

**VETERANS HEALTH ADMINISTRATION  
OFFICE OF PATIENT CARE SERVICES  
TECHNOLOGY ASSESSMENT PROGRAM**

**BRIEF OVERVIEW:**

**ULTRAFILTRATION FOR DECOMPENSATED  
HEART FAILURE**

Prepared by  
Karen Flynn, DDS, MS  
Program Manager

January, 2011

---

# TECHNOLOGY ASSESSMENT PROGRAM

## An Effective Resource for Evidence-based Managers

VA's Technology Assessment Program (TAP) is a national program within the Office of Patient Care Services dedicated to advancing evidence-based decision making in VA. TAP responds to the information needs of senior VA policy makers by carrying out systematic reviews of the medical research literature on health care technologies to determine "what works" in health care. "Technologies" may be devices, drugs, procedures, and organizational and supportive systems used in health care. TAP reports may be used to support better resource management.

TAP provides the *Brief Overview* to help fill the urgent information needs of its VA clients. The *Brief Overview* employs a systematic review methodology to identify and synthesize the best available evidence from the peer-reviewed literature. Content will depend on the availability of information, intended use and desired time frame. It may require some additional reading of documents (provided with the overview for the client) to obtain a full and comprehensive picture of the state of knowledge on the topic.

All TAP products are reviewed internally by TAP's physician advisor and key experts in VA. Additional comments and information on this report can be sent to:

VA Technology Assessment Program • Office of Patient Care Services  
Boston VA Healthcare System (11T) • 150 S. Huntington Ave. • Boston, MA 02130  
Tel. (857) 364-4469 • Fax (857) 364-6587 • [VATAP@va.gov](mailto:VATAP@va.gov)

**A SUMMARY FOR HTA REPORTS**  
**Copyright INAHTA Secretariat 2001**

VATAP is a member of the International Network of Agencies for Health Technology Assessment (INAHTA) [www.inahta.org]. INAHTA developed this checklist<sup>®</sup> as a quality assurance guide to foster consistency and transparency in the health technology assessment (HTA) process. VATAP will add this checklist<sup>®</sup> to its reports produced since 2002.

This summary form is intended as an aid for those who want to record the extent to which a HTA report meets the 17 questions presented in the checklist. It is NOT intended as a scorecard to rate the standard of HTA reports – reports may be valid and useful without meeting all of the criteria that have been listed.

<b>Brief Overview:</b>			
<b>Ultrafiltration for Decompensated Heart Failure</b>			
January 2011			
Item	Yes	Partly	No
<b>Preliminary</b>			
1. Appropriate contact details for further information?	√		
2. Authors identified?	√		
3. Statement regarding conflict of interest?	√		
4. Statement on whether report externally reviewed?	√		
5. Short summary in non-technical language?			√
<b>Why?</b>			
6. Reference to the question that is addressed and context of the assessment?	√		
7. Scope of the assessment specified?	√		
8. Description of the health technology?	√		
<b>How?</b>			
9. Details on sources of information?	√		
10. Information on selection of material for assessment?	√		
11. Information on basis for interpretation of selected data?	√		
<b>What?</b>			
12. Results of assessment clearly presented?	√		
13. Interpretation of the assessment results included?	√		
<b>What Then?</b>			
14. Findings of the assessment discussed?	√		
15. Medico-legal implications considered?			√
16. Conclusions from assessment clearly stated?	√		
17. Suggestions for further actions?	√		

**CONTRIBUTORS TO THIS REVIEW:**

No conflicts of interest.

<b>TAP staff person/position</b>	<b>Role</b>	<b>Responsibilities</b>
<b>Karen Flynn</b> Program Manager Boston	Primary author	Conception and conduct of review: <ul style="list-style-type: none"> <li>• Communication with client;</li> <li>• Clinical search strategy;</li> <li>• Interim information;</li> <li>• Analytic framework;</li> <li>• Draft review;</li> <li>• Final review.</li> </ul>
<b>Elizabeth Adams</b> Health System Specialist Boston	Consultation throughout project	Internal content and format review.
<b>Elaine Alligood</b> Information Specialist Boston	Literature database searches	Database searches: <ul style="list-style-type: none"> <li>• Design/conduct technical strategy;</li> <li>• Choose/manage databases;</li> <li>• Strategy text and references for report;</li> <li>• TAP library/archive.</li> </ul>
<b>Bernard Spence</b> Administrative Officer Boston	Administrative support	<ul style="list-style-type: none"> <li>• Budget/resources;</li> <li>• “Intelligent lay reader” review;</li> <li>• Project tracking;</li> <li>• Web posting/indexing.</li> </ul>
<b>Rebecca Morton</b> Library Technician Boston	Article retrieval	Information retrieval: <ul style="list-style-type: none"> <li>• Full text from print journals and electronic resources;</li> <li>• Manage reference lists.</li> </ul>
<b>Valerie Lawrence</b> Physician Advisor San Antonio	Content and methods review	Final review: <ul style="list-style-type: none"> <li>• Logic/Internal consistency;</li> <li>• Clarity;</li> <li>• Clinical context;</li> <li>• Methods.</li> </ul>
<b>Andrea Gwosdow, Ph.D.</b> <b>Cherie Dewar</b> Gwosdow Associates Boston	Freelance medical writers	Final review: <ul style="list-style-type: none"> <li>• Clarity;</li> <li>• Copyediting.</li> </ul>

**ABBREVIATIONS**

<b>AKI</b> , acute kidney injury	<b>ESRD</b> , end-stage renal disease
<b>ACC</b> , American College of Cardiology	<b>ESV</b> , end-systolic volume
<b>ACE</b> , angiotension-converting enzyme	<b>FDA</b> , Food and Drug Administration
<b>ACS</b> , acute coronary syndrome	<b>GP</b> , general practitioner
<b>ADHF</b> , acute decompensated heart failure	<b>GFR</b> , glomerular filtration rate
<b>AHA</b> , American Heart Association	<b>HBT</b> , home-based telemanagement
<b>AHRQ</b> , Agency for Healthcare Research and Quality	<b>HF</b> , heart failure or hemofiltration
<b>AMI</b> , acute myocardial infarction	<b>HFSA</b> , Heart Failure Society of America
<b>ASGE</b> , American Society of Gastrointestinal Endoscopy	<b>ITT</b> , intention to treat
<b>BNP</b> , B-type natriuretic peptide	<b>IV</b> , intravenous
<b>BP</b> , blood pressure	<b>LOS</b> , length of stay
<b>CAD</b> , coronary artery disease	<b>LR</b> , likelihood ratio
<b>CARRESS</b> , CARdiorenal REScue Study	<b>LV</b> , left ventricle or ventricular
<b>CCT</b> , controlled clinical trial	<b>LVEF</b> , left ventricular ejection fraction
<b>CEP</b> , Center for Evidence-based Purchasing (UK)	<b>MI</b> , myocardial infarction
<b>CHF</b> , congestive heart failure	<b>NHSC</b> , National Horizon Scanning Centre (UK)
<b>CHF Solutions/CHFS</b> , device manufacturer	<b>NHLBI</b> , National Heart, Lung, and Blood Institute (US)
<b>CI</b> , 95% confidence interval	<b>NHS</b> , National; Health Service (UK)
<b>CONSORT</b> , Consolidated Standards of Reporting Trials	<b>NICE</b> , National Institute for Clinical Excellence (UK)
<b>COPD</b> , Chronic Obstructive Pulmonary Disease	<b>NIH</b> , National Institutes of Health
<b>CPAP</b> , continuous positive airway pressure	<b>NIV</b> , non-invasive ventilation
<b>CS</b> , clinical scenario	<b>NIPSV</b> , noninvasive pressure support ventilation
<b>CVA</b> , cerebrovascular accident	<b>NNT</b> , number needed to treat
<b>DMP</b> , disease management program	<b>NPV</b> , negative predictive value
<b>ED</b> , emergency department	<b>NS</b> , not significant
<b>EDV</b> , end-diastolic volume	<b>NT-proBNP</b> , N-terminal pro-B-type natriuretic peptide
<b>EF</b> , ejection fraction	<b>NYHA</b> , New York Heart Association
<b>ESC</b> , European Society of Cardiology	<b>OR</b> , odds ratio
<b>ESC</b> , European Society of Cardiology	

**PPV**, positive predictive value

**QoL**, quality of life

**QUADAS**, quality assessment for studies of diagnostic accuracy

**RCT**, randomized controlled trial

**RN**, registered nurse

**ROC**, receiver operating characteristic

**RPM**, remote patient monitoring

**RR**, relative risk

**RRT**, renal replacement therapy

**SBP**, systolic blood pressure

**Se**, sensitivity

**Sp**, specificity

**STARD**, Standards for Reporting diagnostic accuracy

**STROBE**, strengthening the reporting of observational studies in epidemiology

**TAAG**, Technology Assessment Advisory Group (VHA Office of Patient Care Services)

**UF**, ultrafiltration

**WMD**, weighted mean difference

## BRIEF OVERVIEW:

# ULTRAFILTRATION FOR DECOMPENSATED HEART FAILURE

## BACKGROUND

VHA's Technology Assessment Advisory Group (TAAG) asked the Technology Assessment Program (TAP) for a literature review to support the use of ultrafiltration in decompensated heart failure patients in VA patient care.

TAP's approach was to search first for available systematic reviews, technology assessments, and guidelines as a means of quickly gauging the overall status of research. TAP then updated review searches to identify any subsequently published review-eligible studies that would alter the original review conclusions.

## METHODS

### Searches

TAP repeatedly searched PubMed, MEDLINE, INAHTA databases, EMBASE, and the Cochrane Library using the terms "ultrafiltration", "decompensated heart failure", "volume overload", and "cardiorenal syndrome". Searches for subsequently published review-eligible primary research focused on ultrafiltration rather than alternate interventions. Final updated searches were conducted on October, 1, 2010.

