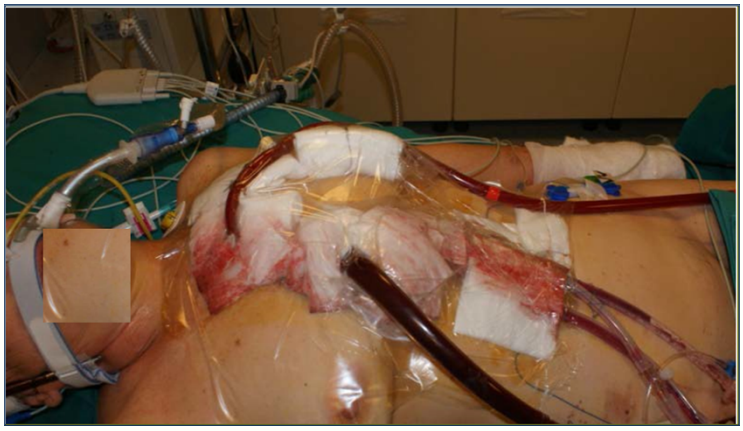
ECMO



Extremely Intensive and Invasive Treatment

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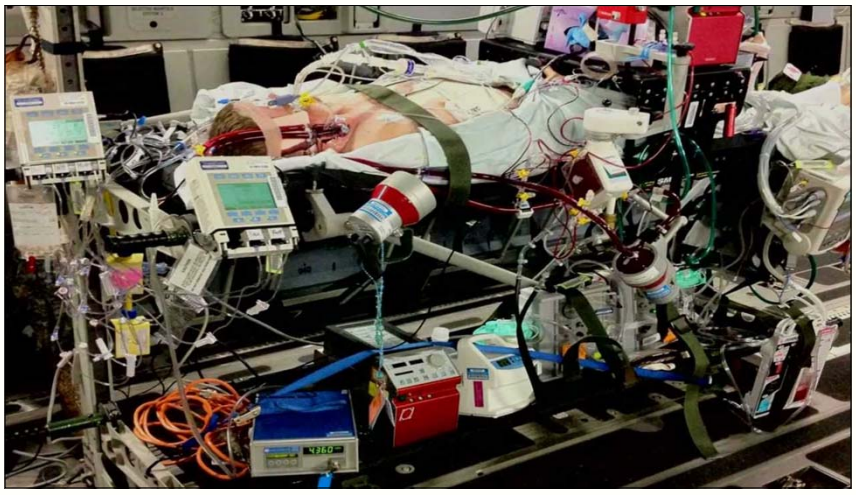
ECMO



ECMO Can Be Lifesaving

Joint medevac team transports critically-ill Marine from Japan to Hawaii *13th Air Force Public Affairs / Published March 29, 2012*

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ECMO

Agency Medical Director Concerns

- **Safety = High**
- **Efficacy = High**
- **Cost = High**

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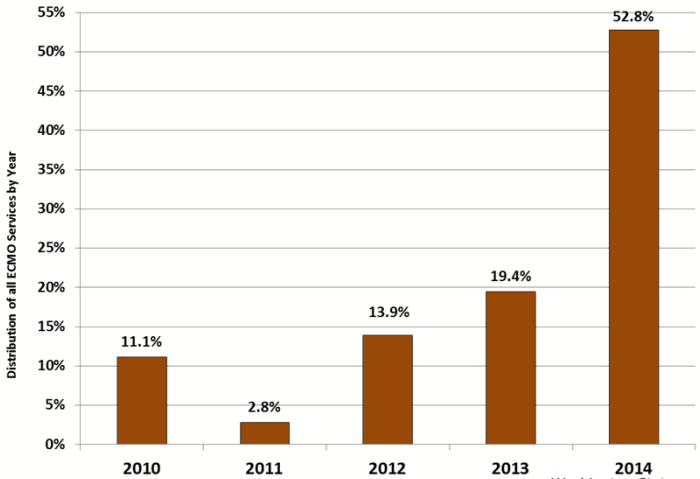
ECMO

CHART 1

PEBB/UMP, MEDICARE PEBB, L & I, MEDICAID FEE-FOR-SERVICE, AND MEDICAID MANAGED CARE
2010 – 2014: ECMO
5-YEAR DISTRIBUTION OF ALL UNIQUE PATIENTS >17 YEARS OLD RECEIVING ECMO



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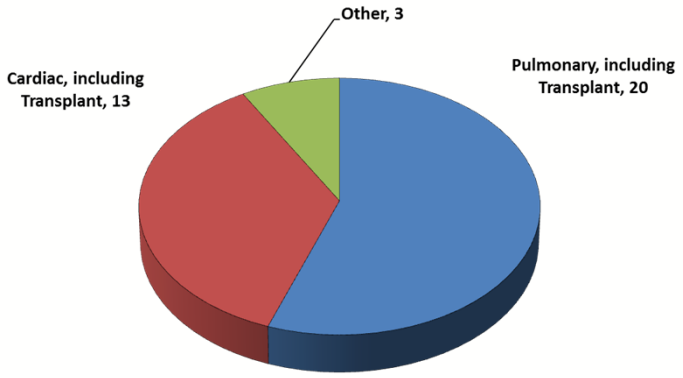
ECMO

CHART 2
PEBB/UMP, MEDICARE PEBB, L & I, MEDICAID FEE-FOR-SERVICE, AND MEDICAID MANAGED CARE
2010 – 2014 EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)
DISTRIBUTION OF SUMMARY DIAGNOSES FOR ECMO PATIENTS GREATER THAN 17 YEARS OLD



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ECMO

CHART 2
PEBB/UMP, MEDICARE PEBB, L & I, MEDICAID FEE-FOR-SERVICE, AND MEDICAID MANAGED CARE
2010- 2014 UTILIZATION: SITE OF SERVICE
DISTRIBUTION OF ECMO PROVIDERS FOR PATIENTS ≥17 YEARS OLD

University of Washington and Legacy Emmanuel* (OR)	**58%**
Other State facilities	**36%**
Out-of-State	**6%**

* *Legacy Emmanuel receives all ECMO referral for the Legacy Health Care System; including SW Washington facilities*

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ECMO

ECMO

Utilization by Day

- Median Usage: 2 days
- Average Usage: 3.5 days
- Range: 1 – 27 days

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ECMO

Current State Agency Policy

- **Medicaid** – Covered without conditions
- **PEBB** – Covered with conditions for adults
- **Labor & Industries** – Covered; prior authorization required
- **Corrections** – Covered without conditions

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ECMO

Extracorporeal Life Support Organization (ELSO) Guidelines & Training Standards

- Indications for ECLS (ECMO) include acute severe heart or lung failure with high mortality risk despite optimal conventional therapy
- ECMO is considered for use in patients at ≥50% mortality risk and indicated in most circumstances at ≥80% mortality risk
- Specific indications, e.g.:
  - Primary or secondary hypoxic respiratory failure
  - CO2 retention on mechanical ventilation despite high Pplat (>30 cm H2O)

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ECMO

ELSO Guidelines & Training Standards, cont'd

- Specific relative contraindications, e.g.:
  - Conditions incompatible with normal life if patient recovers
  - Chronic organ dysfunction (emphysema, cirrhosis, renal failure)
- Facility and training standards
  - Includes active involvement in ELSO and participation in ELSO registry
  - Specifies training standards for staff performing ECMO

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ECMO

Agency Medical Director Concerns

- **Effectiveness evidence base is weak, but, in summary:**
  - Insufficient for cardiac support compared to ventricular assist device (VAD)
  - Low quality evidence favors ECMO for (appropriately selected) respiratory failure compared to optimized conventional mechanical ventilation
  - Insufficient to support "bridge to transplant" compared to cardiopulmonary bypass
  - Low quality evidence suggests extracorporeal CPR (eCPR) using ECMO is non-inferior to conventional CPR

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ECMO

Agency Medical Director Concerns, cont'd

- Significant risk of harms (e.g., bleeding, limb ischemia, unspecified complications) must be weighed against setting of extremely high mortality risk in which ECMO is used
- High cost (estimated $100-500K in evidence report) must be weighed against prospect of full or near-full recovery in patients with potential for substantial life expectancy with good function

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ECMO

Agency Recommendations

- **Cover with conditions**
  - In appropriately selected cases of respiratory failure with or without potentially reversible circulatory failure/shock OR
  - In perioperative period for lung and heart transplants OR
  - As bridge to VAD OR
  - For eCPR for in-hospital cardiac arrest OR
  - For eCPR in accidental deep hypothermia AND
  - Only at a facility participating in the ELSO case registry
- **Not covered**
  - For cardiac support in lieu of VAD
  - For eCPR for cardiac arrest outside the hospital setting, other than accidental deep hypothermia

