**Table D-2. Quality and applicability for KQ 2 studies**

| **Study** | **Index Tests/Comparators** | **Quality** | **Limitations to Applicability** |
| --- | --- | --- | --- |
| Andreassen, 200662 | * BNP * Cardiac index * Functional class * RHC-mPAP * RHC-PVR * RHC-sPAP * RAP * Mortality | Good | * None |
| Badesch, 201263  Badesch 201164 | * BNP | Good | * Included patients did not match the review question |
| Barst, 199665 | * mPAP | Good | * None |
| Bendayan, 200266 | * Uric acid * 6MWD (absolute) * Functional class * Mortality * RHC-CO * RHC-mPAP | Good | * None |
| Benza, 201067 | * BNP >180 * BNP<50 * Pericardial effusion * Mortality | Good | * None |
| Bernus, 200968 | * BNP * Cardiac index * Peak TRV * PCWP * RHC-mPAP * RHC-PVR * Right atrial pressure * RV size * TRV | Good | * None |
| Bharani, 200769 | * sPAP | Fair | * Intervention (active arm) was not similar to that used in routine clinical practice |
| Borges, 200670 | * RIMP/MPI/Tei index * RV size * 6MWD (absolute) * RHC-PVR | Good | * None |
| Brierre, 201071 | * mPAP * mPAP >= 49 * Pericardial effusion * RIMP/MPI/Tei index * RIMP/MPI/Tei index ≥0.98 * TAPSE * Mortality | Good | * Outcomes were not measured for sufficiently long duration of treatment |
| Bustamante-Labarta, 200272 | * RA size * Survival free from lung transplant | Good | * None |
| Campana, 200473 | * BNP * Cardiac index * FAC * RV size * TAPSE * mPAP * Right atrial pressure * RVEF | Good | * None |
| Cella, 200974 | * RVSP * Nitric oxide * 6MWD (change) | Good | * None |
| Channick, 200175  Badesch 200276 | * mPAP | Good | * Potential adverse events associated with testing or treatment were not measured or reported |
| Chin, 200777 | * BNP * 6MWD (absolute) * PCWP * RHC-CO * RHC-mPAP * RHC-PVR * Right atrial pressure | Good | * None |
| Dimitroulas, 200778 | * BNP | Good | * None |
| D’Alto, 201079 | * BNP | Fair | * None |
| Dyer, 200680 | * RIMP/MPI/Tei index * RHC-mPAP | Fair | * None |
| Elstein, 200481 | * BNP * Tricuspid insufficiency | Good | * None |
| Fahmy Elnoamany, 200782 | * Endothelin-1 * sPAP * RHC-sPAP * RIMP/MPI/Tei Index * RVEF | Fair | * None |
| Feliciano, 200583 | * RIMP/MPI/Tei index | Good | * None |
| Fijalkowska, 200684 | * BNP * FAC * Pericardial effusion * RA size * RIMP/MPI/Tei index * RV size * Troponin T * 6MWD (absolute) * Cardiac index * Functional class * Peak TRV * RHC-mPAP * RHC-PVR * Right atrial pressure * Mortality | Good | * None |
| Filusch, 201085 | * cTroponin T * hsTroponin T * BNP * Mortality * WHO class | Good | * Surrogate outcomes were not sufficiently clinically relevant |
| Forfia, 200686 | * TAPSE * RHC-PVR * Mortality | Good | * None |
| Friedberg, 200687 | * mPAP * BNP * sPAP * RHC-mPAP * RHC-sPAP | Good | * Included patients did not match the review question * Study included patients with a wide variety of conditions in addition to the target population |
| Galie, 200888  Oudiz 200989  Shapiro 201290 | * BNP | Good | * None |
| Gan, 200691 | * BNP * 6MWD (absolute) * Cardiac index * RHC-mPAP * RHC-PVR * Right atrial pressure * RVEF | Good | * None |
| Ghio, 201092 | * FAC * Pericardial effusion * RIMP/MPI/Tei index * sPAP * TAPSE * Mortality | Good | * Study population was inadequately described to assess the applicability of this study * Target condition as defined by the reference standard did not match the review question |
| Ghofrani, 200293 | * BNP * cGMP * RHC-PVR | Fair | * Surrogate outcomes were not sufficiently clinically relevant |
| Goto, 201094 | * BNP * sPAP * RHC-mPAP * RHC-sPAP | Good | * Study population was inadequately described to assess the applicability of this study * Participants had widely differing degrees of disease severity * Included patients did not match the review question |
| Grapsa, 200795 | * RIMP/MPI/Tei index * Pericardial effusion * RA size * TRV | Good | * None |
| Grubstein, 200896 | * sPAP * RHC-sPAP | Fair | * None |
| Haddad, 200997 | * mPAP * sPAP * RHC-mPAP * RHC-sPAP | Good | * None |
| Halank, 201198 | * BNP * Median | Fair | * None |
| Hampole, 200999 | * BNP * Mortality | Good | * None |
| Heresi, 2012100 | * cTnl (detectable vs. nondetectable) * BNP * NYHA class * RA size * 6MWD | Good | * None |
| Heresi, 2010101 | * BNP * 6MWD (absolute) * Cardiac index * RHC-mPAP * RHC-PVR * Right atrial pressure * Mortality | Good | * None |
