



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	17
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	44
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	69
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	109
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	109
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	109
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	121
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	121
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	134
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	134
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	130
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	132
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	134
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	132
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	132
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	134
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	133
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	135
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	132
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	107



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Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	154
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	154
Study characteristics	17	Cite each included study and present its characteristics.	156
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	156
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	160
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	168
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	168
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	172
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	173
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	202
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	202
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	223
	23b	Discuss any limitations of the evidence included in the review.	233
	23c	Discuss any limitations of the review processes used.	235
	23d	Discuss implications of the results for practice, policy, and future research.	236
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	295
Competing interests	26	Declare any competing interests of review authors.	293
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	302

Supplementary TABLE 1 | Risk of bias assessment based on the NOS

Study	Selection			Definit ion of the control s	Compa rability	Ascertain ment of exposur e	Exposure		Total scores
	Adequate definition of cases	Represe ntativen ess of cases	Selecti on of the control s		Control for importan t factor		Same method of ascertainment	Nonres ponse rate	
Mariko Kogo, et al ⁸	★	★	★	★	★★☆	★	★	★	8
Di He, et al ¹⁶	★	★	★	★	★★☆	★	☆	★	7
Rogelio Perez- Padilla1, et al ¹⁴	★	★	★	☆	★★☆	★	☆	☆	5
Rina Kanetake, et.al ¹⁷	★	★	★	★	★★★	☆	☆	☆	6
Yasuyoshi Washio, et al ¹⁸	★	★	★	★	★★★	★	★	☆	8
Di He, et al ¹⁹	★	☆	★	★	★★☆	☆	★	☆	5
Daniel H Higbee, et al ²⁰	★	★	★	★	★★★	☆	★	★	8
Emily S, et al ²¹	★	★	★	★	★★☆	★	☆	★	7
Jacob Louis Marott, et al ¹²	★	★	★	★	★★★	★	☆	★	8
Spyridon Fortis, et al ²²	★	★	★	☆	★★☆	★	☆	☆	5

Kendra A. Young, et al ²³	★	☆	★	★	★★☆	★	☆	☆	5
Sara Renata Alex Wijnant, et al ²⁴	★	★	★	★	★★☆	★	★	★	8
Hye Jung Park, et al ²⁵	★	★	☆	☆	★★☆	★	★	★	6
Emily S. Wan, et al ¹⁵	★	★	☆	☆	★★☆	☆	★	★	5

Supplementary TABLE 2 |

SNP	other_allele.exposure	effect_allele.exposure	beta.exposure	se.exposure	pval.exposure	eaf.exposure	F
				0.00361			35.29
rs301805	T	G	0.021468	3	2.80E-09	0.559	99
rs300172				0.00389			73.90
3	G	A	0.033512	8	8.12E-18	0.321	009
rs666983				0.00439			34.99
9	C	T	0.026004	6	3.36E-09	0.204	992
rs218612				0.00358			52.79
2	A	T	0.026057	6	3.61E-13	0.561	994
rs755550				0.00355			46.09
7	C	T	-0.02414	6	1.14E-11	0.496	986
rs205058				0.00370			30.70
6	G	C	-0.02055	8	3.00E-08	0.355	005
rs120421				0.00356			38.99
07	T	C	-0.02228	8	4.22E-10	0.527	999
rs120252				0.00533			38.19
37	A	C	-0.033	9	6.52E-10	0.124	993
rs204685				0.00447			30.70
0	C	T	-0.02481	8	3.03E-08	0.187	014
rs672872				0.00473			56.10
6	T	C	0.035449	3	6.73E-14	0.829	011
rs100478				0.00357			70.19
7	G	A	0.029923	1	5.27E-17	0.581	985
rs267889				0.00364			30.40
7	G	A	0.020087	3	3.51E-08	0.625	008
rs758557				0.00372			36.09
9	C	G	0.0224	8	1.88E-09	0.505	985
				0.00373			66.59
rs266047	G	A	-0.03051	9	3.36E-16	0.529	971