### Included were:

- Systematic reviews and subsequently published eligible studies addressing use of ultrafiltration or alternate interventions to manage or prevent fluid overload in adults with acutely decompensated chronic heart failure;
- Peer-reviewed published in English from 2000 to October 2010;
- Comparative studies;
- Analytic and cost studies or economic evaluations.

### Excluded were:

- Narrative reviews, letters, and other publications lacking primary patient-based data and/or explicit methods descriptions;
- Articles judged unintelligible by at least two TAP staff;
- Inaccurately indexed or otherwise irrelevant to our charge;
- Descriptive studies: single cases or case series;
- Laboratory or other pre-clinical studies;
- Previous or duplicate publications of the same material;
- Preliminary studies: Cochrane protocols; pilot or feasibility studies.

"Quasi-systematic" reviews, i.e., those indexed or titled as systematic but which, on close examination, do not meet criteria or are inadequately reported to judge. They often attend to some details of truly systematic methods, but miss their essential spirit of critical analysis.

**Literature appraisal**

The progression of epidemiologic studies, or the epidemiologic study cycle, confirming the existence and magnitude of an association between exposure and disease, or intervention and outcome, is well-documented (Ibrahim, 1985; Mausner and Kramer, 1985; Lilienfeld and Stolley, 1994; Muir Gray, 1997): it begins with observational, hypothesis-generating studies such as single case or case series reports, then on to cross-sectional (also known as survey, correlational, or ecological) studies, which ascertain exposure and disease in populations at the same point in time, then progresses through analytic, hypothesis-testing studies (case-control or cohort, from which relative risk or estimates can be calculated), and culminates in the randomized controlled trial (RCT) confirming causality.

The systematic review, synthesizing multiple primary studies, provides an ultimate level of evidence, as do economic evaluations using efficacy data from reviews, and ideally collecting resource data during the course of randomized trials that also supply causal evidence.

One author (Flynn) selected, critically appraised and synthesized the information in this report.

**Systematic reviews**

Systematic reviews (detailed below) qualify as reproducible science and their production requires a threshold level of available primary research. Published systematic reviews thus provide an immediately accessible overview of the general status of a body of research literature. Conversely, the lack of published high-quality systematic reviews indicates a corresponding lack of published research.

The most recent guidelines (Dickstein, 2008; Hunt 2005; HFSA, 2006) report consensus recommendations for acute and chronic heart failure: as quasi-systematic reviews not focused on ultrafiltration, these guidelines are not included in the tables.

Cook (1995 and 1997) defines systematic reviews: *“Systematic reviews are scientific investigations in themselves, with pre-planned methods and an assembly of original studies as their “subjects”. They synthesize the results of multiple primary investigations by using strategies that limit bias and random error...”*

The same authors further specify characteristics of systematic reviews and contrast them with traditional narrative reviews: the latter synthesize articles without reporting methods of selection or quality assessment criteria, and thus do not qualify as reproducible unbiased science.

Systematic reviews:

- Ask a focused clinical question;
- Conduct a comprehensive search for relevant studies using an explicit search strategy;
- Uniformly apply criteria for inclusion and exclusion of studies;
- Rigorously and critically appraise included studies;
- Provide detailed analyses of the strengths and limitations of included studies;
- May include primary studies, which TAP generally considers redundant. However, in this case, the single most relevant RCT [Costanzo (2007): the UNLOAD trial], cited in reviews and assessments, is abstracted Appendix Table 2 as a point of reference for ongoing research.

## RESULTS

TAP's searches identified a total of 406 citations, of which we retrieved 80 for full-text review and ultimately included 23 (Table 1). Only three systematic reviews that focused on ultrafiltration met the inclusion criteria. They are abstracted in detail in Appendix Table 2.

The list of subsequently published eligible studies is equally slender: one among three studies reports additional results from the referenced UNLOAD trial (Costanzo, 2007 and 2010) already included by Colechin (2007).

TAP identified several systematic reviews on alternative interventions and related topics that may help inform care management of decompensated heart failure (Tables 1 and Appendix Table 2).

**Table 1. Overview of included studies**

Citation	Content	Setting
<b>Systematic reviews, technology assessments, economic studies for ultrafiltration</b>		
Bradley (2009)	Cost consequences	Decision model analysis
Colechin (2007)	Systematic review of cost impact	UK evidence-based purchasing
NHSC (2006)	Aquadex FlexFlow®	UK Horizon Scanning brief
<b>Reference study for ultrafiltration</b>		
Costanzo (2007)	Included by Colechin (2007)	UNLOAD trial
<b>Subsequently published review eligible primary studies</b>		
Allen (2010)	Continuous vs. bolus dosing of diuretics	Patients hospitalized with HF and volume overload: eligible for Salvador (2005)
Costanzo (2010)	UF vs. diuretic: secondary/clinical outcomes at 90 days	UNLOAD trial
Rogers (2008)	UF vs. furosemide	Effects on renal function
<b>Related reviews</b>		
Ditewig (2010)	Heart failure	Self-management programs
Porapakham (2010)	NT-proBNP guided therapy	Chronic heart failure
Inglis (Cochrane; 2010)	Telephone support or telemonitoring in chronic heart failure	All-cause mortality; CHF hospitalizations; QoL; acceptability; costs
Kramer (2010)	Ventricular remodeling	Effects on HF mortality with reduced EF
Zhou (2010)	Pleural effusion due to HF	Diagnostic value of NT-proBNP
Giordano (2009)	Home telemanagement vs. usual care	Rehospitalization for chronic HF
Klersy (2009)	Remote monitoring	Chronic HF
Felker (2009)	BNP- vs. symptom-guided therapy	1996-2009
Polisena (2009)	Home telehealth	Economic evaluations
Balion (AHRQ; 2006)	BNP and NT-proBNP	Diagnosis and prognosis of heart failure
Faris (Cochrane; 2006)	Harms and benefits of diuretics	Chronic heart failure
Masip (2005)	Noninvasive ventilation	Acute cardiogenic pulmonary edema
Roccaforte (2005)	Disease management programs	Clinical outcomes
Salvador (Cochrane; 2005)	Continuous infusion vs. bolus injection of loop diuretics	ADHF
McAlister (2004)	Multidisciplinary strategies	Risks for readmission
Phillips (2004)	Discharge planning	Older patients: readmission, mortality, LOS, QoL, costs

## CONCLUSIONS/DISCUSSION

One ultrafiltration device, the Aquadex FlexFlow system (CHF Solutions, Brooklyn Park MN) has been FDA approved for marketing in the US since December 2006 for temporary (up to eight hours) treatment of patients with fluid overload who have failed diuretic therapy and for extended (longer than eight hours) treatment of patients with fluid overload who have failed diuretic therapy and require hospitalization (FDA 2006).

FDA stipulates that treatment be administered by a health care provider under physician supervision and that both provider and physician have been trained in extracorporeal therapies. FDA's approval letter does not explicitly reference published studies, but it is reasonable to assume that FDA reviewers identified the same trials included by Colechin (2007; Appendix Table 2), with the exception of Costanzo (UNLOAD trial; 2007 and 2010 also in Appendix Table 2), which was published after the date of the FDA letter and remains the only RCT to address ultrafiltration. Colechin (2007) thus provides the most recent and comprehensive systematic review of ultrafiltration for acute decompensated heart failure and provides the core evidence considered by TAP in the present review.

TAP identified no recently published evidence to materially change NHS/CEP conclusions (Colechin, 2007):

*“CEP finds that ultrafiltration has significant potential to become a routine therapy for excess fluid removal in patients with congestive heart failure. However, further work is needed to establish the patient groups who would benefit most, the optimal rates of fluid removal, the conditions for termination of therapy, and the cost savings associated with long-term quality of life benefits.”*

These conclusions can be transferred to the US in 2011. Additional shortcomings of the available literature include those described by Colechin, as well as:

- Lack of blinding, which may be understandably difficult in the case of a bulky bedside device;
- Lack of explicit power calculations and correspondingly small numbers of patients in clinical trials, which may reflect the relative lack of reliable estimates of clinically significant effects for ultrafiltration in available research on which such calculations would be based;
- Lack of follow-up beyond two to three months;
- Reliance on intermediate or surrogate outcomes such as fluid volume removed or weight lost, rather than longer term outcomes such as quality of life or heart failure-specific mortality.
- The device manufacturer is a significant presence in the only published (Costanzo, 2007; 2010) and ongoing trials (Table 3).

The systematic reviews and assessments in Table 1 do not report significant adverse events or safety concerns, but studies may not have been adequately powered or followed patients for long enough to detect uncommon adverse events. Post-marketing surveillance for a device only available since late 2006 may also be inadequate for detecting uncommon or late adverse events. Kidney dysfunction with overzealous volume reduction has been observed (Testani, 2010) and is under investigation for ultrafiltration (Appendix Table 3).

The related reviews sections of Tables 1 and 2 provide insights into organization of care interventions that may reduce incidence of acute decompensation and the need for ultrafiltration. These include: patient education for self-monitoring, comprehensive discharge

planning with post-discharge support, telemonitoring, and multidisciplinary management that have been shown to improve CHF outcomes and reduce rehospitalization rates.

Finally, TAP's searches of AHRQ's database of ongoing trials ([www.clinicaltrials.gov](http://www.clinicaltrials.gov); detailed in Appendix Table 3) failed to identify in-progress studies likely to provide definitive answers any time in the near future. Studies listed in Table 3 continue to focus on a research agenda similar to that outlined by Colechin: patient selection and technical refinement rather than large multicenter trials for longer-term outcomes.

