

Appendix 1

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Table S1 Studies inclusion criteria and pulmonary hypertension definition (excluding the studies with Eisenmenger syndrome only)

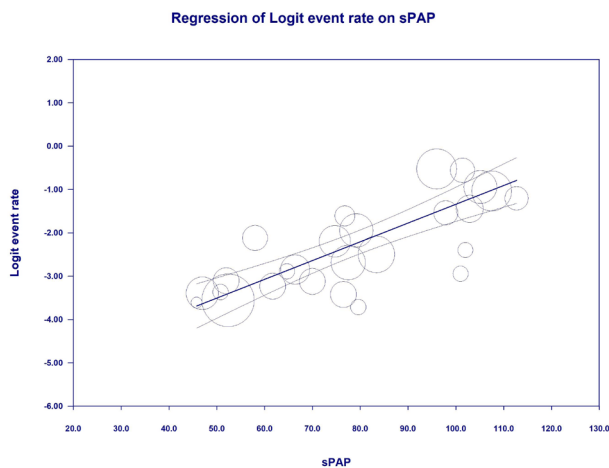
Study	Inclusion criteria/definition of PH
Tahir 1995 (20)	Twenty mothers with coexisting PH were analyzed, and 20 mothers without PH served as controls at Universiti Kebangsaan Malaysia between January 1989 and December 1991
Bonnin 2005 (21)	All pregnant women followed at Antoine Beclere Hospital, France (1992–2002) for known or newly diagnosed PH during pregnancy
Jaïs 2012 (22)	Pregnancies from July 2007 to June 2010 in PAH patients across 13 centers in Europe, USA, and Australia. PAH diagnosed via right heart catheterization
Katsuragi 2012 (23)	Forty-two pregnant women with PAH from January 1982 to December 2007
Ma 2012 (24)	Pregnant women with PH at Peking Union Medical College Hospital between January 1999 and December 2008
Duarte 2013 (25)	Pregnant patients with PAH treated at five US institutions from January 1999 to January 2009
Subbaiah 2013 (26)	Pregnant women with PAH delivering at ≥ 28 weeks from July 2006 to July 2012 in India. PAH defined as sPAP ≥ 30 mmHg
Monagle 2015 (27)	All patients admitted for PH management during pregnancy at Monash Medical Center (1994–February 2009)
Ladouceur 2017 (18)	Women with PAH-CHD from seven French centers (1997–2015)
Sliwa 2016 (28)	All pregnant patients with RVSP >30 mmHg at rest, measured by TTE or RHC. Excluded RVSP elevation due to obstruction/pulmonary stenosis
Dolgun 2018 (29)	Patients with PAH at a tertiary care center in Türkiye (2008–2015)
Meng 2017 (30)	Retrospective review (2001–2015) of pregnant women with PH across four academic institutions. PH defined as mPAP >25 mmHg
Zhao 2018 (31)	249 women with PH at Beijing Anzhen Hospital (2012–2015). PH defined by mPAP ≥ 25 mmHg (TTE or RHC)
Gong 2018 (32)	39 consecutive pregnant women with PH (2006–2012). PH defined as sPAP ≥ 40 mmHg
Li 2019 (19)	PAH-CHD patients at Beijing Anzhen Hospital (2011–2016). mPAP >25 mmHg or TTE with TRV + other structural parameters
Su 2022 (51)	Pregnant women with PH or delivery at Peking Union Medical College Hospital (2009–2018). PH defined as mPAP >25 mmHg or sPAP >35 mmHg
Zhang 2018 (34)	Idiopathic PAH patients pregnant or aborted between 2010 and 2016 at Beijing Anzhen Hospital
Zhu 2018 (35)	78 pregnancies with PH delivering at Sun Yat-sen University (2007–2017). PH defined as sPAP >30 mmHg
Weldegerima 2019 (36)	Prospective registry of PH in pregnancy at Mekelle University Hospital, Ethiopia (2016–2017)