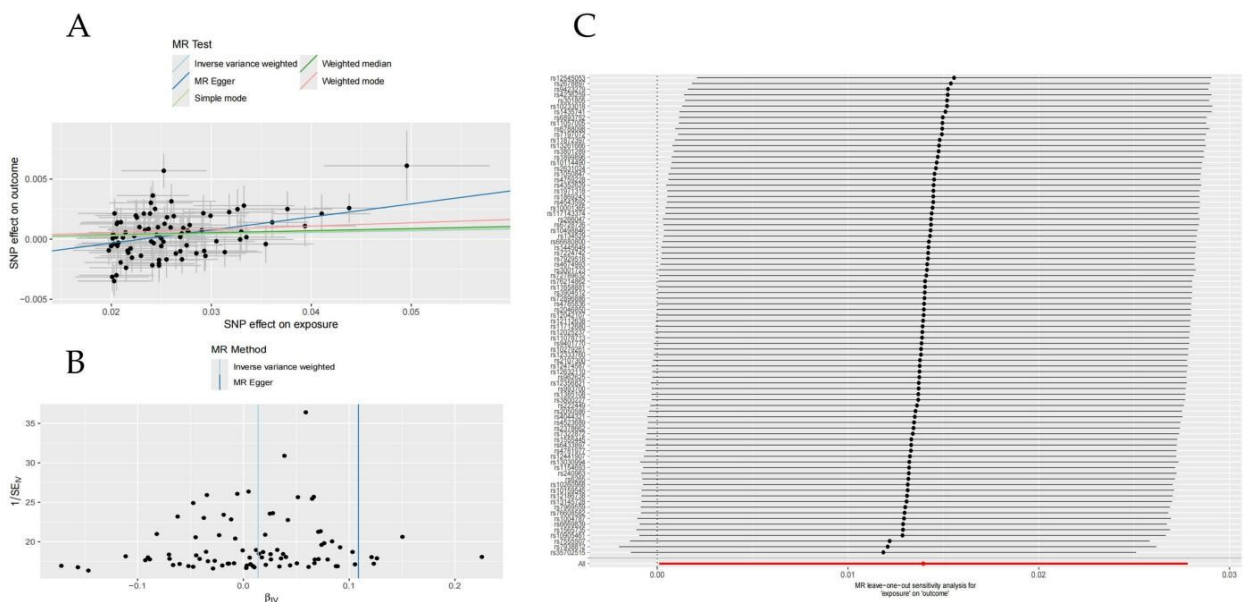
rs357025				0.00423				35.60
15	G	T	0.025244	1	2.43E-09	0.162		013
rs130309				0.00355				
94	G	A	0.036093	6	3.56E-24	0.485		103
rs144564				0.00356				45.29
9	T	C	0.023993	5	1.68E-11	0.525		98
rs124745				0.00358				59.50
87	G	T	0.027633	2	1.25E-14	0.404		032
rs643389				0.00405				30.60
7	T	C	0.022448	8	3.16E-08	0.754		015
rs210730				0.00492				30.49
0	C	G	-0.0272	5	3.27E-08	0.845		995
rs467499				0.00443				32.29
3	A	G	-0.02521	6	1.32E-08	0.207		99
rs186924				0.00356				30.69
3	T	C	0.019741	3	2.97E-08	0.481		996
rs126321				0.00375				38.79
10	A	G	-0.02338	3	4.78E-10	0.647		998
rs117126				0.00457				34.89
80	A	C	-0.02705	8	3.51E-09	0.174		991
rs678809				0.00368				72.20
8	A	T	-0.03135	9	1.91E-17	0.623		012
rs666808				0.00365				30.80
00	G	T	-0.02027	3	2.83E-08	0.397		015
rs115469				0.00491				44.10
3	A	G	0.032622	2	3.12E-11	0.856		013
rs962625				0.00403				34.50
A	G	G	0.023718	8	4.37E-09	0.24		013
rs993700				0.00429				36.50
T	C	C	-0.02593	2	1.53E-09	0.766		005
rs116068				0.00358				33.49
5	C	G	0.020772	9	7.20E-09	0.478		989
rs131457				0.00366				40.29
28	G	C	-0.02325	3	2.14E-10	0.358		996
rs100013				0.00364				47.10
65	G	A	-0.02499	2	6.65E-12	0.405		017
rs689375				0.00407				34.99
2	A	G	-0.0241	4	3.25E-09	0.766		998
rs435262				0.00356				59.49
9	C	T	-0.02753	9	1.22E-14	0.492		974
rs121867				0.00502				43.89
38	G	T	-0.03326	1	3.42E-11	0.154		992
rs727896				0.00528				38.70
32	C	T	-0.03289	6	5.02E-10	0.12		002
rs138510				0.00415				35.19
8	C	T	0.024662	7	3.00E-09	0.239		998
rs404432				0.00371				56.29
1	A	G	-0.02784	1	6.08E-14	0.642		994