| Hinderliter, 1997102 | * FAC * Pericardial effusion * RV size * sPAP * TRV * 6MWD (absolute) * Cardiac index * RHC-mPAP * Right atrial pressure * RHC-sPAP | Fair | * Outcomes were not measured for sufficiently long duration of treatment * Potential adverse events associated with testing or treatment were not measured or reported |
| Hiramoto, 2009103 | * BNP * Endothelin-1 | Fair | * None |
| Ho, 2009104 | * RIMP/MPI/Tei Index * FAC * BNP * sPAP * RVEF | Good | * None |
| Homma, 2001105 | * sPAP * RHC-sPAP | Good | * None |
| Jacobs, 2009106 | * BNP | Fair | * None |
| Kaya, 2012107 | * RV size * RA size * sPAP * S’ | Good | * None |
| Keogh, 2011108 | * sPAP | Fair | * None |
| Knirsch, 2011109 | * BNP | Good | * Study population was inadequately described to assess the applicability of this study * Study included patients with a wide variety of conditions in addition to the target population * Cointerventions/treatments did not adequately reflect routine clinical practice * Outcomes were not measured for sufficiently long duration of treatment |
| Kopec, 2012110 | * BNP * ET-1 | Fair | * Index test, its conduct, or interpretation differed from the review question |
| Lammers, 2009111 | * BNP * 6MWD (absolute) * Functional class | Good | * None |
| Langleben, 1999112 | * Endothelin-1 | Good | * None |
| Leuchte, 2005113 | * Change in BNP * BNP * Change in : * 6MWD (absolute) * Cardiac index * RHC-CO * RHC-mPAP * RHC-PVR * Right atrial pressure | Good | * None |
| Lorenzen, 2011114 | * BNP * Uric acid * Mortality | Good | * None |
| Machado, 200629 | * BNP * BNP ≥160, unadjusted ≥160, adjusted log10, adjusted log10, unadjusted * 6MWD (absolute) * mPAP * PCWP * RA size * RHC-CO * RHC-dPAP * RHC-PVR * RHC-sPAP * RV size * TRV * Mortality | Poor | * None |
| Machado, 2004115 | * Nitric oxide * sPAP * mPAP * RHC-sPAP | Fair | * None |
| Mahapatra, 2006116 | * RIMP/MPI/Tei Index * RVSP * Mortality | Fair | * None |
| Mathai, 2011117 | * FAC * Peak TRV * Pericardial effusion * RA size * TAPSE * Mortality | Fair | * None |
| Mauritz, 2011118 | * BNP | Good | * None |
| McLaughlin, 2010119  Frantz, 2012120 | * BNP | Good | * None |
| Michelakis, 2002121 | * cGMP | Fair | * Surrogate outcomes were not sufficiently clinically relevant * Outcomes were not measured for sufficiently long duration of treatment * Potential adverse events associated with testing or treatment were not measured or reported |
| Minniti, 2009122 | * BNP * TRV | Poor | * None |
| Montani, 2007123 | * Endothelin-1 * Cardiac index * RHC-PVR * Right atrial pressure | Fair | * Participants were at widely differing points in natural history of disease * Intervention (active arm) was not similar to that used in routine clinical practice |
| Morishita, 2009124 | * Pericardial effusion * RA size * RA size * BNP * Functional class | Good | * None |
| Mukerjee, 2003125 | * BNP * RHC-mPAP * RHC-PVR | Good | * None |
| Nagaya, 2000126 | * ANP * BNP * PCWP * RHC-CO * RHC-mPAP * Right atrial pressure * Mortality * RHC-PVR * Right atrial pressure * RV size | Good | * None |
| Nakayama, 2007127 | * BNP | Fair | * None |
| Nath, 2005128 | * Peak TRV * RIMP/MPI/Tei Index * RV size * sPAP * TRV * Functional class | Good | * Participants were at widely differing points in natural history of disease * Participants had widely differing degrees of disease severity |
| Nickel, 2012129 | * BNP * Uric acid * Mortality | Fair | * None |
| Nickel, 2008130 | * BNP * Uric acid * Composite outcome (death or lung transplantation) | Fair | * Participants were at widely differing points in natural history of disease * Participants had widely differing degrees of disease severity |
| Njaman, 2007131 | * Uric acid * Mortality | Good | * None |
| Ogawa, 2012132 | * BNP | Fair | * None |
| Park, 2004133 | * sPAP * BNP * Clinical event | Fair | * None |
| Pyxaras, 2011134 | * sPAP * mPAP * RHC-sPAP * RHC-mPAP | Good | * None |
| Raymond, 2002135 | * FAC * Peak TRV * Pericardial effusion * RA size * Mortality * Composite outcome (death or transplantation) | Fair | * None |
| Rhodes, 2011136 | * BNP * 6MWD (absolute) * Cardiac index * PCWP * RHC-PVR * Right atrial pressure * Mortality | Good | * Participants were at widely differing points in natural history of disease * Participants had widely differing degrees of disease severity |
