Supplementary Appendix
Manuscript Title

A Systematic Review with Meta-analysis of Biomarkers for detection of Pulmonary Arterial Hypertension

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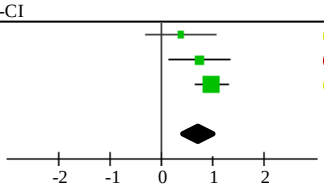
Fig. S1

Fig. S1 Summarized risk of bias table, P; patients, I; index (biomarker) test, R; reference test (diagnosis), T; flow and timing. QUADAS-2.

Fig. S2 Haematologic markers

a **PDW**, %

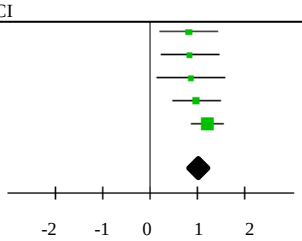
Study	Type	PAH Mean	n	Control Mean	n	Weight	Std. Mean Difference Random, 95%-CI	Risk of Bias P I R T
Yaoita, N. et al., (2014).	PAH	15.6±2.4	19	14.6±2.7	15	18%	0.4 [-0.3, 1.1]	? ? + ?
Yildiz, A. et al., (2013).	PAH	18.1±1.2	25	17.4±0.6	22	23%	0.8 [0.2, 1.3]	- + + +
Zheng Y.G. et al., (2015).	**iPAH**	**14.3±2.9**	**82**	**11.9±1.9**	**82**	**58%**	**1.0 [0.7, 1.3]**	? ? + +
Total effect PAH		p<0.00001	126		119	100%	0.8 [0.5, 1.1]	
Mean difference (mean, 95% CI)		1.42 % [0.16, 2.67]						



b **MPV**, fL

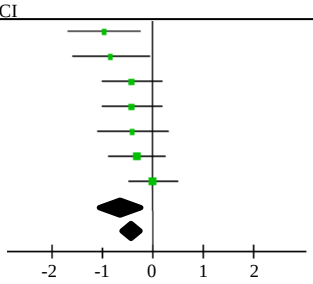
Study	Type	PAH Mean	n	Control Mean	n	Weight	Std. Mean Difference Random, 95%-CI	Risk of Bias P I R T
Yildiz, A. et al., (2013).	PAH	9.0±1.4	25	8.0±0.8	22	14%	0.8 [0.2, 1.4]	- + + ?
Varol, E. et al., (2011).	PAH	8.7±0.9	22	8.0±0.7	25	14%	0.8 [0.2, 1.4]	- ? + ?
Kereveur, A. et al., (2000).	PAH	9.3±1.1	16	8.5±0.7	19	9%	0.9 [0.2, 1.6]	? ? + ?
Can, M. et al., (2010).	PAH	9.1±1.0	34	8.2±0.8	34	19%	1.0 [0.5, 1.5]	- ? + ?
Zheng, Y.G. et al., (2015).	**iPAH**	**11.4±0.9**	**82**	**10.3±0.9**	**82**	**44%**	**1.2 [0.9, 1.6]**	? ? + +
Total effect PAH		p<0.00001	179		182	100%	1.0 [0.8, 1.3]	
Mean difference (mean, 95% CI)		0.95 fL [0.76, 1.13]						

*Yaoita, N. et al., (2014) excluded (control group severe CVD)



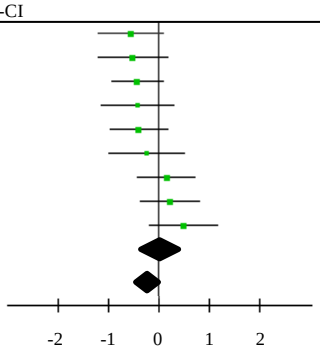
c **Thrombocytes**, 10^9/L

Study	Type	PAH Mean	n	Control Mean	n	Weight	Std. Mean Difference Random, 95%-CI	Risk of Bias P I R T
Decker, I. et al., (2011).	**iPAH**	**207±88**	**30**	**286±70**	**12**	**11%**	**-0.9 [-1.6, -0.2]**	+ ? + ?
Vrigkou, E. et al., (2019).	PAH	223±8	30	253±48	10	10%	-0.8 [-1.5, -0.1]	- ? + +
Varol, E. et al., (2011).	PAH	230±68	22	255±56	25	15%	-0.4 [-1.0, 0.2]	- ? + ?
Yildiz, A. et al. (2013).	PAH	231±53	25	272±39	22	15%	-0.4 [-1.0, 0.3]	- + + ?
Yaoita, N. et al., (2014).	**iPAH**	**197±61**	**19**	**224±77**	**15**	**11%**	**-0.4 [-1.1, 0.3]**	? ? + ?
Yaylali, Y.T. et al., (2019).	PAH	231±53	21	250±63	35	17%	-0.3 [-0.9, 0.2]	- ? + +
Can, M.M. et al., (2010).	PAH	238±87	34	237±65	34	21%	0.0 [-0.5, 0.5]	- ? + ?
Total effect iPAH		**p=0.02**	**49**		**27**	**23%**	**-0.7 [-1.2, -0.1]**	
Total effect PAH		p=0.001	181		153	100%	-0.4 [-0.6, -0.2]	
Mean difference (mean, 95% CI)		-23.9 10^9/L [-38.6, -9.2]						



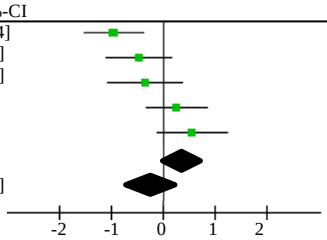
d **Hb**, g/dL

Study	Type	PAH Mean	n	Control Mean	n	Weight	Std. Mean Difference Random, 95%-CI	Risk of Bias P I R T
Suzuki, S., et al. (2016).	PAH	12.9±2.7	14	14.0±1.5	30	11%	-0.6 [-1.2, 0.1]	? ? ? +
Yaoita, N., et al. (2014).	PAH	12.2±1.5	19	13.1±1.9	15	10%	-0.5 [-1.2, 0.2]	? ? + ?
Estephan, L. E., et al. (2019).	PAH	12.9±1.9	47	13.7±1.7	22	15%	-0.4 [-1.0, 0.1]	+ + + ?
Varol, E., et al. (2011).	PAH	13.4±1.7	22	14.1±1.9	25	9%	-0.4 [-1.0, 0.2]	- ? + +
Gabrielli, L. A., et al. (2011).	**iPAH**	**14.0±4.0**	**14**	**15.0±4.0**	**14**	**12%**	**-0.2 [-1.0, 0.5]**	- ? + ?
Vrigkou, E., et al. (2019)	PAH	13.2±2.8	30	14.3±1.5	10	9%	-0.1 [-0.8, 0.7]	? + + ?
Yildiz, A., et al. (2013).	PAH	13.8±3.0	25	13.4±1.5	22	13%	0.2 [-0.4, 0.7]	- + + +
Zhu, T., et al. (2019).	**iPAH**	**14.3±2.4**	**27**	**13.8±1.5**	**20**	**11%**	**0.2 [-0.2, 0.8]**	? + + +
Decker, I., et al. (2011).	PAH	13.9±1.3	30	13.3±1.0	12	10%	0.5 [-0.2, 1.]	+ ? + ?
Total effect iPAH		**p=0.82**	**41**		**34**	**19%**	**0.1 [-0.4, 0.5]**	
Total effect PAH		p=0.15	228		170	100%	-0.2 [-0.4, 0.1]	
Mean difference (mean, 95% CI)		-0.59 g/dL [-1.23, 0.06]						



e **Hct**, %

Study	Type	PAH Mean	n	Control Mean	n	Weight	Std. Mean Difference Random, 95%-CI	Risk of Bias P I R T
Yaylali, Y. T., et al. (2019).	PAH	36.9±5.5	21	42.2±5.2	35	21%	-1.0 [-1.6, -0.4]	- ? + +
Suzuki, S., et al. (2016).	PAH	39.0±7.4	14	41.7±4.3	30	20%	-0.5 [-1.1, 0.2]	? ? ? +
Vrigkou, E., et al. (2019)	PAH	42.4±4.2	30	43.9±3.7	10	19%	-0.4 [-1.1, 0.4]	- ? + +
Zhu, T., et al. (2019).	**iPAH**	**43.5±7.0**	**27**	**42.0±3.9**	**20**	**21%**	**0.3 [-0.3, 0.8]**	? + + +
Decker, I., et al. (2011).	**iPAH**	**42.5±3.82**	**30**	**40.4±3.1**	**12**	**19%**	**0.6 [-0.1, 1.2]**	+ ? + ?
Total effect iPAH		**p=0.09**	**57**		**32**	**39%**	**0.4 [-0.1, 0.8]**	
Total effect PAH		p=0..46	122		107	100%	-0.2 [-0.8, 0.3]	
Mean difference (mean, 95% CI)		-1.07 % [-3.91, 1.76]						



f **Leukocytes**, 10^9/L

Study	Type	PAH Mean	n	Control Mean	n	Weight	Std. Mean Difference Random, 95%-CI	Risk of Bias P I R T
Gabrielli, L.A. et al., (2011).	**iPAH**	**8.6±1.0**	**14**	**9.2±1.0**	**14**	**12%**	**-0.6 [-1.3, 0.2]**	? ? + ?
Decker I. et al., (2011).	**iPAH**	**6.0±1.0**	**12**	**7.0±1.8**	**30**	**13%**	**-0.6 [-1.3, 0.1]**	+ ? + ?
Varol, E. et al., (2011).	PAH	6.5±1.8	25	7.1±1.4	22	16%	-0.4 [-1.0, 0.2]	- ? + ?
Vrigkou, E. et al., (2011).	PAH	6.8±1.1	10	7.1±2.0	30	12%	-0.2 [-0.9, 0.6]	- ? + +
Yaoita, N. et al., (2014).	PAH	5.6±1.4	15	5.5±1.5	19	13%	0.0 [-0.6, 0.7]	? ? + ?
Yildiz, A. et al., (2013).	PAH	8.0±1.8	25	8.3±2.2	22	17%	0.1 [-0.4, 0.7]	- + + ?
Yaylali, Y.T. et al., (2019).	PAH	7.4±1.8	35	6.4±2.2	21	17%	0.5 [0.0, 1.1]	- ? + +
Total effect iPAH		**p=0.03**	**26**		**44**	**23%**	**-0.6 [-1.1, -0.1]**	
Total effect PAH		p=0.34	133		161	100%	-0.1 [-0.4, 0.2]	
Mean difference (mean, 95% CI)		-0.23 10^9/L [-0.70,0.24]						

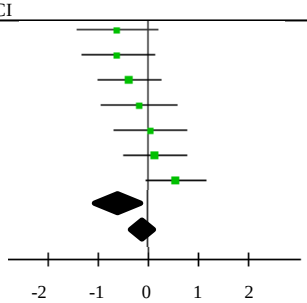


Fig. S2 Forest plots of non-selected haematologic biomarkers, including; PDW; platelet distribution width, MPV; mean platelet volume, thrombocytes, Hb; hemoglobin, Hct; hematocrit, leukocytes. Risk of bias (QUADAS-2), P: patient inclusion, I; index-test (biomarker), R; reference standard (diagnosis), T; flow and timing. Publications pressed in bold measured biomarker levels in iPAH and/or hPAH uniquely.

Fig. S3

Metabolic markers

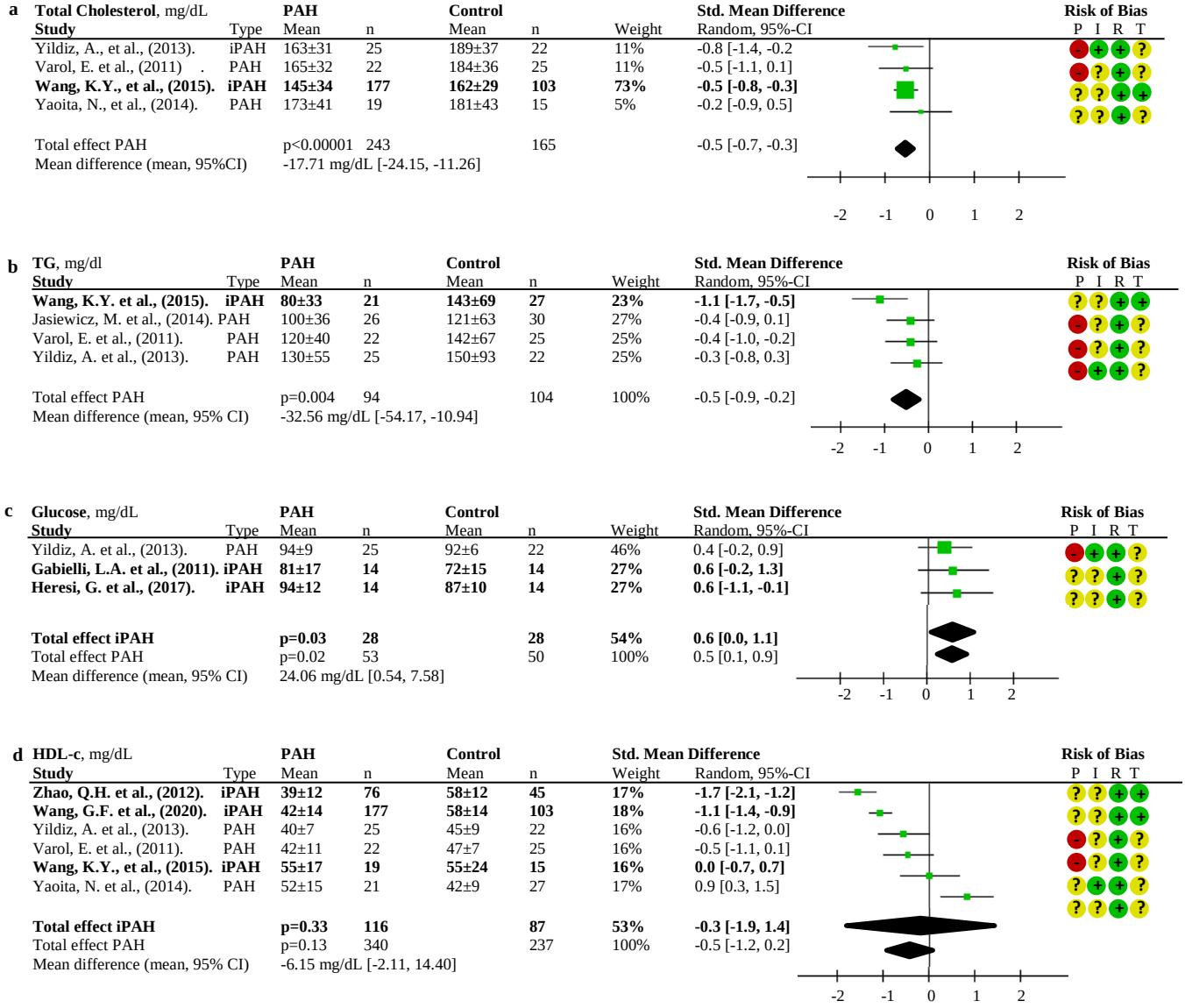


Fig. S3 Forest plots of non-selected metabolic biomarkers, including total cholesterol, TG; triglycerides, glucose, HDL-c; high density lipid-cholesterol. risk of bias (QUADAS-2), P: patient inclusion, I; index-test (biomarker), R; refence standard (diagnosis), T; flow and timing. Publications pressed in bold measured biomarker levels in iPAH and/or hPAH uniquely.

Fig. S4

Coagulation markers

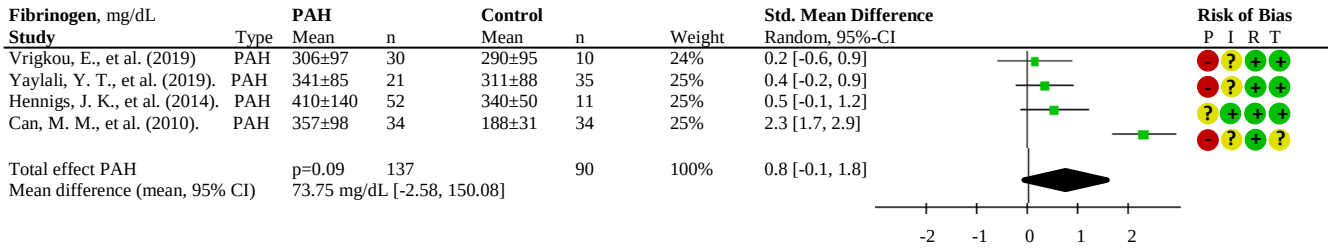


Fig. S4 Forest plots of non-selected coagulation biomarkers, including fibrinogen. Risk of bias (QUADAS-2), P: patient inclusion, I; index-test (biomarker), R; reference standard (diagnosis), T; flow and timing. Publications pressed in bold measured biomarker levels in iPAH and/or hPAH uniquely.