Hartopo 2019 (37)	Retrospective registry of pregnant patients with uncorrected septal defects at Dr. Sardjito Hospital (2012–2017)
Keepanasseril 2019 (38)	PH pregnancies at JIPMER, India (2011–2017)
Herrera 2022 (39)	PH pregnancies at Parkland Memorial and UT Southwestern Hospitals (2006–2017). PH: sPAP >30 mmHg (TTE) or >20 mmHg (RHC)
Ekici 2022 (40)	45 PH pregnancies followed at Ege University Hospital, Türkiye (2009–2018)
Prasad 2022 (41)	PH pregnancies at Amrita Institute, India (2008–2018)
Lai 2021 (42)	PH pregnancies admitted to Second Xiangya Hospital (2004–2016). PH: sPAP >30 mmHg
Luo 2020 (43)	PAH pregnancies at Xiangya Hospitals (2004–2016). PH: mPAP ≥ 25 mmHg or sPAP >36 mmHg
Yang 2021 (44)	PH pregnancies screened by TTE at Renji Hospital (2012–2018)
Kamp 2021 (9)	All PAH pregnancies between 2007 and 2019
Liu 2021 (45)	Obstetric PH patients at Air Force Medical University Hospital (2011–2020)
Miao 2022 (46)	PH pregnancies from 2001–2020 at Renji Hospital. mPAP >25 mmHg or sPAP >35 mmHg
Shahid 2021 (47)	PH pregnancies followed and delivered at Narowal Hospital, Pakistan (2020)
Budhram 2023 (48)	PH pregnancies at Inkosi Albert Luthuli Hospital, South Africa (2016–2018). PH: mPAP ≥ 25 mmHg
Liao 2022 (49)	Patients with sPAP ≥ 30 mmHg and at least one echo with TRV ≥ 2.8 m/s
Marshall 2022 (50)	PH defined as RVSP >35 mmHg or TRV ≥ 2.8 m/s on TTE. Managed between 2004–2018
Su 2022 (51)	94 PH pregnancies at Guangxi Medical University (2015–2020). PH: mPAP ≥ 25 mmHg
Tokgöz 2022 (52)	35 women diagnosed with PAH during or within 6 months postpartum
Chen 2023 (10)	PH pregnancies admitted at Second Xiangya Hospital (2004–2020). PH: sPAP >35 mmHg
Dai 2023 (53)	25 PH pregnancies admitted to Fujian Medical University (2018–2022). PH: sPAP >30 mmHg
Jha 2023 (54)	PAH or ES pregnancies from June 2020 to June 2022
Liu 2023 (55)	PH pregnancies at Beijing Anzhen Hospital (2010–2019). PH: sPAP >40 mmHg
Lv 2023 (56)	PH pregnancies at Guangzhou Medical University (2011–2020). PH: sPAP ≥ 36 mmHg
Piao 2023 (57)	PAH pregnancies at Anzhen Hospital (2007–2013). PH: mPAP >25 mmHg
Zhang 2023 (8)	CHD-associated PH across 7 tertiary hospitals (1993–2019). PH: mPAP ≥ 20 mmHg or RV-RA gradient ≥ 30 mmHg
Zhou 2021 (58)	PAH pregnancies at Peking Union Medical College Hospital (2000–2018). PAH: mPAP ≥ 25 mmHg with PCWP ≤ 15 mmHg
Kang 2024 (59)	PH pregnancies terminated at West China Second Hospital (2009–2022). PH: sPAP >35 mmHg (TTE)
McNeil 2024 (60)	PH pregnancies at Duke Medical Center (2014–2020). PH defined as RVSP ≥ 35 mmHg, or mPAP >25 mmHg, or history with vasodilator therapy