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ECMO

Agency Recommendations, cont'd

- Monitor results of IRB-approved clinical trials for any warranted re-review

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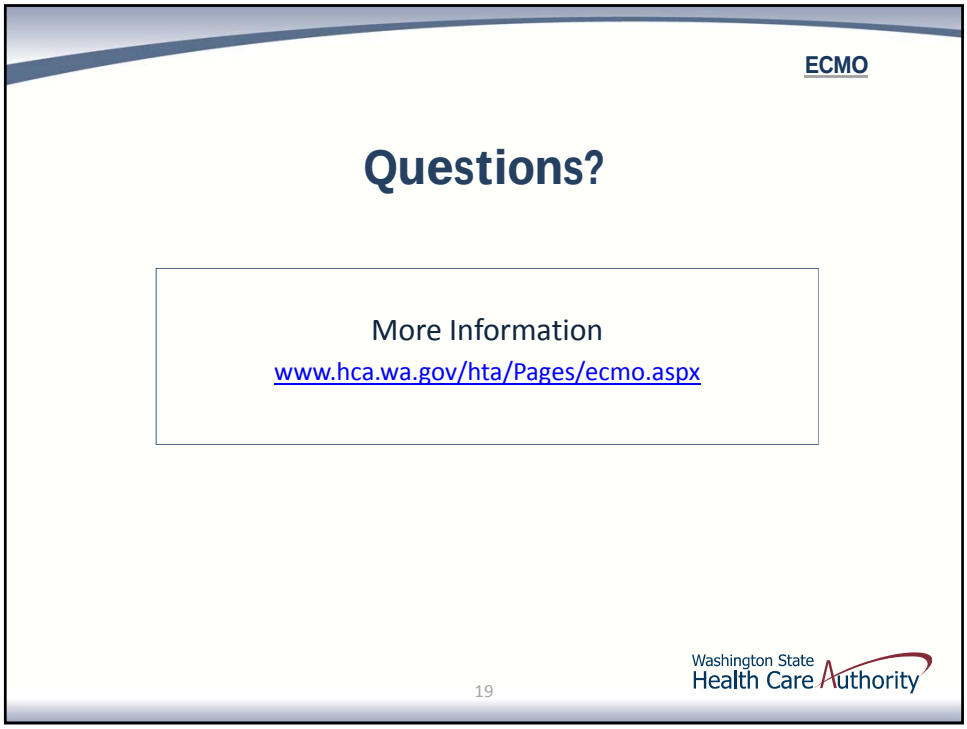
ECMO
Questions?
More Information
www.hca.wa.gov/hta/Pages/ecmo.aspx
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Washington State Health Care Authority
Health Technology Assessment

Order of Scheduled Presentations:

Extracorporeal Membrane Oxygenation

	Name
1	
2	
3	
4	
5	
6	

No requests to provide public comment were received.

Extracorporeal Membrane Oxygenation (ECMO)

An Assessment of
Comparative Clinical Effectiveness
& Comparative Value

Presented to the Washington State Health Care Authority by
Elizabeth Russo, MD
March 18, 2016

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Agenda

- Background
- Key Questions
- Project Scope: PICOTS, Results of Literature Review
- Evidence Ratings

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Background

- Extracorporeal membrane oxygenation (ECMO) is a form of life support that provides cardiopulmonary assistance outside the body
- ECMO may be used to support lung function for severe respiratory failure or heart function for severe cardiac failure
- Well-established treatment for infants with lung and heart failure but early studies of ECMO in adults showed poor survival rates

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Background

- **1979**: Zapol's *JAMA* study of adults in respiratory failure treated with ECMO vs. mechanical ventilation found similar (10%) survival in both groups
- **Since 2000**: technological advancements improved safety and broadened the application
  - Heparin-coated cannulae, new oxygenators, more efficient pumps
  - Less specialty staffing required
  - 2009 H1N1 pandemic increased demand

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ECMO Circuitry and Terminology

- **Veno-venous (VV) ECMO:** pulmonary support
- **Veno-arterial (VA) ECMO:** cardiac and pulmonary support
- **Extracorporeal carbon dioxide removal ($ECCO_2$-R, pECLA, iLA):** ventilatory support

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ECMO Circuitry

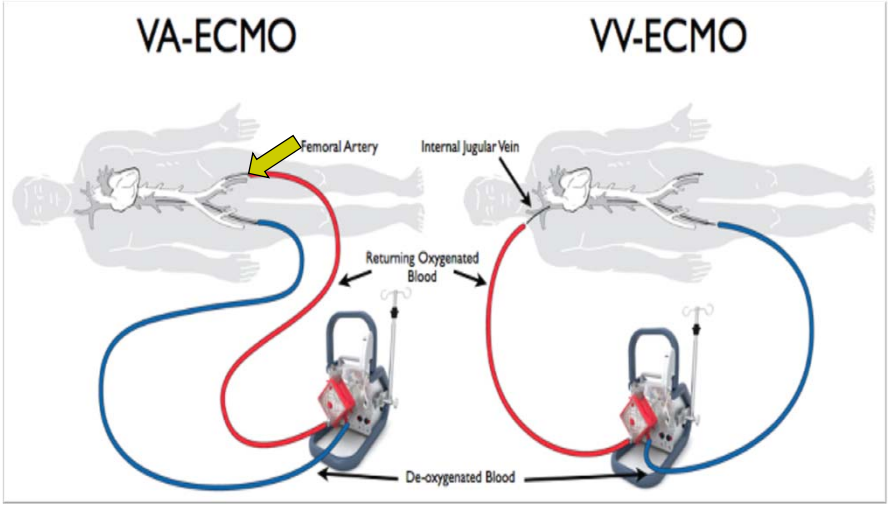

Image: http://ccforum.biomedcentral.com/articles/10.1186/cc9229

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Key Questions

1. What is the comparative clinical effectiveness of ECMO versus conventional treatment strategies in adults?

2. What are the rates of adverse events and other potential harms associated with ECMO compared to conventional treatment strategies?

3. What is the differential effectiveness and safety of ECMO according to sociodemographic factors, severity of the condition for which ECMO is used, setting in which ECMO is implemented, time of ECMO initiation (early vs. late), and duration of time on ECMO?

4. What are the costs and potential cost-effectiveness of ECMO relative to conventional treatment strategies?

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Project Scope: PICOTS

Population:

- Adults (age ≥18 years) with severe respiratory and/or cardiac failure

Intervention:

- Veno-venous ECMO
- Veno-arterial ECMO
- $ECCO_2$-R

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Project Scope

Comparators

- Conventional intensive care management with endotracheal intubation and ventilation
- Ventricular assist devices (VADs)
- Traditional cardiopulmonary bypass

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Project Scope

Outcomes:

- All-cause mortality
- Length of hospital stay
- Survival to discharge
- Disability
- Device-related complications and other adverse outcomes
- Health-related quality of life, longer-term health status, and other measures of well-being
- Costs and cost-effectiveness

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Project Scope

Timing:

- January 2000-January 2016

Study Designs:

- Randomized controlled trials (RCTs)
- Observational studies (comparative cohort, case-control)
- Case series ≥ 150 patients
- Study quality evaluated using USPSTF criteria: evidence review focused on good quality studies only

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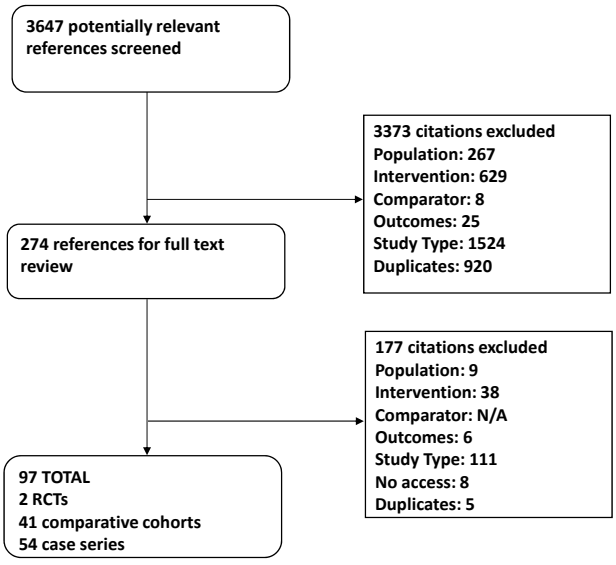
Results of Literature Search



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Quality of Evidence

- Growing evidence base – largely comparative study designs with diverse patient populations, settings, technologies, disease entities, etc.
- Generalizability limited due to variability within and across studies
  - Standards of care
  - Device technologies
  - Clinical decision-making
  - Patient characteristics
  - Retrospective study design
- 2 RCTs, both good quality
- 16 (39%) of 41 comparative studies good quality

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KQ1: What is the comparative clinical effectiveness of ECMO versus conventional treatment strategies in adults (age≥18 years)?

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Study Information	Comparators	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Direction of Effect of ECMO	Comments
Key Question #1: Effectiveness								
ECMO Cardiac support N=79 RCT=0 Cohort studies=1	VAD	Medium	Consistency unknown (single study)	Direct	Imprecise	++ **Low**	Comparable: No differences in in-hospital survival or successful bridging to active therapy	Single retrospective study
ECMO Pulmonary support N=793 RCT=2 Cohort studies=6	Mechanical ventilation	Medium	Inconsistent	Direct	Precise	+++ **Moderate**	Comparable: No consistent differences in survival, length of stay, or disability	Variation in disease entities, disease severity, and in standards of care
ECMO Bridge to transplant N=742 RCT=0 Cohort studies=3	Cardiopulmonary bypass	Medium	Inconsistent	Direct	Imprecise	++ **Low**	Comparable: No survival benefit; shorter length of stay (1 study)	Two studies examined heart transplant; one studied heart-lung transplant
ECMO ECPR N=1,543 RCT=0 Cohort studies=5	Conventional cardiopulmonary resuscitation	Medium	Inconsistent	Direct	Imprecise	++ **Low**	Comparable: Short-term survival benefit is lost in longer-term. One study showed neurologic benefit	Only one study reported positive survival benefit in longer term.

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ECMO for Cardiac Support

- 1 study of ECMO vs. mini-VAD using retrospective chart review of adults hospitalized with cardiogenic shock (Chamogeorgakis)
- ECMO showed no benefit for the following:
  - Weaning from mechanical support
  - In-hospital survival
  - Bridging to long-term support/transplant

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ECMO for Pulmonary Support

- 2 RCTs and 6 observational studies comparing mechanical ventilation with VV-ECMO/VA-ECMO or $ECCO_2$-R (Bein, Peek, Del Sorbo, Kluge, Noah, Pham, Tsai, Guirand)
- Bein: RCT of 79 adults w/ ARDS received av$ECCO_2$-R or conventional low tidal volume ventilation
  - No statistical differences in mortality, organ failure, days without ventilation, length of hospital or ICU stay between groups

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ECMO for Pulmonary Support (cont.)

