Supplementary Material

Inhaled therapies targeting prostacyclin pathway in pulmonary hypertension due to COPD: systematic review

**Abdullah A. Alqarni1,2\*, Abdulelah M. Aldhahir3, Heba M. Bintalib4,5, Jaber S. Alqahtani6, Rayan A. Siraj7, Mansour Majrshi8,9, Abdulkareem A. AlGarni10,11, Abdallah Y. Naser12, Sara A. Alghamdi13 and Hassan Alwafi14

1Department of Respiratory Therapy, Faculty of Medical Rehabilitation Sciences, King Abdulaziz University, Jeddah, Saudi Arabia, 2Respiratory Therapy Unit, King Abdulaziz University Hospital, Jeddah, Saudi Arabia, 3Respiratory Therapy Department, Faculty of Applied Medical Sciences, Jazan University, Jazan, Saudi Arabia, 4Department of Respiratory Care, King Saud bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia, 5King Abdullah International Medical Research Centre, Jeddah, Saudi Arabia, 6Department of Respiratory Care, Prince Sultan Military College of Health Sciences, Dammam, Saudi Arabia, 7Department of Respiratory Care, College of Applied Medical Sciences, King Faisal University, Al Ahsa, Saudi Arabia, 8National Heart and Lung Institute, Imperial College London, London, UK, 9Respiratory Medicine, Royal Brompton Hospital, London, UK, 10King Abdulaziz Hospital, The Ministry of National Guard Health Affairs, Al Ahsa, Saudi Arabia, 11King Saud bin Abdulaziz University for Health Sciences, College of Applied Medical Sciences, Al Ahsa, Saudi Arabia, 12Department of Applied Pharmaceutical Sciences and Clinical Pharmacy, Faculty of Pharmacy, Isra University, Amman, Jordan, 13Respiratory Care Department, Mediclinic Almurjan Hospital, Jeddah, Saudi Arabia, 14Faculty of Medicine, Umm Al-Qura University, Mecca, Saudi Arabia**

