

Web Appendix 1:

Literature search strategy

BTS Acute Hypercapnic Respiratory Failure (AHRF) write-up

Sources to be searched for the guidelines;

Cochrane Database of Systematic Reviews (CDSR)
Database of Abstracts of Reviews of Effects (DARE)
MEDLINE and MEDLINE In-Process
EMBASE

Dates searched: 1990 onwards
All study types
English language only
Human only

Cochrane Library (includes CDSR and DARE)

<http://www.thecochranelibrary.com>

Searched online 10/11/10

- #1 MeSH descriptor Asthma explode all trees 8740
- #2 asthma*:ti,ab,kw 19621
- #3 wheez*:ti,ab,kw 925
- #4 MeSH descriptor Bronchial Spasm explode all trees 349
- #5 bronchospas*:ti,ab,kw 998
- #6 (bronch* near/3 spas*):ti,ab,kw 429
- #7 MeSH descriptor Bronchoconstriction explode all trees 491
- #8 bronchoconstrict*:ti,ab,kw 1911
- #9 (bronch* near/3 constrict*):ti,ab,kw 74
- #10 MeSH descriptor Bronchial Hyperreactivity, this term only 526
- #11 MeSH descriptor Respiratory Hypersensitivity, this term only 194
- #12 ((bronchial* or respiratory or airway* or lung*) near/3 (hypersensitiv* or allerg* or insufficiency)):ti,ab,kw 1749
- #13 MeSH descriptor Pulmonary Disease, Chronic Obstructive explode all trees 1656
- #14 ("chronic obstructive pulmonary disease" or COPD):ti,ab,kw 5746
- #15 MeSH descriptor Cystic Fibrosis explode all trees 940
- #16 (cystic* near/3 fibros*):ti,ab,kw 2349
- #17 mucoviscidos*:ti,ab,kw 43
- #18 MeSH descriptor Neuromuscular Diseases explode all trees 4126
- #19 ((neuromuscular* or neuro muscular* or chest wall*) near/1 (disease* or deformit*)):ti,ab,kw 248
- #20 MeSH descriptor Obesity Hypoventilation Syndrome, this term only 6
- #21 "obesity hypoventilation syndrome":ti,ab,kw 12
- #22 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21) 33413
- #23 ((hypercapni* near/10 "respiratory fail*") or AHRF):ti,ab,kw 16
- #24 MeSH descriptor Hypercapnia, this term only 262

#25 MeSH descriptor Respiratory Insufficiency explode all trees 1497
#26 (#24 AND #25) 55
#27 (#23 OR #26) 66
#28 (#22 AND #27), from 1990 to 2010 48

Of 48 results in total Cochrane Library 3 were from Cochrane Database of Systematic Reviews (CDSR) and 1 from Database of Reviews of Effects (DARE).