- Peek: CESAR trial of 180 adults w/ respiratory failure received VV-ECMO or conventional low tidal volume ventilation
- No mandated management protocol; ECMO patients transferred to one hospital w/ institutional protocols
- Less mortality and severe disability with ECMO (37% vs. 53%; p=0.03) but no independent mortality benefit
- Longer median hospital stay with ECMO (35 vs. 17 days)

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ECMO for Pulmonary Support (cont.)

- 4/6 observational studies found lower in-hospital mortality (8-49% in ECMO vs. 35-76% in comparator arms) (Del Sorbo, Noah, Tsai, Guirand)
- 4 studies reporting on length of hospitalization found comparable or longer stay with ECMO (Del Sorbo, Kluge, Pham, Guirand)
- Inconclusive impact on the following:
  - Morbidity
  - Disability
  - Quality of life (trend toward improvement in CESAR trial but failed to reach statistical significance)

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ECMO as Bridge to Transplant

- 3 observational studies of perioperative ECMO as a bridge to (heart/lung) transplant vs. non-ECMO (Bittner, Jayarajan) or cardiopulmonary bypass (Bitner, Ius, Jayarajan)
- ECMO recipients had similar (Bittner, Ius) or higher (Jayarajan) mortality post-discharge; in-hospital mortality inconsistent
- ECMO associated with decreased hospital stay (mean 12.4 vs. 39.4 days) but may have been skewed by higher mortality (Jayarajan)
- Disability, health-related quality of life, or functional outcomes not examined

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ECMO as Cardiopulmonary Resuscitation (ECPR)

- 5 observational studies examined ECPR vs. conventional CPR (Chou, Kim, Lin, Sakamoto, Shin)
- All studies used retrospectively analyzed data
- Inconsistent findings on mortality:
  - 4/5 studies reported improvement for in- or out-of-hospital cardiac arrest that disappeared at later follow-up in 3 studies
  - 1 study reported sustained mortality benefit up to 2 years

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ECMO as Cardiopulmonary Resuscitation (ECPR) (cont.)

- No significant difference in length of hospitalization (Kim) in only study in which LOS evaluated
- Lin reported better neurological outcomes within ECPR group at discharge, but no difference at 3 months
- Sakamoto reported better neurological outcomes up to 6 months

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KQ2: What are the rates of adverse events and other potential harms associated with ECMO compared to conventional treatment strategies?

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Study Information	Comparators	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Direction of Effect of ECMO	Comments
Key Question #2: Harms								
Bleeding	Various	Medium	Consistent	Direct	Imprecise	+++ **Moderate**	2.5-25%	Heterogeneous patient populations
Limb ischemia	Various	Medium	Consistent	Direct	Precise	++++ **High**	2.5%-7.6%	Heterogeneous patient populations
Cannulation site complications	Various	Medium	Consistent	Direct	Imprecise	+++ **Moderate**	1-23.1%	Heterogeneous patient populations

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Limitations of Assessing Harms Associated with ECMO

- Harms underreported in most studies
- No ratings of complication severity
- Most studies underpowered to detect differences or do not report complications in comparator groups
- High variability in available estimates with little correlation between rates of adverse events and duration of follow-up
- Insufficient evidence to evaluate whether complications differ by indication
- Insufficient evidence to evaluate whether complications vary by type of ECMO

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Harms Associated with ECMO

Indication	Study & Indication	Patients with Complications	Bleeding	Limb Ischemia	Cannulation Site Complications
Cardiac Support	**Chamogeorgakis et al. 2013[27]** 61 patients treated with VA-ECMO for post-infarction- or decompensated cardiomyopathy-related cardiogenic shock	8 (13.1%)	2 (2.5%)$^{\beta}$	6 (7.6%)$^{\beta}$	8 (13.1%)$^{\pi}$
Pulmonary Support	**Bein et al. 2013[2]** 40 patients with ARDS treated with avECCO$_2$-R	3 (7.5%)	-	1 (2.5%)	2 (5%)
	Peek et al. 2009[11] 90 patients with ARDS randomized to receive VV-ECMO (68 treated)	2 (2%)	-	-	1 (1%)*
	Del Sorbo et al. 2015[33] 25 patients with acute hypercapnic respiratory failure due to exacerbation of COPD treated with ECCO$_2$-R	13 (52%)	4 (16%)	-	1 (4%)
	Guirand et al. 2014[37] 26 trauma patients with life-threatening acute hypoxemic respiratory failure treated with VV-ECMO	23 (88%)	4 (15%)	-	0
	Pham et al. 2013[35] 123 patients with H1N1-associated ARDS treated with VV- or VA-ECMO	65 (53%)	-	-	-

*Percent of 90 randomized to ECMO (68 patients [75%] actually treated with ECMO)
$^{\beta}$Percent of total patient population of 61 ECMO and 18 VAD
$^{\pi}$All complications were limb complicates related to cannulation site

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Harms Associated with ECMO (cont'd)

Indication	Study & Indication	Patients with Complications	Bleeding	Limb Ischemia	Cannulation Site Complications
Bridge to Transplant	**Bittner et al. 2012**[41] Perioperative VA-ECMO support for 27 patients undergoing lung transplantation	-	4 (14.8%)	0	-
	Ius et al. 2012[42] 46 patients undergoing lung transplant were supported perioperatively with VA-ECMO	-	-	2 (4.3%)	5 (11%)
CPR	**Kim et al. 2014**[64] 52 patients with out-of-hospital cardiac arrest treated with ECPR	16 (30.8%)	13 (25%)	3 (6.8%)	12 (23.1%)[µ]

[µ]12 bleeding events were at cannulation site

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KQ3: What is the differential effectiveness and safety of ECMO according to sociodemographic factors, severity of the condition for which ECMO is used, setting in which ECMO is implemented, time of ECMO initiation (early vs. late), and duration of time on ECMO?

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Study Information	Comparators	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Direction of Effect of ECMO	Comments
Key Question #3: Differential ECMO effects and risk factors								
Age	Various	Medium	Inconsistent	Direct	Imprecise	++ **Low**	Limited and conflicting evidence that older age predicts survival and positive neurologic outcomes	
Gender	Various	Medium	Inconsistent	Direct	Imprecise	++ **Low**	Limited evidence that male gender predicts survival	
Dialysis	Various	Medium	Inconsistent	Direct	Imprecise	++ **Low**	Limited evidence that dialysis is associated with ECMO survival	Associations only found in case series

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Differential Effectiveness of ECMO

- Insufficient evidence on differential effectiveness of ECMO according to race/ethnicity, disease severity, setting, time of initiation, or duration of time on ECMO
- Age
  - CESAR trial found no differential effect between treatment with ECMO or conventional ventilation by age group
  - Evidence inconsistent to determine whether age is an independent predictor of survival

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Differential Effectiveness of ECMO (cont.)

- Gender
  - No RCTs evaluated role of gender on ECMO-related outcomes
  - 4/5 comparative cohort studies did not find gender to be an independent predictor of ECMO
- Renal Replacement Therapy/Dialysis
  - Tsai found that neither RRT nor dialysis were predictors of survival to discharge for ARDS patients who received ECMO
  - ELSO registry data, however, indicates that RRT/dialysis is associated with higher mortality among ECMO recipients.

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KQ4: What are the costs and potential cost-effectiveness of ECMO relative to conventional treatment strategies?

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Study Information	Comparators	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence	Direction of Effect of ECMO	Comments
Key Question #4: Costs and Cost-Effectiveness								
ECMO use	Mechanical Ventilation	Medium	Consistency unknown (one study)	Direct	Imprecise	**++ Low**	Cost-effectiveness $7,000 - $35,000 per LY or QALY gained; incremental costs in US of $100,000 - $500,000	Two studies of cost-effectiveness in non-US settings

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Economic Impact of ECMO: Published Evidence

- Cost-effectiveness of VV-ECMO in adults with respiratory failure: CESAR trial
  - Mean cost per patient $65,519 higher than conventional treatment (in 2005 USD)
  - Cost-effectiveness at 6 months exceeded $2 million per QALY gained
  - Cost-effectiveness over lifetime: $31,112 (95% CI 12,317 – 95,507) per QALY gained
- Cost-effectiveness of VA-ECMO in adults with cardiac arrest or cardiotoxicant-induced shock: St. Onge
  - Incremental cost per life-year $7,185 (2013 Canadian dollars) assuming 100% and 83% survival for cardiac arrest and severe shock, respectively
  - Incremental cost per life-year $34,311 using lower survival estimates

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Economic Impact of ECMO: Published Evidence (cont'd)

- Resource use trends in US for critically ill adults treated with ECMO: Maxwell
  - Nationwide Inpatient Sample Database 1998-2009
  - Average cost per admission $344,009 (2009 USD)
    - Mean total costs increased from <$200,000/patient to almost $500,000/patient
  - Total costs highest for patients with heart transplant ($722,123 per patient) and lowest for patients post-cardiotomy ($273,429 per patient)
- Sauer used the same database between 2006 and 2011:
  - Estimated median cost per patient of $120,000 in 2011**