Fig. S5

Inflammation

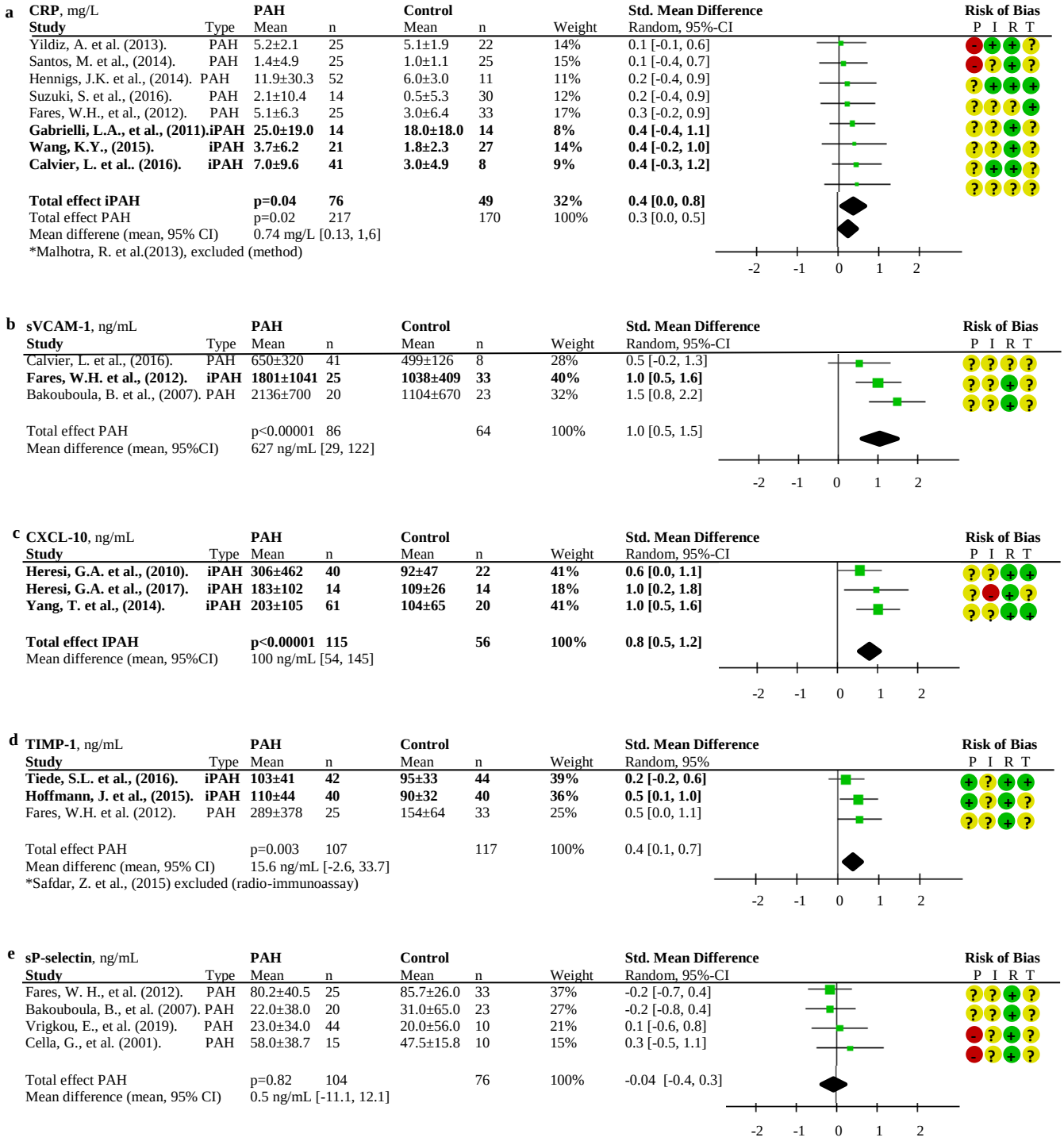


Fig. S5 Forest plots of non-selected inflammatory biomarkers, including; sVCAM-1; circulating vascular cell adhesion molecule-1, CXCL-10; C-X-C motif chemokine ligand-10, CRP; C-reactive protein, TIMP-1; tissue inhibitors of metalloproteinases-1, sP-selectin; soluble P-selectin. Risk of bias (QUADAS-2), P: patient inclusion, I; index-test (biomarker), R; reference standard (diagnosis), T; flow and timing. Publications pressed in bold measured biomarker levels in iPAH and/or hPAH uniquely.

Fig. S6

Renal

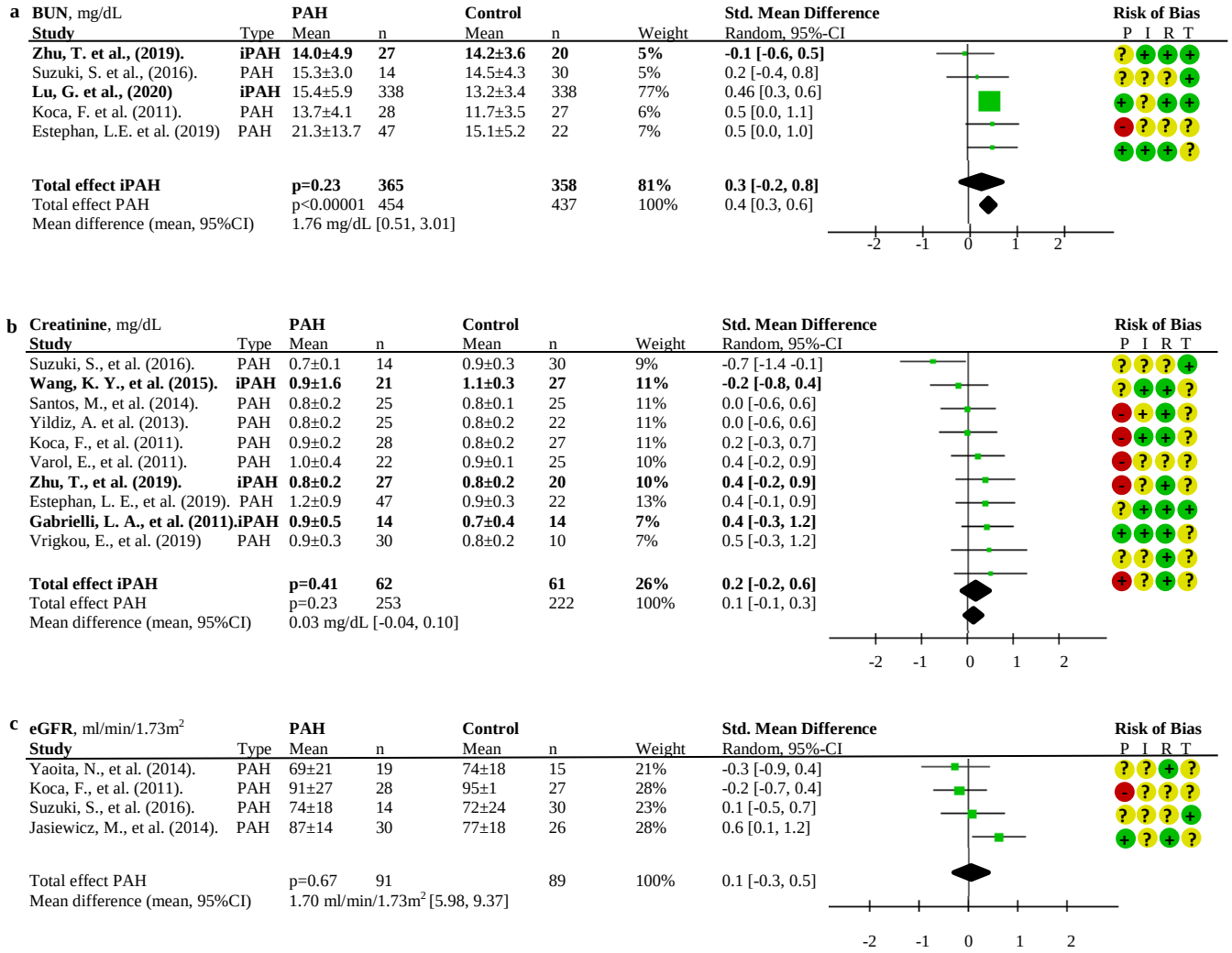


Fig. S6 Forest plots of non-selected renal biomarkers, including; BUN; brain urea nitrogen, creatinine, eGFR; estimated glomerular filtration rate. Risk of bias (QUADAS-2), P: patient inclusion, I; index-test (biomarker), R; reference standard (diagnosis), T; flow and timing. Publications pressed in bold measured biomarker levels in iPAH and/or hPAH uniquely.

Fig. S7

Hepatic

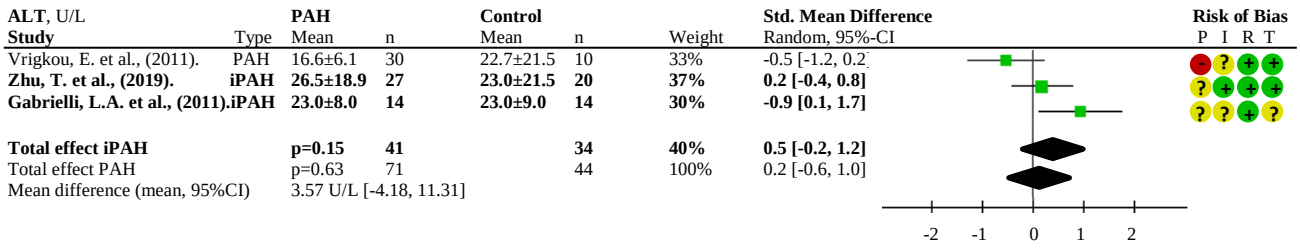
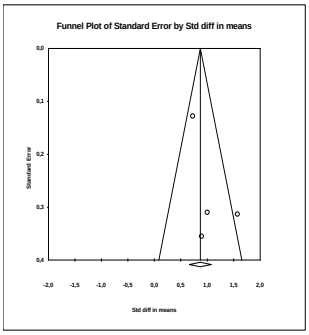


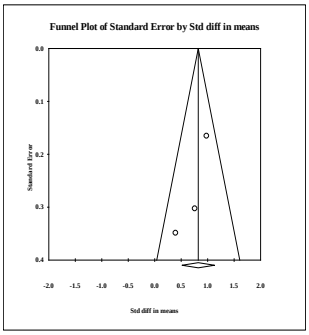
Fig. S7 Forest plots of non-selected hepatic biomarkers, including; ALT; alanine transaminase. Risk of bias (QUADAS-2), P: patient inclusion, I; index-test (biomarker), R; reference standard (diagnosis), T; flow and timing. Publications pressed in bold measured biomarker levels in iPAH and/or hPAH uniquely.

Figure S8

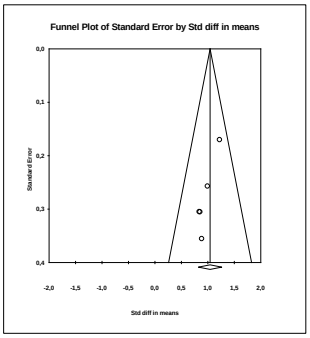
a. RDW



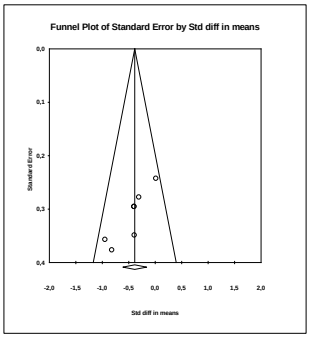
b. PDW



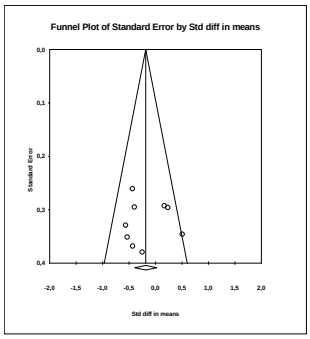
c. MPV



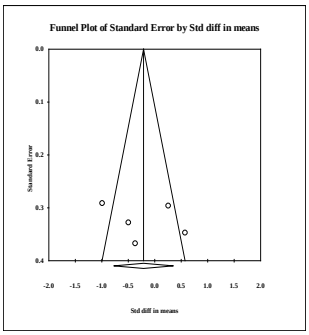
d. Thrombocytes



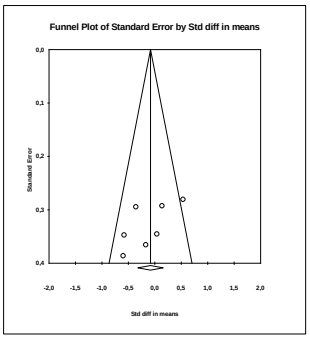
e. Hb



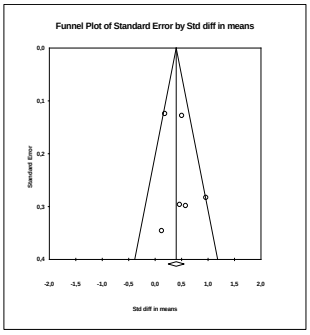
f. Hct



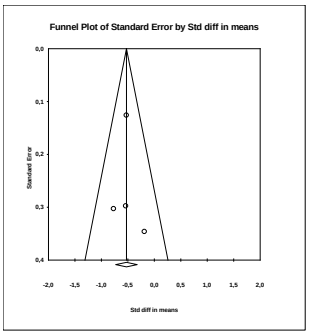
g. Leukocytes



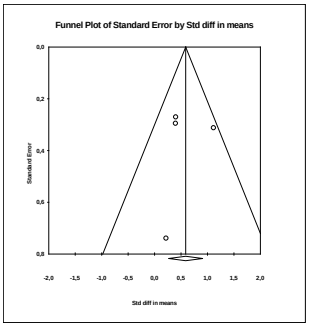
h. LDL-c



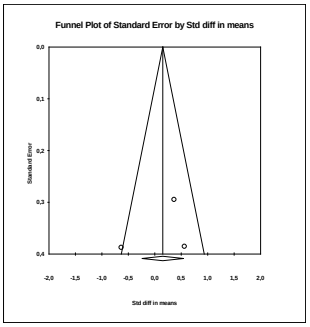
i. Total cholesterol



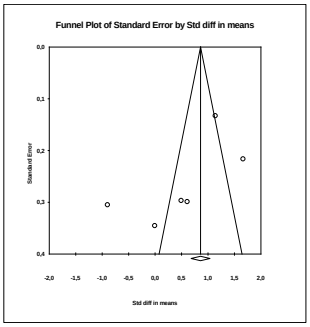
j. TG



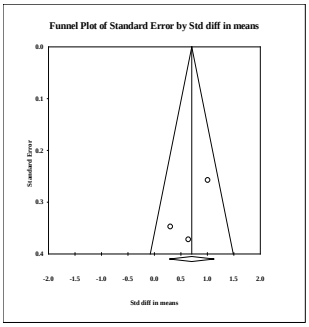
k. Glucose (fasted)