| Sadushi-Kolici, 2012137 | * Pericardial effusion * Mortality | Fair | * None |
| Schumann, 2010138 | * BNP * sPAP | Good | * Participants were at widely differing points in natural history of disease * Participants had widely differing degrees of disease severity |
| Sebbag, 2001139 | * RIMP/MPI/Tei Index * SPAP | Good | * Participants were at widely differing points in natural history of disease * Participants had widely differing degrees of disease severity * Potential adverse events associated with testing or treatment were not measured or reported |
| Shimony, 2012140 | * Pericardial effusion (prevalent v incident) * Mortality | Fair | * None |
| Simeoni, 200849 | * BNP | Good | * Participants were at widely differing points in natural history of disease * Participants had widely differing degrees of disease severity * Included patients did not match the review question * Study excluded participants with other conditions that might be easily confused with PAH such as PH due to heart failure, thrombotic disease, COPD * Study included patients with a wide variety of conditions in addition to the target population |
| Soon, 2011141 | * BNP | Good | * Participants were at widely differing points in natural history of disease * Participants had widely differing degrees of disease severity |
| Souza, 2007142 | * BNP * 6MWD (absolute) * Cardiac index * Functional class * RHC-mPAP * RHC-PVR * Right atrial pressure | Good | * None |
| Taguchi, 2012143 | * BNP | Good | * None |
| Takatsuki, 2012144 | * TRJv * RV size * BNP | Good | * None |
| Takatsuki, 2012145 | * BNP | Good | * None |
| Takatsuki, 2012146 | * BNP (BNP and NT-proBNP) * 6MWD * RHC-mPAP * RHC-RAP * RHC-PVRi * RHC-CI * TRJv | Good | * None |
| Takeda, 2010147 | * BNP * Mortality | Good | * None |
| Torbicki, 2003148 | * FAC * BNP * Pericardial effusion * RA size * Troponin T * Mortality | Good | * None |
| Utsunomiya, 2011149 | * BNP * RA size * RIMP/MPI/Tei Index * Mortality | Fair | * None |
| Utsunomiya, 2009150 | * RA size * Right atrial pressure * RIMP/MPI/Tei Index | Good | * None |
| Van Albada, 2008151 | * Uric acid * Cardiac index * Mortality * RHC-mPAP * RHC-PVR | Good | * Potential adverse events associated with testing or treatment were not measured or reported |
| Vizza, 2012152 | * ET-1 * BNP * WHO FC * RHC-mPAP * RHC-CI * RHC-PVR * Clinical worsening | Good | * None |
| Vizza, 2008153 | * Endothelin-1 * BNP | Good | * None |
| Voelkel, 2000154 | * Uric acid * RHC-mPAP * Right atrial pressure | Good | * None |
| Williams, 200661 | * BNP * 10-fold increase from baseline levels | Fair | * None |
| Wilkins, 2005155 | * RV size * Cardiac index * RIMP/MPI/Tei Index * RA size * BNP | Good | * None |
| Yamada, 2012156 | * BNP * Uric acid * Mortality * Hospitalization | Good | * None |
| Yanagisawa, 2012157 | * BNP | Good | * None |
| Yang, 2012158 | * RV size * mPAP | Fair | * None |
| Yoshida, 2012159 | * BNP * mPAP | Fair | * None |
| Zafrir, 2007160 | * RA size * RIMP/MPI/Tei Index * RVEF | Good | * None |
| Zeng, 2011161 | * BNP | Good | * None |
| Zhao, 2012162 | * Uric acid * Mortality | Good | * None |

Abbreviations: 6MWD=6-minute walk distance; BNP=brain natriuretic peptide; CHF=congestive heart failure; CTEPH=chronic thromboembolic pulmonary hypertension; CVD=collagen vascular disease; DLCO=diffusion capacity of the lung for carbon monoxide; FAC=fractional area change; mPAP=mean pulmonary artery pressure; MPI=myocardial performance index; NT-proBNP=N-terminal pro-B-type natriuretic peptide; NYHA=New York Heart Association; PAH=pulmonary arterial hypertension; PH=pulmonary hypertension; PPH=primary pulmonary hypertension; PVR=pulmonary vascular resistance; RA=right atrium; RHC=right heart catheterization; RIMP=right index of myocardial performance; RV=right ventricle; RVEF=right ventricular ejection fraction; S’=tricuspid lateral annular systolic velocity; sPAP=systolic pulmonary artery pressure; SSc=systemic sclerosis; TAPSE=tricuspid annular plane systolic excursion; TDI=tissue Doppler imaging; TRV=tricuspid regurgitant jet velocity; VSD=ventricular septal defect; VTIRVOT=velocity-time integral of right ventricular outflow tract