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Integrated Evidence Ratings

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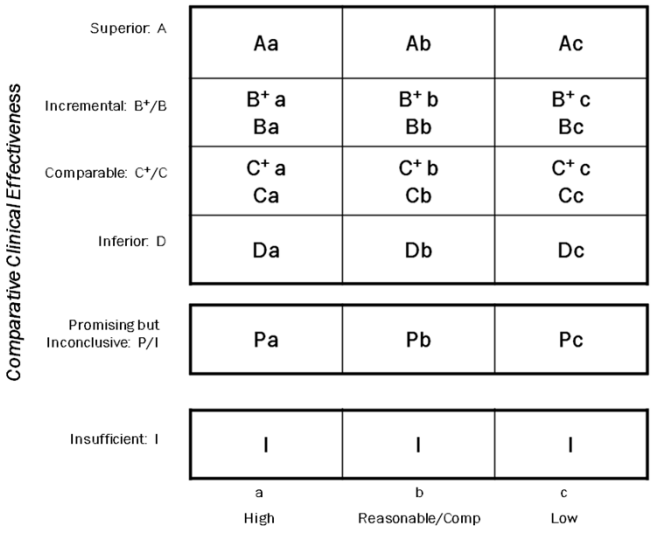
ICER Rating Matrix



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Evidence Ratings by Clinical Indication

- Cardiac support: ECMO vs. mini-VAD
  - Insufficient (I/Low Value)
- Pulmonary support: ECMO vs. mechanical ventilation
  - Comparable or Better (C+c/Low Value)
- Bridge to transplant: ECMO vs. cardiopulmonary bypass
  - Insufficient (I/Low Value)
- Cardiopulmonary resuscitation: ECPR vs. conventional CPR
  - Comparable (Cc/Low Value)

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Clinical Practice Guidelines

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Practice Guidelines

Extracorporeal Life Support Organization (ELSO 2010)

- **Patient selection**: Acute heart/lung failure with high mortality risk
- **Setting**: Tertiary centers with tertiary level adult ICU in location that can support ≥6 cases/center/year; participation in ELSO registry
- **Training**: Training and certification at accredited institutions according to clinical specialty area (e.g., perfusion)

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Practice Guidelines

- **AHA (2010):** ECPR may be considered when time without blood flow is brief and cardiac arrest is reversible or pending cardiac transplantation or revascularization in patients <75
- **American Thoracic Society (1997):** should be applied selectively by experienced, well-supported centers to those patients with disease refractory to other therapies
- **NICE (2014):** Patients whose conditions are refractory to other treatments and who have acute heart failure that is likely to recover spontaneously (e.g., myocarditis) or for whom there is a clear plan for subsequent intervention (e.g., heart transplant). Should be carried out by specialized clinical teams

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Payer Coverage Policies

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CMS & Private Insurer Coverage

- No national or local coverage determinations for ECMO in adults identified from CMS
- Aetna covers ECMO for adults at high risk of death with reversible causes of respiratory or cardiac failure that is unresponsive to other measures
- Premera Blue Cross and the Regence Group cover ECMO for treatment of cardiac or respiratory failure that is potentially reversible or as bridge to heart and/or lung transplant

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Ongoing Trials

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Ongoing Clinical Trial

- Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA) in France
- Estimated primary completion date February 2016
- Estimated enrollment: 331
- Duration of follow-up: ≥90 days
- Experimental arm: VV-ECMO
- Comparator arm: EXPRESS trial maximal pulmonary recruitment group (standard ARDS management)
- Primary outcome measure: all cause mortality on day 60

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Thank you

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Appendix: Quality Criteria

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Quality Ratings: USPSTF criteria

Outcome Studies:

- **Good:**
  - Comparable groups with no or low attrition; intent-to-treat analysis used in RCTs
  - Reliable and valid measurement instruments used
  - Clear description of intervention and comparator(s)
  - All important outcomes considered
  - Attention to confounders in design and analysis
- **Fair:**
  - Generally comparable groups, some differential follow-up may occur; intent-to-treat analysis used in RCTs
  - Acceptable measurement instruments used
  - Some but not all important outcomes considered
  - Some but not all potential confounders are accounted for
- **Poor:**
  - Noncomparable groups and/or differential follow-up; lack of intent-to-treat analysis for RCTs
  - Unreliable or invalid measurement instruments used (including not masking outcome assessment)
  - Key confounders given little or no attention

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Additional slides

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Long-Term Outcomes of ECMO

- 5/18 studies reported outcomes beyond 1 year following ECMO and hospital discharge
  - 2 transplant studies reported higher 1-yr and 5-yr mortality among ECMO patients (Bittner, Jayarajan)
  - 1 transplant study reported lower 1-yr mortality (Ius)
  - 1 ECPR study found comparable 1-yr mortality (Lin)
  - 1 ECPR study found lower 1-yr and 2-yr mortality (Shin)

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Long-Term Outcomes of ECMO (cont.)

- From pediatric literature, Hamutcu reported greater incidence of lung injury among ECMO survivors treated as neonates 5, 8, and 12 years later compared to healthy controls
- Sensorineural hearing loss associated with ECMO use among children 1-10 years later
- Challenging to distinguish long-term developmental outcomes from underlying disease processes

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Table ES-2: Summary of evidence for ECMO used to provide cardiac support

Study (Setting and Time)	Population	Intervention	Control (p values for comparison to intervention group)	Follow-up and Outcomes
Chamogeorgakis et al. 2013[27] (Cleveland, OH: single site; January 2006-September 2011)	Cardiogenic shock	ECMO (n=61) Mean age: 58 years 72.2% male 77.8% postinfarction	mp-VAD (n=18) Mean age: 53 years (p=0.121) 80.3% male (p=0.519) 52.5% postinfarction (p=0.063)	Mean follow-up 14.3 months Successfully weaned: ECMO 33.3% mp-VAD 19.7% (p=0.336) In-hospital survival: ECMO 50.0% mp-VAD 49.2% (p>0.999) Bridge to long-term support or transplant: ECMO 27.8% mp-VAD 31.1% (p>0.999)

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Table ES-3: Summary of evidence from RCTs for ECMO used to provide pulmonary support

Study (Setting and Time)	Population	Intervention	Control	Follow-up and Outcomes
Bein et al. 2013[2] (Germany and Austria: multi-site; September 2007-December 2010)	ARDS (American-European Consensus Conference definition) No LV failure Mechanical ventilation < 1 wk	avECCO$_2$-R treatment (iLA AV, Novalung, Heilbronn, Germany) (n=40) Mean age: 49.8 years 95% male Murray score: 2.8 BMI: 28.6 Pulmonary ARDS: 78% PaO2/FiO2: 152 ± 37	Conventional ventilation (maintaining 6mL/kg/PBW tidal volumes) (n=39) Mean age: 48.7 years 77% male Murray score: 2.7 BMI: 28.8 Pulmonary ARDS: 95% PaO2/FiO2: 168 ± 37	Follow-up outcomes assessed at 60 days Primary outcomes: Days w/o assisted ventilation in a 28-day period: avECCO$_2$-R 10.0 ± 8 Ventilation 9.3 ± 9 (NS) Days w/o assisted ventilation in a 60-day period: avECCO$_2$-R 33.2 ± 20 Ventilation 29.2 ± 21 (NS) Secondary outcome: Non-pulmonary organ failure free days-60: avECCO$_2$-R 21.0 ± 14 Ventilation 23.9 ± 15 (NS) Murray score on day 10: avECCO$_2$-R 2.2 ± 0.6 Ventilation 2.1 ± 0.5 (NS) Length of stay in hospital (days): avECCO$_2$-R 46.7 ± 33 Ventilation 35.1 ± 17 (NS) Length of stay in ICU (days): avECCO$_2$-R 31.3 ± 23 Ventilation 22.9 ± 11 (NS) In-hospital mortality: avECCO$_2$-R 17.5% Ventilation 15.4% (NS)

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Table ES-3: Summary of evidence from RCTs for ECMO used to provide pulmonary support (cont'd)

Peek et al. 2009[11] (UK: multi-site; July 2001-August 2006)	Severe respiratory failure (potentially reversible)	ECMO (n=90) Mean age: 39.9 years 57% male Murray score: 3.5 PaO2/FiO2 75.9 APACHE II score: 19.68 Pneumonia primary diagnosis: 62%	Conventional management (n=90) Mean age: 40.4 years 59% male Murray score: 3.4 PaO2/FiO2: 75.0 APACHE II score: 19.9 Pneumonia primary diagnosis: 59%	Follow-up outcomes assessed at 6 months: Death or severe disability: ECMO 37% Ventilation 53% RR: 0.69 (95% C.I.: 0.05-0.97; p=0.03) Died ≤6 mos or before discharge: ECMO 37% Ventilation 45% RR: 0.73 (95% CI: 0.52-1.03; p=0.07) Median days between randomization and death: ECMO 15 Ventilation 5 Median length of stay in hospital (days): ECMO 35.0 (IQR 15.6-74.) Ventilation 17.0 (IQR 4.8-45.3) Median length of stay in ICU (days): ECMO 24.0 IQR 13.0-40.5) Ventilation 13.0 (IQR 11.0-16.0) Overall health status (VAS; 0-100; higher score is better): ECMO 67.9 Ventilation 65.9 (NS)

NS=non-significant

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Table ES-4: Summary of evidence from observational studies for ECMO used to provide pulmonary support