CHD, congenital heart disease; ES, Eisenmenger syndrome; mPAP, mean pulmonary arterial pressure; PAH, pulmonary arterial hypertension; PCWP, pulmonary capillary wedge pressure; PH, pulmonary hypertension; RA, right atrium; RHC, right heart catheter; RV, right ventricle; RVSP, right ventricular systolic pressure; sPAP, systolic pulmonary artery pressure; TRV, tricuspid regurgitation velocity; TTE, transthoracic echocardiogram.

Table S2 Pulmonary hypertension severity classifications across the studies

Study	Pulmonary hypertension severity classifications
Jaïs 2012 (22)	Severe PAH defined as “non-responders” to PAH medications
Katsuragi 2012 (23)	Mild PH: TTE sPAP 30–50 mmHg or RHC mPAP 25–40 mmHg. Severe PH: TTE sPAP \geq 50 mmHg or RHC mPAP \geq 40 mmHg
Ma 2012 (24)	Mild: 25–49 mmHg, Moderate: 50–79 mmHg, Severe: $>$ 80 mmHg (method unclear)
Subbaiah 2013 (26)	Mild PH: TTE sPAP 30–50 mmHg, Severe PH: TTE sPAP \geq 50 mmHg
Monagle 2015 (27)	Mild: sPAP 30–40 mmHg, Moderate: sPAP 40–70 mmHg, Severe: sPAP $>$ 70 mmHg
Sliwa 2016 (28)	Mild: RVSP 30–50 mmHg, Moderate: RVSP 50–70 mmHg, Severe: RVSP $>$ 70 mmHg
Meng 2017 (30)	Mild: RHC mPAP 25–49 mmHg, Severe: mPAP $>$ 49 mmHg or TTE sPAP $>$ 69 mmHg
Zhao 2018 (31)	Mild: sPAP 25–50 mmHg, Moderate: sPAP 50–80 mmHg, Severe: sPAP $>$ 80 mmHg
Gong 2018 (32)	Mild: 40–79 mmHg, Severe: sPAP \geq 80 mmHg
Sun 2018 (51)	RHC: Mild mPAP 25–35 mmHg, Moderate 36–45 mmHg, Severe $>$ 45 mmHg. TTE: Mild sPAP 35–55 mmHg, Moderate 56–75 mmHg, Severe $>$ 75 mmHg
Zhang 2018 (34)	Mild: mPAP 25–49 mmHg, Severe: mPAP $>$ 50 mmHg or sPAP $>$ 69 mmHg
Zhu 2018 (35)	Mild: sPAP 30–49 mmHg, Moderate: 50–69 mmHg, Severe: $>$ 69 mmHg
Weldegerima 2019 (36)	Severe PH: sPAP $>$ 70 mmHg
Hartopo 2019 (37)	Severe PH: RVSP $>$ 90 mmHg based on TTE and TRV + signs of PH
Keepanasseril 2019 (38)	PH: RVSP $>$ 40 mmHg at rest (TTE or RHC)
Herrera 2022 (39)	Mild: TTE sPAP 30–40 mmHg, Moderate: 40–50 mmHg, Severe: RHC mPAP $>$ 40 mmHg or sPAP $>$ 50 mmHg
Ekici 2022 (40)	Mild: sPAP 35–55 mmHg, Moderate: 56–75 mmHg, Severe: $>$ 75 mmHg
Lai 2021 (42)	Moderate: sPAP $<$ 50 mmHg, Severe: $>$ 50 mmHg (TTE)
Luo 2020 (43)	Mild: sPAP 36–50 mmHg, Severe: sPAP $>$ 50 mmHg
Yang 2021 (44)	PAH defined by TTE: TRV $>$ 2.8 m/sec plus other signs, excluding left heart disease
Liu 2021 (45)	Mild: RVSP 30–50 mmHg, Moderate: 50–70 mmHg, Severe: $>$ 70 mmHg
Miao 2022 (46)	RHC: Mild mPAP 25–35 mmHg, Moderate 36–45 mmHg, Severe $>$ 45 mmHg. TTE: Mild sPAP $<$ 50 mmHg, Moderate 50–79 mmHg, Severe $>$ 80 mmHg
Budhram 2023 (48)	Mild: mPAP 25–50 mmHg, Moderate: 50–89 mmHg, Severe: \geq 90 mmHg
Liao 2022 (49)	Mild: sPAP 30–49 mmHg, Moderate: 50–79 mmHg, Severe: \geq 80 mmHg
Su 2022 (51)	Mild: sPAP 25–49 mmHg, Moderate: 50–79 mmHg, Severe: \geq 80 mmHg
Chen 2023 (10)	Mild: sPAP 35–60 mmHg, Severe: $>$ 60 mmHg
Dai 2023 (53)	Severe PH: sPAP $>$ 80 mmHg
Liu 2023 (55)	Mild: sPAP $<$ 50 mmHg, Moderate: 50–70 mmHg, Severe: $>$ 70 mmHg
Piao 2023 (57)	Mild: sPAP 40–49 mmHg, Moderate: 50–79 mmHg, Severe: $>$ 80 mmHg
Zhang 2023 (8)	Mild: mPAP 20–40 mmHg or RV-RA gradient 30–50 mmHg, Moderate-Severe: mPAP $>$ 40 mmHg or RV-RA gradient $>$ 50 mmHg
Zhou 2021 (58)	Mild: sPAP 30–49 mmHg, Moderate: 50–79 mmHg, Severe: $>$ 79 mmHg
Kang 2024 (59)	Mild: sPAP 36–49 mmHg, Moderate: 50–69 mmHg, Severe: \geq 70 mmHg
McNeil 2024 (60)	Mild: mPAP 25–49 mmHg, Severe: mPAP $>$ 50 mmHg (RHC) or sPAP $>$ 70 mmHg (TTE)

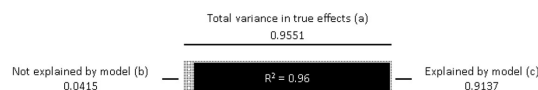
CHD, congenital heart disease; ES, Eisenmenger syndrome; mPAP, mean pulmonary arterial pressure; PAH, pulmonary arterial hypertension; PCWP, pulmonary capillary wedge pressure; PH, pulmonary hypertension; RA, right atrium; RHC, right heart catheter; RV, right ventricle; RVSP, right ventricular systolic pressure; sPAP, systolic pulmonary artery pressure; TRV, tricuspid regurgitation velocity; TTE, transthoracic echocardiogram.