				0.00442				32.69
rs222449	A	T	-0.02532	8	1.08E-08	0.793	998	
rs104988				0.00355				33.60
46	C	T	0.02061	6	6.62E-09	0.473	009	
rs940177				0.00398				48.40
0	G	A	0.027731	6	3.47E-12	0.273	019	
rs380022				0.00405				31.60
7	A	G	0.022812	8	1.93E-08	0.701	001	
				0.00483				72.00
rs240963	T	C	-0.04104	7	2.16E-17	0.836	027	
rs423625				0.00355				48.49
9	T	G	-0.02477	7	3.35E-12	0.499	991	
rs102609				0.00360				31.69
68	G	A	-0.02032	9	1.75E-08	0.597	999	
rs132465				0.00373				39.40
63	C	G	-0.02346	8	3.45E-10	0.526	006	
rs121126				0.00404				36.80
38	A	G	-0.02453	3	1.34E-09	0.275	002	
rs380128								34.80
9	A	C	-0.02206	0.00374	3.74E-09	0.351	01	
rs123337				0.00480				36.60
60	T	C	-0.02905	1	1.44E-09	0.204	002	
rs102330				0.00355				57.89
18	A	G	0.027069	7	2.75E-14	0.503	974	
rs102792				0.00366				34.20
61	G	A	-0.02142	3	5.00E-09	0.619	019	
rs156573				0.00446				71.09
5	T	A	-0.03762	1	3.42E-17	0.212	983	
rs132616				0.00355				57.20
66	G	T	-0.02689	6	3.90E-14	0.522	012	
rs125450				0.00363				31.09
53	A	G	0.020281	7	2.43E-08	0.397	997	
rs263102				0.00402				32.50
4	A	G	-0.02296	8	1.18E-08	0.737	016	
rs189989				0.00388				46.29
6	C	T	0.026448	7	1.04E-11	0.286	989	
rs454359				0.00356				37.89
2	T	C	0.021931	2	7.46E-10	0.468	986	
rs101144				0.00453				31.70
90	G	A	-0.02551	2	1.81E-08	0.198	006	
rs237866				0.00356				34.50
2	G	A	0.020948	6	4.16E-09	0.556	016	
rs109054				0.00414				33.40
61	T	C	-0.02396	5	7.35E-09	0.718	006	
rs101595				0.00372				49.59
45	C	G	0.02625	7	1.84E-12	0.375	983	
rs792137				0.00355				51.20
8	G	C	-0.02546	8	8.26E-13	0.463	021	

rs123568				0.00504				60.79
21	G	C	0.03937	9	6.27E-15	0.14		99
rs942327				0.00370				30.60
9	C	G	-0.02051	8	3.21E-08	0.641		003
rs452368				0.00364				31.99
9	A	G	-0.02061	3	1.55E-08	0.408		998
				0.00457				48.19
rs6265	C	T	-0.03179	8	3.77E-12	0.203		997
rs792951				0.00428				32.00
8	A	G	0.024238	5	1.56E-08	0.765		001
rs793881				0.00363				144.9
2	T	G	0.043791	7	2.71E-33	0.424		998
rs110570				0.00357				34.20
05	A	G	-0.02093	9	4.85E-09	0.43		001
rs475922				0.00393				30.40
8	G	C	-0.02169	4	3.58E-08	0.27		001
rs796955				0.00395				37.89
9	A	G	-0.02438	9	7.31E-10	0.688		996
rs197131				0.00492				33.49
8	C	T	0.028507	5	7.06E-09	0.141		998
rs390451				0.00357				35.00
2	G	A	-0.02116	7	3.23E-09	0.429		013
rs954072				0.00355				30.19
9	A	T	-0.01955	8	3.82E-08	0.501		995
rs732287				0.00433				34.80
2	C	T	-0.02557	5	3.58E-09	0.782		002
rs762148				0.00454				30.20
62	A	C	-0.02499	7	3.99E-08	0.202		001
rs143574				0.00359				67.09
1	G	A	0.029415	1	2.64E-16	0.425		991
rs124419				0.00452				41.70
07	C	A	-0.02921	3	1.06E-10	0.186		011
rs719707				0.00416				35.29
2	C	T	-0.02477	9	2.77E-09	0.238		989
rs478197				0.00436				29.90
7	T	C	-0.02387	5	4.54E-08	0.205		017
rs478583				0.00365				31.29
6	T	C	-0.02047	9	2.26E-08	0.398		984
rs105084				0.00358				36.29
7	C	T	-0.02162	9	1.67E-09	0.505		994
rs116588				0.00361				31.09
81	A	G	0.020136	1	2.43E-08	0.418		999
rs110787				0.00360				31.30
13	A	G	-0.02017	6	2.23E-08	0.454		003
rs722474				0.00365				32.10
2	C	T	-0.02071	5	1.43E-08	0.595		001
rs728968				0.00483				30.90
86	G	C	-0.02689	7	2.75E-08	0.144		007

rs650814					0.00358			33.29
4	C	G	-0.02069	6	7.97E-09	0.563	987	
rs118723					0.00409			36.59
97	G	A	-0.02477	5	1.43E-09	0.252	996	
rs766085								36.00
82	C	A	-0.04956	0.00826	1.94E-09	0.0389	003	
rs155544					0.00382			34.79
5	A	T	0.022555	3	3.65E-09	0.337	994	
rs117143					0.00526			30.90
374	T	C	0.02929	9	2.76E-08	0.12	001	
					0.00366			29.80
rs134529	T	C	-0.01998	1	4.85E-08	0.349	009	

Supplementary FIGURE 1 | Sensitivity analyses and visual validation. (A) The scatter plot demonstrated a consistent positive trend between SNP-exposure and SNP-outcome effects, supporting the directional validity of both IVW and MR-Egger estimates. (B) Funnel plot indicated low heterogeneity of instrumental variables. (C) Leave-one-out sensitivity analysis confirmed robustness, as exclusion of individual SNPs yields stable effect estimates for both IVW and MR-Egger, with overlapping confidence intervals, indicating no undue influence from any single genetic variant.



Supplementary FIGURE 2 | Forest plots depicting the comparisons of clinical characteristics and spirometry parameters between progressive PRISm and nonprogressive individuals with PRISm.