Study (Setting and Time)	Population	Intervention	Control (p values for comparison to intervention group)	Follow-up and Outcomes
Del Sorbo et al. 2015 [33] (Italy: two sites; May 2011-November 2013)	Hypercapnic (COPD) risk of respiratory failure	$ECCO_2$-R + noninvasive ventilation (n=25) Mean age: 70.7 years FEV_1: 30.80 Simplified Acute Physiology (SAP) II score (0-163; increases with illness severity): 36.52	Noninvasive ventilation (NIV) (matched n=21) Mean age: 70.4 years (p=0.8778) FEV_1: 28.7 (p=0.6374) SAP II score: 36.14 (p=0.6364)	28 days Endotracheal intubation during the 28 d after ICU admission (ref: NIV-only) HR=0.27 (95% CI: 0.07-0.98; p=0.047) Intubation rate: $ECCO_2$-R+NIV 12% NIV 33% (p=0.1495) In-hospital mortality: $ECCO_2$-R+NIV 8% (95% CI: 1.0-26.0) NIV 35% (95% CI: 18.0-57.5) (p=0.0347) Median length of stay in hospital (days): $ECCO_2$-R+NIV 24 (IQR 21-28) NIV 22 (IQR 13-36) (p=0.8007) Median length of stay in ICU (days): $ECCO_2$-R+NIV 8 (IQR 7-10) NIV 12 (IQR 6-15) (p= 0.1943)

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Table ES-4: Summary of evidence from observa-tional studies for ECMO used to provide pulmonary support (cont'd)

Kluge et al. 2012 [34] (Germany: multi-site; January 2007-December 2010)	Acute hypercapnic respiratory failure unresponsive to noninvasive ventilation	PECLA device (n=21) Median age: 58 years 48% male COPD diagnosis 66.7% Median SAPS II score: 39 Median PaO2/FiO2: 208 Median $PaCO_2$: 84.0 mmHg	Ventilation (matched n=21) Median age: 58 years (NS) 43% male COPD 66.7% (NS) Median SAP II score: 40 (NS) Median PaO2/FiO2: 179 (NS) Median $PaCO_2$: 65.0 mmHg (p=0.001)	6-month follow-up duration 28-day mortality: PECLA 24% Ventilation 19% (p=0.845) 6-month mortality: PECLA 33% Ventilation 33% (p=0.897) Median length of stay in hospital (days): PECLA 23 (Range 4-137) Ventilation 42 (4-248) (p=0.056) Median length of stay in ICU (days): PECLA 15 (Range 4-137) Ventilation 30 (4-66) (p=0.263)

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Table ES-4: Summary of evidence from observational studies for ECMO used to provide pulmonary support (cont'd)

Noah et al. 2011 [32] (UK: multi-site; September 2009-January 2010)	H1N1-related ARDS CESAR trial entry criteria[11]	ECMO-referred (n=75) Mean age: 36.5 Mean PaO2/FiO2: 54.9 mmHg Mean SOFA score: 9.1 Currently/recently pregnant: 26.7% BMI<18.6: 5.3% 18.6<BMI<40: 84.0% BMI≥40: 10.7%	Non-ECMO-referred (GenMatched n=75) Mean age: 37.1 (NS) Mean PaO2/FiO2: 55.2 mmHg Mean SOFA score: 8.9 (NS) Currently/recently pregnant: 26.7% (NS) BMI<18.6: 1.3% (NS) 18.6<BMI<40: 88.0% (NS) BMI≥40: 10.7% (NS)	Follow-up duration not reported Mortality: ECMO-referred 24% Non-ECMO-referred 50.7% GenMatched RR 0.47 (95% CI: 0.31-0.72; p=0.001)

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Table ES-4: Summary of evidence from observational studies for ECMO used to provide pulmonary support (cont'd)

Pham et al. 2013 [35] (France: multi-site; July 2009 to March 2010)	H1N1-related ARDS	ECMO treatment in the first week of ARDS (n=52) Mean age: 45 years 58% male Mean BMI: 30 Mean PaO_2/FiO_2: 70 Mean $PaCO_2$: 56 mmHg Murray score: 3.3	Non-ECMO treatment in severe H1N1-related ARDS (matched n=52) Mean age: 45 years (NS) 56% male (NS) Mean BMI: 31 (NS) Mean PaO_2/FiO_2: 60 (NS) Mean $PaCO_2$: 55 mmHg (p=NS) Murray score: 3.3 (NS)	Follow-up duration not reported Median length of mechanical ventilation (days): ECMO 22 (IQR 11.7-35) Non-ECMO 13.5 (IQR 7-21) (p<0.01) Median length of stay in ICU (days): ECMO 27 (IQR 12-52) Non-ECMO 19.5 (9-26) (p=0.04) Mortality: ECMO 50% Non-ECMO 40% (p=0.44)

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Table ES-4: Summary of evidence from observational studies for ECMO used to provide pulmonary support (cont'd)

Tsai et al. 2015 [36] (Taiwan: single site; January 2007 to December 2012	ARDS	ECMO (n=45) • VV-ECMO (n=37) • VA-ECMO (n=8) Mean age: 56 years 71% male Mean PaO_2/FiO_2: 92.9 APACHE II score: 25 SOFA score: 11.9 RRT: 40% Chronic dialysis: 15.6%	Low tidal volume ventilation (APACHE score-matched n=45) Mean age: 56 years (NS) 75% male (NS) Mean PaO_2/FiO_2: 123.5 (NS) APACHE II score: 25 (NS) SOFA score: 10.2 (NS) RRT: 17.8% (p=0.020) Chronic dialysis: 8.9% (NS)	6-month follow-up duration In-hospital mortality: ECMO 48.9% Ventilation 75.6% (p=0.009)

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Table ES-4: Summary of evidence from observational studies for ECMO used to provide pulmonary support (cont'd)

Guirand et al. 2014 [37] (California: two sites; January 2001-December 2009)	Acute hypoxemic respiratory failure in trauma patients Defined as $PaO_2/FiO_2 \leq 80$ with $FiO_2 > 0.9$ without evidence of cardiogenic pulmonary edema and Murray score ≥3.0	VV-ECMO (n=26) Included in age and PaO_2/FiO_2-matched analysis (n=17) Mean age: 30.9 years 71% male 88% Blunt trauma Mean PaO_2/FiO_2: 52.1 Murray score: 3.9 35% RRT	Conventional ventilation (n=76) Included in age and PaO_2/FiO_2-matched analysis (n=17) Mean age: 34.1 years (NS) 88% male (NS) 65% Blunt trauma (NS) Mean PaO_2/FiO_2: 51.1 (NS) Murray score: 3.8 (NS) 24% RRT (NS)	60-day follow-up duration Mean length of mechanical ventilation (days): ECMO 28.5 Ventilation 15.4 (p=0.105) Mean length of stay in hospital (days): ECMO 45.9 Ventilation 21.1 (0.040) Mean length of stay in ICU (days): ECMO 38.5 Ventilation 18.2 (p=0.064)

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Table ES-5: Summary of evidence for ECMO used as ECPR

Study (Setting and Time)	Patient Population	ECPR	Conventional CPR	Follow-up Duration
Chou et al., 2014[44] (Single center Taiwan: 2006-2010)	in-hospital cardiac arrest	n=43 Treated with ECPR Mean age 60.5	n=23 Mean age 69.6	Until discharge (NR)
Kim et al., 2014[45] (Single Center Korea: 2006-2013)	out-of-hospital cardiac arrest	n=52 in propensity matched group Mean age: 54 M/F: 40/12 Comorbidity score: 0	n=52 in propensity matched group Mean age: 54 (NS) M/F: 38/14 (NS) Comorbidity score: 0 (NS)	3 months post-cardiac arrest
Lin et al., 2010[46] (Single Center Taiwan: 2004-2006)	in-hospital cardiac arrest responders	n=27 in propensity-matched group Mean age 59 Male 77.8%	n=27 in propensity matched group Mean age 60 (NS) 85.2% (NS)	1 year
Sakamoto et al. 2014[47] (Multicenter Japan: 2008-2011)	out-of-hospital cardiac	n=260 Mean Age: 56.3 Male: 90.4%	n=194 Mean Age: 58.1 (NS) Male: 88.7% (NS)	6 months
Shin et al. (Shin 2011, Shin 2013)[48,49] (Korea: 2003-2009)	Patients with witnessed in-hospital cardiac arrests at Samsung Medical Center; ages 18-80	n=60 in propensity-matched group Treated with ECPR (Capiox bypass system)	n=60 in propensity-matched group Treated with CCPR	2 years

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Washington State Health Care Authority
Health Technology Assessment

Final Key Questions and Background

Extracorporeal Membrane Oxygenation (ECMO)

Background

Extracorporeal membrane oxygenation (ECMO) is a form of life support that provides cardiopulmonary assistance outside the body. ECMO may be used to support lung function for severe respiratory failure or heart function for severe cardiac failure. An ECMO circuit can be set up as veno-venous (VV) or veno-arterial (VA). VV-ECMO provides external gas exchange, bypassing the lungs and protecting them from high tidal volumes of ventilation that would otherwise be needed to oxygenate and ventilate the patient. VV-ECMO is indicated for patients with potentially reversible respiratory failure, including those with severe acute respiratory distress syndrome (ARDS), primary graft dysfunction following lung transplant, and trauma to the lungs.

VA-ECMO provides the same external gas exchange as VV-ECMO, but also augments blood flow in settings of severe cardiac injury. VA-ECMO is indicated for patients with cardiac failure, including cardiogenic shock unresponsive to typical intensive care medicines and cardiac arrest that does not respond to cardiopulmonary resuscitation (CPR). VA-ECMO may also be used for patients following heart surgery or as a bridge to heart transplantation. Both VA- and VV-ECMO may be used intraoperatively as a planned alternative to traditional cardiopulmonary bypass in selected patient populations (e.g., lung or heart transplantation).

Other external gas exchange systems provide similar functions without the pump component of VV- or VA-ECMO. These arteriovenous extracorporeal lung assist (pECLA) devices bypass the lungs, but not the heart, and use the patient's blood pressure in order to sustain circulation of the externally oxygenated blood.[1-3] Because of the requirement for adequate cardiac function, these systems have more limited application.