Main results for Model 1, Random effects (MM), Z-Distribution, Logit event rate

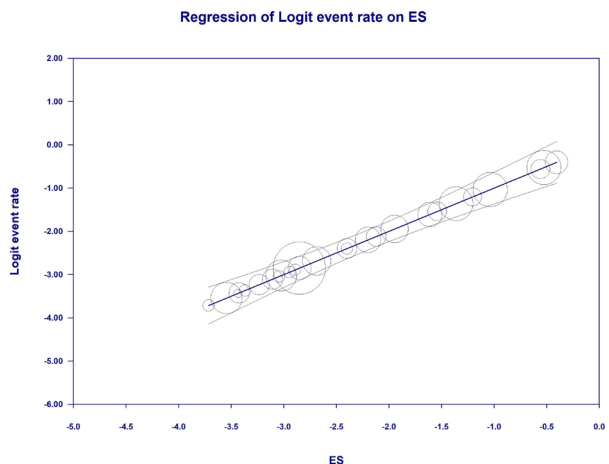
Covariate	Coefficient	Standard Error	95% Lower	95% Upper	Z-value	2-sided P-value
Intercept	-5.6673	0.4397	-6.5291	-4.8054	-12.89	0.0000
sPAP	0.0433	0.0054	0.0326	0.0539	7.98	0.0000

R² for Model 1, Random effects (MM), Z-Distribution, Logit event rate



$$R^2 = \frac{\text{Explained (c)}}{\text{Total (a)}} = \frac{0.9137}{0.9551} = 0.96$$

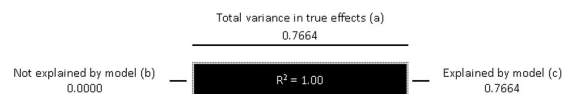
Figure S1 Meta-regression exploring the relationship between the mean sPAP in the included studies and maternal mortality in the pregnant patient with PH. As indicated in the accompanying table, the correlation was statistically significant and able to explain 96% (R^2) of between-study variance in maternal mortality rate. R^2 calculation: (I) to compute the total variance (of all studies about the grand mean), we run the regression with no covariates; (II) to compute the variance not explained by the model (of all studies about the regression line), we run the regression with the covariates; (III) the difference between these values gives us the variance explained by the model. PH, pulmonary hypertension; sPAP, systolic pulmonary artery pressure.



Main results for Model 1, Random effects (MM), Z-Distribution, Logit event rate

Covariate	Coefficient	Standard Error	95% Lower	95% Upper	Z-value	2-sided P-value
Intercept	-0.0000	0.2322	-0.4552	0.4552	-0.00	1.0000
ES	1.0000	0.0966	0.8107	1.1893	10.36	0.0000

R² for Model 1, Random effects (MM), Z-Distribution, Logit event rate



$$R^2 = \frac{\text{Explained (c)}}{\text{Total (a)}} = \frac{0.7664}{0.7664} = 1.00$$

Figure S2 Meta-regression exploring the relationship between the Eisenmenger syndrome proportion in the included studies and maternal mortality in the pregnant patient with PH. As indicated in the accompanying table, the correlation was statistically significant and able to explain 100% (R^2) of between-study variance in maternal mortality rate. R^2 calculation: (I) to compute the total variance (of all studies about the grand mean), we run the regression with no covariates; (II) to compute the variance not explained by the model (of all studies about the regression line), we run the regression with the covariates; (III) the difference between these values gives us the variance explained by the model. ES, Eisenmenger syndrome; PH, pulmonary hypertension.

Table S3 Neonatal/fetal outcomes in pulmonary hypertension pregnancies

Characteristics	Percentage	Number of studies
Neonatal/fetal death	211/4,087 (5%)	48
Timing of death		
Spontaneous abortion/intrauterine fetal death	44/125 (35%)	33
Neonatal death after delivery	32/125 (26%)	33
Stillbirth	29/125 (23%)	33
Death with the mother during pregnancy/delivery	28/125 (22%)	33
Etiology of maternal PH		
Congenital heart disease	76/138 (55%)	26
Idiopathic PAH	13/138 (9%)	26
Other causes	49/138 (36%)	26
Severity of PH in pregnancy		
Mild/moderate	63/154 (41%)	26
Severe	91/154 (59%)	26

PAH, pulmonary arterial hypertension; PH, pulmonary hypertension.

