**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, 201263Badesch 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, 200175Badesch 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, 200888Oudiz 200989Shapiro 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, 2010119Frantz, 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