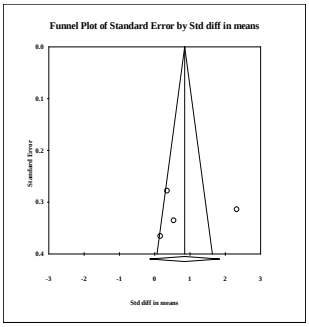
l. HDL-c



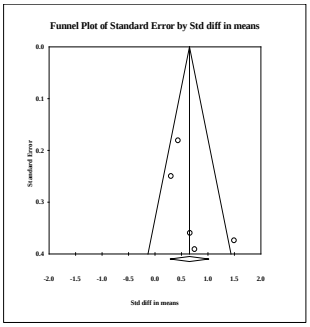
m. D-dimer



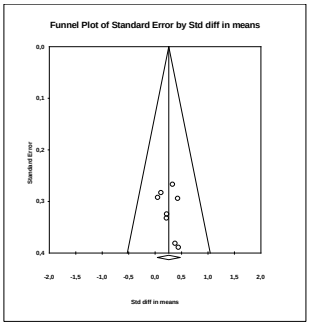
n. Fibrinogen



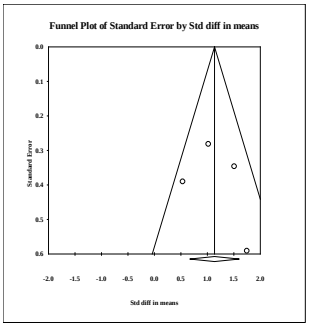
o. IL-6



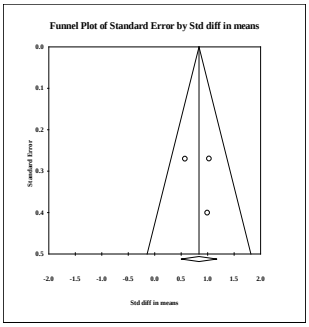
p. CRP



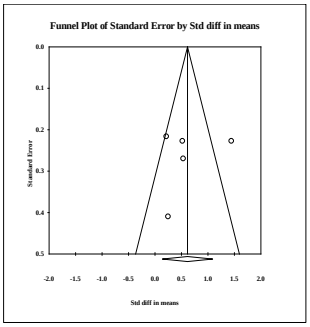
q. sVCAM



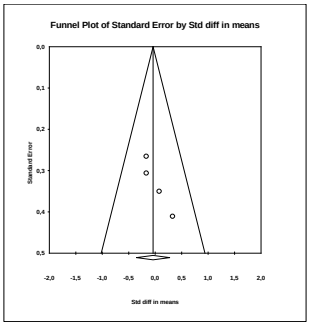
r. CXCL-10



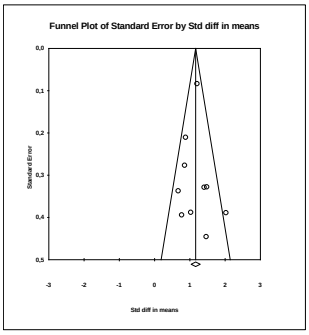
s. TIMP-1



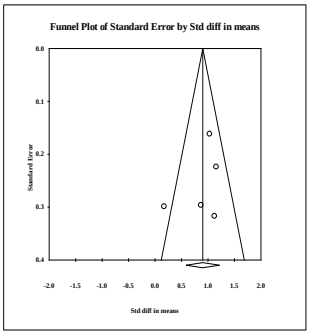
t. sP-selectin



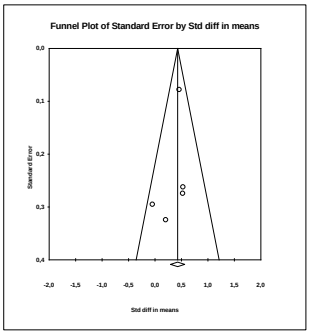
u. NT-proBNP



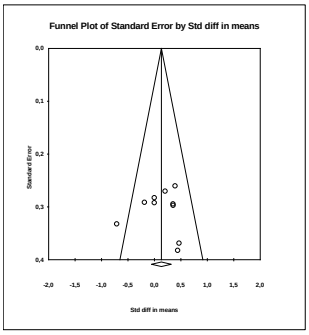
v. UA



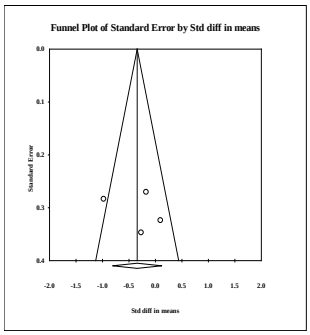
w. BUN



x. Creatinine



y. eGFR



z. ALT

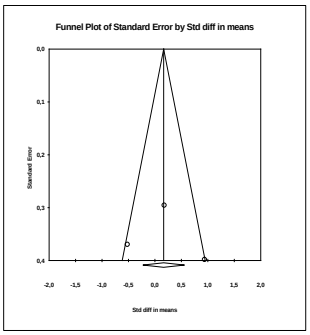


Fig. S8 Funel plots of all meta-analysis indicating publication bias. X-axis; standardized difference in means, y-axis; standard error. Each dot represents one publication.

Table S1

Search strategy Biomarkers

PubMed 887 results (28 January, 2021)

Search	Query	Results
#8	(#1 AND #2 AND (#3 OR #4 OR #5 OR #6 OR #7))	887
#7	"Blood"[Mesh] OR "blood*"[tiab] OR "Plasma"[Mesh] OR "plasma*"[tiab] OR "Serum"[Mesh] OR "serum*"[tiab] OR "sera*"[tiab] OR "Urine"[Mesh] OR "urin*"[tiab]	4519455
#6	"adipogenesis inhibitory factor"[tiab] OR "amcf i"[tiab] OR "antiheparin factor"[tiab] OR "autocrine motility factor"[tiab] OR "b cell differentiation factor"[tiab] OR "b cell growth factor"[tiab] OR "b cell proliferating factor"[tiab] OR "b cell stimulatory factor"[tiab] OR "beta 2 thromboglobulin"[tiab] OR "beta thromboglobulin"[tiab] OR "bsf 1"[tiab] OR "bsf 2"[tiab] OR "Chemokines, CC"[Mesh] OR "chemotactic factor"[tiab] OR "chemotactic peptide"[tiab] OR "colony stimulating factor"[tiab] OR "colony stimulating factors"[tiab] OR "csif 10"[tiab] OR "ctla 8"[tiab] OR "Cytokines"[mesh] OR "cytotoxic t lymphocyte associated antigen"[tiab] OR "eosinophil differentiation factor"[tiab] OR "epidermal cell derived thymocyte activating factor"[tiab] OR "erythrocyte burst promoting factor"[tiab] OR "gamma thromboglobulin"[tiab] OR "gdf 15"[tiab] OR "growth and development factor"[tiab] OR "growth differentiation factor 15"[tiab] OR "heparin neutralizing protein"[tiab] OR "heparin neutralizing proteins"[tiab] OR "hepatocyte growth factor"[tiab] OR "hepatocyte stimulating factor"[tiab] OR "hybridoma growth factor"[tiab] OR "ifn beta 2"[tiab] OR "ifn gamma inducing factor"[tiab] OR "il 1"[tiab] OR "il 10"[tiab] OR "il 11"[tiab] OR "il 12"[tiab] OR "il 12p35"[tiab] OR "il 12p40"[tiab] OR "il 13"[tiab] OR "il 15"[tiab] OR "il 16"[tiab] OR "il 17"[tiab] OR "il 17a"[tiab] OR "il 17b"[tiab] OR "il 17c"[tiab] OR "il 17d"[tiab] OR "il 17e"[tiab] OR "il 17f"[tiab] OR "il 18"[tiab] OR "il 1ra"[tiab] OR "il 23 p19"[tiab] OR "il 23"[tiab] OR "il 23p19"[tiab] OR "il 3"[tiab] OR "il 4"[tiab] OR "il 5"[tiab] OR "il 6"[tiab] OR "il 7"[tiab] OR "il 8"[tiab] OR "il 9"[tiab] OR "kit ligand"[tiab] OR "lcf factor"[tiab] OR "lymphocyte activating factor"[tiab] OR "lymphocyte chemoattractant factor"[tiab] OR "lymphocyte mitogenic factor"[tiab] OR "lymphopoietin 1"[tiab] OR "macrophage cell factor"[tiab] OR "macrophage granulocyte inducer"[tiab] OR "macrophage inflammatory protein"[tiab] OR "macrophage inflammatory proteins"[tiab] OR "mast cell growth factor"[tiab] OR "mcgf 2"[tiab] OR "mgdf factor"[tiab] OR "mgi 1"[tiab] OR "mgi 2"[tiab] OR "monocyte chemotactic proteins"[tiab] OR "mpl ligand"[tiab] OR "myeloid cell growth inducer"[tiab] OR "myeloid differentiation inducing protein"[tiab] OR "myeloproliferative leukemia virus oncogene ligand"[tiab] OR "natural killer cell stimulatory factor"[tiab] OR "neutrophil activating peptide"[tiab] OR "neutrophil activation factor"[tiab] OR "Orphan Nuclear Receptors"[Mesh] OR "p cell stimulating factor"[tiab] OR "plasmacytoma growth factor"[tiab] OR "prostate differentiation factor"[tiab] OR "protein inducer mgi"[tiab] OR "Receptors, Chemokine"[Mesh] OR "Receptors, Cytokine"[Mesh] OR "Receptors, Interleukin-7"[Mesh] OR "recombinant g csf"[tiab] OR "recombinant gm csf"[tiab] OR "ro 23 6019"[tiab] OR "ro 236019"[tiab] OR "ru 49637"[tiab] OR "scatter factor"[tiab] OR "steel factor"[tiab] OR "stem cell factor"[tiab] OR "t cell growth factor"[tiab] OR "t cell replacing factor"[tiab] OR "t cell stimulating factor"[tiab] OR "t helper factor"[tiab] OR "thrombocytopoiesis stimulating factor"[tiab] OR "thymocyte stimulating factor"[tiab] OR "b cell activating factor"[tiab] OR "b cell maturation protein a"[tiab] OR "b lymphocyte activating factor"[tiab] OR "b lymphocyte stimulator"[tiab] OR "betac interleukin receptor subunit"[tiab] OR "br3 b cell activation factor receptor"[tiab] OR "cd 127"[tiab] OR "cd134l protein"[tiab] OR "cd27l protein"[tiab] OR "cd95l"[tiab] OR "csf2rb receptor"[tiab] OR "cytokine receptor gp130"[tiab] OR "enbrel"[tiab] OR "erelzi"[tiab] OR "gp130 signal transducer"[tiab] OR "il6st gp130"[tiab] OR "leukemia inhibitory factor oncostatin m shared receptor"[tiab] OR "leukemia inhibitory factor receptor"[tiab] OR "lin"[tiab] OR "lin+"[tiab] OR "nf kappa b receptor activator"[tiab] OR "nf kappab receptor activator"[tiab] OR "oncostatin m leukemia inhibitory factor shared receptor"[tiab] OR "oncostatin m receptor beta"[tiab] OR "oncostatin m type i receptor"[tiab] OR "oncostatin m type ii receptor"[tiab] OR "osteoclast differentiation factor"[tiab] OR "p145 c kit"[tiab] OR "p145c kit"[tiab] OR "proto oncogene protein c kit"[tiab] OR "proto oncogene protein fms"[tiab] OR "proto oncogene protein kit"[tiab] OR "proto oncogene proteins c kit"[tiab] OR "rankl"[tiab] OR "receptor activator of nf kappa b"[tiab] OR "receptor activator of nf kappab"[tiab] OR "receptor activator of nuclear factor kappa b"[tiab] OR "sgp130"[tiab] OR "signal transducer gp130"[tiab] OR "signal transducing receptor gp130"[tiab] OR "soluble glycoprotein 130"[tiab] OR "soluble gp130"[tiab] OR "t b cell activating molecule"[tiab] OR "t cell gp39 antigen"[tiab] OR "tall 1 protein"[tiab] OR "tnfr fc fusion protein"[tiab] OR "tnfrsf11a protein"[tiab] OR "tnfrsf5 receptor"[tiab] OR "tnfrsf8 receptor"[tiab] OR "tnfsf13b"[tiab] OR "tnr 001"[tiab] OR "tnr001"[tiab] OR "tntr fc"[tiab] OR "trance protein"[tiab] OR "trance r"[tiab] OR "transmembrane activator and caml interactor protein"[tiab] OR "tweakr"[tiab] OR "4 1bb ligand*"[tiab] OR "4 1bbl protein*"[tiab] OR "apo 1 antigen*"[tiab] OR "b cell maturation antigen*"[tiab] OR "baff ligand*"[tiab] OR "baff receptor*"[tiab] OR "bcgf"[tiab] OR "bcma protein*"[tiab] OR "ber h2 antigen*"[tiab] OR "blys protein*"[tiab] OR "c fms protein*"[tiab] OR "c kit protein*"[tiab] OR "c kit receptor*"[tiab] OR "catabolin*"[tiab] OR "ccl1"[tiab] OR "ccl11"[tiab] OR "ccl17"[tiab] OR "ccl18"[tiab] OR "ccl19"[tiab] OR "ccl2"[tiab] OR "ccl20"[tiab] OR "ccl21"[tiab] OR "ccl22"[tiab] OR "ccl24"[tiab] OR "ccl26"[tiab] OR "ccl27"[tiab] OR "ccl3"[tiab] OR "ccl4"[tiab] OR "ccl5"[tiab] OR "ccl7"[tiab] OR "ccl8"[tiab] OR "ccr"[tiab] OR "ccr1"[tiab] OR "ccr10"[tiab] OR "ccr2"[tiab] OR "ccr3"[tiab] OR "ccr4"[tiab] OR "ccr5"[tiab] OR "ccr6"[tiab] OR "ccr7"[tiab] OR "ccr8"[tiab] OR "cd115 antigen*"[tiab] OR "cd116 antigen*"[tiab] OR "cd117 antigen*"[tiab] OR "cd118 antigen*"[tiab] OR "cd127"[tiab] OR "cd130 antigen*"[tiab] OR "cd131 antigen*"[tiab] OR "cd134 antigen*"[tiab] OR "cd134 ligand*"[tiab] OR "cd137 ligand*"[tiab] OR "cd153 antigen*"[tiab] OR "cd154 antigen*"[tiab] OR "cd178 antigen*"[tiab] OR "cd254 antigen*"[tiab] OR "cd257 antigen*"[tiab] OR "cd265 antigen*"[tiab] OR "cd266 antigen*"[tiab] OR "cd267 antigen*"[tiab] OR "cd268 antigen*"[tiab] OR "cd27 ligand*"[tiab] OR "cd30 antigen*"[tiab] OR "cd30 ligand*"[tiab] OR "cd357 antigen*"[tiab] OR "cd40 antigen*"[tiab] OR "cd40 ligand*"[tiab] OR "cd40l"[tiab] OR "cd70 antigen*"[tiab] OR "cd95 antigen*"[tiab] OR "cd95 ligand*"[tiab] OR "cdw40 antigen*"[tiab] OR "chemokin*"[tiab] OR "chemokine*"[tiab] OR "colony stimulating factor receptor*"[tiab] OR "csf 1 receptor*"[tiab] OR "csf receptor*"[tiab] OR "ctla8"[tiab] OR "cx3c"[tiab] OR "cxcl8"[tiab] OR "cxcr"[tiab] OR "cxcr3"[tiab] OR "cxcr4"[tiab] OR "cxcr5"[tiab] OR "cxcr6"[tiab] OR "cytokin*"[tiab] OR "ectodysplasin*"[tiab] OR "erythropoietin receptor*"[tiab] OR "erythropoietin*"[tiab] OR "etanercept"[tiab] OR "fas antigen*"[tiab] OR "fas cell surface death receptor*"[tiab] OR "fas ligand*"[tiab] OR "fas receptor*"[tiab] OR "fasl protein*"[tiab] OR "fms proto oncogene protein*"[tiab] OR "fn14 receptor*"[tiab] OR "g csf receptor*"[tiab] OR "glucocorticoid induced tnfr related protein*"[tiab] OR "gm csf receptor*"[tiab] OR "gp130 transducing protein*"[tiab] OR "granulocyte colony stimulating factor receptor*"[tiab] OR "hematopoieti*"[tiab] OR "hepatopoietin*"[tiab] OR "il1"[tiab] OR "il10"[tiab] OR "il11"[tiab] OR "il12"[tiab] OR "il13"[tiab] OR "il15"[tiab] OR "il16"[tiab] OR "il17"[tiab] OR "il17a"[tiab] OR "il17b"[tiab] OR "il17c"[tiab] OR "il17d"[tiab] OR "il17e"[tiab] OR "il17f"[tiab] OR "il18"[tiab] OR "il23"[tiab] OR "il3"[tiab] OR "il4"[tiab] OR "il5"[tiab] OR "il6"[tiab] OR "il7"[tiab] OR "il8"[tiab] OR "il9"[tiab] OR "interferon*"[tiab] OR "interleukin*"[tiab] OR "ki 1 antigen*"[tiab] OR "kit proto oncogene protein*"[tiab] OR "lif receptor*"[tiab] OR "lineage negative"[tiab] OR "lymphokine*"[tiab] OR "lymphotoxin*"[tiab] OR "m csf receptor*"[tiab] OR "macrophage colony stimulating factor receptor*"[tiab] OR "monocyte chemoattractant protein*"[tiab] OR "monocyte chemotactic protein*"[tiab] OR "opgl protein*"[tiab] OR "osm lif receptor*"[tiab] OR "osteoprotegerin ligand*"[tiab] OR "ox40 ligand*"[tiab] OR "ox40 receptor*"[tiab] OR "ox40l	1211502