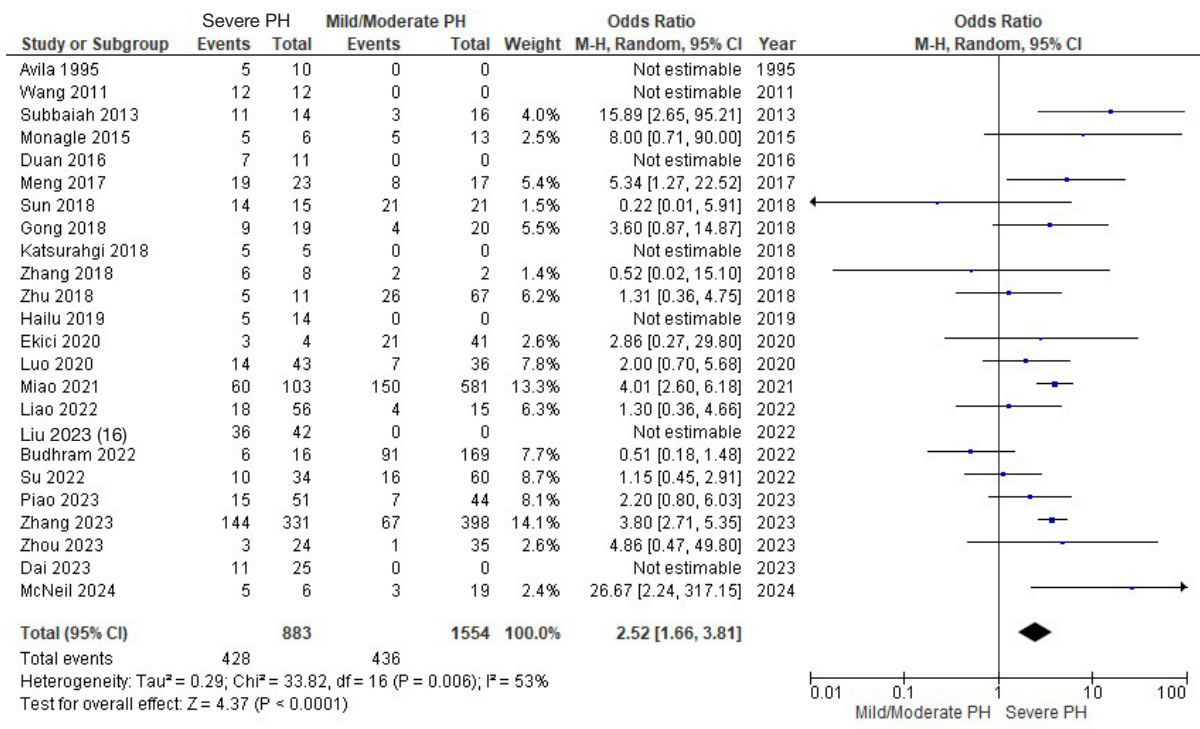


Figure S3 Prematurity rate in severe PH vs. mild/moderate PH (16). CI, confidence interval; PH, pulmonary hypertension.