MEDLINE and MEDLINE In-Process

Searched 10/11/10 via OVID interface

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1950 to Present

- 1 exp Asthma/ (93432)
- 2 asthma\$.ti,ab. (100573)
- 3 wheez\$.ti,ab. (8231)
- 4 exp Bronchial Spasm/ (3968)
- 5 bronchospas\$.ti,ab. (4313)
- 6 (bronch\$ adj3 spas\$).ti,ab. (466)
- 7 exp Bronchoconstriction/ (3412)
- 8 bronchoconstrict\$.ti,ab. (7608)
- 9 (bronch\$ adj3 constrict\$).ti,ab. (542)
- 10 Bronchial Hyperreactivity/ (6039)
- 11 Respiratory Hypersensitivity/ (8074)
- 12 ((bronchial\$ or respiratory or airway\$ or lung\$) adj3 (hypersensitiv\$ or hyperreactiv\$ or allerg\$ or insufficiency)).ti,ab. (18594)
- 13 exp Pulmonary Disease, Chronic Obstructive/ (14840)
- 14 ("chronic obstructive pulmonary disease" or COPD).ti,ab. (25184)
- 15 exp Cystic Fibrosis/ (25090)
- 16 (cystic\$ adj3 fibros\$).ti,ab. (27909)
- 17 mucoviscidos\$.ti,ab. (1364)
- 18 exp Neuromuscular Diseases/ (214713)
- 19 ((neuromuscular\$ or neuro muscular\$ or chest wall\$) adj (disease\$ or deformit\$)).ti,ab. (3840)
- 20 Obesity Hypoventilation Syndrome/ (536)
- 21 "obesity hypoventilation syndrome".ti,ab. (212)
- 22 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (410750)
- 23 ((hypercapni\$ adj10 "respiratory fail\$") or AHRF).ti,ab. (497)
- 24 Hypercapnia/ and exp Respiratory Insufficiency/ (1166)
- 25 23 or 24 (1492)
- 26 22 and 25 (537)
- 27 limit 26 to humans (516)
- 28 limit 27 to english language (337)
- 29 limit 28 to yr="1990 -Current" (266)

EMBASE

Searched 10/11/10 via OVID interface

EMBASE 1980 to 2010 Week 44

- 1 exp Asthma/ (141201)
- 2 asthma\$.ti,ab. (119971)
- 3 wheez\$.ti,ab. (9572)
- 4 exp Bronchospasm/ (18984)
- 5 bronchospas\$.ti,ab. (5045)
- 6 (bronch\$ adj3 spas\$).ti,ab. (489)
- 7 broncho-constrict\$.ti,ab. (138)
- 8 bronchoconstrict\$.ti,ab. (8360)
- 9 (bronch\$ adj3 constrict\$).ti,ab. (585)
- 10 Bronchus Hyperreactivity/ (10884)
- 11 Respiratory tract allergy/ (5750)
- 12 ((bronchial\$ or respiratory or airway\$ or lung\$) adj3 (hypersensitiv\$ or hyperreactiv\$ or allerg\$ or insufficiency)).ti,ab. (21525)
- 13 exp Chronic Obstructive Lung Disease/ (48577)
- 14 ("chronic obstructive pulmonary disease" or COPD).ti,ab. (30332)
- 15 exp Cystic Fibrosis/ (34168)
- 16 (cystic\$ adj3 fibros\$).ti,ab. (30559)
- 17 mucoviscidos\$.ti,ab. (1399)
- 18 exp Neuromuscular Disease/ (102458)
- 19 ((neuromuscular\$ or neuro muscular\$ or chest wall\$) adj (disease\$ or deformit\$)).ti,ab. (4419)
- 20 Obesity Hypoventilation Syndrome/ (698)
- 21 "obesity hypoventilation syndrome".ti,ab. (249)
- 22 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (367416)
- 23 ((hypercapni\$ adj10 "respiratory fail\$") or AHRF).ti,ab. (592)
- 24 Hypercapnia/ and exp Respiratory Failure/ (1396)
- 25 23 or 24 (1666)
- 26 22 and 25 (859)
- 27 limit 26 to humans (793)
- 28 limit 27 to english language (565)
- 29 limit 28 to yr="1990 -Current" (521)

Results

Database	Results	After deduplication	Custom 4 field
Cochrane Database of Systematic Reviews	3	3	CDSR 10/11/10
Database of Abstracts of Reviews of Effects	1	1	DARE 10/11/10
MEDLINE and MEDLINE In-Process	266	260	MEDLINE 10/11/10
EMBASE	521	318	EMBASE 10/11/10
Total	791	582	

All results saved to Endnote X3 library BTS AHRF guidelines.enl

Update searches September 2013

Search strategies as previously except terms for sleep apnea added (lines 22-24 in all strategies).