	protein*"[tiab] OR "rank ligand*"[tiab] OR "recombinant human dimeric tnf receptor type ii igg fusion protein*"[tiab] OR "ro236019"[tiab] OR "ru49637"[tiab] OR "scf receptor*"[tiab] OR "stem cell factor receptor*"[tiab] OR "taci receptor*"[tiab] OR "tcgf"[tiab] OR "thank protein*"[tiab] OR "thrombocytopoietin*"[tiab] OR "thrombopoietin*"[tiab] OR "tnfrsf6 receptor*"[tiab] OR "tnt receptor fusion protein*"[tiab] OR "trance receptor*"[tiab] OR "tweak receptor*"[tiab] OR "transforming growth factor*"[tiab] OR "tumor necrosis factor*"[tiab]	
#5	"Blood Cells"[Mesh] OR "blood cell*"[tiab] OR "thrombocyt*"[tiab] OR "platelet*"[tiab] OR "erythrocyt*"[tiab] OR "hemocyt*"[tiab] OR "leukocyt*"[tiab] OR "reticulocyt*"[tiab] OR "granulocyt*"[tiab] OR "mononuclear cell*"[tiab] OR "stem cell*"[tiab] OR "progenitor cell*"[tiab] OR "mother cell*"[tiab] OR "colony forming"[tiab] OR "basophil*"[tiab] OR "eosinophil*"[tiab] OR "neutrophil*"[tiab] OR "lymphocyt*"[tiab] OR "monocyt*"[tiab] OR "killer cell*"[tiab] OR "nk cell*"[tiab] OR "precursor cell*"[tiab] OR "suppressor cell*"[tiab] OR "myelocyt*"[tiab] OR "myeloblast*"[tiab] OR "B-cell*"[tiab] OR "T-cell*"[tiab] OR "T helper cel*"[tiab] OR "Treg*"[tiab] OR "macrophage*"[tiab] OR "myeloid cell*"[tiab] OR "dendritic cell*"[tiab] OR "antigen-presenting cell*"[tiab] OR "immune cell*"[tiab] OR "inflammatory cell*"[tiab] OR "CD4"[tiab] OR "CD8"[tiab]	2350640
#4	"Extracellular Vesicles"[Mesh] OR "microparticle*"[tiab] OR "microvesicle*"[tiab] OR "exosom*"[tiab] OR "ectosom*"[tiab] OR "extracellular vesicle*"[tiab] OR "exovesicle*"[tiab] OR "apoptotic bod*"[tiab]	46380
#3	"MicroRNAs"[Mesh] OR "MicroRNA*"[tiab] OR "Micro RNA*"[tiab] OR "miRNA*"[tiab] OR "pri-miRNA*"[tiab] OR "stRNA*"[tiab] OR "Small Temporal RNA*"[tiab] OR "pre-miRNA*"[tiab] OR "lncRNA* "[tiab] OR "non-coding RNA*"[tiab] OR "noncoding RNA*"[tiab] OR "ncRNA*"[tiab]	150417
#2	("Biomarkers"[Mesh] OR "biomarker*"[tiab] OR "marker*"[tiab] OR "indicator*"[tiab])	1729998
#1	("Familial Primary Pulmonary Hypertension"[Mesh] OR "pulmonary arterial hypertensi*"[tiab] OR "pulmonary artery hypertensi*"[tiab] OR "idiopathic pulmonary hypertens*"[tiab] OR "hereditary pulmonary hypertens*"[tiab] OR "heritable pulmonary hypertens*"[tiab] OR "primary pulmonary hypertensi*"[tiab] OR "primary pulmonary hypertens*"[tiab])	16546

Embase.com 1506 results, 736 excluding conference abstracts (28 January, 2021)

No.	Query	Results
#10	#9 NOT 'conference abstract'/it	736
#9	#8 NOT ([animals]/lim NOT [humans]/lim)	1506
#8	#1 AND #2 AND (#3 OR #4 OR #5 OR #6 OR #7)	1740
#7	'urine'/exp OR 'blood'/exp OR 'blood*':ti,ab,kw OR 'plasma*':ti,ab,kw OR 'serum*':ti,ab,kw OR 'sera*':ti,ab,kw OR 'urin*':ti,ab,kw	6345741
#6	'cytokine'/exp OR 'orphan nuclear receptor'/exp OR 'cytokine receptor'/exp OR 'adipogenesis inhibitory factor*':ti,ab,kw OR 'amcf i':ti,ab,kw OR 'antiheparin factor*':ti,ab,kw OR 'autocrine motility factor*':ti,ab,kw OR 'apo 1 antigen*':ti,ab,kw OR 'b cell differentiation factor*':ti,ab,kw OR 'b cell growth factor*':ti,ab,kw OR 'b cell proliferating factor*':ti,ab,kw OR 'b cell stimulatory factor*':ti,ab,kw OR 'beta 2 thromboglobulin':ti,ab,kw OR 'beta thromboglobulin':ti,ab,kw OR 'bsf 1':ti,ab,kw OR 'bsf 2':ti,ab,kw OR 'b cell activating factor*':ti,ab,kw OR 'b cell maturation protein a':ti,ab,kw OR 'b lymphocyte activating factor*':ti,ab,kw OR 'b lymphocyte stimulator':ti,ab,kw OR 'betac interleukin receptor subunit':ti,ab,kw OR 'br3 b cell activation factor receptor':ti,ab,kw OR 'b cell maturation antigen*':ti,ab,kw OR 'baff ligand*':ti,ab,kw OR 'baff receptor*':ti,ab,kw OR 'bcgf':ti,ab,kw OR 'bcma protein*':ti,ab,kw OR 'ber h2 antigen*':ti,ab,kw OR 'blys protein*':ti,ab,kw OR 'chemotactic factor*':ti,ab,kw OR 'chemotactic peptid*':ti,ab,kw OR 'colony stimulating factor*':ti,ab,kw OR 'csif 10':ti,ab,kw OR 'ctla 8':ti,ab,kw OR 'cytotoxic t lymphocyte associated antigen':ti,ab,kw OR 'cd 127':ti,ab,kw OR 'cd134l protein':ti,ab,kw OR 'cd27l protein':ti,ab,kw OR 'cd95l':ti,ab,kw OR 'csf2rb receptor':ti,ab,kw OR 'cytokine receptor gp130':ti,ab,kw OR 'c fms protein*':ti,ab,kw OR 'c kit protein*':ti,ab,kw OR 'c kit receptor*':ti,ab,kw OR 'catabolin*':ti,ab,kw OR 'ccl1*':ti,ab,kw OR 'ccl2*':ti,ab,kw OR 'ccl3*':ti,ab,kw OR 'ccl4':ti,ab,kw OR 'ccl5':ti,ab,kw OR 'ccl7':ti,ab,kw OR 'ccl8':ti,ab,kw OR 'ccr':ti,ab,kw OR 'ccr1*':ti,ab,kw OR 'ccr2':ti,ab,kw OR 'ccr3':ti,ab,kw OR 'ccr4':ti,ab,kw OR 'ccr5':ti,ab,kw OR 'ccr6':ti,ab,kw OR 'ccr7':ti,ab,kw OR 'ccr8':ti,ab,kw OR 'cd115 antigen*':ti,ab,kw OR 'cd116 antigen*':ti,ab,kw OR 'cd117 antigen*':ti,ab,kw OR 'cd118 antigen*':ti,ab,kw OR 'cd127':ti,ab,kw OR 'cd130 antigen*':ti,ab,kw OR 'cd131 antigen*':ti,ab,kw OR 'cd134 antigen*':ti,ab,kw OR 'cd134 ligand*':ti,ab,kw OR 'cd137 ligand*':ti,ab,kw OR 'cd153 antigen*':ti,ab,kw OR 'cd154 antigen*':ti,ab,kw OR 'cd178 antigen*':ti,ab,kw OR 'cd254 antigen*':ti,ab,kw OR 'cd257 antigen*':ti,ab,kw OR 'cd265 antigen*':ti,ab,kw OR 'cd266 antigen*':ti,ab,kw OR 'cd267 antigen*':ti,ab,kw OR 'cd268 antigen*':ti,ab,kw OR 'cd27 ligand*':ti,ab,kw OR 'cd30 antigen*':ti,ab,kw OR 'cd30 ligand*':ti,ab,kw OR 'cd357 antigen*':ti,ab,kw OR 'cd40 antigen*':ti,ab,kw OR 'cd40 ligand*':ti,ab,kw OR 'cd40l':ti,ab,kw OR 'cd70 antigen*':ti,ab,kw OR 'cd95 antigen*':ti,ab,kw OR 'cd95 ligand*':ti,ab,kw OR 'cdw40 antigen*':ti,ab,kw OR 'chemokin*':ti,ab,kw OR 'chemokine*':ti,ab,kw OR 'csf 1 receptor*':ti,ab,kw OR 'csf receptor*':ti,ab,kw OR 'ctla8':ti,ab,kw OR 'cx3c':ti,ab,kw OR 'cxcl8':ti,ab,kw OR 'cxcr':ti,ab,kw OR 'cxcr3':ti,ab,kw OR 'cxcr4':ti,ab,kw OR 'cxcr5':ti,ab,kw OR 'cxcr6':ti,ab,kw OR 'cytokin*':ti,ab,kw OR 'eosinophil differentiation factor':ti,ab,kw OR 'epidermal cell derived thymocyte activating factor':ti,ab,kw OR 'erythrocyte burst promoting factor':ti,ab,kw OR 'enbrel':ti,ab,kw OR 'erelzi':ti,ab,kw OR 'ectodysplasin*':ti,ab,kw OR 'erythropoietin receptor*':ti,ab,kw OR 'erythropoietin*':ti,ab,kw OR 'etanercept':ti,ab,kw OR 'fas antigen*':ti,ab,kw OR 'fas cell surface death receptor*':ti,ab,kw OR 'fas ligand*':ti,ab,kw OR 'fas receptor*':ti,ab,kw OR 'fasl protein*':ti,ab,kw OR 'fms proto oncogene protein*':ti,ab,kw OR 'fn14 receptor*':ti,ab,kw OR 'gamma thromboglobulin':ti,ab,kw OR 'gdf 15':ti,ab,kw OR 'growth and development factor':ti,ab,kw OR 'growth differentiation factor 15':ti,ab,kw OR 'gp130 signal transducer':ti,ab,kw OR 'g csf receptor*':ti,ab,kw OR 'glucocorticoid induced tnfr related protein*':ti,ab,kw OR 'gm csf receptor*':ti,ab,kw OR 'gp130 transducing protein*':ti,ab,kw OR 'heparin neutralizing protein':ti,ab,kw OR 'heparin neutralizing proteins':ti,ab,kw OR 'hepatocyte growth factor':ti,ab,kw OR 'hepatocyte stimulating factor':ti,ab,kw OR 'hybridoma growth factor':ti,ab,kw OR 'hematopoieti*':ti,ab,kw OR 'hepatopoietin*':ti,ab,kw OR 'ifn beta 2':ti,ab,kw OR 'ifn gamma inducing factor':ti,ab,kw OR 'il 1':ti,ab,kw OR 'il 10':ti,ab,kw OR 'il 11':ti,ab,kw OR 'il 12':ti,ab,kw OR 'il 12p35':ti,ab,kw OR 'il 12p40':ti,ab,kw OR 'il 13':ti,ab,kw OR 'il 15':ti,ab,kw OR 'il 16':ti,ab,kw OR 'il 17':ti,ab,kw OR 'il 17a':ti,ab,kw OR 'il 17b':ti,ab,kw OR 'il 17c':ti,ab,kw OR 'il 17d':ti,ab,kw OR 'il 17e':ti,ab,kw OR 'il 17f':ti,ab,kw OR 'il 18':ti,ab,kw OR 'il 1ra':ti,ab,kw OR 'il 23 p19':ti,ab,kw OR 'il 23':ti,ab,kw OR 'il 23p19':ti,ab,kw OR 'il 3':ti,ab,kw OR 'il 4':ti,ab,kw OR 'il 5':ti,ab,kw OR 'il 6':ti,ab,kw OR 'il 7':ti,ab,kw OR 'il 8':ti,ab,kw OR 'il 9':ti,ab,kw OR 'il6st gp130':ti,ab,kw OR 'il1':ti,ab,kw OR 'il10':ti,ab,kw OR 'il11':ti,ab,kw OR 'il12':ti,ab,kw OR 'il13':ti,ab,kw OR 'il15':ti,ab,kw OR 'il16':ti,ab,kw OR 'il17':ti,ab,kw OR 'il17a':ti,ab,kw OR 'il17b':ti,ab,kw OR 'il17c':ti,ab,kw OR 'il17d':ti,ab,kw OR 'il17e':ti,ab,kw OR 'il17f':ti,ab,kw OR 'il18':ti,ab,kw OR 'il23':ti,ab,kw OR 'il3':ti,ab,kw OR 'il4':ti,ab,kw OR 'il5':ti,ab,kw OR 'il6':ti,ab,kw OR 'il7':ti,ab,kw OR 'il8':ti,ab,kw OR 'il9':ti,ab,kw OR 'interferon*':ti,ab,kw OR 'interleukin*':ti,ab,kw OR 'kit ligand':ti,ab,kw OR 'lcf factor':ti,ab,kw OR 'ki 1 antigen*':ti,ab,kw OR 'kit proto oncogene protein*':ti,ab,kw OR 'lymphocyte activating factor':ti,ab,kw OR 'lymphocyte chemoattractant factor':ti,ab,kw OR 'lymphocyte mitogenic factor':ti,ab,kw OR 'lymphopoietin 1':ti,ab,kw OR 'leukemia inhibitory factor oncostatin m shared receptor':ti,ab,kw OR 'leukemia inhibitory factor receptor':ti,ab,kw OR 'lin':ti,ab,kw OR 'lin+':ti,ab,kw OR 'lif receptor*':ti,ab,kw OR 'lineage negative':ti,ab,kw OR 'lymphokine*':ti,ab,kw OR 'lymphotoxin*':ti,ab,kw OR 'macrophage cell factor':ti,ab,kw OR 'macrophage granulocyte inducer':ti,ab,kw OR 'macrophage inflammatory	2048571