## REFERENCES

- Allen LA, Turer AT, Dewald T, Stough WG, Cotter G, O'Connor CM. Continuous versus bolus dosing of Furosemide for patients hospitalized for heart failure. *The American journal of cardiology*, 2010; 105(12): 1794-1797.
- Alvarado CJ, Anderson AG, Maki DG. Microbiologic assessment of disposable sterile endoscopic sheaths to replace high-level disinfection in reprocessing: a prospective clinical trial with nasopharyngoscopes. *American Journal of Infection Control*, 2009; 37(5): 408-413.
- Andrade JG, Stadnick E, Virani SA. The role of peripheral ultrafiltration in the management of acute decompensated heart failure. *Blood Purification*, 2010; 29(2): 177-182.
- Arnold JMO, Howlett JG, Mann E, Svendsen AM, Dorian P, Jong P, et al. Canadian Cardiovascular Society Consensus Conference recommendations on heart failure update 2007: Prevention, management during intercurrent illness or acute decompensation, and use of biomarkers. *Canadian Journal of Cardiology*, 2007; 23(1): 21-45.
- Bagshaw SM, Berthiaume LR, Delaney A, Bellomo R. Continuous versus intermittent renal replacement therapy for critically ill patients with acute kidney injury: a meta-analysis. *Critical Care Medicine*, 2008; 36(2): 610-617.
- Balion C. (AHRQ. Agency for Healthcare Research and Quality): Rockville. Testing for BNP and NT-proBNP in the Diagnosis and Prognosis of Heart Failure, 437 Pgs. *Evidence Report/Technology Assessment*, 2006. Report Number: 142, <http://www.ahrq.gov/downloads/pub/evidence/pdf/BNP/BNP.pdf>
- Bart BA, Boyle A, Bank AJ, Anand I, Olivari MT, Kraemer M, et al. Ultrafiltration versus usual care for hospitalized patients with heart failure: the Relief for Acutely Fluid-Overloaded Patients With Decompensated Congestive Heart Failure (RAPID-CHF) trial. *Journal of the American College of Cardiology*, 2005; 46(11): 2043-2046.
- Bradley SM, Levy WC, Veenstra DL. Cost-consequences of ultrafiltration for acute heart failure: a decision model analysis. *Circulation: Cardiovascular Quality and Outcomes*, 2009; 2(6): 566-573.
- Clark RA, Inglis SC, McAlister FA, Cleland JG, Stewart S. Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis. *British Medical Journal*, 2007; 334(7600): 942.
- Colechin ES, Bower L, Sims AJ. (NHS. Centre for Evidence-based Purchasing): Newcastle upon Tyne. Ultrafiltration therapy for fluid overload in heart failure, 45 Pgs. 2007. Report Number: CEP 07016,
- Cook DJ, Guyatt GH, Laupacis A, Sackett DL, Goldberg RJ. Clinical recommendations using levels of evidence for antithrombotic agents. *Chest*, 1995; 108(4 Suppl): 227S-230S.
- Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: synthesis of best evidence for clinical decisions. *Annals of Internal Medicine*, 1997; 126(5): 376-380. *Epub:1997/03/01*.
- Costanzo MR, Guglin ME, Saltzberg MT, Jessup ML, Bart BA, Teerlink JR, et al. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. *Journal of the American College of Cardiology*, 2007; 49(6): 675-683.
- Costanzo MR, Saltzberg MT, Jessup M, Teerlink JR, Sobotka PA. Ultrafiltration is associated with fewer rehospitalizations than continuous diuretic infusion in patients with decompensated heart failure: results from UNLOAD. *Journal of Cardiac Failure*, 2010; 16(4): 277-284.

- Costanzo MR, Ronco C. Extracorporeal fluid removal in heart failure patients. *Contributions to Nephrology*, 2010a; 165: 236-243.
- de Lissovoy G, Fraeman K, Teerlink JR, Mullahy J, Salon J, Sterz R, et al. Hospital costs for treatment of acute heart failure: economic analysis of the REVIVE II study. *The European Journal of Health Economics*, 2010; 11(2): 185-193.
- DesCoteaux JG, Blackmore K, Parsons L. A prospective comparison of the costs of reusable and limited-reuse laparoscopic instruments. *Canadian Journal of Surgery. Journal Canadien de Chirurgie*, 1998; 41(2): 136-141.
- Dickstein K. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: application of natriuretic peptides (Reply). *European Heart Journal*, 2008.
- Ditewig JB, Blok H, Havers J, van Veenendaal H. Effectiveness of self-management interventions on mortality, hospital readmissions, chronic heart failure hospitalization rate and quality of life in patients with chronic heart failure: a systematic review. *Patient Education and Counseling*, 2010; 78(3): 297-315.
- Endoscopy ASfG. ASGE guidelines for clinical application: Establishment of gastrointestinal endoscopy areas. *Gastrointestinal Endoscopy*, 1999; 50(6): 910-912.
- Faris R, Flather MD, Purcell H, Poole-Wilson PA, Coats AJ. Diuretics for heart failure. *Cochrane Database of Systematic Reviews*, 2006;(1): CD003838.
- FDA. Food and Drug Administration. (FDA Center for Devices and Radiological Health, Office of Device Evaluation): Rockville. 510(k) Summary Aquadex FlexFlow System, 4 Pgs., December 13, 2006. <http://www.fda.gov/cdrh/pdf6/K062922.pdf>
- Felker GM, Hasselblad V, Hernandez AF, O'Connor CM. Biomarker-guided therapy in chronic heart failure: a meta-analysis of randomized controlled trials. *American Heart Journal*, 2009; 158(3): 422-430.
- Fengler TW, Pahlke H, Bisson S, Kraas E. The clinical suitability of laparoscopic instrumentation. A prospective clinical study of function and hygiene. *Surgical Endoscopy*, 2000; 14(4): 388-394.
- Flessner MF, Zsom L, Juncos L. Ultrafiltration versus diuretics in congestive heart failure. *American Journal of the Medical Sciences*, 2010; 340(1): 38-41.
- Giordano A, Scalvini S, Zanelli E, Corra U, Longobardi GL, Ricci VA, et al. Multicenter randomised trial on home-based telemanagement to prevent hospital readmission of patients with chronic heart failure. *International Journal of Cardiology*, 2009; 131(2): 192-199.
- Guyatt GH, Sackett DL, Sinclair JC, Hayward R, Cook DJ, Cook RJ. Users' guides to the medical literature. IX. A method for grading health care recommendations. Evidence-Based Medicine Working Group. *JAMA*, 1995; 274(22): 1800-1804.
- Heart Failure Society of America, (HFSA). Evaluation and management of patients with acute decompensated heart failure. *Journal of Cardiac Failure*, 2006; 12(1): 86-103.
- Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. *Circulation*, 2005; 112(12): 154-235.
- Ibrahim MA. Epidemiology and Health Policy. Rockville: Aspen, 1985.

- Inglis SC, Clark RA, McAlister FA, Ball J, Lewinter C, Cullington D, et al. Structured telephone support or telemonitoring programmes for patients with chronic heart failure. *Cochrane Database of Systematic Reviews*, 2010; 8: CD007228.
- Kimmery MB, Burnett DA, Carr-Locke DL, DiMarino AJ, Jensen DM, Katon R, et al. ASGE technology assessment position paper: Transmission Of Infection By Gastrointestinal Endoscopy. *Gastrointestinal Endoscopy*, 1993; 39(6): 885-888.
- Klersy C, De Silvestri A, Gabutti G, Regoli F, Auricchio A. A meta-analysis of remote monitoring of heart failure patients. *Journal of the American College of Cardiology*, 2009; 54(18): 1683-1694.
- Kollef MH, Napolitano LM, Solomkin JS, Wunderink RG, Bae IG, Fowler VG, et al. Health care-associated infection (HAI): a critical appraisal of the emerging threat-proceedings of the HAI Summit. *Clinical Infectious Diseases*, 2008; 47 Suppl 2: S55-99.
- Kramer DG, Trikalinos TA, Kent DM, Antonopoulos GV, Konstam MA, Udelson JE. Quantitative evaluation of drug or device effects on ventricular remodeling as predictors of therapeutic effects on mortality in patients with heart failure and reduced ejection fraction: a meta-analytic approach. *Journal of the American College of Cardiology*, 2010; 56(5): 392-406.
- Levy PD, Penugonda N, Guglin M. Treatment of massive fluid overload as a result of constrictive pericarditis with ultrafiltration in the emergency department. *Annals of Emergency Medicine*, 2008; 51(3): 247-250.
- Liang KV, Williams AW, Greene EL, Redfield MM. Acute decompensated heart failure and the cardiorenal syndrome. *Critical Care Medicine*, 2008; 36(1 Suppl): S75-S88.
- Lilienfeld DE, Stolley PD. Foundations of Epidemiology. 3rd. New York: Oxford University Press, 1994.
- Maric B, Kaan A, Ignaszewski A, Lear SA. A systematic review of telemonitoring technologies in heart failure. *European Journal of Heart Failure*, 2009; 11(5): 506-517.
- Masip J, Roque M, Sanchez B, Fernandez R, Subirana M, Exposito JA. Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and meta-analysis. *JAMA*, 2005; 294(24): 3124-3130.
- Mausner JS, Kramer S. Mausner & Bahn Epidemiology: An Introductory Text. 2nd. Philadelphia: WB Saunders, 1985.
- McAlister FA, Lawson FM, Teo KK, Armstrong PW. A systematic review of randomized trials of disease management programs in heart failure. *The American Journal of Medicine*, 2001; 110(5): 378-384.
- McAlister FA, Stewart S, Ferrua S, McMurray JJ. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. *Journal of the American College of Cardiology*, 2004; 44(4): 810-819.
- Mohammed AA, van Kimmenade RR, Richards M, Bayes-Genis A, Pinto Y, Moore SA, et al. Hyponatremia, natriuretic peptides, and outcomes in acutely decompensated heart failure: results from the International Collaborative of NT-proBNP Study. *Circulation: Heart failure*, 2010; 3(3): 354-361.
- Muir Gray JA. Evidence-Based Healthcare: How to Make Health Policy and Management Decisions. New York: Churchill Livingstone, 1997.
- Mulrow CD, Cook DJ, Davidoff F. Systematic reviews: critical links in the great chain of evidence. *Annals of Internal Medicine*, 1997; 126(5): 389-391.