Cochrane Library (includes CDSR and DARE)

<http://www.thecochranelibrary.com>

Searched online 26/09/13

- #1 MeSH descriptor Asthma explode all trees 8988
- #2 asthma*:ti,ab,kw 21116
- #3 wheez*:ti,ab,kw 1033
- #4 MeSH descriptor Bronchial Spasm explode all trees 353
- #5 bronchospas*:ti,ab,kw 1037
- #6 (bronch* near/3 spas*):ti,ab,kw 435
- #7 MeSH descriptor Bronchoconstriction explode all trees 512
- #8 bronchoconstrict*:ti,ab,kw 1995
- #9 (bronch* near/3 constrict*):ti,ab,kw 77
- #10 MeSH descriptor Bronchial Hyperreactivity, this term only 538
- #11 MeSH descriptor Respiratory Hypersensitivity, this term only 199
- #12 ((bronchial* or respiratory or airway* or lung*) near/3 (hypersensitiv* or allerg* or insufficiency)):ti,ab,kw 1969
- #13 MeSH descriptor Pulmonary Disease, Chronic Obstructive explode all trees 2053
- #14 ("chronic obstructive pulmonary disease" or COPD):ti,ab,kw 7252
- #15 MeSH descriptor Cystic Fibrosis explode all trees 1015
- #16 (cystic* near/3 fibros*):ti,ab,kw 2663
- #17 mucoviscidos*:ti,ab,kw 124
- #18 MeSH descriptor Neuromuscular Diseases explode all trees 4782
- #19 ((neuromuscular* or neuro muscular* or chest wall*) near/1 (disease* or deformit*)):ti,ab,kw 282
- #20 MeSH descriptor Obesity Hypoventilation Syndrome, this term only 6
- #21 "obesity hypoventilation syndrome":ti,ab,kw 21
- #22 MeSH descriptor: [Sleep Apnea, Obstructive] explode all trees 698
- #23 (obstructive near/2 (sleep near/1 apn*)):ti,ab,kw 1680
- #24 (OSA or OSAHS):ti,ab 669
- #22 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) 39284
- #23 ((hypercapni* near/10 "respiratory fail*") or AHRF):ti,ab,kw 119
- #24 MeSH descriptor Hypercapnia, this term only 286
- #25 MeSH descriptor Respiratory Insufficiency explode all trees 1651
- #26 (#24 AND #25) 62
- #27 (#23 OR #26) 156
- #28 (#22 AND #27), from 1990 to 2010 115

Of 115 results in total Cochrane Library 3 were from Cochrane Database of Systematic Reviews (CDSR) and 1 from Database of Reviews of Effects (DARE). All were found in previous searches.

MEDLINE and MEDLINE In-Process

Searched 27/09/13 via OVID interface

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

- 1 exp Asthma/ (109608)
- 2 asthma\$.ti,ab. (124274)
- 3 wheez\$.ti,ab. (10472)
- 4 exp Bronchial Spasm/ (4128)
- 5 bronchospas\$.ti,ab. (4788)
- 6 (bronch\$ adj3 spas\$).ti,ab. (485)
- 7 exp Bronchoconstriction/ (4034)
- 8 bronchoconstrict\$.ti,ab. (8573)
- 9 (bronch\$ adj3 constrict\$).ti,ab. (627)
- 10 Bronchial Hyperreactivity/ (7399)
- 11 Respiratory Hypersensitivity/ (8877)
- 12 ((bronchial\$ or respiratory or airway\$ or lung\$) adj3 (hypersensitiv\$ or hyperreactiv\$ or allerg\$ or insufficiency)).ti,ab. (22143)
- 13 exp Pulmonary Disease, Chronic Obstructive/ (24228)
- 14 ("chronic obstructive pulmonary disease" or COPD).ti,ab. (37278)
- 15 exp Cystic Fibrosis/ (29195)
- 16 (cystic\$ adj3 fibros\$).ti,ab. (34386)
- 17 mucoviscidos\$.ti,ab. (1374)
- 18 exp Neuromuscular Diseases/ (249376)
- 19 ((neuromuscular\$ or neuro muscular\$ or chest wall\$) adj (disease\$ or deformit\$)).ti,ab. (4909)
- 20 Obesity Hypoventilation Syndrome/ (614)
- 21 "obesity hypoventilation syndrome".ti,ab. (300)
- 22 exp Sleep Apnea, Obstructive/ (11665)
- 23 (obstructive adj2 (sleep adj apn*)).ti,ab. (15471)
- 24 (OSA or OSAHS).ti,ab. (7349)
- 25 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 (509093)
- 26 ((hypercapni\$ adj10 "respiratory fail\$") or AHRF).ti,ab. (670)
- 27 Hypercapnia/ and exp Respiratory Insufficiency/ (1304)
- 28 26 or 27 (1750)
- 29 25 and 28 (699)
- 30 limit 29 to humans (663)
- 31 limit 30 to english language (463)
- 32 limit 31 to yr="1990 -Current" (390)