ECMO is a well-established treatment for infants with lung and heart failure and has become a standard of care in many pediatric care centers.[4] In contrast, the evidence base for its use among adults is still emerging. Early studies of ECMO in adults found ECMO to be associated with poor survival rates.[5,6] However several developments have prompted renewed interest and wider utilization of ECMO in recent years.[7] First, technological advancements have improved the safety of the technique and broadened the application to include ambulating patients.[15] Technological improvements include heparin-coated cannulae, new oxygenators, and pumps.[8] Second, more recent clinical trials have shown improved survival without severe disability with ECMO compared to conventional ventilator support.[9] Finally, the 2009 H1N1 pandemic spurred increased demand for ECMO at rates higher than previously seen, resulting in additional evidence of a survival benefit.[10,11] Figure 1 on page 7 depicts major advancements in the development and implementation of ECMO over time.

Policy Context

Due to the expense and intensity of critical care, guidelines about how to implement life-sustaining and life-saving technologies warrant careful attention. Although consensus around when ECMO is indicated is still developing, the use of ECMO has grown in recent years and continues to rise subsequent to the H1N1 pandemic in 2009.[12] Because the availability of ECMO is limited and requires specialized medical care, liberalizing its use in the intensive care or operating room settings has important policy implications.

Proposed Scope

The Washington State Health Care Authority has commissioned ICER to conduct a systematic review of the published literature on the use of extracorporeal membrane oxygenation in 1) critically ill adult patients with severe respiratory or cardiac failure, and 2) adult patients who receive ECMO as a planned intra-operative procedure. Evidence will be culled from randomized controlled trials (RCTs), systematic reviews, and high-quality observational studies. Specific details on the proposed scope (Population, Intervention, Comparators, and Outcomes [PICO]) are detailed in the following sections.

Population

This review will examine the use of ECMO in adults (age≥18 years) with severe respiratory and/or cardiac failure hospitalized in intensive care unit settings. Specifically, our review will focus on the use of ECMO in patients with severe acute respiratory distress syndrome, patients who are unable to maintain sufficient cardiac output (e.g., as a bridge therapy to heart transplantation), patients who received ECMO during advanced cardiac life support (e.g., extracorporeal CPR), or patients with other reversible etiologies. Additionally, we will include studies of patients for whom ECMO was used as a planned intra-operative procedure.

Intervention

The intervention of interest will be the use of ECMO in the intensive care or operating room setting as a means of supporting the circulation of oxygenated blood. Our review will focus on pump-driven veno-venous and veno-arterial ECMO but will also include pumpless extracorporeal lung assist (pECLA) systems.

Comparators

The primary comparator of interest in critical care settings will be conventional intensive care management with endotracheal intubation and ventilation. In the operating room setting, the primary comparator will be traditional cardiopulmonary bypass. We will also include comparisons between distinct systems of extracorporeal life support (e.g., pump-driven vs. pump-free gas exchange systems) where literature is available.

Outcomes

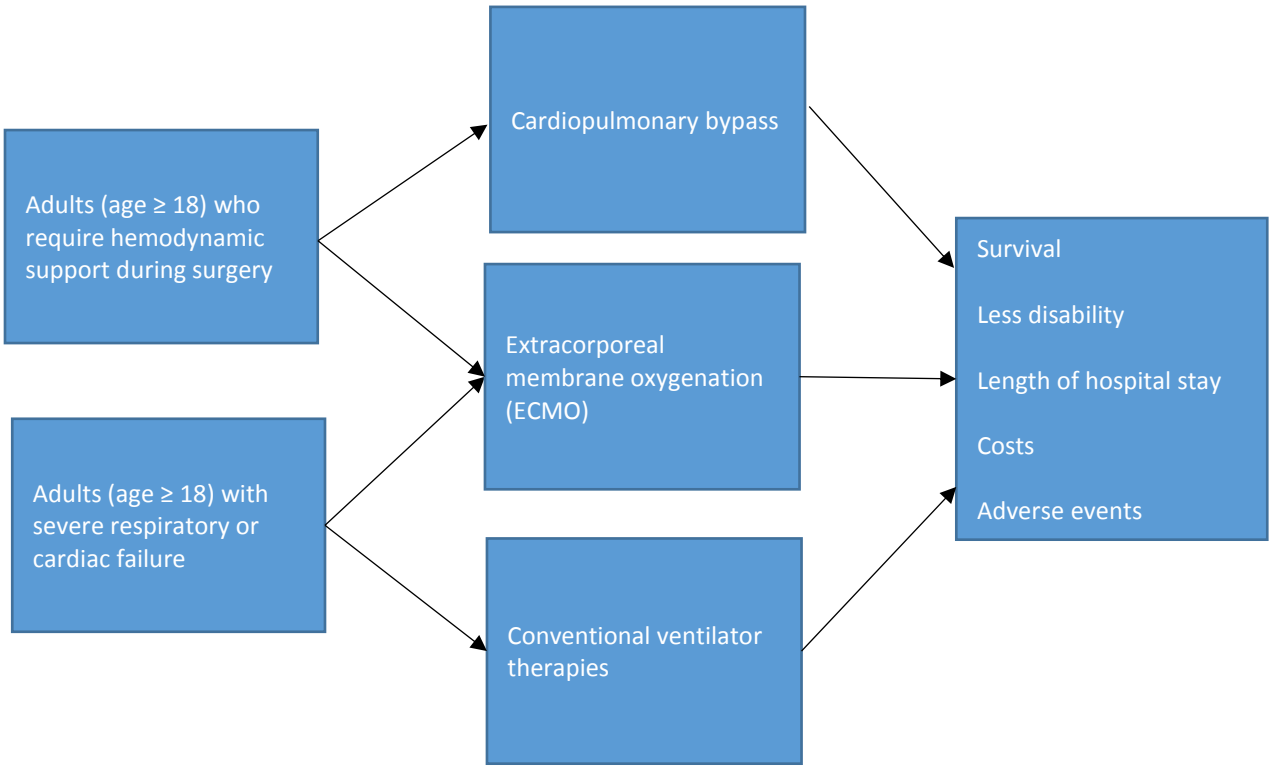
Outcomes of interest will include: 1) all-cause mortality; 2) length of hospital stay; 3) survival to discharge; 4) disability (as reported by study authors); 5) device-related complications and other adverse outcomes; 6) health-related quality of life, longer-term health status, and other measures of

well-being; and 7) costs and cost-effectiveness of ECMO. We will use available economic literature to evaluate treatment-related costs, long-term costs of care, and indirect costs (e.g., productivity loss, caregiver burden) of ECMO compared to conventional treatment. In addition, we will also analyze the budgetary impact of ECMO in a setting germane to the Washington HCA. Our budget impact analysis will focus on the direct medical costs associated with ECMO (i.e., treatment and management of complications).

Analytic Framework

The proposed analytic framework for this project is depicted below. It is expected that studies will vary substantially in terms of their entry criteria and technological application of ECMO. In addition, we anticipate that available RCTs may have inadequate statistical power or other quality concerns due to the difficulty of recruiting and randomizing participants, the inability to blind, high crossover rates, and potential protocol violations.

Analytical Framework: Extracorporeal Membrane Oxygenation



Methodology

Evidence Synthesis

We propose a systematic review of all RCTs, good and fair-quality comparative cohort studies, and prior systematic reviews of the effectiveness and safety of ECMO in adults (age≥18 years), as compared to alternative treatment approaches. Information will also be extracted from selected case series that meet specific quality criteria (e.g., consecutive sample, clearly defined entry criteria, sample retention), but will be summarized separately.

Of note, although the first report of successful ECMO in an adult patient was published in 1972, case selection, ventilation strategies, extracorporeal circuit design, and disease management have since undergone substantial changes.[9,13,14,15] We will therefore limit our literature search to publications since 2000, which describe ECMO with updated technologies. The full search strategy will include articles in MEDLINE, EMBASE, the Cochrane Register of Controlled Trials, and the Databases of Abstracts of Reviews of Effects (DARE) maintained by the University of York. We will supplement electronic searches with a manual review of retrieved references.

We will synthesize data on relevant outcomes quantitatively if feasible (i.e., if more than two studies are available with limited clinical heterogeneity between studies) and will generate qualitative evidence tables for each key question. As necessary, we will augment the evidence base with a non-systematic summary of evidence drawn from the literature around pediatric ECMO; while such evidence is not strictly generalizable to adult populations, it may provide useful context for the evaluation of ECMO in adults.

Quality Assessment

We will use criteria published by the US Preventive Services Task Force (USPSTF) to assess the quality of RCTs and comparative cohort studies, using the categories "good," "fair," or "poor."[16] Overall strength of evidence for each key question will be described as "high," "moderate," or "low," and will utilize the evidence domains employed in the AHRQ approach.[17] In keeping with standards set by the Washington HCA, however, assignment of strength of evidence will focus primarily on study quality, quantity of available studies, and consistency of findings.

In addition, summary ratings of the comparative clinical effectiveness and comparative value of the procedures of interest (i.e., *across* multiple key questions) will be assigned using ICER's integrated evidence rating matrix.[18] The matrix has been employed in previous Washington HCA assessments of bariatric surgery, virtual colonoscopy, coronary CT angiography, proton bean therapy, and breast imaging in special populations. The matrix can be found in the Appendix to this document.

Key Questions

We suggest a number of key questions as central to this review. Each question is listed below, along with the source for the evidence necessary to address it.

1. What is the comparative clinical effectiveness of ECMO versus conventional treatment strategies in adults (age≥18 years)?

   Sources: RCTs, good-quality comparative cohort studies, and good-quality systematic reviews

2. What are the rates of adverse events and other potential harms associated with ECMO compared to conventional treatment strategies?