National Horizon Scanning Centre. (NHSC): Birmingham. Ultrafiltration for acute decompensated heart failure: horizon scanning technology briefing, 6 Pgs. *Technology Briefing*, March 30, 2006.

Nelson DB, Jarvis WR, Rutala WA, Foxx-Orenstein A, Isenberg G, Dash Georgia P, et al. Multi-society guideline for reprocessing flexible gastrointestinal endoscopes. *Diseases of the Colon and Rectum*, 2004; 47(4): 413-421.

Peacock WF, Costanzo MR, De Marco T, Lopatin M, Wynne J, Mills RM, et al. Impact of intravenous loop diuretics on outcomes of patients hospitalized with acute decompensated heart failure: insights from the ADHERE registry. *Cardiology*, 2009; 113(1): 12-19.

Phillips CO, Wright SM, Kern DE, Singa RM, Shepperd S, Rubin HR. Comprehensive discharge planning with postdischarge support for older patients with congestive heart failure: a meta-analysis. *JAMA*, 2004; 291(11): 1358-1367.

Polisena J, Coyle D, Coyle K, McGill S. Home telehealth for chronic disease management: a systematic review and an analysis of economic evaluations. *International Journal of Technology Assessment in Health Care*, 2009; 25(3): 339-349.

Porapakkham P, Zimmet H, Billah B, Krum H. B-type natriuretic peptide-guided heart failure therapy: A meta-analysis. *Archives of Internal Medicine*, 2010; 170(6): 507-514.

Rey JF, Bjorkman D, Duforest-Rey D, Axon A, Seanz RF, M., Mine T, et al. World Gastroenterology Organization, WGO/OMED practice guideline: endoscope disinfection. 2005. [http://www.guidelines.gov/summary/summary.aspx?doc\\_id=9543&nbr=005088&string=Rey+AND+2005+AND+endoscope+AND+disinfection](http://www.guidelines.gov/summary/summary.aspx?doc_id=9543&nbr=005088&string=Rey+AND+2005+AND+endoscope+AND+disinfection).

Roccaforte R, Demers C, Baldassarre F, Teo KK, Yusuf S. Effectiveness of comprehensive disease management programmes in improving clinical outcomes in heart failure patients. A meta-analysis. *European Journal of Heart Failure*, 2005; 7(7): 1133-1144.

Rogers HL, Marshall J, Bock J, Dowling TC, Feller E, Robinson S, et al. A randomized, controlled trial of the renal effects of ultrafiltration as compared to furosemide in patients with acute decompensated heart failure. *Journal of Cardiac Failure*, 2008; 14(1): 1-5.

Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical Epidemiology: A Basic Science for Clinical Medicine. 2nd ed. Boston: Little Brown & Company, 1991.

Salvador DR, Rey NR, Ramos GC, Punzalan FE. Continuous infusion versus bolus injection of loop diuretics in congestive heart failure. *Cochrane Database of Systematic Reviews*, 2005;(3): CD003178.

Sanchez Jose E, Ortega T, Rodriguez C, Diaz M, Beatriz, Martin M, et al. Efficacy of peritoneal ultrafiltration in the treatment of refractory congestive heart failure. *Nephrology, Dialysis, Transplantation*, 2010; 25(2): 605-610.

Testani JM, Chen J, McCauley BD, Kimmel SE, Shannon RP. Potential effects of aggressive decongestion during the treatment of decompensated heart failure on renal function and survival. *Circulation*, 2010; 122(3): 265-272.

Zhou Q, Ye ZJ, Su Y, Zhang JC, Shi HZ. Diagnostic value of N-terminal pro-brain natriuretic peptide for pleural effusion due to heart failure: a meta-analysis. *Heart*, 2010; 96(15): 1207-1211.

APPENDIX

Table 2. Abstracted details of studies listed in Table 1

Citation	Design/methods	Results/Conclusions
<b>Ultrafiltration reviews</b>		
Bradley (2009)	<p><b>Decision model:</b></p> <ul style="list-style-type: none"> <li>• Outcomes and costs: ultrafiltration vs. IV diuretics for index and subsequent (within 90 days) hospitalizations;</li> <li>• Outcomes from Costanzo (2007: UNLOAD); device and time costs supplied by UNLOAD investigators;</li> <li>• Perspectives: society; Medicare; hospital payer.</li> </ul>	<p><b>Results by perspective:</b></p> <ul style="list-style-type: none"> <li>• Society perspective: 86% probability that ultrafiltration is more expensive (base case, \$13,469/patient treated with ultrafiltration vs. \$11,610 for diuretics);</li> <li>• Medicare : &gt;99% probability that ultrafiltration would save costs;</li> <li>• Hospital: 97% probability that ultrafiltration would be more expensive;</li> <li>• Sensitivity analyses: cost estimates most influenced by length of index hospitalization; number of days rehospitalized; number and cost of hemofilters.</li> </ul> <p><b>Conclusions:</b> <i>“Despite a reduction in rehospitalization rates, it is unlikely that ultrafiltration results in cost savings from a societal perspective. The discordance in costs between societal, Medicare, and hospital perspectives underscores the importance of payer perspective in formulating strategies and reimbursement structures to reduce heart failure rehospitalizations.”</i></p>
Colechin (2007)	<p>NHS Centre for evidence-based purchasing systematic review with cost impact analysis: Can ultrafiltration be used as an alternative to intravenous diuretics for heart failure patients admitted with fluid overload?</p> <ul style="list-style-type: none"> <li>• Medline searches conducted March 2007;</li> <li>• Included: double blind RCTs in humans with heart failure;</li> <li>• Quality assessment by Cochrane criteria;</li> <li>• Cost impact analysis: differences in costs/patient with 12 hr Aquadex system treatment vs. standard treatment with loop diuretics.</li> </ul>	<p>39 studies with 1174 patients (mean study size, 30.2; range, 4-200):</p> <p><b>Study availability:</b></p> <ul style="list-style-type: none"> <li>• 7 experimental studies used a broadly similar study design (heart failure patients randomized to treatment with UF vs. conventional diuretics) and enrolled a total of 358 patients (mean 60, median 38, range 16-200, mean age 62 years);</li> <li>• One study compared two different UF protocols;</li> <li>• None of the 32 observational studies used a formal cohort or case-control design.</li> </ul> <p><b>HF guidelines:</b></p> <ul style="list-style-type: none"> <li>• NICE: no explicit mention of UF, but patients unresponsive to drug therapy should have specialist referral for other options;</li> <li>• ES: algorithm for diuretic in acute HF; UF or dialysis should be considered if diuretics ineffective;</li> <li>• AHA/ACC: discussed for patients with refractory end stage HF and renal dysfunction.</li> </ul> <p><b>Heterogeneity among studies:</b></p> <ul style="list-style-type: none"> <li>• The studies used different protocols for UF (including termination conditions), had different primary outcome measures, and different durations of follow-up;</li> <li>• In some of the experimental studies, patients receiving UF continued to receive diuretics;</li> <li>• Total volume of fluid removed was the only common outcome measure, but this depended on UF</li> </ul>

Citation	Design/methods	Results/Conclusions
		<p>protocol;</p> <ul style="list-style-type: none"> <li>• There was insufficient homogeneity among the RCTs to conduct a meta-analysis for any outcome measure;</li> <li>• Two of the RCTs were supported by the device manufacturer.</li> </ul> <p><b>Study patients:</b></p> <ul style="list-style-type: none"> <li>• RCTs: no differences between groups in severity of heart failure (as measured by NYHA score) or urinary output prior to UF;</li> <li>• In one study all patients had severe left ventricular systolic dysfunction, but remaining studies did not specify;</li> <li>• Comorbidities: no common inclusion or exclusion criteria. In general, patients with hemodynamic instability, arrhythmia, valvular heart disease, or artificial pacemakers were excluded. Some studies excluded patients with anginas pectoris, systolic hypotension, or conditions related to lung water, but other studies included patients with these conditions.</li> </ul> <p><b>Overall:</b></p> <ul style="list-style-type: none"> <li>• Insufficient evidence from RCTs to permit a systematic review or meta-analysis satisfying Cochrane criteria;</li> <li>• Authors acknowledge practical and ethical difficulties of conducting RCTs in this patient group.</li> </ul> <p><b>Cost analysis:</b></p> <ul style="list-style-type: none"> <li>• Assumptions: both UF and diuretic require 30 min preparation time for patient and equipment; hematocrit test requiring 5 minutes of RN time carried out every 15 min for first hour of UF to establish flow rate; diuretic treatment based on Costanzo (2007, below) with bolus injections at an average dose of 181mg daily for 48 hrs; and post-discharge care would be the same for both groups;</li> <li>• Costs related to direct hospital treatment of fluid overload in heart failure only, no after-discharge care or adverse event costs included.</li> </ul> <p><b>Cost/patient results:</b></p> <ul style="list-style-type: none"> <li>• Non-ICU: £2379.39 for UF; £771.39 for diuretics;</li> <li>• ICU: £3758 for UF; £3318 for diuretics;</li> <li>• Results were sensitive to changes in rates of readmission and emergency visits;</li> <li>• Analysis was limited by the data available: further research is needed on resource use associated with UF in subgroups of CHF patients, particularly those with diuretic resistance, where there may be greater potential for UF benefit. Further collection of data on adverse events, long-term quality of life, and post-discharge care is also needed.</li> </ul>