EMBASE

Searched 30/09/13 via OVID interface

EMBASE 1980 to 2013 Week 39

- 1 exp Asthma/ (177683)
- 2 asthma\$.ti,ab. (152226)
- 3 wheez\$.ti,ab. (12953)
- 4 exp Bronchospasm/ (21844)
- 5 bronchospas\$.ti,ab. (5876)
- 6 (bronch\$ adj3 spas\$).ti,ab. (526)
- 7 broncho-constrict\$.ti,ab. (158)

- 8 bronchoconstrict\$.ti,ab. (9403)
- 9 (bronch\$ adj3 constrict\$).ti,ab. (712)
- 10 Bronchus Hyperreactivity/ (11818)
- 11 Respiratory tract allergy/ (7357)
- 12 ((bronchial\$ or respiratory or airway\$ or lung\$) adj3 (hypersensitiv\$ or hyperreactiv\$ or allerg\$ or insufficiency)).ti,ab. (26959)
- 13 exp Chronic Obstructive Lung Disease/ (67738)
- 14 ("chronic obstructive pulmonary disease" or COPD).ti,ab. (48181)
- 15 exp Cystic Fibrosis/ (45596)
- 16 (cystic\$ adj3 fibros\$).ti,ab. (40999)
- 17 mucoviscidos\$.ti,ab. (1464)
- 18 exp Neuromuscular Disease/ (128222)
- 19 ((neuromuscular\$ or neuro muscular\$ or chest wall\$) adj (disease\$ or deformit\$)).ti,ab. (5759)
- 20 Obesity Hypoventilation Syndrome/ (918)
- 21 "obesity hypoventilation syndrome".ti,ab. (396)
- 22 exp sleep disordered breathing/ (8656)
- 23 (obstructive adj2 (sleep adj apn*)).ti,ab. (20263)
- 24 (OSA or OSAHS).ti,ab. (10232)
- 25 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 (495526)
- 26 ((hypercapni\$ adj10 "respiratory fail\$") or AHRF).ti,ab. (857)
- 27 Hypercapnia/ and exp Respiratory Failure/ (1816)
- 28 26 or 27 (2257)
- 29 25 and 28 (1233)
- 30 limit 29 to humans (1131)
- 31 limit 30 to english language (871)
- 32 limit 31 to yr="1990 -Current" (827)
- 33 limit 32 to embase (771)

Results

Database	Results	After deduplication against previous results	After deduplication	Custom 4 field
Cochrane Database of Systematic Reviews	3	0	0	n/a
Database of Abstracts of Reviews of Effects	1	0	0	n/a
MEDLINE and MEDLINE In-Process	390	65	65	MEDLINE update 27/09/13
EMBASE	771	287	243	EMBASE update 30/09/13
Total	1165	352	308	

All 308 results saved to Endnote X6 library BTS AHRF guideline update 2013.enl

Clinical questions

NIV

1. Indication for NIV and comparison with conservative and invasive mechanical ventilation

COPD

In which patients should NIV be the first line treatment

When should we use NIV in these patient groups?