	protein':ti,ab,kw OR 'macrophage inflammatory proteins':ti,ab,kw OR 'mast cell growth factor':ti,ab,kw OR 'mcgf 2':ti,ab,kw OR 'mgdf factor':ti,ab,kw OR 'mgi 1':ti,ab,kw OR 'mgi 2':ti,ab,kw OR 'monocyte chemotactic proteins':ti,ab,kw OR 'mpl ligand':ti,ab,kw OR 'myeloid cell growth inducer':ti,ab,kw OR 'myeloid differentiation inducing protein':ti,ab,kw OR 'myeloproliferative leukemia virus oncogene ligand':ti,ab,kw OR 'm csf receptor*':ti,ab,kw OR 'monocyte chemoattractant protein*':ti,ab,kw OR 'monocyte chemotactic protein*':ti,ab,kw OR 'natural killer cell stimulatory factor*':ti,ab,kw OR 'neutrophil activating peptide':ti,ab,kw OR 'neutrophil activation factor':ti,ab,kw OR 'nf kappa b receptor activator':ti,ab,kw OR 'nf kappab receptor activator':ti,ab,kw OR 'p cell stimulating factor':ti,ab,kw OR 'oncostatin m leukemia inhibitory factor shared receptor':ti,ab,kw OR 'oncostatin m receptor beta':ti,ab,kw OR 'oncostatin m type i receptor':ti,ab,kw OR 'oncostatin m type ii receptor':ti,ab,kw OR 'osteoclast differentiation factor':ti,ab,kw OR 'opgl protein*':ti,ab,kw OR 'osm lif receptor*':ti,ab,kw OR 'osteoprotegerin ligand*':ti,ab,kw OR 'ox40 ligand*':ti,ab,kw OR 'ox40 receptor*':ti,ab,kw OR 'ox40l protein*':ti,ab,kw OR 'plasmacytoma growth factor':ti,ab,kw OR 'prostate differentiation factor':ti,ab,kw OR 'protein inducer mgi':ti,ab,kw OR 'p145 c kit':ti,ab,kw OR 'p145c kit':ti,ab,kw OR 'proto oncogene protein c kit':ti,ab,kw OR 'proto oncogene protein fms':ti,ab,kw OR 'proto oncogene protein kit':ti,ab,kw OR 'proto oncogene proteins c kit':ti,ab,kw OR 'recombinant g csf':ti,ab,kw OR 'recombinant gm csf':ti,ab,kw OR 'ro 23 6019':ti,ab,kw OR 'ro 236019':ti,ab,kw OR 'ru 49637':ti,ab,kw OR 'rankl':ti,ab,kw OR 'receptor activator of nf kappa b':ti,ab,kw OR 'receptor activator of nf kappab':ti,ab,kw OR 'receptor activator of nuclear factor kappa b':ti,ab,kw OR 'rank ligand*':ti,ab,kw OR 'recombinant human dimeric tnf receptor type ii igg fusion protein*':ti,ab,kw OR 'ro236019':ti,ab,kw OR 'ru49637':ti,ab,kw OR 'scatter factor':ti,ab,kw OR 'steel factor':ti,ab,kw OR 'stem cell factor':ti,ab,kw OR 'sgp130':ti,ab,kw OR 'signal transducer gp130':ti,ab,kw OR 'signal transducing receptor gp130':ti,ab,kw OR 'soluble glycoprotein 130':ti,ab,kw OR 'soluble gp130':ti,ab,kw OR 'scf receptor*':ti,ab,kw OR 'stem cell factor receptor*':ti,ab,kw OR 't cell growth factor':ti,ab,kw OR 't cell replacing factor':ti,ab,kw OR 't cell stimulating factor':ti,ab,kw OR 't helper factor':ti,ab,kw OR 'thrombocytopoiesis stimulating factor':ti,ab,kw OR 'thymocyte stimulating factor':ti,ab,kw OR 't b cell activating molecule':ti,ab,kw OR 't cell gp39 antigen':ti,ab,kw OR 'tall 1 protein':ti,ab,kw OR 'tnfr fc fusion protein':ti,ab,kw OR 'tnfrsf11a protein':ti,ab,kw OR 'tnfrsf5 receptor':ti,ab,kw OR 'tnfrsf8 receptor':ti,ab,kw OR 'tnfsf13b':ti,ab,kw OR 'tnr 001':ti,ab,kw OR 'tnr001':ti,ab,kw OR 'tntr fc':ti,ab,kw OR 'trance protein':ti,ab,kw OR 'trance r':ti,ab,kw OR 'transmembrane activator and caml interactor protein':ti,ab,kw OR 'tweakr':ti,ab,kw OR 'taci receptor*':ti,ab,kw OR 'tcgf':ti,ab,kw OR 'thank protein*':ti,ab,kw OR 'thrombocytopoietin*':ti,ab,kw OR 'thrombopoietin*':ti,ab,kw OR 'tnfrsf6 receptor*':ti,ab,kw OR 'tnt receptor fusion protein*':ti,ab,kw OR 'trance receptor*':ti,ab,kw OR 'tweak receptor*':ti,ab,kw OR 'transforming growth factor*':ti,ab,kw OR 'tumor necrosis factor*':ti,ab,kw OR '4 1bb ligand*':ti,ab,kw OR '4 1bbl protein*':ti,ab,kw	
#5	'blood cell'/exp OR 'blood cell*':ti,ab,kw OR 'thrombocyt*':ti,ab,kw OR 'platelet*':ti,ab,kw OR 'erythrocyt*':ti,ab,kw OR 'hemocyt*':ti,ab,kw OR 'leukocyt*':ti,ab,kw OR 'reticulocyt*':ti,ab,kw OR 'granulocyt*':ti,ab,kw OR 'mononuclear cell*':ti,ab,kw OR 'stem cell*':ti,ab,kw OR 'progenitor cell*':ti,ab,kw OR 'mother cell*':ti,ab,kw OR 'colony forming':ti,ab,kw OR 'basophil*':ti,ab,kw OR 'eosinophil*':ti,ab,kw OR 'neutrophil*':ti,ab,kw OR 'lymphocyt*':ti,ab,kw OR 'monocyt*':ti,ab,kw OR 'killer cell*':ti,ab,kw OR 'nk cell*':ti,ab,kw OR 'precursor cell*':ti,ab,kw OR 'suppressor cell*':ti,ab,kw OR 'myelocyt*':ti,ab,kw OR 'myeloblast*':ti,ab,kw OR 'b-cell*':ti,ab,kw OR 't-cell*':ti,ab,kw OR 't helper cel*':ti,ab,kw OR 'treg*':ti,ab,kw OR 'macrophage*':ti,ab,kw OR 'myeloid cell*':ti,ab,kw OR 'dendritic cell*':ti,ab,kw OR 'antigen-presenting cell*':ti,ab,kw OR 'immune cell*':ti,ab,kw OR 'inflammatory cell*':ti,ab,kw OR 'cd4':ti,ab,kw OR 'cd8':ti,ab,kw	3208435
#4	'microparticle*':ti,ab,kw OR 'microvesicle*':ti,ab,kw OR 'exosom*':ti,ab,kw OR 'ectosom*':ti,ab,kw OR 'extracellular vesicle*':ti,ab,kw OR 'exovesicle*':ti,ab,kw OR 'apoptotic bod*':ti,ab,kw	64493
#3	'microrna'/exp OR 'microrna*':ti,ab,kw OR 'micro rna*':ti,ab,kw OR 'mirna*':ti,ab,kw OR 'pri-mirna*':ti,ab,kw OR 'strna*':ti,ab,kw OR 'small temporal rna*':ti,ab,kw OR 'pre-mirna*':ti,ab,kw OR 'lncrna*':ti,ab,kw OR 'non-coding rna*':ti,ab,kw OR 'noncoding rna*':ti,ab,kw OR 'ncrna*':ti,ab,kw	209930
#2	'biological marker'/exp OR 'biomarker*':ti,ab,kw OR 'marker*':ti,ab,kw OR 'indicator*':ti,ab,kw	1876051
#1	'pulmonary arterial hypertens*':ti,ab,kw OR 'pulmonary artery hypertens*':ti,ab,kw OR 'idiopathic pulmonary hypertensi*':ti,ab,kw OR 'primary pulmonary hypertens*':ti,ab,kw OR 'heritable pulmonary hypertensin':ti,ab,kw OR 'hereditary pulmonary hypertens*':ti,ab,kw	28468

Clarivate Analytics/ Web of Science Core Collection 976 results (28 January, 2021)

Set	Result	
#8	#1 AND #2 AND (#3 OR #4 OR #5 OR #6 OR #7) *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	976
#7	TS=("blood*" OR "plasma*" OR "serum*" OR "sera*" OR "urin*") *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	4312314

#6	TS=("adipogenesis inhibitory factor*" OR "amcf i" OR "antiheparin factor*" OR "autocrine motility factor*" OR "apo 1 antigen*" OR "b cell differentiation factor*" OR "b cell growth factor*" OR "b cell proliferating factor*" OR "b cell stimulatory factor*" OR "beta 2 thromboglobulin" OR "beta thromboglobulin" OR "bsf 1" OR "bsf 2" OR "b cell activating factor*" OR "b cell maturation protein a" OR "b lymphocyte activating factor*" OR "b lymphocyte stimulator" OR "betac interleukin receptor subunit" OR "br3 b cell activation factor receptor" OR "b cell maturation antigen*" OR "baff ligand*" OR "baff receptor*" OR "bcgf" OR "bcma protein*" OR "ber h2 antigen*" OR "blys protein*" OR "chemotactic factor*" OR "chemotactic peptid*" OR "colony stimulating factor*" OR "csif 10" OR "ctla 8" OR "cytotoxic t lymphocyte associated antigen" OR "cd 127" OR "cd 134l protein" OR "cd27l protein" OR "cd95l" OR "csf2rb receptor" OR "cytokine receptor gp130" OR "c fms protein*" OR "c kit protein*" OR "c kit receptor*" OR "catabolin*" OR "ccl1*" OR "ccl2*" OR "ccl3*" OR "ccl4" OR "ccl5" OR "ccl7" OR "ccl8" OR "ccr" OR "ccr1*" OR "ccr2" OR "ccr3" OR "ccr4" OR "ccr5" OR "ccr6" OR "ccr7" OR "ccr8" OR "cd115 antigen*" OR "cd116 antigen*" OR "cd117 antigen*" OR "cd118 antigen*" OR "cd127" OR "cd130 antigen*" OR "cd131 antigen*" OR "cd134 antigen*" OR "cd134 ligand*" OR "cd137 ligand*" OR "cd153 antigen*" OR "cd154 antigen*" OR "cd178 antigen*" OR "cd254 antigen*" OR "cd257 antigen*" OR "cd265 antigen*" OR "cd266 antigen*" OR "cd267 antigen*" OR "cd268 antigen*" OR "cd27 ligand*" OR "cd30 antigen*" OR "cd30 ligand*" OR "cd357 antigen*" OR "cd40 antigen*" OR "cd40 ligand*" OR "cd40l" OR "cd70 antigen*" OR "cd95 antigen*" OR "cd95 ligand*" OR "cdw40 antigen*" OR "chemokin*" OR "chemokine*" OR "csf 1 receptor*" OR "csf receptor*" OR "ctla8" OR "cx3c" OR "cxcl8" OR "cxcr" OR "cxcr3" OR "cxcr4" OR "cxcr5" OR "cxcr6" OR "cytokin*" OR "eosinophil differentiation factor" OR "epidermal cell derived thymocyte activating factor" OR "erythrocyte burst promoting factor" OR "enbrel" OR "erelzi" OR "ectodysplasin*" OR "erythropoietin receptor*" OR "erythropoietin*" OR "etanercept" OR "fas antigen*" OR "fas cell surface death receptor*" OR "fas ligand*" OR "fas receptor*" OR "fasl protein*" OR "fms proto oncogene protein*" OR "fn14 receptor*" OR "gamma thromboglobulin" OR "gdf 15" OR "growth and development factor" OR "growth differentiation factor 15" OR "gp130 signal transducer" OR "g csf receptor*" OR "glucocorticoid induced tnfr related protein*" OR "gm csf receptor*" OR "gp130 transducing protein*" OR "heparin neutralizing protein" OR "heparin neutralizing proteins" OR "hepatocyte growth factor" OR "hepatocyte stimulating factor" OR "hybridoma growth factor" OR "hematopoieti*" OR "hepatopoietin*" OR "ifn beta 2" OR "ifn gamma inducing factor" OR "il 1" OR "il 10" OR "il 11" OR "il 12" OR "il 12p35" OR "il 12p40" OR "il 13" OR "il 15" OR "il 16" OR "il 17" OR "il 17a" OR "il 17b" OR "il 17c" OR "il 17d" OR "il 17e" OR "il 17f" OR "il 18" OR "il 1ra" OR "il 23 p19" OR "il 23" OR "il 23p19" OR "il 3" OR "il 4" OR "il 5" OR "il 6" OR "il 7" OR "il 8" OR "il 9" OR "il6st gp130" OR "il1" OR "il10" OR "il11" OR "il12" OR "il13" OR "il15" OR "il16" OR "il17" OR "il17a" OR "il17b" OR "il17c" OR "il17d" OR "il17e" OR "il17f" OR "il18" OR "il23" OR "il3" OR "il4" OR "il5" OR "il6" OR "il7" OR "il8" OR "il9" OR "interferon*" OR "interleukin*" OR "kit ligand" OR "lcf factor" OR "ki 1 antigen*" OR "kit proto oncogene protein*" OR "lymphocyte activating factor" OR "lymphocyte chemoattractant factor" OR "lymphocyte mitogenic factor" OR "lymphopoietin 1" OR "leukemia inhibitory factor oncostatin m shared receptor" OR "leukemia inhibitory factor receptor" OR "lin" OR "lin+" OR "lif receptor*" OR "lineage negative" OR "lymphokine*" OR "lymphotoxin*" OR "macrophage cell factor" OR "macrophage granulocyte inducer" OR "macrophage inflammatory protein" OR "macrophage inflammatory proteins" OR "mast cell growth factor" OR "mcgf 2" OR "mgdf factor" OR "mgi 1" OR "mgi 2" OR "monocyte chemotactic proteins" OR "mpl ligand" OR "myeloid cell growth inducer" OR "myeloid differentiation inducing protein" OR "myeloproliferative leukemia virus oncogene ligand" OR "m csf receptor*" OR "monocyte chemoattractant protein*" OR "monocyte chemotactic protein*" OR "natural killer cell stimulatory factor*" OR "neutrophil activating peptide" OR "neutrophil activation factor" OR "nf kappa b receptor activator" OR "nf kappab receptor activator" OR "p cell stimulating factor" OR "oncostatin m leukemia inhibitory factor shared receptor" OR "oncostatin m receptor beta" OR "oncostatin m type i receptor" OR "oncostatin m type ii receptor" OR "osteoclast differentiation factor" OR "opgl protein*" OR "osm lif receptor*" OR "osteoprotegerin ligand*" OR "ox40 ligand*" OR "ox40 receptor*" OR "ox40l protein*" OR "plasmacytoma growth factor" OR "prostate differentiation factor" OR "protein inducer mgi" OR "p145 c kit" OR "p145c kit" OR "proto oncogene protein c kit" OR "proto oncogene protein fms" OR "proto oncogene protein kit" OR "proto oncogene proteins c kit" OR "recombinant g csf" OR "recombinant gm csf" OR "ro 23 6019" OR "ro 236019" OR "ru 49637" OR "rankl" OR "receptor activator of nf kappa b" OR "receptor activator of nf kappab" OR "receptor activator of nuclear factor kappa b" OR "rank ligand*" OR "recombinant human dimeric tnf receptor type ii igg fusion protein*" OR "ro236019" OR "ru49637" OR "scatter factor" OR "steel factor" OR "stem cell factor" OR "sgp130" OR "signal transducer gp130" OR "signal transducing receptor gp130" OR "soluble glycoprotein 130" OR "soluble gp130" OR "scf receptor*" OR "stem cell factor receptor*" OR "t cell growth factor" OR "t cell replacing factor" OR "t cell stimulating factor" OR "t helper factor" OR "thrombocytopoiesis stimulating factor" OR "thymocyte stimulating factor" OR "t b cell activating molecule" OR "t cell gp39 antigen" OR "tall 1 protein" OR "tnfr fc fusion protein" OR "tnfrsf11a protein" OR "tnfrsf5 receptor" OR "tnfrsf8 receptor" OR "tnfsf13b" OR "tnr 001" OR "tnr001" OR "tntr fc" OR "trance protein" OR "trance r" OR "transmembrane activator and caml interactor protein" OR "tweakr" OR "taci receptor*" OR "tcgf" OR "thank protein*" OR "thrombocytopoietin*" OR "thrombopoietin*" OR "tnfrsf6 receptor*" OR "tnt receptor fusion protein*" OR "trance receptor*" OR "tweak receptor*" OR "transforming growth factor*" OR "tumor necrosis factor*" OR "4 1bb ligand*" OR "4 1bbl protein*") *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	1316499
# 5	TS=("blood cell*" OR "thrombocyt*" OR "platelet*" OR "erythrocyt*" OR "hemocyt*" OR "leukocyt*" OR "reticulocyt*" OR "granulocyt*" OR "mononuclear cell*" OR "stem cell*" OR "progenitor cell*" OR "mother cell*" OR "colony forming" OR "basophil*" OR "eosinophil*" OR "neutrophil*" OR "lymphocyt*" OR "monocyt*" OR "killer cell*" OR "nk cell*" OR "precursor cell*" OR "suppressor cell*" OR "myelocyt*" OR "myeloblast*" OR "B-cell*" OR "T-cell*" OR "T helper cel*" OR "Treg*" OR "macrophage*" OR "myeloid cell*" OR "dendritic cell*" OR "antigen-presenting cell*" OR "immune cell*" OR "inflammatory cell*" OR "CD4" OR "CD8") *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	2677862
#4	TS=("microparticle*" OR "microvesicle*" OR "exosom*" OR "ectosom*" OR "extracellular vesicle*" OR "exovesicle*" OR "apoptotic bod*") *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	73190
#3	TS=("MicroRNA*" OR "Micro RNA*" OR "miRNA*" OR "pri-miRNA*" OR "stRNA*" OR "Small Temporal RNA*" OR "pre-miRNA*" OR "lncRNA*" OR "non-coding RNA*" OR "noncoding RNA*" OR "ncRNA*") *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	170639
#2	TS=("biomarker*" OR "marker*" OR "indicator*") *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	1719569
# 1	TS=("pulmonary arterial hypertens*" OR "pulmonary artery hypertens*" OR "idiopathic pulmonary hypertensi*" OR "primary pulmonary hypertens*" OR "heritable pulmonary hypertensin" OR "hereditary pulmonary hypertens*") *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	21537