Citation	Design/methods	Results/Conclusions
		<p><b>Conclusions for cost analysis:</b> <i>“The cost impact analysis was used to estimate the impact that treating fluid overload with Aquadex in heart failure patients would have on NHS resources associated with hospital care, compared with standard diuretic treatment. The analysis showed that the cost of treatment was significantly increased, but hospital care costs were reduced overall and the cost of consumables accounted for the majority of the higher treatment cost.”</i></p> <p><b>Among RCTs which compared a single UF treatment with IV diuretics:</b></p> <ul style="list-style-type: none"> <li>• UF was at least as effective in removing fluid;</li> <li>• UF was effective in diuretic-resistant patients;</li> <li>• UF-treated patients showed sustained (up to 3 months) improvement in exercise test performance;</li> <li>• UF effectiveness on observational studies was in broad agreement with results from RCTs;</li> <li>• No evidence suggested that UF is unsafe, but some studies suggested that UF carries greater risk at high rates of fluid removal, particularly in heart failure patients.</li> </ul> <p><b>Summary:</b> <i>“Ultrafiltration appears to be safe and well tolerated by most CHF patients. Further studies are needed to establish the safe maximum rate of fluid removal, especially for patients in advanced stages of the disease and also to measure the long-term mortality rate.”</i></p> <p><b>Conclusions:</b> <i>“CEP finds that ultrafiltration has significant potential to become a routine therapy for excess fluid removal in patients with congestive heart failure. However, further work is needed to establish the patient groups who would benefit most, the optimal rates of fluid removal, the conditions for termination of therapy, and the cost savings associated with long-term quality of life benefits.”</i></p>
NHSC (2006)	<p>Horizon scanning briefing: Ultrafiltration: (Aquadex FlexFlow aquapheresis system):</p> <ul style="list-style-type: none"> <li>• Target group: acute decompensated heart failure patients (with very severe peripheral edema and fluid overload who have not responded adequately or rapidly to conventional therapy;</li> <li>• Place of use: secondary care/general non-specialist hospital; or tertiary care;</li> <li>• Other related guidance under development: Nesiritide for acute decompensated heart failure.</li> </ul>	<p><b>3 RCTs with 261 patients</b> tabulated:</p> <ul style="list-style-type: none"> <li>• Primary outcomes: weight loss, fluid removal, dyspnea score change;</li> <li>• At 48 hrs: 38% greater weight loss and 28% greater fluid removal vs. standard care;</li> <li>• At 90 days: 50% reduction in readmissions and 52% reduction in emergency or clinic visits vs. standard care;</li> <li>• Hemodynamic stability, median 3213 ml fluid removed;</li> <li>• Weight loss, 91.9±17.5 kg to 89.3±17.3 kg;</li> <li>• Adverse events: none in 2/3 trials; 1 catheter site infection in one trial.</li> </ul> <p>Existing comparators/treatments:</p> <ul style="list-style-type: none"> <li>• Diuretic in acute pulmonary edema;</li> <li>• IV vasodilators (nitrates);</li> <li>• IV inotropes: in severe exacerbations, usually in intensive care;</li> <li>• Treatment of precipitating cause: infection, arrhythmia, hypertension, myocardial infarction, anemia;</li> </ul>

Citation	Design/methods	Results/Conclusions
		<ul style="list-style-type: none"> <li>• Conventional ultrafiltration: high blood flow rates and large bore vascular access, mainly in intensive care or renal department settings;</li> <li>• Once stable, treatment aims to relieve symptoms, improve exercise tolerance, reduce exacerbations and mortality by: ACE inhibitors or angiotensin-II receptor antagonists; diuretics; beta-blockers (stable heart failure); digoxin (for patients with atrial fibrillation); cardiac resynchronization.</li> </ul> <p><b>Costs:</b> Aquadex FlexFlow, £12,000; new filter and blood circuit for each patient, £600 (multiple treatments may be required for severe cases).</p> <p><b>Potential or intended impact:</b> Speculative, but may include decreased length of stay, reduced referrals, and reduced re-admissions.</p>
<p>Costanzo (2007)</p>	<p>RCT:</p> <ul style="list-style-type: none"> <li>• Included by Colechin (2007);</li> <li>• Patients over 18 yrs hospitalized for HF (28 US centers with experience in ultrafiltration) with <math>\geq 2</math> signs of hypervolemia randomized to UF or IV diuretics and followed 90 days or until death;</li> <li>• All patients had dietary sodium and fluid restrictions;</li> <li>• Power calculations implied (100 subjects/arm) but not explicitly reported;</li> <li>• Not blinded;</li> <li>• Sponsored by and with investigator ties to device manufacturer;</li> <li>• Exclusions: acute coronary syndrome; serum creatinine <math>&gt; 3.0</math>mg/dL; systolic BP <math>\leq 90</math> mm Hg; hematocrit <math>&gt; 45\%</math>; unattainable venous access; requirement for IV pressors; vasoactive drug use during hospitalization before randomization; used of iodinated radiocontrast; comorbidities expected to prolong hospitalization; contraindication to anticoagulation; systemic infection; heart transplant;</li> <li>• Primary end points: weight loss and dyspnea at 48 hrs after randomization;</li> <li>• Secondary endpoints: 48 hr functional capacity;</li> </ul>	<p><b>200 patients randomized:</b></p> <ul style="list-style-type: none"> <li>• 100/group;</li> <li>• <math>63 \pm 15</math> years;</li> <li>• 79% male;</li> <li>• 71% with EF <math>\leq 40\%</math>.</li> </ul> <p><b>Results:</b></p> <ul style="list-style-type: none"> <li>• At 48 hrs: weight (<math>5.0 \pm 3.1</math>kg vs. <math>3.1 \pm</math>kg; <math>p = 0.001</math>) and net fluid loss (<math>4.6</math> vs. <math>3.1</math> L; <math>p = 0.001</math>) were greater in UF group;</li> <li>• Dyspnea scores were similar;</li> <li>• At 90 days: UF group had fewer patients hospitalized for HF (18% vs. 32%; <math>P = 0.037</math>); HF rehospitalizations (<math>0.22 \pm 0.54</math> vs. <math>0.46 \pm 0.76</math>; <math>P = 0.022</math>); rehospitalization days/patient (<math>1.4 \pm 4.2</math> vs. <math>3.8</math>; <math>P = 0.022</math>); and unscheduled visits (21% vs. 44%; <math>P = 0.009</math>);</li> <li>• No serum creatinine differences between groups;</li> <li>• Deaths: 9 in UF group; 11 in diuretics group.</li> </ul> <p><b>Conclusions:</b> <i>“In decompensated HF, ultrafiltration safely produces greater weight and fluid loss than intravenous diuretics, reduces 90-day resource utilization for HF, and is an effective alternate therapy.”</i></p>

Citation	Design/methods	Results/Conclusions
	<p>HF re-hospitalizations or unscheduled visits in 90 days;</p> <ul style="list-style-type: none"> <li>Safety endpoints: renal function; electrolytes; blood pressure.</li> </ul>	
<b>Subsequently published review-eligible primary studies for ultrafiltration</b>		
<p>Costanzo (2010)</p>	<p>RCT:</p> <ul style="list-style-type: none"> <li>Patients over 18 yrs hospitalized for HF (28 US centers with experience in ultrafiltration) with <math>\geq 2</math> signs of hypervolemia randomized to UF or IV diuretics and followed 90 days or until death;</li> <li>All patients had dietary sodium and fluid restrictions;</li> <li>Power calculations implied (100 subjects/arm) but not explicitly reported;</li> <li>Not blinded;</li> <li>Sponsored by and with investigator ties to device manufacturer;</li> <li>Exclusions: acute coronary syndrome; serum creatinine <math>&gt; 3.0</math> mg/dL; systolic BP <math>\leq 90</math> mm Hg; hematocrit <math>&gt; 45\%</math>; unattainable venous access; requirement for IV pressors; vasoactive drug use during hospitalization before randomization; used of iodinated radiocontrast; comorbidities expected to prolong hospitalization; contraindication to anticoagulation; systemic infection; heart transplant;</li> <li>Primary end points: weight loss and dyspnea at 48 hrs after randomization;</li> <li>Secondary endpoints: 48 hr functional capacity; HF re-hospitalizations or unscheduled visits in 90 days;</li> <li>Safety endpoints: renal function; electrolytes; blood pressure.</li> </ul>	<p><b>100 subjects/group:</b></p> <ul style="list-style-type: none"> <li>UF or standard IV diuretics as continuous infusion (32) or bolus injection (68) by choice of treating physician;</li> <li>48 hr weight loss reported in Costanzo (2007), above;</li> <li>At 90 days: UF group had fewer patients hospitalized for HF than continuous IV infusion or bolus injection (18% vs. 39% vs. 29%; <math>P = 0.054</math>); HF rehospitalizations (<math>0.23 \pm 0.54</math> vs. <math>0.54 \pm 0.79</math> vs. <math>0.42 \pm 0.75</math>; <math>P = 0.046</math>); rehospitalization days/patient (<math>1.4 \pm 4.1</math> vs. <math>4.9 \pm 10.5</math>; <math>P = 0.044</math>); and unscheduled visits (22% vs. 52% vs. 40%; <math>P = 0.015</math>);</li> <li>No serum creatinine differences between groups;</li> <li>Deaths: 9 in UF group; 11 in diuretics group.</li> </ul> <p><b>Conclusions:</b> <i>“Despite similar weight loss with UF and continuous diuretic infusion, fewer HF hospitalizations occurred only with UF. Removal of isotonic fluid by HF compared with hypotonic urine by diuretics more effectively reduces total body sodium in congested HF patients.”</i></p>
<p>Allen (2010)</p>	<p>RCT: continuous vs. bolus diuretics for patients hospitalized with HF and volume overload:</p> <ul style="list-style-type: none"> <li>Duke University Medical Center, 1999-2005;</li> </ul>	<p><b>41 subjects (21 bolus, 20 continuous):</b></p> <ul style="list-style-type: none"> <li>NS differences for baseline characteristics except gender: mean age, <math>60 \pm 15</math> yrs; mean ejection fraction, <math>35 \pm 19\%</math>, mean creatinine, <math>1.9 \pm 1.2</math> mg/dl;</li> </ul>