What arterial blood gas values should determine when ventilatory support should be started

What physiological parameters indicate need for NIV

Are there direct comparisons between NIV and IMV in patients with COPD

Other conditions

How do other patients with hypercapnic exacerbation differ from those with COPD (group for which there is the largest evidence base by far)

Neuromuscular disease – For this consider both acute (de novo) and acute on chronic

Obesity hypoventilation

Chest wall deformity

2. Contra-indications and adverse patient characteristics

What are the contra-indications for NIV

Relative

Absolute

What is the evidence for these contraindications

Is there positive evidence of harm or just consensus

What investigations should be performed prior to starting NIV

Key words

Side effects

Limitations

3. Machines, masks, modes, and monitoring

What type of machine is best and/or safest for delivering acute NIV?

Pressure, volume, proportional assist ventilation (PAV), volume assured pressure support, neurally adjusted ventilatory assist (NAVA)

Pressure support v pressure control

Is there a role for negative pressure ventilation?

What settings should be chosen when NIV initiated

What are the best interfaces to use?

What patient characteristics determine which interface best first choice

Full face mask, nasal mask, nasal pillows, helmet, total face mask

Where should exhalation port be positioned

What infection control measures should be taken

What parameters should be monitored and when

Continuous or intermittent (frequency)

Respiratory rate, arterial blood gas tensions, pulse rate, expired tidal volume, leak, measure of synchrony, Visual analogue comfort scores, Visual analogue dyspnoea scores

Should humidifiers be used

Heated

Cold

Heat and moisture exchangers

Should sedation be used

How should oxygen be used during acute NIV - when and how?

How should patients receiving NIV receive nebulised drugs?

What are the appropriate clinical environs for management of acute hypercapnic respiratory failure?

What recommendations can be made about equipment and monitoring? (do not include ventilators)

What recommendations can be made about staffing and skill / training mix for each disease group and environment?

4. Patient pathways ie placement, monitoring and weaning NIV.

What parameters are useful in deciding need for NIV?

What are the primary targets for evaluating effectiveness of treatment? (RR, pH, PCO₂ etc)

In which clinical areas should NIV be delivered? (Are there any specific requirements that determine whether it should be ward or ED, HDU or ICU?)

What clinical parameters determine the best location for providing NIV?

Which staff should provide acute NIV?

What are the specific aspects of NIV that are different from IMV such as communication, nutrition, mobilisation, chest physio etc

How should NIV be weaned?

What physiological parameters should be achieved before NIV is weaned or discontinued?

Should NIV be restarted if patient deteriorates and if needed does this change outcome?

What should be the target number of hours of NIV

In first 24 hours

In total

What are the general care measures which need to be instituted for patients on NIV?

What is the best position for a patient receiving NIV – prone, supine, 45 degrees etc

Is there a role for decontamination of the upper respiratory tract

Should patients have invasive monitoring

Urinary catheters

Central lines

Arterial lines

5. Complications and trouble shooting

How do we adjust the settings for patients not improving?

How should we identify complications and how do we correct them (eg pressure sores)?

What are the complications associated with NIV

How can they be prevented?

Sputum clearance/bronchoscopy/cough assist

Invasive mechanical ventilation (IMV) questions

For each of the following questions the populations under consideration are:

1. Asthma
2. COPD
3. Cystic fibrosis
4. Chest wall and neuromuscular disease (acco. Cochrane)
5. Obesity hypoventilation syndrome
6. Invasively mechanically ventilated patients

Starting IMV

Who should be ventilated? Move to care planning

What are the indications for IMV?

What modes of Ventilation should be employed initially/subsequently?

Where and when?