Wiley/Cochrane Library 87 results (28 January, 2021)

ID	Search	Hits
#8	#1 AND #2 AND (#3 OR #4 OR #5 OR #6 OR #7)	83
#7	(blood* OR plasma* OR serum* OR sera* OR urin*):ti,ab,kw	461866
#6	((“pulmonary arterial” NEXT hypertens*) OR (“pulmonary artery” NEXT hypertens*) OR (“idiopathic pulmonary” NEXT hypertensi*) OR (“primary pulmonary” NEXT hypertens*) OR (“heritable pulmonary” NEXT hypertens*) OR (“hereditary pulmonary” NEXT hypertens*)):ti,ab,kw	1606
#5	(biomarker* OR marker* OR indicator*):ti,ab,kw	92775
#4	(MicroRNA* OR (Micro NEXT RNA*) OR miRNA* OR pri-miRNA* OR stRNA* OR (“Small Temporal” NEXT RNA*) OR pre-miRNA* OR lncRNA* OR (non-coding NEXT RNA*) OR (noncoding NEXT RNA*) OR ncRNA*):ti,ab,kw	1127
#3	(microparticle* OR microvesicle* OR exosom* OR ectosom* OR (extracellular NEXT vesicle*) OR exovesicle* OR (apoptotic NEXT bod*)):ti,ab,kw	769
#2	((blood NEXT cell*) OR thrombocyt* OR platelet* OR erythrocyt* OR hemocyt* OR leukocyt* OR reticulocyt* OR granulocyt* OR (mononuclear NEXT cell*) OR (stem NEXT cell*) OR (progenitor NEXT cell*) OR (mother NEXT cell*) OR “colony forming” OR basophil* OR eosinophil* OR neutrophil* OR lymphocyt* OR monocyt* OR (killer NEXT cell*) OR (nk NEXT cell*) OR (precursor NEXT cell*) OR (suppressor NEXT cell*) OR myelocyt* OR myeloblast* OR B-cell* OR T-cell* OR (“T helper” NEXT cell*) OR Treg* OR macrophage* OR myeloid cell* OR (dendritic NEXT cell*) OR (“antigen-presenting” NEXT cell*) OR (immune NEXT cell*) OR (inflamm* NEXT cell*) OR CD4 OR CD8 OR “stem cell factor receptor”):ti,ab,kw	118610
#1	(("adipogenesis inhibitory" NEXT factor*) OR ("amcf i") OR (antiheparin NEXT factor*) OR ("autocrine motility" NEXT factor*) OR ("apo 1" NEXT antigen*) OR ("b-cell differentiation" NEXT factor*) OR ("b-cell growth" NEXT factor*) OR ("b cell proliferating" NEXT factor*) OR ("b cell stimulatory" NEXT factor*) OR ("beta 2 thromboglobulin") OR ("beta thromboglobulin") OR (bsf 1) OR (bsf 2) OR ("b cell activating" NEXT factor*) OR ("b cell maturation protein a") OR ("b lymphocyte activating" NEXT factor*) OR ("b lymphocyte stimulator") OR ("betac interleukin receptor subunit") OR ("br3 b cell activation factor receptor") OR ("b cell maturation" NEXT antigen*) OR (baff NEXT ligand*) OR (baff NEXT receptor*) OR (bcgf) OR ("bcma protein") OR ("ber h2" NEXT antigen*) OR ("blys protein") OR (chemotactic NEXT factor*) OR ("chemotactic peptid") OR ("colony stimulating" NEXT factor*) OR ("csif 10") OR ("ctla 8") OR ("cytotoxic t lymphocyte associated" NEXT antigen*) OR ("cd 127") OR ("cd134l protein") OR ("cd27l protein") OR ("cd95l") OR ("csf2rb receptor") OR ("cytokine receptor gp130") OR ("c fms protein") OR ("c kit protein") OR ("c kit receptor") OR (catabolin*) OR (ccl1*) OR (ccl2*) OR (ccl3*) OR ("ccl4") OR ("ccl5") OR ("ccl7") OR ("ccl8") OR ("ccr") OR (ccr1*) OR ("ccr2") OR ("ccr3") OR ("ccr4") OR ("ccr5") OR ("ccr6") OR ("ccr7") OR ("ccr8") OR (cd115 NEXT antigen*) OR (cd116 NEXT antigen*) OR (cd117 NEXT antigen*) OR (cd118 NEXT antigen*) OR ("cd127") OR (cd130 NEXT antigen*) OR (cd131 NEXT antigen*) OR (cd134 NEXT antigen*) OR (cd134 NEXT ligand*) OR (cd137 NEXT ligand*OR cd153 NEXT antigen*) OR (cd154 NEXT antigen*) OR (cd178 NEXT antigen*) OR (cd254 NEXT antigen*) OR (cd257 NEXT antigen*) OR (cd265 NEXT antigen*) OR (cd266 NEXT antigen*) OR (cd267 NEXT antigen*) OR (cd268 NEXT antigen*) OR (cd27 NEXT ligand*) OR (cd30 NEXT antigen*) OR (cd30 NEXT ligand*) OR (cd357 NEXT antigen*) OR (cd40 NEXT antigen*) OR (cd40 NEXT ligand*) OR ("cd40l") OR (cd70 NEXT antigen*) OR (cd95 NEXT antigen*) OR (cd95 NEXT ligand*) OR (cdw40 NEXT antigen*) OR (chemokin*) OR ("csf 1 receptor") OR ("csf receptor") OR ("ctla8") OR ("cx3c") OR ("cxcl8") OR ("cxcr") OR ("cxcr3") OR ("cxcr4") OR ("cxcr5") OR ("cxcr6") OR (cytokin*) OR ("eosinophil differentiation factor") OR ("epidermal cell derived thymocyte activating factor") OR ("erythrocyte burst promoting factor") OR ("enbrel") OR ("erelzi") OR (ectodysplasin*) OR ("erythropoietin") OR ("etanercept") OR (fas NEXT antigen*) OR ("fas cell surface death receptor") OR (fas NEXT ligand*) OR ("fas receptor") OR ("fasl protein") OR ("fms proto oncogene protein") OR ("fn14 receptor") OR ("gamma thromboglobulin") OR ("gdf 15") OR ("growth and development factor") OR ("growth differentiation factor 15") OR ("gp130 signal transducer") OR ("g csf receptor") OR ("glucocorticoid induced tnfr related protein") OR ("gm csf receptor") OR ("gp130 transducing protein") OR ("heparin neutralizing protein") OR ("heparin neutralizing proteins") OR ("hepatocyte growth factor") OR ("hepatocyte stimulating factor") OR ("hybridoma growth factor") OR (hematopoieti*) OR (hepatopoietin*) OR ("ifn beta 2") OR ("ifn gamma inducing factor") OR ("il 1") OR ("il 10") OR ("il 11") OR ("il 12") OR ("il 12p35") OR ("il 12p40") OR ("il 13") OR ("il 15") OR ("il 16") OR ("il 17") OR ("il 17a") OR ("il 17b") OR ("il 17c") OR ("il 17d") OR ("il 17e") OR ("il 17f") OR ("il 18") OR ("il 1ra") OR ("il 23 p19") OR ("il 23") OR ("il 23p19") OR ("il 3") OR ("il 4") OR ("il 5") OR ("il 6") OR ("il 7") OR ("il 8") OR ("il 9") OR ("il6st gp130") OR ("il1") OR ("il10") OR ("il11") OR ("il12") OR ("il13") OR ("il15") OR ("il16") OR ("il17") OR ("il17a") OR ("il17b") OR ("il17c") OR ("il17d") OR ("il17e") OR ("il17f") OR ("il18") OR ("il23") OR ("il3") OR ("il4") OR ("il5") OR ("il6") OR ("il7") OR ("il8") OR ("il9") OR (interferon*) OR (interleukin*) OR (kit NEXT ligand*) OR ("lcf factor") OR ("ki 1" NEXT antigen*) OR ("kit proto oncogene protein") OR ("lymphocyte activating" NEXT factor*) OR ("lymphocyte chemoattractant" NEXT factor*) OR ("lymphocyte mitogenic" NEXT factor*) OR ("lymphopoietin 1") OR ("leukemia inhibitory oncostatin m shared receptor") OR ("leukemia inhibitory factor receptor") OR ("lin") OR ("lif receptor") OR ("lineage negative") OR (lymphokine*) OR (lymphotoxin*) OR ("macrophage cell" NEXT factor*) OR ("macrophage granulocyte inducer") OR ("macrophage inflammatory protein") OR ("macrophage inflammatory proteins") OR ("mast cell growth" NEXT factor*) OR ("mcgf 2") OR (mgdf NEXT factor*) OR ("mgi 1") OR ("mgi 2") OR ("monocyte chemotactic proteins") OR ("mpl ligand") OR ("myeloid cell growth inducer") OR ("myeloid differentiation inducing protein") OR ("myeloproliferative leukemia virus oncogene ligand") OR ("m csf receptor") OR ("monocyte chemoattractant protein") OR ("monocyte chemotactic protein") OR ("natural killer cell stimulatory" NEXT factor*) OR ("neutrophil activating peptide") OR ("neutrophil activation" NEXT factor*) OR ("nf kappa b receptor activator") OR ("nf kappab receptor activator") OR ("p cell stimulating" NEXT factor*) OR ("oncostatin m leukemia inhibitory factor shared receptor") OR ("oncostatin m receptor beta") OR ("oncostatin m type i receptor") OR ("oncostatin m type ii receptor") OR ("osteoclast differentiation factor") OR ("opgl protein") OR ("osm lif receptor") OR (osteoprotegerin NEXT ligand*) OR (ox40 NEXT ligand*) OR ("ox40 receptor") OR ("ox40l protein") OR ("plasmacytoma growth factor") OR ("prostate differentiation" NEXT factor*) OR ("protein inducer mgi") OR ("p145 c kit") OR ("p145c kit") OR ("proto oncogene protein c kit") OR ("proto oncogene protein fms") OR ("proto oncogene protein kit") OR ("proto oncogene proteins c kit") OR ("recombinant g csf") OR ("recombinant gm csf") OR ("ro 23 6019") OR ("ro 236019") OR ("ru 49637") OR ("rankl") OR ("receptor activator of nf kappa b") OR ("receptor activator of nf kappab") OR ("receptor activator of nuclear factor kappa b") OR (rank NEXT ligand*) OR ("recombinant human dimeric tnf receptor type ii igg fusion protein") OR ("ro236019") OR ("ru49637") OR (scatter NEXT factor) OR ("steel factor") OR ("stem cell factor") OR ("sgp130") OR ("signal transducer gp130") OR ("signal transducing receptor gp130") OR ("soluble glycoprotein 130") OR ("soluble gp130") OR ("scf receptor") OR ("stem cell factor receptor") OR ("t cell growth" NEXT factor*) OR ("t cell replacing" NEXT factor*) OR ("t cell stimulating" NEXT factor*) OR ("t helper" NEXT factor*) OR ("thrombocytopoiesis stimulating" NEXT factor*) OR ("thymocyte stimulating" NEXT factor*) OR ("t b cell activating molecule") OR ("t cell gp39 antigen") OR ("tall 1 protein") OR ("tnfr fc fusion protein") OR ("tnfrsf11a protein") OR ("tnfrsf5 receptor") OR ("tnfrsf8 receptor") OR ("tnfsf13b") OR ("tnr 001") OR ("tnr001") OR ("tntr fc") OR ("trance protein") OR ("trance r") OR	74840

	("transmembrane activator and caml interactor protein") OR ("tweakr") OR ("taci receptor") OR ("tcgf") OR ("thank protein") OR (thrombocytopoietin*) OR (thrombopoietin*) OR ("tnfrsf6 receptor") OR ("tnt receptor fusion protein") OR ("trance receptor") OR ("tweak receptor") OR ("transforming growth" NEXT factor*) OR ("tumor necrosis" NEXT factor*) OR ("4 1bb" NEXT ligand*) OR ("4 1bbl protein")):ti,ab,kw	

Search Omics (28th of January 2021)

Search		Query #1 and #2	Items found
PubMed	#1	"Familial Primary Pulmonary Hypertension"[Mesh] OR "pulmonary arterial hypertensi*"[tiab] OR "pulmonary artery hypertensi*"[tiab] OR "idiopathic pulmonary hypertens*"[tiab] OR "hereditary pulmonary hypertens*"[tiab] OR "heritable pulmonary hypertens*"[tiab] OR "primary pulmonary hypertensi*"[tiab] OR "primary pulmonary hypertens*"[tiab]	148
	#2	"Glycomics"[Mesh] OR "Proteomics"[Mesh] OR "Metabolomics"[Mesh] OR "glycom*"[tiab] OR "proteom*"[tiab] OR "metabolom*"[tiab] OR "lipidom*"[tiab] OR "transcriptom*"[tiab]	
Embase	#1	('pulmonary arterial hypertens*' OR 'pulmonary artery hypertens*' OR 'idiopathic pulmonary hypertensi*' OR 'primary pulmonary hypertens*' OR 'heritable pulmonary hypertensin' OR 'hereditary pulmonary hypertens*'):ti,ab,kw	309
	#2	'glycomics'/exp OR 'proteomics'/exp OR 'metabolomics'/exp OR 'lipidomics'/exp OR 'transcriptomics'/exp OR ('glycom*' OR 'proteom*' OR 'metabolom*' OR 'lipidom*' OR 'transcriptom*'):ti,ab,kw	
Web of Science	#1	TS=("pulmonary arterial hypertens*" OR "pulmonary artery hypertens*" OR "idiopathic pulmonary hypertensi*" OR "primary pulmonary hypertens*" OR "heritable pulmonary hypertensin" OR "hereditary pulmonary hypertens*")	183
	#2	TS=("glycom*" OR "proteom*" OR "metabolom*" OR "lipidom*" OR "transcriptom*")	
Cochrane	#1	(("pulmonary arterial" NEXT hypertens*) OR ("pulmonary artery" NEXT hypertens*) OR ("idiopathic pulmonary" NEXT hypertensi*) OR ("primary pulmonary" NEXT hypertens*) OR ("heritable pulmonary" NEXT hypertens*) OR ("hereditary pulmonary" NEXT hypertens*)):ti,ab,kw	3
	#2	(glycom* OR proteom* OR metabolom* OR lipidom* OR transcriptom*):ti,ab,kw	

Table S2

	Question 1	**Question 2**	**Question 3**	**Question 4**
Patient inclusion (P) **Risk of bias:** 0 or 1 = low risk 2 = unclear risk 3 or 4 = high risk	Was a consecutive or random sample of patients enrolled? Random = +1 point	Was a case-control design avoided? Case-control = +1	Did the study avoid inappropriate exclusions? No = +1 point	Did the study report data for iPAH uniquely? No = +1 point
Index test (I) **Risk of bias:** 0 = low risk 1 = unclear risk 2 = high risk	Were the index test results interpreted without knowledge of the reference standard? No= +1 point	If a threshold was used, was it predifined or based on an ROC? No ROC = +1	-	-
Reference test (R) **Risk of bias:** 0 = low risk 1 = high risk	Is a diagnosis made by RHC? Echocardiography = + 1	Was the reference standard interpreted without knowledge of the of the index test? No = +1	-	-
Flow and timing (T) **Risk of bias:** 0 = low risk 1 = unclear risk 2 = high risk	Was the index test before the reference standard and initiation of treatment? No = +1	Did all patients receive the same reference standard? No = +1	Were all patients inlcuded in the analysis? No = +1	-

Table S2 Adjusted risk of bias assessment tool according to the QUADAS-2.