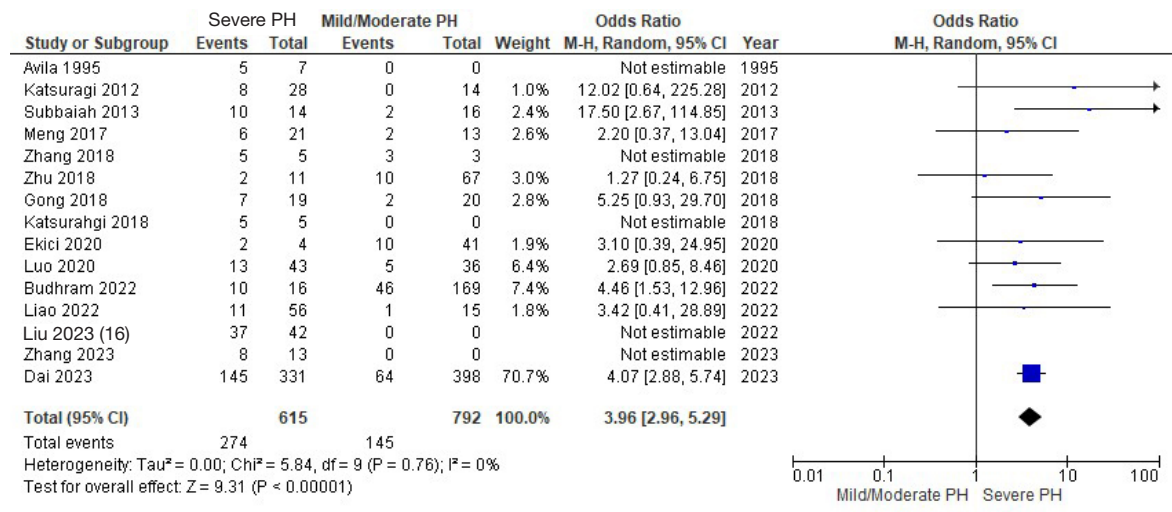
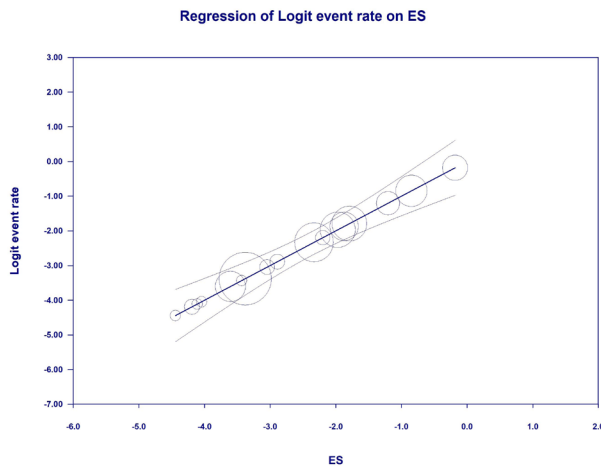


Figure S4 Small gestational age in severe PH vs. mild/moderate PH (16). CI, confidence interval; PH, pulmonary hypertension.



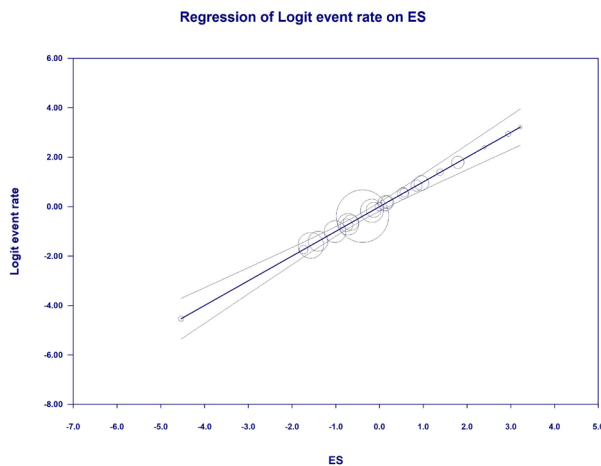
Main results for Model 1, Random effects (MM), Z-Distribution, Logit event rate

Covariate	Coefficient	Standard Error	95% Lower	95% Upper	Z-value	2-sided P-value
Intercept	0.0000	0.3458	-0.6777	0.6777	0.00	1.0000
ES	1.0000	0.1329	0.7395	1.2605	7.52	0.0000

R² for Model 1, Random effects (MM), Z-Distribution, Logit event rate

$$\begin{array}{l}
 \text{Total variance in true effects (a)} \\
 \hline
 0.9028 \\
 \text{Not explained by model (b)} \quad 0.0000 \quad \text{Explained by model (c)} \quad 0.9028 \\
 \hline
 R^2 = \frac{\text{Explained (c)}}{\text{Total (a)}} = \frac{0.9028}{0.9028} = 1.00
 \end{array}$$

Figure S5 Meta-regression exploring the relationship between the Eisenmenger syndrome proportion in the included studies and neonatal mortality rate. As indicated in the accompanying table, the correlation was statistically significant and able to explain 100% (R^2) of between-study variance in maternal mortality rate. R^2 calculation: (I) to compute the total variance (of all studies about the grand mean), we run the regression with no covariates; (II) to compute the variance not explained by the model (of all studies about the regression line), we run the regression with the covariates; (III) the difference between these values gives us the variance explained by the model. ES, Eisenmenger syndrome.