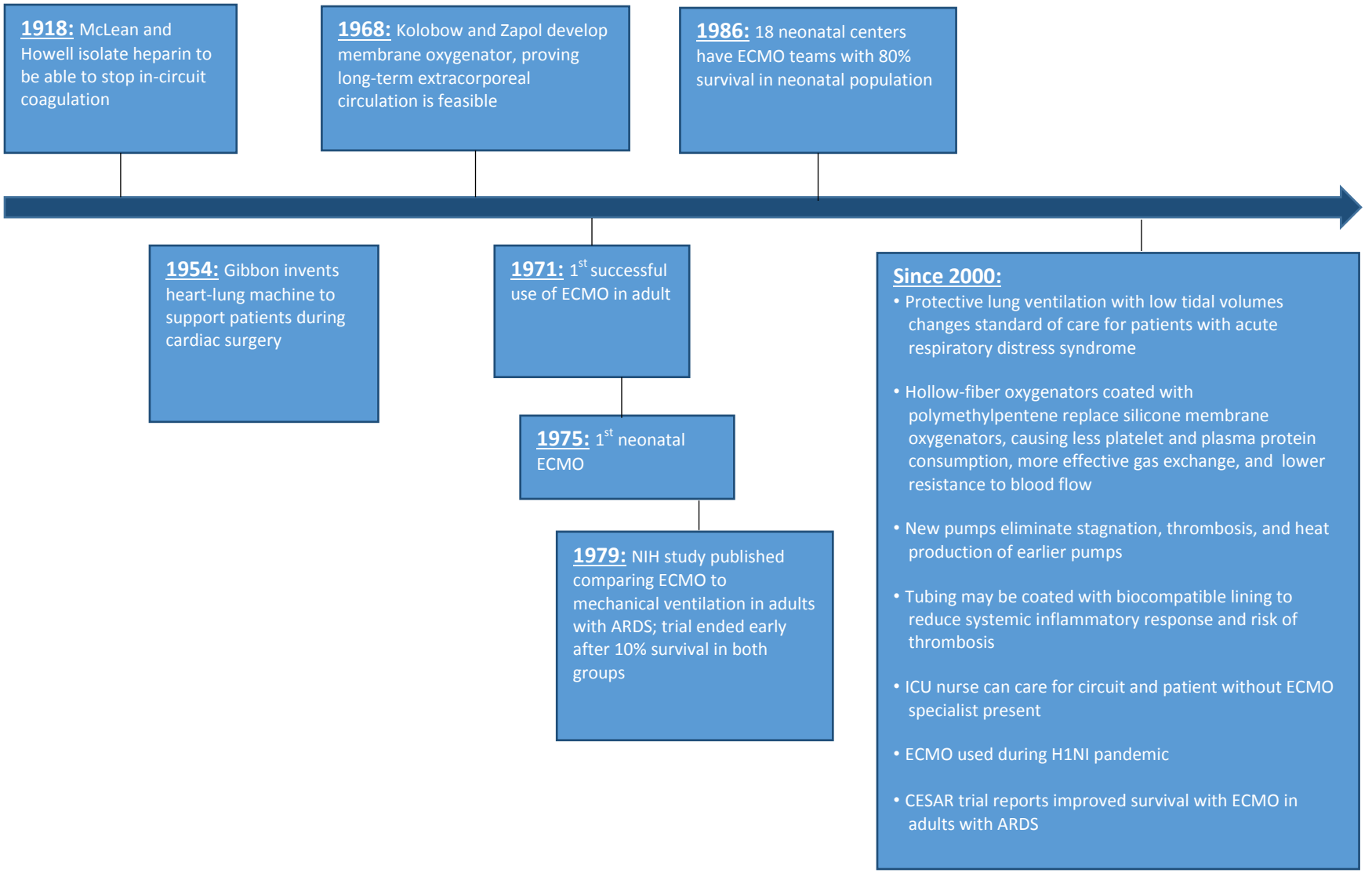
   Sources: RCTs, good-quality comparative cohort studies, good-quality systematic reviews, and case series that meet specific quality criteria (i.e., consecutive sample, clearly defined entry criteria, sample retention)

3. What is the differential effectiveness and safety of ECMO according to sociodemographic factors (e.g., age, sex, race or ethnicity), severity of the condition for which ECMO is used (e.g., Murray score or APACHE score), setting in which ECMO is implemented (e.g., specialized ECMO centers), time of ECMO initiation (early vs. late), and duration of time on ECMO?

   Sources: RCTs, good-quality comparative cohort studies, good-quality systematic reviews, and case series that meet specific quality criteria (i.e., consecutive sample, clearly defined entry criteria, sample retention)

4. What are the costs and potential cost-effectiveness of ECMO relative to conventional treatment strategies?

   Sources: Published economic evaluations, Washington State claims data


1918: McLean and Howell isolate heparin to be able to stop in-circuit coagulation
1954: Gibbon invents heart-lung machine to support patients during cardiac surgery
1968: Kolobow and Zapol develop membrane oxygenator, proving long-term extracorporeal circulation is feasible
1971: 1st successful use of ECMO in adult
1975: 1st neonatal ECMO
1979: NIH study published comparing ECMO to mechanical ventilation in adults with ARDS; trial ended early after 10% survival in both groups
1986: 18 neonatal centers have ECMO teams with 80% survival in neonatal population
Since 2000:
• Protective lung ventilation with low tidal volumes changes standard of care for patients with acute respiratory distress syndrome
• Hollow-fiber oxygenators coated with polymethylpentene replace silicone membrane oxygenators, causing less platelet and plasma protein consumption, more effective gas exchange, and lower resistance to blood flow
• New pumps eliminate stagnation, thrombosis, and heat production of earlier pumps
• Tubing may be coated with biocompatible lining to reduce systemic inflammatory response and risk of thrombosis
• ICU nurse can care for circuit and patient without ECMO specialist present
• ECMO used during H1NI pandemic
• CESAR trial reports improved survival with ECMO in adults with ARDS

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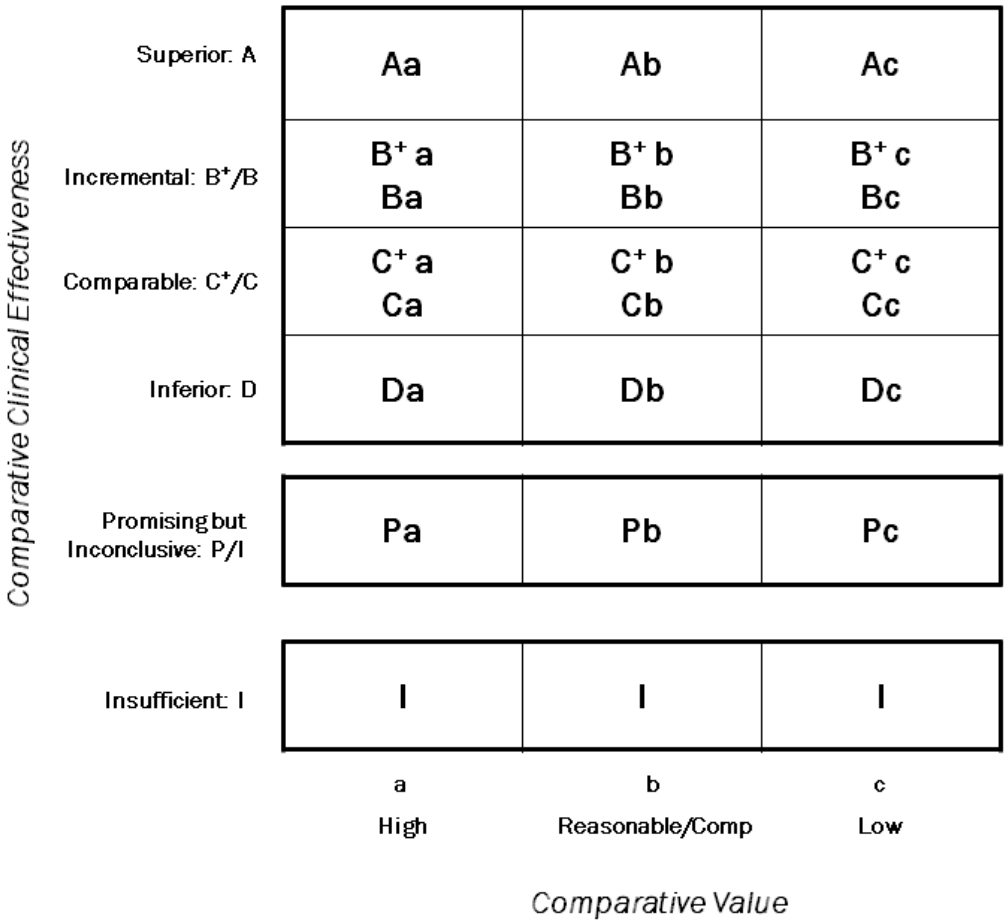
APPENDIX: ICER INTEGRATED EVIDENCE RATING™

(Compares an intervention of interest to a reference comparator)



For additional information on key questions and public comments.

HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on three questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are evidence-based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective[1] as expressed by the following standards[2]:

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms[3]:

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.

[1] Based on Legislative mandate: See RCW 70.14.100(2).

[2] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

[3] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

Using evidence as the basis for a coverage decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. Availability of Evidence:

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. Sufficiency of the Evidence:

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence[4] using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- The amount of evidence (sparse to many number of evidence or events or individuals studied);
- Consistency of evidence (results vary or largely similar);
- Recency (timeliness of information);
- Directness of evidence (link between technology and outcome);
- Relevance of evidence (applicability to agency program and clients);
- Bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

[4] Based on GRADE recommendation: http://www.gradeworkinggroup.org/FAQ/index.htm

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. Factors for Consideration - Importance

At the end of discussion a vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- Risk of event occurring;
- The degree of harm associated with risk;
- The number of risks; the burden of the condition;
- Burden untreated or treated with alternatives;
- The importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- The degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- Value variation based on patient preference.

