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**Title:** Gas exchange measures during six minute walk test are more sensitive to disease severity than walk distance

Prof. Norman 507 Morris n.morris@griffith.edu.au<sup>1,2</sup>, Helen 508 Seale helen\_seale@health.qld.gov.au<sup>2</sup>, Prof. Bruce 509 Johnson johnson.bruce@mayo.edu.au<sup>3</sup> and Dr. Fiona 510 Kermeen fiona\_kermeen@health.qld.gov.au<sup>2</sup>. <sup>1</sup> School of Rehabilitation Sciences, Griffith University, Gold Coast, QLD, Australia ; <sup>2</sup> Queensland Lung Transplant Service, The Prince Charles Hospital, Brisbane, QLD, Australia and <sup>3</sup> Cardiovascular Diseases, Mayo Clinic, Rochester, MN, United States .

**Body:** Introduction: In pulmonary hypertension (PH) the 6-min walk distance (6MWD) differentiates patients based on WHO Functional Class (FC), however its relationship to other indices of disease severity such as pulmonary artery pressure (PAP) and vascular resistance (PVR) is unclear. There is evidence that indices of gas exchange obtained during exercise such as breathing efficiency (BE: VE/VECO<sub>2</sub>) and end tidal CO<sub>2</sub> (PETCO<sub>2</sub>) relate to disease severity, hence the purpose of this study was to examine the relationship between disease severity and gas exchange measures made during a 6MWT. Method: 50 patients (49 ± 17 yr, FC=2.2±0.5), completed a 6MWT whilst gas exchange was measured simultaneously. End exercise 6MWD, BE, PETCO<sub>2</sub> and a non-invasive gas exchange estimate of pulmonary vascular capacitance (PCAP=oxygen pulse x PETCO<sub>2</sub>) were correlated with resting echocardiography measures of RV systolic pressure (RVSP). In a subgroup (n=15, FC=2.3±0.5, Category 1 PH) resting right heart catheterisations (RHC) were performed and PAP and PVR determined. Result: The mean 6MWD was 504±102m. There was no relationship between 6MWD and RVSP (70±23 mmHg, r=-0.15, p=0.51) however end exercise BE (42±10, r=0.63), PETCO<sub>2</sub> (27.2±7.1 mmHg, r=-0.60) and PCAP (204 ± 107, r=-0.47) were significantly (p<0.01) related to RVSP. In the subgroup of RHC patients only end exercise PETCO<sub>2</sub> (25.7±5.8 mmHg) and PCAP (186±94) were significantly correlated with PVR (PETCO<sub>2</sub>: r=-0.46, PCAP: r=-0.56) and PAP (PETCO<sub>2</sub>: r=-0.44, PCAP: r=-0.56). Conclusion: Non-invasive gas exchange measures may be a useful addition to the 6MWD and provide a more sensitive method for PH screening and tracking response to therapy.