**\* Correspondence:**Abdullah A. Alqarni; aaalqarni1@kau.edu.sa

**Appendices**

Search strategy for the systematic review

# Table S1: Search strategy in Medline, Embase, Cochrane and Scopus

|  |
| --- |
| **Search strategy in Ovid MEDLINE(R) and embase** |
|  |
| 1 exp Lung Diseases, Obstructive/ 231884 |
| 2 (chronic adj2 (air\* adj2 obstruct\*)).kf,fx,tw. 2305 |
| 3 ((lung\* or pulmon\* or respirat\* or bronchopulmon\*) adj3 obstruct\*).kf,fx,tw. 73558 |
| 4 (COAD or COBD or COPD).kf,fx,tw. 56809 |
| 5 ((centriacinar\* or centrilobular\* or focal or panacinar\* or panlobular\* or pulmonar\*) adj2 emphysem\*).kf,fx,tw. 7378 |
| 6 exp Bronchitis/ 31090 |
| 7 "bronchit\*".ab,kf,ti,fx. 24800 |
| 8 exp Hypoxia/ 87544 |
| 9 hypoxia.kf,fx,tw. 132808 |
| 10 (oxygen adj4 (lack\* or deprivation\*)).kf,fx,tw. 9261 |
| 11 1 or 2 or 3 or 4 or 5 or 6 or 7 278312 |
| 12 8 or 9 or 10 179321 |
| 13 11 or 12 453757 |
| 14 exp Hypertension/ 311077 |
| 15 (hypertension or (blood adj2 pressure\*)).kf,fx,tw. 673464 |
| 16 14 or 15 738087 |
| 17 exp Epoprostenol/ 12873 |
| 18 (Epoprostenol or prostacyclin or treprostinil or iEPO or PGI2 or tyvaso or flolan).kf,fx,tw. 18577 |
| 19 exp Iloprost/ 2110 |
| 20 (iloprost or ventavis).kf,fx,tw. 2625 |
| 21 17 or 18 or 19 or 20 22680 |
| 22 13 and 16 24465 |
| 23 21 and 22 333 |
| 24 Limit 23 to English |
| **Search strategy in Scopus** |
| ( TITLE-ABS-KEY ( \*obstructive AND lung AND diseases\* ) OR TITLE-ABS-KEY ( ( chronic AND air\* AND obstruct\* ) ) OR TITLE-ABS-KEY ( ( coad OR cobd OR copd ) ) OR TITLE-ABS-KEY ( ( ( centriacinar\* OR centrilobular\* OR focal OR panacinar\* OR panlobular\* OR pulmonar\* ) emphysem\* ) ) OR TITLE-ABS-KEY ( bronchitis ) OR TITLE-ABS-KEY ( ( oxygen AND lack\* OR deprivation\* ) ) AND TITLE-ABS-KEY ( hypertension ) OR TITLE-ABS-KEY ( ( hypertension OR ( \*blood AND pressure\* ) ) ) AND TITLE-ABS-KEY ( ( epoprostenol OR prostacyclin OR treprostinil OR iepo OR pgi2 OR tyvaso OR flolan ) ) OR TITLE-ABS-KEY ( iloprost OR ventavis ) ) AND ( LIMIT-TO ( LANGUAGE , "English" ) ) |
| **Search strategy in Cochrane** |
| ID Search Hits |
| #1 MeSH descriptor: [Lung Diseases, Obstructive] explode all trees 20954 |
| #2 (chronic NEXT (air\* and obstruct\*)):ti,ab,kw OR ((coad OR cobd OR copd)):ti,ab,kw OR ((centriacinar\* OR centrilobular\* OR focal OR panacinar\* OR panlobular\* OR pulmonar\* ) NEXT (emphysem\* )):ti,ab,kw OR ((lung\* or pulmon\* or respirat\* or bronchopulmon\*) NEXT (obstruct\*)):ti,ab,kw (Word variations have been searched) 23974 |
| #3 MeSH descriptor: [Bronchitis] explode all trees 1907 |
| #4 (bronchit\*):ti,ab,kw (Word variations have been searched) 4540 |
| #5 #1 or #2 or #3 or #4 39651 |
| #6 MeSH descriptor: [Hypoxia] explode all trees 2433 |
| #7 (hypoxia):ti,ab,kw 7295 |
| #8 (oxygen NEXT (lack\* or deprivation\*)):ti,ab,kw 23 |
| #9 #6 or #7 or #8 7310 |
| #10 #5 or #9 46568 |
| #11 MeSH descriptor: [Hypertension] explode all trees 20110 |
| #12 (hypertension or (blood NEXT pressure\*)):ti,ab,kw 139798 |
| #13 #11 or #12 139798 |
| #14 MeSH descriptor: [Epoprostenol] explode all trees 542 |
| #15 ((Epoprostenol or prostacyclin or treprostinil or iEPO or PGI2 or tyvaso or flolan)):ti,ab,kw 1667 |
| #16 MeSH descriptor: [Iloprost] explode all trees 228 |
| #17 ((iloprost or ventavis)):ti,ab,kw 508 |
| #18 #14 or #15 or #16 or #17 1965 |
| #19 #10 AND #13 3827 |
| #20 #18 AND #19 36 |

Risk Of Bias Assessment

**Table S2: Summary of the Cochrane risk of bias in non-randomized studies assessment**

|  |  |  |  |
| --- | --- | --- | --- |
| Domain | Bajawa et al, 2017 | Wang et al. 2017 | Dernaika et al. 2010 |
| Bias due to confounding | Low | Low | Low |
| Bias in selection of participants into the study | Low | Low | Low |
| Bias in classification of interventions | Low | Low | Low |
| Bias due to deviations from intended interventions | Low | Low | Low |
| Bias due to missing data | Low | Low | Low |
| Bias in measurement of outcomes | Low | Low | Low |
| Bias in selection of the reported result | Medium | Low | Low |
| Overall bias | Medium bias | Low bias | Low bias |

**Table S3: Summary of the Cochrane risk of bias in randomized studies (crossover) trials assessment**

|  |  |
| --- | --- |
| Domain | Boeck et al. 2012 |
| Risk of bias arising from the randomization process | Low |
| Risk of bias arising from period and carryover effects | Low |
| Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Low |
| Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Low |
| Risk of bias due to missing outcome data | Low |
| Risk of bias in measurement of the outcome | Low |
| Risk of bias in selection of the reported result | Low |
| Overall bias | Low bias |