Citation	Design/methods	Results/Conclusions
	<ul style="list-style-type: none"> <li>• Eligibility for trial: primary diagnosis, ADHF; &lt; 24 hrs from hospital presentation; volume overload (pulmonary congestion on x-ray or pro-BNP. Upper limit of normal for age);</li> <li>• Exclusions: ESRD or anticipated need for renal replacement therapy, pregnancy, not expected to survive;</li> <li>• Computer-generated randomization;</li> <li>• Sample size calculation: 41 subjects;</li> <li>• Blinding not reported.</li> </ul>	<ul style="list-style-type: none"> <li>• Mean furosemide doses similar over first 48 hours;</li> <li>• NS differences in outcomes to hospital day 3 or discharge and all patients survived to discharge.</li> </ul> <p><b>Conclusions:</b> <i>“There were no substantial differences between bolus injection and continuous infusion of equal doses of furosemide for the treatment of patients hospitalized with heart failure. Given the high prevalence of heart failure hospitalization and the disparate results of small studies regarding optimal dosing of loop diuretics to treat these patients, larger multicenter blinded studies are needed.”</i></p>
Rogers (2008)	<p>RCT:</p> <ul style="list-style-type: none"> <li>• Consequences of UF vs. standard IV diuretic (furosemide) on renal function;</li> <li>• Patient selection: hospitalized for ADHF; EF&lt; 40%; ≥ 2 signs of hypervolemia;</li> <li>• Primary outcomes: GFR (iothalamate), renal plasma flow (measured by para-aminohippurate); before fluid removal and at 48 hrs;</li> <li>• Secondary end points: urine output and net fluid removal at 48 hrs.</li> </ul>	<p>19 patients (59±16 yrs; 68% male):</p> <ul style="list-style-type: none"> <li>• 9 randomized to UF, 10 to IV furosemide;</li> <li>• Change in GFR (-3.4 ±7.7 ml/min vs. -3.6 ± 115 ml/min; p = .966) and filtration fraction (-6.9 ± 13.6 ml/min vs.. -3.9 ± 13.6ml/min; p = .644) after treatment were not significantly different between UF and furosemide groups;</li> <li>• There was no significant difference in net fluid removal (-3211±2345ml for UF vs. -2725±2330ml for furosemide; p = .682);</li> <li>• Urine output during 48 hrs was significantly greater for furosemide (5786 ±2587ml) vs. UF (2286±915ml); p&lt;.001.</li> </ul> <p><b>Conclusions:</b> <i>“During a 48-hour period, UF did not cause any significant differences in renal hemodynamics compared with the standard treatment of intravenous furosemide.”</i></p>
<b>Related reviews/alternate interventions</b>		
Ditewig (2010)	<p><b>Effectiveness of self-management interventions vs. usual care in chronic heart failure: mortality, hospitalizations, QoL:</b></p> <ul style="list-style-type: none"> <li>• Multiple databases, 1966-April 2009;</li> <li>• RCTs evaluating self-management interventions in any format including formal disease management program vs. standard care;</li> <li>• &gt; 18 yrs; no exclusions for severity of disease, literacy, or ethnic group.</li> </ul>	<p><b>19 studies:</b></p> <ul style="list-style-type: none"> <li>• All reported method of randomization and interventions focused on patient education;</li> <li>• 7 did not report blinding: possible selection bias; 7 had baseline differences between groups but did not report adjustment;</li> <li>• Mortality effects: 9 studies (1988 subjects): one study reported significant difference; others, NS;</li> <li>• All-cause hospital readmission: 8 studies (2248 subjects) with mean FU 3098 days: two studies found significant reductions; other 6, NS; but short FU and baseline severity differences;</li> <li>• QoL: 14 studies (2311 subjects) mean FU, 362 days: baseline differences and different QoL instruments.</li> </ul> <p><b>Conclusions:</b> <i>“Currently available studies have methodological shortcomings which might impair validation of self-management intervention effectiveness for mortality, hospitalization and QoL. There is a need for well-designed studies including patient populations with severe co-morbidity and</i></p>

Citation	Design/methods	Results/Conclusions
		<i>psychological disorders, besides recruiting from combined healthcare facilities (primary as well as secondary)."</i>
Inglis (Cochrane; 2010)	<b>Telephone support or telemonitoring vs. standard practice for patients with CHF:</b> <ul style="list-style-type: none"> <li>• Multiple databases, -November 2008;</li> <li>• Peer-reviewed RCTs comparing structured telephone support/telemonitoring to usual care, neither including a home visit or longer than usual (4-6 weeks) clinic FU;</li> <li>• Unpublished abstract data used in sensitivity analyses.</li> </ul>	<b>25 RCTs; 5 published abstracts:</b> <ul style="list-style-type: none"> <li>• 16 RCTs (5613 subjects) evaluated telephone support, 11 (2710) telemonitoring, 2 (included in previous counts) both;</li> <li>• Telemonitoring reduced all-cause mortality: RR, 0.66 (CI, 0.54-0.82; P&lt;0.0001);</li> <li>• Structured telephone support had NS positive effect: RR, 0.88 (CI, 0.67-0.94; P = 0.008);</li> <li>• Both reduced CHF-related hospitalizations: telephone support (RR, 0.77; CI, 0.68-0.87; P&lt;0.0001); telemonitoring (RR, 0.79; CI, 0.67-0.95; P = 0.008); improved QoL in several studies; reduced costs; and were acceptable to patients;</li> <li>• Improvements in prescribing, patient knowledge/self-care, and NYHA functional class were observed.</li> </ul> <p><b>Conclusions:</b> <i>"Structured telephone support and telemonitoring are effective in reducing the risk of all-cause mortality and CHF-related hospitalizations in patients with CHF; they improve quality of life, reduce costs, and improve evidence-based prescribing."</i></p>
Kramer (2010)	<b>Relationship between therapy-induced left ventricular remodeling and longer-term outcomes in patients with LV dysfunction:</b> <ul style="list-style-type: none"> <li>• Medline, - April 2007: large double-blind (except for devices) RCTs evaluating effects of drugs or devices on mortality in CHF (mortality trials);</li> <li>• Second search for articles (-1999) evaluating effects of those interventions and associations with outcomes on remodeling from imaging studies (remodeling trials);</li> <li>• Excluded mortality trials: duplicate publications; meeting abstracts; &lt; 6 mo FU; non-English language; &lt; 500 subjects;</li> <li>• Excluded (remodeling trials): no measurement of LVEF, volume or dimension; FU &lt; 4 weeks.</li> </ul>	<b>30 large RCTs for effects of 25 interventions on mortality:</b> <ul style="list-style-type: none"> <li>• 69,766 subjects with median FU 17 months;</li> <li>• For each intervention mortality trial: 1-22 remodeling trials with 91 drug or device vs. placebo comparisons following 19,921 subjects for median 6 months;</li> <li>• OR for death in mortality trials correlated with effects on LVEF (<math>\rho = -0.51</math>; P&lt;0.01); EDV (<math>\rho = 0.44</math>; P &lt;0.002); ESV (<math>\rho = 0.48</math>; P = 0.0002).</li> </ul> <p><b>Conclusions:</b> <i>"In patients with LVD, short-term, trial-level therapeutic effects of a drug or device on LV remodeling are associated with longer-term-trial-level effects on mortality."</i></p>
Porapakkham (2010)	<b>Benefit of BNP in guiding treatment of CHF:</b> <ul style="list-style-type: none"> <li>• Multiple databases, -Dec 2008;</li> <li>• RCTs in outpatients with CHF;</li> </ul>	<b>8 RCTs (1726 patients):</b> <ul style="list-style-type: none"> <li>• Mean duration, 6 months (3-24);</li> <li>• Significantly lower risk of all-cause mortality (RR, 0.76; CI, 0.63-0.91; P = .003) for BNP group;</li> </ul>