In which patients should IMV be the first line treatment

What physiological parameters indicate need for IMV

Doing IMV

Add: fluid balance/monitoring, value or use of mini-tracheostomy(including high pressure MV through min trach)

What levels of PaO₂/PaCO₂ should be targeted?

What tidal volume is appropriate?

What is the optimal level of PEEP?

Can PEEP be adjusted to aid triggering and/or reduce gas trapping?

What kind of triggers are available to aid for spontaneous breathing?

When should controlled modes of ventilation be used?

What is the role of care bundles?

Is there a benefit in early mobilisation/ rehabilitation?

Is there a benefit in daily sedation holds?

How should end-expiratory lung volume/ gas-trapping be managed?

How do we manage Patient/Ventilator asynchrony? (include triggering)

Is there a role for Helium/Oxygen mixtures?

Is there a role for sputum clearance/ suctioning?

Is there a role for negative pressure ventilation?

Is there a role for oxygen insufflation? (been suggested via trache to aid weaning)

Stopping IMV

When should patients be weaned from mechanical ventilation?

How should patients be weaned from IMV?

What criteria predict successful extubation?

What is the role of protocols/ automation in weaning?

When is the best time to perform tracheostomy?

Is there a role for spontaneous breathing trials?

Is there a benefit in post-extubation NIV?

Care Planning

For each of the following questions the populations under consideration are:

1. Asthma
2. COPD
3. Cystic fibrosis
4. Chest wall and neuromuscular disease (acco. Cochrane)
5. Obesity hypoventilation syndrome

Factors predictive of outcome that contribute to clinical decision making in acute HRF

What is prognosis after first episode of hypercapnic respiratory failure?

What is prognosis if there are recurrent admissions with HRF?

What is prognosis when chronic daytime ventilatory failure develops?

Does degree of hypoxaemia influence outcome in chronic HRF

What prognostic indices exist for each condition? Are they used, practical and do they have validity?

Does current smoking status affect outcome from acute HRF?

Does the degree of acute acidaemia / hypercapnia affect short term prognosis in acute HRF?

Does presence of CXR changes / pneumonia affect short term prognosis?

Does presence of other organ dysfunction affect short term prognosis?

Mention the following but not in depth:

Does LTOT improve long term outcome?

Does home NIV improve long term outcome?

Does completion of pulmonary rehabilitation improve long term outcome?

Does compliance with any other treatment (smoking cessation, LTOT, bronchodilators, home NIV etc) affect long term prognosis?

Mechanics of delivery of care in acute HRF

Is there evidence that access to NIV or IMV is appropriate in UK hospitals?

Is there evidence that resource allocation is equitable?

Is there evidence for quality assessment of acute NIV or ICU management of AHRF?

These questions should be primarily considered by care planning.

Weaning failure and prolonged ventilation after acute HRF

When is a patient receiving prolonged mechanical ventilation considered to be a weaning failure?

What are the reasons for failure to wean?

What interventions improve outcome in weaning failure?

Do weaning centres improve outcome?

Is there an economic justification for weaning centres?

Who should receive home mechanical ventilation (both non invasive and invasive)?

Patient choice and advance care plans (ACP) in acute HRF

Do care plans reduce or prevent unwanted hospital admission, intubation or CPR?

Are there international differences in use and attitude towards ACPs?

How should an ACP be formulated?

What are the resource implications of ACPs?

What are the professional responsibilities (medical, nursing etc) in promoting ACPs?
Is there evidence on longer term quality of life after receiving NIV or invasive mechanical ventilation in each condition?
Is there evidence on short and long term survival after receiving NIV or IMV in each condition?

End of life care in patients with acute HRF

Can end of life be identified in patients with AHRF?
Is there any evidence for how terminal care should be delivered?
Is there a role for specialist palliative care services in AHRF?
Is there an ethical difference between withdrawal of ventilation and withdrawal of other treatments?
Where should discontinuation of ventilation take place?
Are there guidelines available for discontinuing non invasive or IMV?