Table S3 **Author (year)**	**Markers**	**Material**	**Location**	**Con (n)**	**iPAH (n)**	**Exclusively iPAH**	**Treatment**	**Comments inclusion**
Andreassen, A. K., et al. (2006).	NT-proBNP	plasma	RHC (PA)	10	17	yes	incident	-
Calvier, L., et al. (2016).	sVCAM-1	plasma	peripheral vein (non fasting)	8	41	yes	under treatment	included during conference, unclear reference test
Can, M. M., et al. (2010).	Thrombocytes, d-dimer, fibrinogen, MPV	plasma and whole blood	peripheral vein	34	34	no	under treatment	exclusion comorbidity
Cella, G., et al. (2001).	sP-selectin	plasma	peripheral vein	10	15	no	under treatment	-
Decker, I., et al. (2011).	RBC, MCV, thrombocytes, leukocytes, Hb, Hct, RDW	plasma and whole blood	peripheral vein	12	30	yes	under treatment	-
Estephan, L. E., et al. (2019).	BUN, creatinine, Hb	plasma	RHC (specified)	22	47	no	under treatment	Controls RHC
Fares, W. H., et al. (2012).	CRP, NT-proBNP, TIMP-1	serum	RHC (PA)	33	25	no	under treatment	-
Fijalkowska, A., et al. (2006).	NT-proBNP	serum	peripheral vein	9	36	yes	incident	-
Gabrielli, L. A., et al. (2011).	ALT, leukocytes, CRP, glucose (fasted), Hb	plasma and whole blood	peripheral vein	14	14	yes	under treatment	exclusion comorbidity, anti-inflammatory treatment
Hennigs, J. K., et al. (2014).	CRP, fibrinogen, NT-proBNP	plasma	peripheral vein	11	52	no	incident	exclusion comorbidity, controls RHC
Heresi, G. A., et al. (2010).	CXCL-10	serum	peripheral vein	11	10	yes	under treatment	exclusion comorbidity
Heresi, G. A., et al. (2010).	HDL-C, TG	plasma and whole blood	RHC (PA) and peripheral vein	229	69	no	incident	-
Heresi, G. A., et al. (2017).	CXCL-10, glucose (fasted), IL-6	plasma	peripheral vein	14	14	yes	under treatment	exclusion comorbidity
Hoffmann, J., et al. (2015).	TIMP-1	serum	unclear	40	40	yes	under treatment	-
Itoh, T., et al. (2006).	IL-6	serum	peripheral vein	13	28	yes	under treatment	-
Jasiewicz, M., et al. (2014).	Thrombocytes, leukocytes, creatinine, UA	serum and whole blood	peripheral vein (fasted)	24	26	no	under treatment	-
Jiang, X., et al. (2008).	UA	serum	RHC (VCI)	98	78	yes	under treatment	-
Kereveur, A., et al. (2000).	MPV	plasma and whole blood	peripheral vein	19	16	no	under treatment	only patients PGI2
Koca, F., et al. (2011).	BUN, creatinine	serum	peripheral vein	27	28	no	under treatment,	exclusion comorbidity, unclear reference test
Kopeć, G., et al. (2017).	LDL-c	plasma	peripheral vein (fasted)	2431	63	no	under treatment	-
Lu, G.H. et al. (2020).	Creatinine, NT-proBNP	plasma	peripheral vein	338	338	no	under treatment	-
Malhotra, R., et al. (2013).	CRP, NT-proBNP	serum	peripheral vein	56	50	yes	under treatment	-
Nagaya, N., et al. (1999).	UA	serum	peripheral vein (fasted)	30	90	yes	incident	exclusion renal failure
Petrauskas, L. A., et al. (2019).	RDW	unclear	peripheral vein	101	181	no	under treatment	exclusion comorbidity
Prins, K. W., et al. (2018).	IL-6	serum	peripheral vein	10	40	no	incident	-
Renard, S., et al. (2013).	NT-proBNP	plasma	RHC (VCI)	50	49	yes	under treatment	exclusion comorbity
Rhodes, C. J., et al. (2011).	IL-6	plasma	unclear	40	139	yes	under treatment	-
Safdar, Z., et al. (2015).	TIMP-1	serum	peripheral vein	37	68	yes	under treatment	-
Santos, M., et al. (2014).	BNP, creatinine, CRP, glucose (fasted), Hb, HDL-c, TG	serum	peripheral vein	25	25	no	under treatment	exclusion comorbidity, anti-inflammatory treatment
Soon, E., et al. (2010).	IL-6	serum	peripheral vein	21	70	yes	under treatment	-
Suzuki, S., et al. (2016).	BUN, creatinine, CRP, eGFR,	unclear	unclear	30	16	no	incident	-

	Hb, Hct							
Tiede, S. L., et al. (2016).	TIMP-1	plasma	RHC (unclear)	44	42	yes	incident	-
Varol, E., et al. (2011).	platelets, leukocytes, creatinine, Hb, HDL-c, LDL-c, MPV, TG, total cholesterol	plasma and whole blood	peripheral vein	25	22	no	under treatment	exclusion comorbidity, anti-coagulant treatment
Vrigkou, E. et al (2019)	d-dimer, fibrinogen, Hb, Hct, creatinine, leukocytes, thrombocytes,, ALT	plasma	RHC (PA) or peripheral vein	10	30	no	incident	exclusion comorbidity, anti-coagulant treatment
Wang, G. F., et al. (2020).	TG, total cholesterol, glucose (fasted), bilirubin, creatinine,UA, NT-proBNP, LDL-c, HDL-c	serum	peripheral vein	103	177	no	incident	Only Han chineese
Wang, K. Y., et al. (2015).	creatinine, CRP, HDL-c, NT-proBNP, TG	serum	unclear	27	21	yes	under treatment	exclusion comorbidity
Yang, D., et al. (2013).	NT-proBNP	plasma	peripheral vein (fasted)	20	20	yes	incident	exclusion comorbidity
Yang, T., et al. (2014).	CXCL-10	plasma	peripheral vein	20	61	yes	incident	exclusion comorbidity
Yaoita, N., et al. (2014).	thrombocytes, leukocytes, d-dimer, eGFR, Hb, HDL-c, LDL-c, MPV, PDW, total cholesterol, UA	unclear	peripheral vein	15	19	no	under treatment	controls were hypertension, hyperlipidemia, hypertrophic cardiomyopathies and paroxysmal atrial fibrillation
Yaylali, Y. T., et al. (2019).	RBC, MCV, thrombocytes, leukocytes, fibrinogen, Hb, Hct, RDW	plasma and whole blood	peripheral vein	35	21	no	incident	exclusion treatment
Yildiz, A., et al. (2013).	leukocytes, platelets, creatinine, CRP, glucose (fasted), Hb, HDL-c, LDL-c, MPV, PDW, RDW, TG, total cholesterol	plasma and whole blood	peripheral vein (fasted)	22	25	no	under treatment	exclusion comorbidity, anti-coagulation treatment
Zhao, Q. H., et al. (2012).	HDL-c	serum	peripheral vein (fasted)	45	76	yes	incident	exclusion CVD risk factors
Zheng, Y. G., et al. (2015).	MPV, PDW	plasma and whole blood	peripheral vein (fasted)	82	82	yes	incident	exclusion comorbidity, anti-coagulant treatment
Zhu, T., et al. (2019).	ALT, BUN, creatinine, Hb, Hct, NT-proBNP	plasma	peripheral vein, (12 hr fast)	20	27	yes	incident	age > 14 yrs, exclusion comorbidity

Table S3 A detailed overview of 45 included publications, describing markers extracted from the publication, location /type of blood draw, number of control and PAH subjects included, the treatment status of included patients, and concerns regarding inclusion methodology.

Table S4

Marker	Studies (n)	Data distribution	Control (n)	Weighted average	PAH (n)	Weighted average
5-HT, ng/mL	2	mean/SD[#]	28	4.0 ± 1.1	25	7.5 ± 3.7
ADMA, µmol/mL	1	mean/SD	22	0.36 ± 0.05	57	0.53 ± 0.15
	2	median (IQR)	75	0.51 (0.47 – 0.57)	77	0.83 (0.68 – 1.04)
Ang-1, ng/mL	2	median (IQR)	18	4.2 (3.2 – 5.4)	90	13.7 (10.9 – 16.5)
BNP, pg/mL	1	mean/SD	20	34 ± 32	26	141 ± 1233
	8	median (IQR)	203	20 (10 – 37)	266	129 (34 – 457)
Endostatin, ng/mL	2	mean/SD	73	52.9 ± 34.4	65	55.4 ± 48.7
	1	median[#]	39	28.1	37	62.9
ET-1, ng/mL	2	mean/SD	34	0.8 ± 0.4	34	2.0 ± 1.4
	1	median/IQR	9	1.8 ± 1.1	33	2.6 ± 2.2
Gal-3, ng/mL	2	mean/SD	22	7.7 ± 2.0	67	13.2 ± 3.8
	1	median/IQR	10	10.1 (9.0 – 12.7)	15	17.3 (13.2 – 21.1)
HGF, ng/mL	1	median/IQR	62	1.1 (1.0 – 1.3)	52	1.8 (1.3 – 2.6)
HMGB1, ng/mL	2	mean/SD	53	8.6 ± 4.7	50	12.1 ± 7.2
IL-8, pg/mL	1	mean/SD	21	14.3 ± 4.9	70	52.8 ± 148.1
	2	median (IQR)	13	4.5 (4.2 – 5.78)	31	5.5 (3.9 – 8.7)
MCP-1, pg/mL	2	Mean/SD	36	166 ± 152	48	331 ± 180
	1	Median (IQR)	20	79 (49 -93)	29	109 (65 – 142)
MMP-2, ng/mL	2	mean/SD	77	304.7 ± 122.2	67	305.3 ± 101.2
MMP-9, ng/mL	2	mean/SD	77	106 ± 119	67	62.0 ± 75
	1	median (IQR)	37	237 (171 – 370)	68	434 (292 – 663)
Na, mmol/L	2	mean/SD	52	140 ± 2	61	138 ± 4
	1	median/IQR	39	142 (139 – 144)	107	139 (137 – 142)
PlGF, pg/mL	1	mean/SD	40	21.8 ± 1.5	62	45.6 ± 3.5
	2	median/IQR	13	29.5 (20.2 – 41.5)	31	82.9 (53.6 – 126.0)
SCF, ng/mL	1	median/IQR	62	0.80 (0.75 – 0.88)	52	1.0 (0.80 – 1.25)
sE-selectin, ng/mL	2	mean/SD	43	56.7 ± 22.1	40	79.6 ± 44.8
	1	median (IQR)	7	45 (32 – 57)	9	29 (19 – 71)
SOD, pg/mL	1	mean/SD	12	142 ± 25	12	70 ± 30
sVCAM-1, ng/mL	2	mean/SD	41	931 ± 374	66	1086 ± 686
	1	Median (IQR)	7	487 (279 – 1084)	9	1167 (455 – 3454)
TGF-b1, ng/mL	2	mean/SD	12	3.6 ± 1.3	16	2.5 ± 2.0
	1	median (IQR)	61	2.6 (1.9 – 4.3)	216	4.8 (3.2 – 7.9)
Tie-2, ng/mL	2	median (IQR)	15	2.13 (1.83 – 2.3)	103	2.12 (1.88 – 2.20)
TIMP-4, ng/mL	2	mean/SD	77	1.9 ± 1.1	67	1.9 ± 1.6
VEGF, pg/mL	2	mean/SD	41	137 ± 101	66	159 ± 195
	4	median (IQR)	126	109 (69 – 227)	197	180 (125 – 411)
VEGF-A, pg/mL	2	median (IQR)	13	41.2 (25.7 – 60.0)	31	35.4 (23.9 – 42.7)
VEGF-D, ng/mL	2	median (IQR)	12	0.99 (0.95 – 1.11)	31	11.32 (0.71 – 1.44)
	1	mean/SD	8	0.88 ± 0.31	41	0.82 ± 0.51
TNF-a, pg/mL	4	median (IQR)	80	1.8 (1.3 – 2.4)	115	3.7 (2.8 – 5.4)
	2	mean/SD	34	5.5 ± 1.4	98	8.3 ± 3.8

Table S4. Overview of pooled biomarkers described in three or more publications, that were not eligible for meta-analyses due to heterogeneity in data distribution (median with IQR, v.s. mean with SD). 5-HT; serotonin, ADMA; asymetric dimethylarginine, Ang-1; angiopoietin-1, BNP; brain natriuretic protein, ET-1; endothelin-1, Gal-3; galectin-3, HGF; hepatocyte growth factor, HMGB1; high mobility group box 1, IL-8; interleukin-8, MMP-2, -8; matrix metalloproteinase-2 and -8, Na; sodium, PlGF; placental growth factor, SCF; stem cell factor, SOD; superoxide dismutase, sVCAM; soluble vascular cell adhesion molecule, TGF-b1; transfor-g growth factor-b1, Tie-2; angiopoietin-1 receptor-2, TIMP-4; tissue inhibitor of metalloproteinase-4, VEGF; vascular endohtelial growth factor, TNF-a; tissue necrosis factor-a. [#] did not report IQR, or SD.

Table S5

Table S5 Marker	Studies (n)	Data distribution	Control (n)	Weighted average	PAH (n)	Weighted average
Cav-1, pg/mL	1	Mean/SD	27	174 ± 135	21	34 ± 36
	1	Median (IQR)	8	100 (35 – 220)	8	200 (100 – 550)
RBC, cells 10^{12}/L	2	Mean/SD	47	4.77 ± 0.46	51	4.74 ± 0.58
HbA1c, %	2	Mean/SD	44	5.57 ± 0.58	37	5.58 ± 0.60
IL-12, pg/mL	2	Mean/SD	29	32.2 ± 23.3	111	102± 102
K, mEq/L	2	Mean/SD	52	4.13 ± 0.38	61	4.0 ± 0.5
MCV, fL	2	Mean/SD	47	87.3 ± 5.0	51	86.0 ± 7.8
MDA, nmol/L	2	Mean/SD	26	3.55 ± 1.91	112	6.39 ± 1.2
NO, µmol/L	2	Mean/SD	30	53.3 ± 22.3	35	60.4 ± 21.7
OPN, ng/mL	2	Mean/SD	44	22.9 ± 2.7	95	40.7 ± 30.9
Pim-1, ng/mL	2	Mean/SD	115	8.21 ± 3.08	46	23.4 ± 9.7
Se-p, mg/L	1	Mean/SD	20	2.43 ± 0.25	65	3.07 ± 0.57
	1	Median (IQR)	20	5.5 (2.8 – 8.0)	26	14.0 (7.0 – 32.0)
sRAGE, ng/mL	2	Mean/SD	53	775 ± 282	37	1216 ± 596
sST2, ng/mL	2	Mean/SD	34	19.0 ± 6.4	65	34.3 ± 16.1
sTWEAK, pg/mL	2	Median (IQR)	49	343 (269 – 431)	180	195 (192 – 296)
Total bilirubin, mg/dL	2	Mean/SD	45	0.83 ± 0.28	36	0.95 ± 0.53
FGF-2, pg/mL	1	Mean/SD	8	14 ± 24	8	41 ± 42
	1	Median (IQR)	8	30 (14 – 41)	9	12 (8-36)
ENG, ng/mL	1	Mean/SD	56	3.66 ± 0.87	50	5.12 ± 1.34
	1	Median (IQR)	49	4.0 (3.4 – 4.9)	43	5.4 (4.2 – 6.4)
KYN, µmol/L	1	Mean/SD	20	2.6 ± 0.1	20	3.6 (0.2)
	1	Median (IQR)	30	1.9 (1.5 – 2.3)	26	2.8 (2.4 – 3.2)
MCP-1, pg/mL	1	Mean/SD	13	91 ± 18	28	253 ± 127
	1	Median (IQR)	20	79 (49 – 93)	29	109 (65 – 142)
NOx, µmol/L	1	Median (95%-CI)	100	29.2 (21.9 – 34.4)	104	9.7 (6.7 – 12.4)
	1	Median (IQR)	50	11 (5 – 19)	58	23 (15 – 34)
OPG, ng/mL	1	Mean/SD	56	2.89 ± 1.17	50	3.21 ± 1.34
	1	Median (IQR)	35	1.35 (0.82 – 2.02)	28	4.81 (3.52 – 5.87)
PIIINP, ng/mL	1	Mean/SD	37	3.08 ± 0.93	68	5.30 ± 1.87
	1	Median (IQR)	10	4.1 (3.8 – 6.0)	15	4.5 (3.9 – 7.0)
sFLT-1, ng/mL	1	Mean/SD	40	3.09 ± 0.25	62	5.05 ± 0.46
	1	Median (IQR)	5	0.08 (0.06 – 0.08)	22	0.12 (0.09 – 0.14)
TFPI, ng/mL	1	Mean/SD	10	77.68 ± 10.37	15	82.73 ± 34.90
	1	Median (IQR)	29	10.5 (4.0 – 16.0)	16	14.3 (4.0 – 27.6)
Thrombomodulin, ng/mL	1	Mean/SD	10	13.00 ± 7.91	15	8.00 ± 11.62
	1	Median (range)	29	40.6 (14.0 – 117.0)	16	28.4 (6.5 – 54.0)
TRP, µmol/L	1	Mean/SD	20	58.4 ± 3.2	20	47.8 ± 2.4
	1	Median (IQR)	30	40.3 (35.2 – 46.3)	2	52.9 (46.3 – 57.5)
VEGFR-1, pg/mL	1	Mean/SD	56	98.7 ± 41.9	50	132.1 ± 44.6
	1	Median (IQR)	8	80 (61 – 85)	9	125 (101 – 150)

Table S5 Pooled biomarker levels described in two publications. Cav-1; caveolin-1, RBC; red blood cells, HbA1c; hemoglobin A1c, IL-12; interleukin, K; potassium, MCV; mean corpuscular volume, MDA; malondialhyde, NO; nitric oxide, OPN; osteopontin, Pim-1; provirus integration site for moloney murine leukaemia virus kinase, Se-P; selenoproteine-P, sRAGE; receptor advanced glycation end products, sST2; soluble suppression of tumorigenicity, sTWEAK; TNF-related weak inducer of apoptosis, FGF-2; fibroblast growth factor-2, ENG; endoglin, KYN; kynurine, MCP-1; monocyte chemoattractant protein-1, Nox; nitrite NO2- and nitrate NO3-, OPG; osteoprotegerin, PIIINP; N-ter-al propeptide of type III procollagen, sFLT-1; soluble fms-like tyrosine kinase 1, TFPI; tissue factor pathway inhibitor, TRP; tryptophan, VEGFR-1; vascular endothelial growth factor-1.