Citation	Design/methods	Results/Conclusions
	<ul style="list-style-type: none"> <li>Excluded from meta-analysis: ≤20 patients; outcome reported in single study only; or unit of measurement (hospitalizations vs. number of patients hospitalized) precluding meta-analyses.</li> </ul>	<ul style="list-style-type: none"> <li>Subgroup &lt; 75 yrs all-cause mortality also lower (RR, 0.52; CI, 0.33-0.82); P = .005;</li> <li>No reduction in mortality &gt; 75 yrs (RR, 0.94; CI, 0.85-1.34; P = .58);</li> <li>Additional % of patients achieving ACE inhibitor or β-blocker dose targets during trial; 21 and 22 in BNP group, 11.7 vs. 11.7 and 12.5 for usual care.</li> </ul> <p><b>Conclusions:</b> <i>“B-type natriuretic peptide-guided therapy reduces all-cause mortality in patients with chronic HF compared with usual clinical care, especially in patients younger than 75 years. A component of this survival benefit may be due to increased use of agents proven to decrease mortality in chronic HF. However, there does not seem to be a reduction in all-cause hospitalization or an increase in survival free of hospitalization using this approach.”</i></p>
Zhou (2010)	<p><b>N-terminal pro-brain natriuretic peptide for diagnosis of pleural effusion due to heart failure:</b></p> <ul style="list-style-type: none"> <li>Multiple databases, -September 2009;</li> <li>English-language articles addressing diagnostic accuracy (Se, Sp) of NT-proBNP for pleural effusion;</li> <li>Reference standard: multiple tests/clinical criteria (chest radiographs, echocardiogram, response to diuretics);</li> <li>Quality assessment by STARD and QUADAS criteria;</li> <li>Synthesis of results by summary ROC curves.</li> </ul>	<p><b>8 studies (369 cardiac cases/538 controls):</b></p> <ul style="list-style-type: none"> <li>Mean sample size/study, 113 (28-240);</li> <li>Summary estimate pleural NT-proBNP for diagnosis of effusion due to HF: Se, 0.95; (CI, 0.92-0.97); Sp, 0.94 (0.92-0.96); PPV, 14.12 (10.23-19.51); NPV, 0.06 (0.04-0.09); diagnostic OR, 213.87(122.50-373.40).</li> </ul> <p><b>Conclusions:</b> <i>“NT-proBNP levels in pleural fluid showed a high diagnostic accuracy and may help accurately differentiate cardiac from non-cardiac conditions in patients presenting with pleural effusion.”</i></p>
Klersy (2009)	<p><b>Effects of remote monitoring on CHF:</b></p> <ul style="list-style-type: none"> <li>Interventions: Regularly scheduled structured telephone contact or data transmission (via external, wearable, or implantable electronic devices) vs. usual care (in-person MD visits; office, clinic, or ED);</li> <li>Multiple databases – October 2008;</li> <li>RCTs or cohort studies: peer-reviewed full-text published in English Spanish, German, French, or Italian;</li> <li>Evaluated for adherence to CONSORT and STROBE statements (10 point scale);</li> <li>Meta-analysis for primary end points (cumulative mortality or rehospitalization events incidence): RPM vs. usual care;</li> </ul>	<p><b>20 RCTs (6258 subjects with median FU 6 months) and 12 cohort (2354 for 12 months):</b></p> <ul style="list-style-type: none"> <li>RPM significantly associated with lower number of deaths: RR, 0.83 (CI, 0.73-0.95; P = 0.006) in RCTs; RR, 0.53 (0.29-0.96; p &lt;0.001) in cohorts;</li> <li>RPM also significantly associated with decreased hospitalizations: RR, 0.93 (0.87-0.99; p=0.30) in RCTs; RR, 0.52 (0.28-0.96; p&lt;0.001) in cohorts;</li> <li>Decrease in events greater in cohort studies than in RCTs.</li> </ul> <p><b>Conclusions:</b> <i>“RPM confers a significant protective effect in patients with chronic HF compared with usual care.”</i></p>

Citation	Design/methods	Results/Conclusions
	<ul style="list-style-type: none"> <li>Sensitivity and publication bias analyses.</li> </ul>	
Polisena (2009)	<p><b>Home telehealth for chronic disease management:</b></p> <ul style="list-style-type: none"> <li>Multiple databases, 1998-2008;</li> <li>Economic evaluations (including cost studies with assumption that telehealth is at least as effective as usual care);</li> <li>Quality assessment by modified Drummond scale for economic evaluations.</li> </ul>	<p><b>22 studies:</b></p> <ul style="list-style-type: none"> <li>Majority from US; others from Italy, Spain, UK, Canada;</li> <li>21 studies were simple cost analyses, one cost-utility study;</li> <li>Heterogeneity precluded meta-analysis;</li> <li>Most focused on CHF; other diagnoses included diabetes, COPD; or multiple including CHF or COPD;</li> <li>Usual care variably defined: organized home care, other support program, or MD-directed care with/without home care;</li> <li>Results inconsistent and study quality poor.</li> </ul> <p><b>Conclusions:</b> <i>“Current evidence suggests that home telehealth has the potential to reduce costs, but its impact from a societal perspective remains unclear until higher quality studies become available.”</i></p>
Felker (2009)	<p><b>Does titration of therapy based on BNP measurement improve mortality in chronic heart failure?</b></p> <ul style="list-style-type: none"> <li>Multiple databases and meeting proceedings, 1996-2009;</li> <li>Prospective RCTs enrolling patients with heart failure and titrating medical therapy by circulating BNP levels vs. parallel control group; reporting all-cause mortality;</li> <li>No language or publication restrictions;</li> <li>Meta-analysis with sensitivity analyses.</li> </ul>	<p><b>6 RCTs (1627 patients):</b></p> <ul style="list-style-type: none"> <li>Significant mortality advantage for biomarker-guided therapy: HR, 0.69 (CI, 0.55-0.86) without evidence of heterogeneity.</li> </ul> <p><b>Conclusions:</b> <i>“Titration of therapy incorporating serial BNP or N-terminal pro-B-type natriuretic peptide levels is associated with a significant reduction in all-cause mortality compared to usual care in patients with chronic heart failure.”</i></p>
Balion (AHRQ; 2006)	<p><b>Testing for BNP and NT-proBNP in the diagnosis and prognosis of heart failure, addressing these 4 research questions:</b></p> <ol style="list-style-type: none"> <li>Determinants</li> <li>Diagnostic performance in HF</li> <li>Predictive ability for mortality and other cardiac endpoints</li> <li>Value in monitoring treatment.</li> </ol> <ul style="list-style-type: none"> <li>Multiple databases, 1989- Feb 2005;</li> <li>English-language studies measuring BNP and</li> </ul>	<p><b>Conclusions by research question (listed in column to left):</b></p> <ol style="list-style-type: none"> <li><i>“Numerous factors show associations with BNP and NT-proBNP, but value for clinical use is unclear and future research should explore associations, particularly as a function of HF severity.”</i></li> <li><i>“In all settings (ED, specialized clinics, and primary care) both BNP and NT-proBNP have high sensitivity and lower specificity. This would suggest that these measures could serve as a test for ruling out cardiac dysfunction. Measurement of B-type natriuretic peptide levels adds independent information to traditional diagnostic measures for this condition. Large multicenter trials (especially in ED with complex clinical patients) that allow for multivariate analyses to</i></li> </ol>

Citation	Design/methods	Results/Conclusions
	<p>NT-proBNP by methods available to clinical laboratories;</p> <ul style="list-style-type: none"> <li>Quality assessment according to research question: QUADAS for diagnostic accuracy;</li> <li>Qualitative synthesis and meta-analysis.</li> </ul>	<p><i>evaluate variables that contribute to low specificity should be undertaken in the future.</i>"</p> <p>3. "BNP and NT-proBNP have been shown to be independent predictors of mortality and other cardiac composite endpoints for populations with risk of CAD, diagnosed CAD, and diagnosed HF. There were few studies which evaluated B-type natriuretic peptide in populations without known heart failure. All but a single study suggest that these are not sufficiently accurate to be an effective screening test for unrecognized left ventricular dysfunction. Future research should explore the relative merits of b-type natriuretic peptides compared to and combined with other markers of cardiac dysfunction to predict future outcomes."</p> <p>4. "Here is insufficient evidence to demonstrate that BNP and NT-proBNP levels show change in response to therapies to manage the stable chronic HF patient. Future research could include large randomized trials to show whether therapy guided by changes in B-type natriuretic peptides affects outcome."</p>
Faris (Cochrane; 2006)	<p><b>Harms and benefits of diuretics for chronic heart failure:</b></p> <ul style="list-style-type: none"> <li>Multiple databases, 1990-June 2008;</li> <li>RCTS: one diuretic vs. Placebo, one diuretic vs. another active agent (ACE inhibitor; digoxin);</li> <li>Quality assessment criteria: method of treatment allocation/randomization; blinding; completeness of follow-up; handling of withdrawals and exclusions.</li> </ul>	<p><b>14 trials (525 subjects):</b></p> <ul style="list-style-type: none"> <li>Publication dates 1977-1997;</li> <li>Methodologic quality inconsistent: 4/15 used parallel-group design; remainder crossover or withdrawal; most trials too small for adequate statistical power;</li> <li>3 placebo-controlled trials reported mortality data: lower for diuretic than placebo (OR, 0.24; CI, 0.07-0.83; P = 0.02); admissions for worsening heart failure reduced in diuretic groups (OR, 0.07; CI, 0.01-0.52; P = 0.01);</li> <li>4 trials compared diuretic to other agent: diuretic improved exercise capacity (WMD, 0.72; CI, 0.40-1.04; P&lt;0.0001).</li> </ul> <p><b>Conclusions:</b> "The available data from several small trials show that in patients with chronic heart failure, conventional diuretics appear to reduce the risk of death and worsening of heart failure compared to placebo. Compared to active control, diuretics appear to improve exercise capacity."</p>
Roccaforte (2005)	<p><b>Do disease management programs improve outcomes in heart failure?</b></p> <ul style="list-style-type: none"> <li>Multiple database, - December 2004;</li> <li>RCTs enrolling HF patients receiving comprehensive disease management vs. usual care followed in outpatient setting and reporting mortality (HF-specific, all-cause) or rehospitalizations;</li> <li>No language restriction;</li> <li>Quality assessment by Cochrane criteria</li> </ul>	<p><b>33 RCTs:</b></p> <ul style="list-style-type: none"> <li>DMP interventions varied widely: multidisciplinary as defined by investigators (most common, in 7 trials); specialist nurse or pharmacist programs; patient or family education; time of initiation and length of FU varied;</li> <li>Usual care also variable and not consistently well-defined;</li> <li>Mortality reduced by DMP: OR, 0.80 (CI, 0.69-0.93; p = 0.003);</li> <li>All-cause and HF readmissions reduced: OR, 0.76 (CI, 0.69-0.94; p&lt;0.00001);</li> <li>Sensitivity analyses: different DMP approaches apparently equally effective.</li> </ul> <p><b>Conclusions:</b> "DMPs significantly reduce mortality and hospitalizations in HF patients. Because</p>