Main results for Model 1, Random effects (MM), Z-Distribution, Logit event rate

Covariate	Coefficient	Standard Error	95% Lower	95% Upper	Z-value	2-sided P-value
Intercept	-0.0000	0.0735	-0.1441	0.1441	-0.00	1.0000
ES	1.0000	0.0805	0.8422	1.1578	12.42	0.0000

R² for Model 1, Random effects (MM), Z-Distribution, Logit event rate

$$\begin{array}{l}
 \text{Total variance in true effects (a)} \\
 \hline
 0.6729 \\
 \text{Not explained by model (b)} \quad 0.0000 \quad \text{Explained by model (c)} \quad 0.6729 \\
 \hline
 R^2 = \frac{\text{Explained (c)}}{\text{Total (a)}} = \frac{0.6729}{0.6729} = 1.00
 \end{array}$$

Figure S6 Meta-regression exploring the relationship between the Eisenmenger syndrome proportion in the included studies and premature delivery rate. As indicated in the accompanying table, the correlation was statistically significant and able to explain 100% (R^2) of between-study variance in maternal mortality rate. R^2 calculation: (I) to compute the total variance (of all studies about the grand mean), we run the regression with no covariates; (II) to compute the variance not explained by the model (of all studies about the regression line), we run the regression with the covariates; (III) the difference between these values gives us the variance explained by the model. ES, Eisenmenger syndrome.

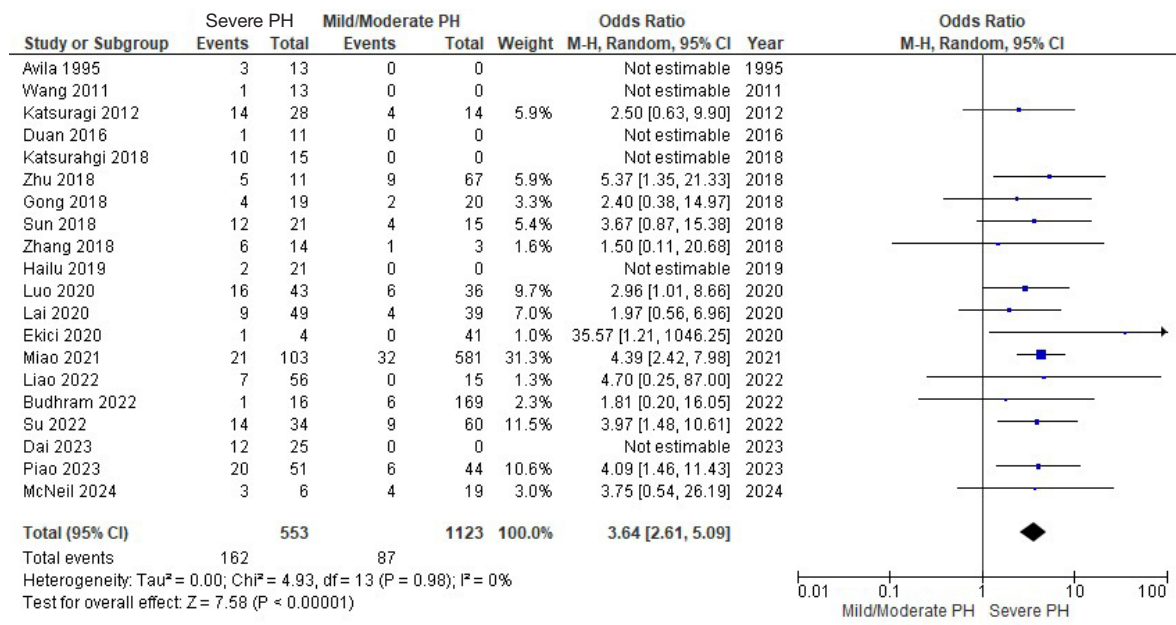


Figure S7 Abortion rate in severe PH vs. mild/moderate PH. CI, confidence interval; PH, pulmonary hypertension.

