Introduction:
Pulmonary arterial hypertension (PAH) may lead to severe circulatory compromise, requiring intensive care. Bone morphogenetic proteins (BMPs) are known to have pivotal roles in organ diseases, including heritable PAH. In PAH, genetic mutations in the type II BMP receptor (BMPR2) are the most common cause of receptor dysfunction. However, it has also recently been demonstrated that aquaporin 1 (Aqp1) dysfunction, apart from its role in acute respiratory distress syndrome (ARDS), may contribute to PAH, highlighting that PAH development may involve more than one pathogenic pathway. Whether reduction in BMPR2 affects Aqp1 is unknown.

Methods:
We studied Aqp1 and the BMP-signalling molecules, SMADs, in BMPR2-silenced human pulmonary microvascular endothelial cells (HPMECs). mRNA levels were measured by RT-PCR, protein by immunoblotting, and Aqp1 function by permeability assays.

Results:
BMPR2-silenced HPMECs exhibited a reduced expression of Aqp1 at a mRNA and protein level. Moreover, BMPR2-silenced HPMECs showed reduced permeability function, implying dysfunctional Aqp1. BMPR2-silenced HPMECs also exhibited reduced expression of SMAD1/5/8 and SMAD2/3 pathways.

Conclusion:
Decreased BMPR2 expression appears to affect Aqp1 at mRNA, protein, and functional levels. To our knowledge, this is the first report to demonstrate that decreased BMPR2 gene expression leads to decreased Aqp1 expression and function in vitro.