Table S6

Marker	Studies (n)	Participants (n)	Mean difference	St. mean difference	OR	p-value
Haematological markers						
RDW, %	4	427	1.83 [1.39, 2.26]	0.98 [0.61, 2.17]	0.49 [0.31, 0,75]	<0.00001
PDW, %	3	245	1.42 [0.16, 2.67]	0.81 [0.50, 1.12]	0.75 [0.45, 1.13]	<0.00001
MPV, fL	5	361	0.95 [0.76, 1.13]	1.0 [0.81, 1.25]	0.68 [0.25, 1.89]	<0.00001
Thrombocytes, 10^9/L	7	334	-23.9 [-38.6, -9.2]	-0.38 [-0.62, -0.15]	0.82 [0.46, 1.46]	0.001
Hb, g/dL	9	400	-0.59 [-1.23, 0.06]	-0.18 [-0.43, 0.07]	6.06 [3.06. 11.99]	0.15
Hct, %	5	229	-1.07 [-3.91, 1.76]	-0.21 [-0.76, 0.34]	0.49 [0.31, 0,75]	0.46
Leukocytes, 10^9/L	7	294	-0.23 [-0.70,0.24]	-0.10 [-0.41, 0.21]	0.75 [0.45, 1.13]	0.52
Metabolic markers						
LDL-c, mg/dL	6	3035	-15.82 [-26.18, -5.46]	-0.44 [-0.65, -0.22]	0.45 [0.30, 0.68]	<0.00001
Total cholesterol, mg/dL	4	408	-17.70 [-24.15, -11.26]	-0.52 [-0.73, -0.32]	0.39 [0.27, 0.56]	<0.00001
TG, mg/dL	4	198	-32.56 [-54.17, -10.94]	-0.52 [-0.87, -0.17]	0.34 [0.17 0.69]	0.004
Glucose (fasted), mg/dL	3	103	24.06 [0.54, 7.58]	0.48 [0.08, 0.87]	1.25 [0.56, 2.75]	0.02
HDL-c, mg/dL	6	577	-6.15 [-2.11, 14.40]	-0.53 [-1.20, 0.15]	0.38 [0.11, 1.31]	0.13
Coagulation markers						
D-dimer, ng/mL	3	142	245.99 [148.55, 343.43]	0.69 [0.27, 1.11]	3.59 [1.67, 7.73]	0.001
Fibrinogen, mg/dL	4	227	73.75 [-2.58, 150.08]	0.84 [-0.14, 1.81]	4.67 [0.78, 28.1]	0.09
Inflammatory markers						
IL-6, pg/mL	5	389	5.01 [2.06, 7.96]	0.64 [0.28, 0.99]	3.26 [1.67, 6.33]	0.0005
CRP, mg/L	8	387	0.74 [0.13, 1,6]	0.25 [0.04, 0.47]	1.60 [1.08, 2.37]	0.02
sVCAM-1, ng/mL	3	150	626.72 [29.38, 1224.07]	1.03 [0.53, 1.52]	7.83 [3.36, 18.26]	<0.00001
CXCL-10, pg/mL	3	171	99.77 [54.53, 145.01]	0.82 [0.49, 1.16]	4.56 [2.47, 8.42]	<0.00001
TIMP-1, ng/mL	3	224	15.58 [-2.56, 33.72]	0.40 [0.13, 0.67]	3.05 [1.29, 7.21]	0.003
sP-selectin, ng/mL	4	180	0.52 [-11.10, 12.14]	-0.04 [0.35, 0.28]	0.89 [0.47, 1.68]	0.82
Cardiac markers						
NT-proBNP, pg/mL	10	1152	1684 [1035, 2330]	1.13 [0.93, 1.33]	7.99 [5.48, 11.62]	<0.00001
Renal markers						
UA, mg/dL	5	441	1.77 [1.06, 2.48]	0.89 [0.58, 1.12]	5.13 [2.90, 9.06]	<0.00001
BUN, mg/dL	5	891	1.76 [0.51, 3.01]	0.43 [0.29, 0.56]	2.17 [1.7, 2.78]	<0.00001
Creatinine, mg/dL	10	475	0.03 [-0.04, 0.10]	0.13 [-0.08, 0.34]	1.27 [0.86, 1.87]	0.23
eGFR, mL/-/1.73 m^2	4	180	1.70 [5.98, 9.37]	0.09 [-0.32, 0.49]	0.53 [0.23, 1.25]	0.67
Hepatic markers						
ALT, U/L	3	115	3.57 [-4.18, 11.31]	0.18 [-0.56, 0.92]	1.40 [0.36, 5.55]	0.37

Table S6. Mean difference, standardized mean difference and OR of 26 meta-analyses. RDW; red cell distribution width, PDW; platelet distribution width,MPV; mean platelet volume, Hb; hemoglobin, Hct; hematocrit, TG; triglycerides, LDL-c; low density lipoprotein, HDL-c; high density lipoprotein, sVCAM-1; circulating vascular cell adhesion molecule-1, CXCL-10; C-X-C motif chemokine ligand-10, IL-6; interleukin-6, TIMP-1; tissue inhibitors of metalloproteinases-1, soluble p-Selectin, CRP; c-reactive protein, NT-proBNP; N-terminal prohormone of brain natriuretic peptide, UA; uric acid, eGFR; estimated glomerular filtration rate, ALT; alanine transaminase. St. mean difference; standardized mean difference. St. mean difference; OR odds ratio.

Table S7

Table S7 Publication bias	**Egger's regression**		**Duval & Tweedie's trim and fill**			**Orwin's fail safe N**	**Funnel plot**
	Intercept	P-value	Original	Studies trimmed	Adjusted	Number of studies*	Figure
Haematological markers							
RDW, %	2.14	0.27	0.98 [0.61, 2.17]	2	0.77 [0.38, 1.14]	10	Fig. S2a
PDW, %	-2.57	0.23	0.81 [0.50, 1.12]	2	0.98 [0.67, 1.30]	8	Fig. S2b
MPV, fL	-2.35	<0.01	1.04 [0.81, 1.25]	3	1.15 [0.96, 1.34]	16	Fig. S2c
Thrombocytes, 10^9/L	-6.02	<0.01	-0.38 [-0.62, -0.15]	3	-0.25 [-0.50, -0.01]	4	Fig. S2d
Hb, g/dL	-0.27	0.94	-0.18 [-0.43, 0.07]	0	-0.18 [-0.43, 0.07]	-	Fig. S2e
Hct, %	6.02	0.62	-0.21 [-0.76, 0.34]	0	-0.21 [-0.76, 0.34]	-	Fig. S2f
Leukocytes, 10^9/L	-6.97	0.11	-0.10 [-0.41, 0.21]	2	-0.04 [-0.35, 0.27]	-	Fig. S2g
Metabolic markers							
LDL-c, mg/dL	-1.07	0.47	-0.44 [-0.65, -0.22]	1	-0.36 [-0.12, -0.61]	4	Fig. S2h
Total cholesterol, mg/dL	0.18	0.89	-0.52 [-0.73, -0.32]	0	-0.52 [-0.73, -0.32]	5	Fig. S2i
TG, mg/dL	0.41	0.88	-0.52 [-0.87, -0.17]	1	-0.61 [-0.94, -0.28]	6	Fig. S2j
Glucose (fasted), mg/dL	-4.51	0.72	0.48 [0.08, 0.87]	0	0.48 [0.08, 0.87]	4	Fig. S2k
HDL-c, mg/dL	5.90	0.15	-0.53 [-1.20, 0.15]	0	-0.53 [-1.20, 0.15]	15	Fig. S2l
Coagulation markers							
D-dimer, ng/mL	-4.84	0.37	0.69 [0.27, 1.11]	2	1.01 [0.54 - 1.48]	6	Fig. S2m
Fibrinogen, mg/dL	-2.38	0.91	0.84 [-0.14, 1.81]	1	1.07 [0.19 - 1.95]	10	Fig. S2n
Inflammatory markers							
IL-6, pg/mL	2.83	0.20	0.64 [0.28, 0.99]	0	0.64 [0.28, 0.99]	7	Fig. S2o
CRP, mg/dL	1.28	0.38	0.25 [0.04, 0.47]	1	0.24 [0.03, 0.45]	1	Fig. S2p
sVCAM-1, ng/mL	1.5	0.67	1.03 [0.53, 1.52]	1	1.04 [0.60, 1.49]	14	Fig. S2q
CXCL-10, pg/mL	1.47	0.78	0.82 [0.49, 1.16]	0	0.82 [0.49, 1.16]	8	Fig. S2r
TIMP-1, ng/mL	-1.98	0.73	0.40 [0.13, 0.67]	1	0.73 [0.29, 1.16]	8	Fig. S2s
sP-selectin, ng/mL	3.34	0.11	-0.04 [0.35, 0.28]	0	-0.07 [-0.42, 0.29]	-	Fig. S2t
Cardiac markers							
NT-proBNP, pg/mL	-0.06	0.94	1.13 [0.93, 1.33]	0	1.13 [0.93, 1.33]	37	Fig. S2u
Renal markers							
UA, mg/dL	-2.11	0.46	0.89 [0.58, 1.12]	1	0.82 [0.53 - 1.12]	14	Fig. S2v
BUN, mg/dL	-0.72	0.40	0.43 [0.29, 0.56]	1	0.43 [0.29, 0.56]	4	Fig. S2w
Creatinine, mg/dL	-0.25	0.94	0.13 [-0.08, 0.34]	1	0.10 [-0.10, 0.31]	-	Fig. S2x
eGFR, mL/-/1.73 m^2	4.87	0.64	0.09 [-0.32, 0.49]	1	-0.07 [-0.09, 0.34]	-	Fig. S2y
Herpetological markers							
ALT, U/L	2.58	0.86	0.18 [-0.56, 0.92]	0	0.18 [-0.56, 0.92]	-	Fig. S2z

Table S7. Estimation of risk of bias by Egger;s regression ($p<0.10$), Duval & Tweedie's trim and fill, and Orwin's fail safe N. PDW; platelet distribution width, RDW; red cell distribution width, MPV; mean platelet volume, Hb; hemoglobin, Hct; hematocrit, TG; triglycerides, LDL-c; low density lipoprotein, HDL-c; high density lipoprotein, sVCAM-1; circulating vascular cell adhesion molecule-1, CXCL-10; C-X-C motif chemokine ligand-10, IL-6; interleukin-6, TIMP-1; tissue inhibitors of metalloproteinases-1, CRP; c-reactive protein, NT-proBNP; N-terminal prohormone of brain natriuretic peptide, UA; uric acid, eGFR; estimated glomerular filtration rate, ALT; alanine transaminase. * publication excluded.

Table S8

Table S8 Publication	Sample size	Sample size	Source	Method	Principle component selection	Validation	Selected principle component
Abdul-Salam, V., et al., 2006.	27 iPAH	26 control	plasma	Proteomics analysis using Mass spec SELDI-TOF MS	ROC curves, AUC	ELISA	C4a des Arg,
Rhodes C.J., et al., 2017.	116 / 174 iPAH	128 control	plasma	Metabolomic profiling using liquid chromatography coupled with mass spectrometry (Metabolon, Durham, NC), logistic regression analysis	Logistic regression analysis	ELISA, validation cohort	Nucleosides (N2,N2-dimethylguanosine, N1-methylinosine), TCA cycle (malate, fumarate), glutamate, fatty acid oxydatin (acylcarnitines), and polyamine metabolites and decreased levels of steroids, sphingomyelins, and phosphatidylcholines
Rafikov, R., et al., 2020.	11 iPAH	23 control	plasma	Metabolomic liquid chromatography coupled with mass spectometry	Supervised clustering analysis	no	TCA cycle, carbohydrates (glycolytic shift). Myo-inositol.
He, Y.Y., 2020.	30 iPAH	30 control	plasma	Metabolomic mass and fragmentation analyses, using liquid chromatography-mass spectrometry	Student t-test ($p < 0.05$),	Validation cohort, rodent, PASMC	Spermine, among 17 other plasma metabolites
Hemnes, A.R., et al., 2019	10 PAH	30 control	plasma	Metabolomics (liquid chromatography-mass spectrometry) and proteomics (SomaLogic aptamer-based assay.)	2-way ANOVA, post hoc tests	Validation cohort, explanted lungs	Long- and medium-chain acylcarnitines (fatty-acid oxidation)
Al-Naamani, N. et al., 2016.	22 PAH	29 control	plasma	Lipidomics using liquid chromatography-mass spectrometry	ROC curves, AUC	Rodent with experimental PAH	Plasma eicosanoids; including 12- and 15-HETE
Amsallem, M., 2021.	121 PAH	76 control	plasma	Proteomics multiplex immunoassay	Regression analysis	Rodent, Cox proportional hazard regression	HGF, Met-c
Bujak, R., 2016.	20 PAH	20 control	plasma	Metabolomic high-performance liquid and gas chromatography (HPLC) coupled with mass spectrometry.	Orthogonal partial least squares discriminant analysis	Glucose tolerance test	Metabolites related to glycolysis, lipid and fatty acid metabolism (acylcarnitines), amino acid metabolism,, TCA and urea cycle
Chen, C. et al., 2020.	40 iPAH	20 control	serum	Metabolomic ultra high-performance liquid and gas chromatography (HPLC) coupled with mass spectrometry.	ROC curves, AUC	Rodent with experimental PAH	LysoPC, PC, decanoylcarnitine (fatty acid oxidation) and l-carnitine
Heresi, G.A., et al., 2020.	31 iPAH	31 control	plasma	Metabolomic high-performance liquid chromatography (HPLC) Online Tandem Mass Spectrometry (LC-MS/MS)	One-way ANOVA, false discovery rate	Random forest analysis	Metabolic profiles
Karamanian, V.A., et al., 2014.	113 PAH	51 control	serum and plasma	Proteomics Multiplex immunoassays	False discovery rate (PaGe)	Random forest analysis, PAEC	EPO, among other growth factors
Mey, J.T., et al., 2020.	21 PAH	31 control	plasma	Metabolomic liquid chromatography coupled with mass spectrometry (Metabolon, Durham, N.C.)	One-way ANOVA	Glucose tolerance test	Acylcarnytines (fatty acid oxidation), fatty acids, ketonic amino-acids
Sanders, J.L., et al., 2019.	26 PAH	26 control	plasma	Metabolomic liquid chromatography coupled with mass spectometry	Two-way ANOVA	Random forest, exercise	higher glycolytic catabolic state (TCA, fatty acid oxydation, glycolysis)
Yu, M., et al., 2007.	20 iPAH	20 control	serum	Metabolomic liquid chromatography coupled with mass spectometry	Statistical test	no	Alpha-1-antitrypsin, vitronectin
Zhang, J. et al., 2009.	10 iPAH	10 control	serum	Proteomics MALDI-TOF-MS, ELISA	Statistical test	no	LRG, among other protein spots