Citation	Design/methods	Results/Conclusions
	<p>(randomization procedure, blinding, ITT analysis, losses to FU);</p> <ul style="list-style-type: none"> <li>• Excluded: subjects included non-HF or data for HF could not be separated; comparison between 2 active interventions without usual care control;</li> <li>• Sensitivity analyses for study quality and program components;</li> <li>• Publication bias assessment.</li> </ul>	<p><i>various types of DMP appear to be similarly effective, the choice of specific programs depends on local health services characteristics, patient population, and available resources.</i>"</p>
<p>Salvador (Cochrane; 2005)</p>	<p><b>Effects and adverse effects of continuous infusion vs. bolus injection of loop diuretics in acutely decompensated heart failure:</b></p> <ul style="list-style-type: none"> <li>• Multiple databases, 1966-2003;</li> <li>• RCTs: continuous infusion vs. bolus IV injection in HF classes III-IV;</li> <li>• Quality assessment by Cochrane criteria.</li> </ul>	<p><b>8 trials (254 subjects):</b></p> <ul style="list-style-type: none"> <li>• Most included trials had low risk for selection, performance, or detection bias, no risk for exclusion bias; all were eligible for meta-analysis;</li> <li>• 7 studies reported urine output: greater for infusion group (WMD, 271cc/24 hr; CI, 93.1-449; p&lt;0.01);</li> <li>• NS differences in electrolyte disturbance;</li> <li>• Lower rate of adverse effects (tinnitus or hearing loss) for infusion (RR, 0.06; CI, 0.01-0.44; p = 0.005);</li> <li>• One study reported LOS; shortened with infusion (WMD, -3.1; CI, -4.06 - -2.20 p&lt;0.0001);</li> <li>• Two studies reported all-cause mortality: better for infusion (RR, 0.52 CI, 0.38-0.71; p&lt;0.0001); cardiac mortality (RR, 0.47; CI, 0.33-0.69; p &lt;0.0001).</li> </ul> <p><b>Conclusions:</b> <i>"Currently available data are insufficient to confidently assess the merit of two methods of giving intravenous diuretics. Based on small and relatively heterogeneous studies, this review showed greater diuresis and a better safety profile when loop diuretic were given as continuous infusion. The existing data does not allow definitive recommendations for clinical practice and larger studies should be done to adequately settle this issue."</i></p>
<p>Masip (2005)</p>	<p>Systematic review: <b>noninvasive ventilation in acute cardiogenic pulmonary edema:</b></p> <ul style="list-style-type: none"> <li>• Multiple databases, 1988-2005;</li> <li>• RCTs, parallel studies and systematic reviews comparing noninvasive ventilation to conventional oxygen therapy in patients with acute pulmonary edema; CPAP or bilevel NIPSV also included.</li> </ul>	<p><b>15 parallel studies:</b></p> <ul style="list-style-type: none"> <li>• Overall, noninvasive ventilation significantly reduced mortality rate by 45% Vs. conventional therapy (RR, 0.55; CI, 0.40-0.78; P= .72);</li> <li>• Rates significant for CPAP (RR, 0.53; CI, 0.35-0.82; P = .44) but not for NIPSV (RR, 0.60; CI, 0.34-1.05; P = .76);</li> <li>• Both modalities showed significant decrease in need to intubate rate: CPAP (RR, 0.40; CI, 0.27-0.58; P = .21); NIPSV (RR, 0.48; CI, 0.32-0.57; P = .20); together (RR, 0.43; CI, 0.32-0.57; P = .20);</li> <li>• There were no differences in intubation or mortality rates in the analysis of studies comparing the 2 techniques.</li> </ul>

Citation	Design/methods	Results/Conclusions
		<p><b>Conclusions:</b> <i>“Noninvasive ventilation reduces the need for intubation and mortality in patients with acute cardiogenic pulmonary edema. Although the level of evidence is higher for CPAP, there are no significant differences in clinical outcomes when comparing CPAP vs. NIPSV.”</i></p>
<p>McAlister (2004)</p>	<p><b>Do multidisciplinary strategies for management of CHF improve outcomes?</b></p> <ul style="list-style-type: none"> <li>• Multiple database, - 2003;</li> <li>• RCTs;</li> <li>• Meta-analysis planned.</li> </ul>	<p><b>29 RCTs (5039 subjects):</b></p> <ul style="list-style-type: none"> <li>• Overall meta-analysis precluded by heterogeneity but a priori groupings for homogeneous interventions were meta-analyzed;</li> <li>• FU care by specialized multidisciplinary team (clinic or non-clinic) reduced HF mortality (RR, 0.75; CI, 0.59-0.96); HF hospitalizations (RR, 0.74; CI, 0.63-0.87); and all-cause hospitalizations (RR, 0.73; CI, 0.52-0.83);</li> <li>• Programs focused on enhancing patient self-care reduced HF hospitalizations (RR, 0.75; CI, 0.57-0.99) but not mortality (RR, 1.14; CI, 0.67-1.94) or all-cause hospitalization (RR, 0.98; CI, 0.809-1.20);</li> <li>• In 15/18 trials evaluating costs: multidisciplinary strategies were cost-saving.</li> </ul> <p><b>Conclusions:</b> <i>“Multidisciplinary strategies for the management of patients with HF reduce HF hospitalizations. Those programs that involve specialized follow-up by a multidisciplinary team also reduce mortality and all-cause hospitalization.”</i></p>
<p>Phillips (2004)</p>	<p><b>Does comprehensive discharge planning and post-discharge support reduce readmission rates for older patients with CHF?</b></p> <ul style="list-style-type: none"> <li>• Multiple databases, -October 2003;</li> <li>• English-language RCTs with detailed descriptions of interventions to modify hospital discharge for CHF patients &gt; 55; vs. usual care and reporting readmission rates;</li> <li>• Quality assessment: method of randomization; blinding; loss to FU;</li> <li>• Publication bias assessed for primary and secondary outcomes.</li> </ul>	<p><b>18 studies from 8 countries (3304 subjects):</b></p> <ul style="list-style-type: none"> <li>• Pooled mean FU, 8 months (3-12);</li> <li>• Fewer intervention patients readmitted vs. controls (555/1590 and 741/1714); RR, 0.75 (CI, 0.64-0.88); NNT, 12;</li> <li>• Secondary outcomes (10 studies): trend to lower all-cause mortality for intervention vs. usual care: RR 0.87 (CI, 0.73-1.03)   p = .60; greater % QoL improvement over baseline (RR, 25.7; CI, 11.0-40.4); and similar or lower charges for medical care per patient per month during index hospitalization, administering intervention, outpatient care and readmission (-\$369; CI, -\$763-\$45; p = .10) for 4 non-US studies and -\$546 ; CI, -\$956--\$115  P = .03) for US studies.</li> </ul> <p><b>Conclusions:</b> <i>“Comprehensive discharge planning plus post-discharge support for older patients with CHF significantly reduced readmission rates and may improve health outcomes such as survival and QoL without increasing costs.”</i></p>

**Table 3. Ongoing studies of ultrafiltration for heart failure**Listed by NIH at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (accessed 10/6/10)

Does not include withdrawn, discontinued, completed or no longer recruiting trials

Purpose/details	Location	Projected completion (if noted)
UF vs. diuretics in ACHF with cardiorenal syndrome: <ul style="list-style-type: none"> <li>• Which therapy is limited by worsening renal function?</li> <li>• N=186 RCT</li> </ul>	Italy	March 2012
UF vs. diuretics: <ul style="list-style-type: none"> <li>• Effects on renal congestion, plasma refill rate, echocardiographic filling pressures, neurohormonal activation, acute kidney injury;</li> <li>• N= 40 RCT</li> </ul>	Belgium	December 2011
Use of blood volume measurement to monitor UF: N= 50 RCT	US private health care system	February 2010
RCT: Effectiveness of UF vs. standard drug treatment for ADHF and cardiorenal syndrome (CARRESS study): <ul style="list-style-type: none"> <li>• Primary outcome: Bivariate (change in weight and creatinine) outcome at 7 days;</li> <li>• Secondary outcomes: weight loss and renal improvement at 7 days; change in renal function at 60 days; change in electrolytes at 7 days; weight change at 60 days; clinical decongestion at 60 days; net fluid loss at 7 days; biomarker change at 60 days; global assessment change at 7 days; LOS; change in oral diuretic dose at 30 and 60 days.</li> </ul>	NHLBI and CHFS; multiple US sites	November 2009
UF vs. usual care: <ul style="list-style-type: none"> <li>• Effects on hemodynamic improvement as measure by pulmonary artery occlusion pressure;</li> <li>• N = 46 RCT</li> </ul>	NxStage Medical (device manufacturer)	January 2009

Table 4. Excluded studies

Citation	Reason for exclusion
Andrade (2010)	Narrative review
Costanzo (2010a)	
Arnold (2007)	
Flessner (2010)	Case report
Dickstein (2010)	Quasi-systematic
Maric (2009)	
HFSA (2006)	
Hunt (2005)	
Bart (2005)	Feasibility trial covered by Colechin (2007)
deLissovoy (2010)	Outside charge
Mohammed (2010)	Not RCT
Sanchez (2010)	Case series
Alvarado (2009)	Pre-clinical
Bagshaw (2008)	Outside charge
Peacock (2009)	Not RCT or CCT
Kollef (2008)	Narrative review
Clark (2007)	Duplicates Inglis (2010)
Jafri (2007)	Outside charge
Nelson (2004)	Narrative review
Rey (2005)	Narrative review
McAlister (2001)	Previous version of McAlister (2004)
Rutala (2001)	Narrative review
Fengler (2000)	Unintelligible
ASGE (1999)	Narrative review
DesCouteaux (1998)	Intermediate outcomes/technical performance
Kimmery (1993)	Narrative review

## VA TECHNOLOGY ASSESSMENT PROGRAM

### ***Mission Statement***

To enhance the health of Veterans and the nation by providing and fostering technology assessment for evidence-based health care

### ***Values***

***Integrity and pride*** in the work that we do

***Quality*** products that are clinically valid and methodologically transparent

***Objectivity*** in evaluating and presenting research evidence

***Commitment*** to continuous quality improvement and to the guiding principles of evidence based practices

***Flexibility*** in responding to changes in VA and the larger healthcare environment

***Innovation*** in designing products and their dissemination to best meet VA's needs

***Accessibility*** of products