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document:

What are the key factors and health outcomes and what evidence is there?

Safety Outcomes	Safety Evidence
Mortality	
Device-related complications/adverse outcomes	
Disability	
Efficacy – Effectiveness Outcomes	**Efficacy / Effectiveness Evidence**
All-cause mortality	
Length of stay	
Survival to discharge	
Disability	
Health-related quality of life	

Long-term health status	
Special Population / Considerations Outcomes	**Special Populations/ Considerations Evidence**
Cost Outcomes	**Cost Evidence**
Costs	
Cost-effectiveness	

Medicare Coverage and Guidelines

[From Page 12 of the Final Evidence Report]

Centers for Medicare and Medicaid Services:

There are currently no National Coverage Decisions published from the Centers for Medicare and Medicaid services.

[From pages 8-11 of the Final Evidence Report]

Extracorporeal Life Support Organization (ELSO) (2010)

http://www.elso.org/resources/Guidelines.aspx

Indications for ECMO include acute severe heart or lung failure with high mortality risk despite optimal conventional therapy. ECMO is considered for use in patients at ≥50% mortality risk and indicated in most circumstances at ≥80% mortality risk. Specific indications include the following:

- Primary or secondary hypoxic respiratory failure
    - 50% mortality risk is associated with a $PaO_2/FiO_2 < 150$ on $FiO_2 > 90\%$ and/or Murray Lung Injury Score 2-3.
    - 80% mortality risk is associated with a $PaO_2/FiO_2 < 100$ on $FiO_2 > 90\%$ and/or Murray Lung Injury Score 3-4 despite optimal care for 6 hours or more.
    - H1N1 disease progression can be very fast (12-24 hours to arrest), so there is a low threshold for failure of optimal therapy.
- CO2 retention on mechanical ventilation despite high Pplat (>30 cm H2O)
- Severe air leak syndromes
- Bridge to lung transplant

- Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care)
- Cardiogenic shock
    - Inadequate tissue perfusion manifested as hypotension and low cardiac output despite adequate intravascular volume.
    - Shock persists despite volume administration, inotropes and vasoconstrictors, and intraaortic balloon counterpulsation if appropriate.
    - Acute myocardial infarction
    - Myocarditis
    - Peripartum cardiomyopathy
    - Decompensated chronic heart failure
    - Post cardiotomy shock
    - Septic shock is an indication in some centers
    - Bridge to cardiac transplant
- ECMO to aid cardiopulmonary resuscitation in patients who have an easily reversible event and have had excellent CPR

Contraindications are relative, balancing the risks of the procedure (including diversion of limited resources) vs. the potential benefits. Relative contraindications include the following:

- Conditions incompatible with normal life if the patient recovers (e.g., massive cranial or cerebral destruction, sustained lack of cardiac or pulmonary function in patients who are not transplant candidates, other circumstances that make temporary cardiopulmonary support clinically futile)
- Mechanical ventilation at high settings ($FiO_2 > .9$, $P_{plat} > 30$) for ≥ 7 days
- Major pharmacologic immunosuppression (absolute neutrophil count <400 /mm^3)
- Preexisting conditions which affect the quality of life (CNS status, recent CNS hemorrhage, end stage malignancy, risk of systemic bleeding with anticoagulation)
- Age and size of patient (e.g., increasing risk with increasing age)
- Chronic organ dysfunction (emphysema, cirrhosis, renal failure)
- Compliance (financial, cognitive, psychiatric, or social limitations)
- Prolonged CPR without adequate tissue perfusion
- Contraindication for anticoagulation
- Obesity
- DNR orders
- Unsuccessful CPR (no return of spontaneous circulation) for 5-30 minutes. ECPR may be indicated on prolonged CPR if good perfusion and metabolic support is documented.

Settings for ECMO

- ECMO centers should be located in tertiary centers with a tertiary level Adult Intensive Care Unit

- ECMO Centers should be located in geographic areas that can support a minimum of 6 ECMO patients per center per year.
- The cost effectiveness of providing fewer than 6 cases per year combined with the loss, or lack of clinical expertise associated with treating fewer than this number of patients per year should be taken into account when developing a new program.
- ECMO Centers should be actively involved in ELSO including participation in the ELSO Registry.

ECMO Training

- ECMO nurses should have completed their programs at approved schools of nursing and have achieved passing scores on their state written exams
- ECMO respiratory therapists should have completed their programs at accredited schools of respiratory therapy and have successfully completed the registry examination for advanced level practitioners and be recognized as Registered Respiratory Therapists (RRT) by the National Board of Respiratory Care (NBRC).
- ECMO perfusionists should have completed their programs at accredited schools of perfusion and have national certification through the American Board of Cardiovascular Perfusion (ABCP).
- ECMO physicians should have successfully completed institutional training requirements for their clinical specialty.
- Other medical personnel such as biomedical engineers or technicians who received specific ECMO training and have practiced as ECMO specialists should complete the equivalent training in ECMO management as the other specialists and document skills as ECMO specialists. These personnel can be approved institutionally as ECMO specialists under the "grandfather" principle.

American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care (AHA) (2010) [79]

http://circ.ahajournals.org/content/122/18_suppl_3/S720.full.pdf+html

Both CBP and ECMO are sophisticated techniques for circulating blood outside the body with or without extracorporeal oxygenation with the goal of supporting circulation without a functioning cardiac pump. Extracorporeal CPR (ECPR) requires highly trained personnel. Although limited by small sample sizes and unbalanced comparison groups, case series and observational studies support use of ECPR for cardiac arrest in patients <75 years old with reversible conditions. AHA considers the evidence base insufficient to recommend ECPR routinely for patients in cardiac arrest (Class IIb, level C recommendation), but concludes that ECPR may be considered when time without blood flow is brief and cardiac arrest is reversible or pending cardiac transplantation or revascularization.

International Society of Heart and Lung Transplantation (ISHLT) (2010)

http://www.guideline.gov/content.aspx?id=45068

For diseases or conditions requiring heart transplantation, the recommendation for using ECMO support in peri-operative management of mechanical circulatory support is to consider the risk of infection, immobility, and need for anticoagulation. This recommendation received a Class IIb consideration for usefulness and efficacy less well established by the evidence, which itself was based on a consensus of expert opinion and small studies.

The absence of objective evidence of myocardial recovery within 3-5 days should trigger consideration of mechanical circulatory support as a bridge to recovery or heart transplantation or withdrawal of life-

sustaining therapy. This Class IIb recommendation is based on less well-established evidence and expert opinion.

American Thoracic Society (1997)
http://www.thoracic.org/statements/resources/archive/acute1-5.pdf
Extracorporeal membrane oxygenation (ECMO) and CO_2 ($ECC0_2$-R) removal in the management of ARDS has enabled patients treated by experienced medical teams to continue extracorporeal support for weeks, with eventual successful discontinuation. However, the methodology remains extremely resource intensive and beset by complications, particularly intracranial hemorrhage. The technique should be applied selectively by experienced, well-supported centers to those patients with disease refractory to other therapies. Other simpler measures (e.g., prone positioning) have demonstrated improved oxygenation in many patients with ARDS.

National Institute for Health and Care Excellence (NICE) (2014)
https://www.nice.org.uk/guidance/ipg482
NICE found adequate evidence on the efficacy of using ECMO for adults with acute heart failure but described uncertainty about which patients would benefit from the procedure. There is also evidence of high incidence of serious complications. Therefore, the procedure is indicated only with special arrangements for clinical governance, consent and audit, or research.

ECMO for acute heart failure in adults should only be carried out by clinical teams with specific training and expertise in the procedure. NICE encourages further research into ECMO for acute heart failure including clear documentation of patient selection and indications for the use of ECMO. Outcome measures should include survival, quality of life, and neurological status.

The Committee emphasized the importance of a strategy for management after ECMO before undertaking the procedure. Patient selection should include only patients whose conditions are refractory to other treatments and who have acute heart failure that is likely to recover spontaneously (e.g., myocarditis) or for whom there is a clear plan for subsequent intervention (e.g., heart transplant). ECMO may need to be withdrawn for patients whose heart failure will not recover or is not suitable for further treatment.

Clinical Committee Findings and Decisions

Efficacy Considerations

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?

- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value?
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy?
    - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices?

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
    - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
    - Adverse effect on health that can result in lasting harm or can be life-threatening?
- Other morbidity concerns?
- Short term or direct complication versus long term complications?
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives?
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?

Next Step: Cover or No Cover

If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions

If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?

- Refer to evidence identification document and discussion.
- Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
- Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:

- What are the known conditions/criteria and evidence state
- What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Clinical Committee Evidence Votes

First Voting Question

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective				
Safe				
Cost-effective				

Discussion

Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second Vote

Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____Not Covered ____ Covered Unconditionally ___ Covered Under Certain Conditions

Discussion Item

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Next Step: Proposed Findings and Decision and Public Comment

At the next public meeting the committee will review the proposed findings and decision and consider any public comments as appropriate prior to a vote for final adoption of the determination.

1) Based on public comment was evidence overlooked in the process that should be considered?

2) Does the proposed findings and decision document clearly convey the intended coverage determination based on review and consideration of the evidence?

Next Step: Final Determination

Following review of the proposed findings and decision document and public comments:

Final Vote

Does the committee approve the Findings and Decisions document with any changes noted in discussion?

If yes, the process is concluded.

If no, or an unclear (i.e., tie) outcome Chair will lead discussion to determine next steps.