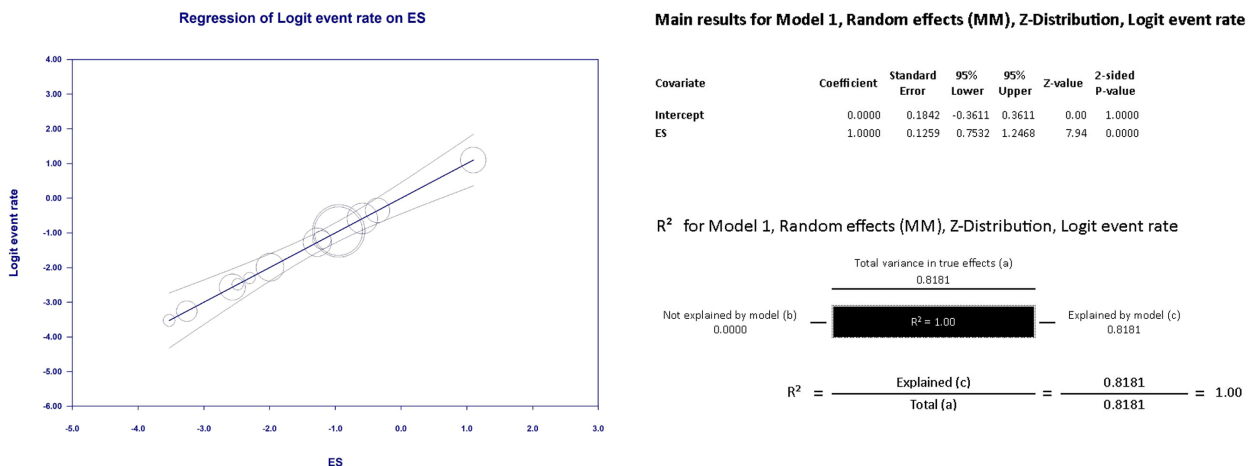


Figure S8 Meta-regression exploring the relationship between the Eisenmenger syndrome proportion in the included studies and abortion rate. As indicated in the accompanying table, the correlation was statistically significant and able to explain 100% (R²) of between-study variance in maternal mortality rate. R² calculation: (I) to compute the total variance (of all studies about the grand mean), we run the regression with no covariates; (II) to compute the variance not explained by the model (of all studies about the regression line), we run the regression with the covariates; (III) the difference between these values gives us the variance explained by the model. ES, Eisenmenger syndrome.

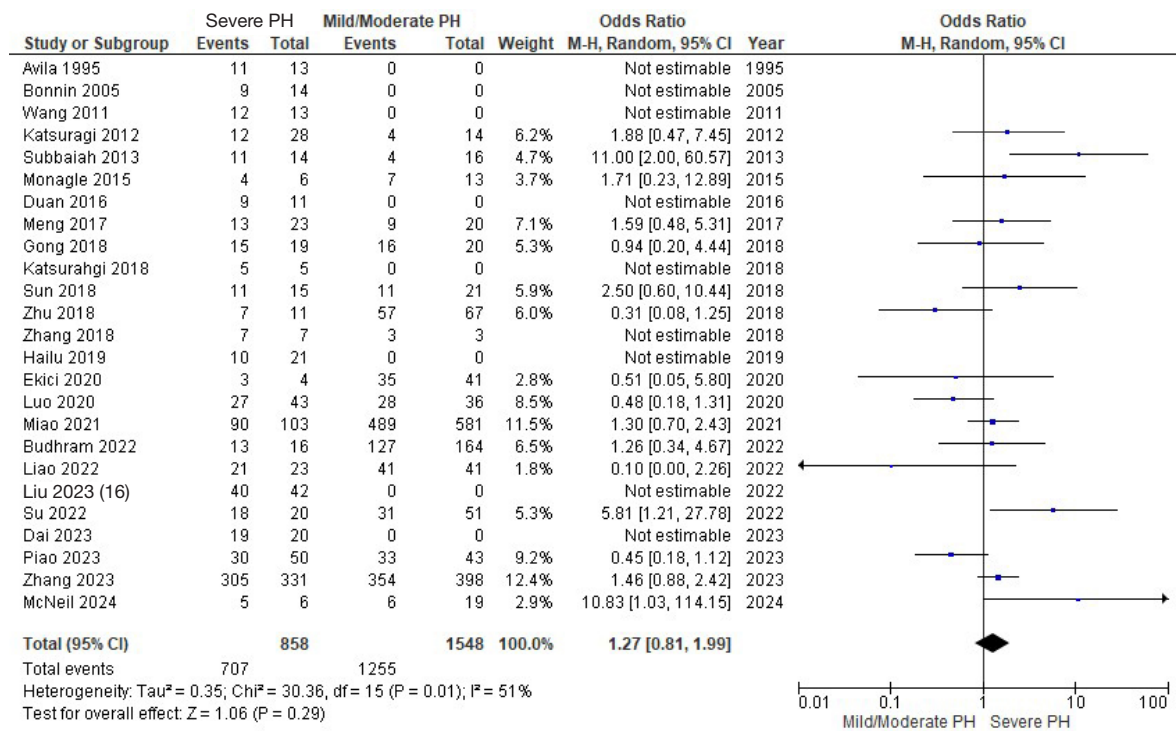


Figure S9 C-section rate in severe PH vs. mild/moderate PH (16). CI, confidence interval; PH, pulmonary hypertension.