Supplementary

Appendix 1 Search strategy

Database	Search terms	No. of studies generated
PubMed	#1 (Lung Neoplasms[MeSH Terms]) OR (Neoplasm, Lung[Title/Abstract])) OR (Neoplasms, Pulmonary[Title/Abstract])) OR (Pulmonary Neoplasm[Title/Abstract])) OR (Lung Cancers[Title/Abstract] OR Cancer, Pulmonary[Title/Abstract])) OR (Pulmonary Cancers[Title/Abstract])) OR (Cancer of Lung[Title/Abstract]) #2 (Volatile Organic Compounds[MeSH Terms])) OR (Organic Compound, Volatile[Title/Abstract])) OR (VOCs[Title/Abstract])) OR (Volatile organic breath components[Title/Abstract]) #3 (exhaled) OR (breath) #4 #1 AND #2 AND #3	1249
Embase	#1 'lung tumor'/exp #2 'lung tumor':ab,ti OR 'broncho-pulmonary neoplasm':ab,ti OR 'broncho-pulmonary tumo':ab,ti OR 'bronchopulmonary neoplasm':ab,ti OR 'bronchopulmonary tumor':ab,ti OR 'lung neoplasia':ab,ti OR 'lung neoplasm':ab,ti OR 'lung neoplasms':ab,ti OR 'lung tumorigenesis':ab,ti OR 'lung tumour':ab,ti OR 'neoplasia of the lung':ab,ti OR 'neoplastic lung':ab,ti OR 'pulmonary neoplasia':ab,ti OR 'pulmonary neoplasm':ab,ti OR 'pulmonary tumor':ab,ti OR 'pulmonary tumorigenesis':ab,ti OR 'pulmonary tumour':ab,ti OR 'tumor of the lung':ab,ti OR 'tumor, lung':ab,ti OR 'tumorigenesis in the lung':ab,ti OR 'tumour, lung':ab,ti #3 'volatile organic compound'/exp #4 'volatile organic compound':ab,ti OR 'organic compound, volatile':ab,ti OR 'volatile organic compounds':ab,ti #5 #1 OR #2	569
Web of Science	#1 ((TS=(Volatile Organic Compounds) OR AB=(Organic Compound, Volatile OR VOCs OR Volatile organic breath components)) #2 (TS=(Lung Neoplasms) OR AB=(Neoplasm, Lung OR Neoplasms, Pulmonary OR Pulmonary Neoplasm OR Lung Cancers OR Cancer, Pulmonary OR Pulmonary Cancers OR Cancer of Lung)) #3 (TS=(exhaled OR breath)) #4 #1 AND #2 AND #3	698
Cochrane Library	#1 MeSH descriptor: [Lung Neoplasms] explode all trees #2(Neoplasm, Lung OR Neoplasms, Pulmonary OR Pulmonary Neoplasm OR Lung Cancers OR Cancer, Pulmonary OR Pulmonary Cancers OR Cancer of Lung):ti,ab,kw #3 #1 AND #2 #4 MeSH descriptor: [Volatile Organic Compounds] explode all trees #5(Organic Compound, Volatile OR VOCs OR Volatile organic breath components):ti,ab,kw #6 #4 AND #5 #7 #3 AND #6	7

https://dx.doi.org/https://dx.doi.org/10.21037/jtd-24-1001

Appendix 2 Details of participants and the Newcastle-Ottawa Quality Assessment Scale scores in the included studies

Details of participants

Study	Information of patients						Analysis Platform
	Patients With Lung Cancer, No.	Cancer Stage	Smoker In Cancer	Smoker In Control	Groups	Setting	
Phillips *et al.*, 1999 (1)	60	I-IV or unknown	NR	NR	LC, HC	USA	GC-MS
Yu *et al.*, 2005 (2)	15	II-IV	9	0	LC, HC	China	GC-MS
Phillips *et al.*, 2007 (3)	193	Mixed	33	78	LC, HC	USA	GC-MS
Wehinger *et al.*, 2007 (4)	17	I-V	9	60	LC, HC	Austria	PTR-MS
Phillips *et al.*, 2008 (5)	193	Mixed	NR	NR	LC, HC	USA	GC-MS
Bajtarevic *et al.*, 2009 (6)	285	NR	68	84	LC, HC	NR	PTR-MS, GC-MS
Gaspar *et al.*, 2009 (7)	18	NR	NR	NR	LC, HC	Portugal	GC-MS
Ligor *et al.*, 2009 (8)	65	NR	28	7	LC, HC	Austria	GC-MS
Peng *et al.*, 2009 (9)	40	III-IV	0	17	LC, HC	Israel	GC-MS
Westhoff *et al.*, 2009 (10)	32	0-IV	7	12	LC, HC	Germany	IMS
Fuchs *et al.*, 2010 (11)	12	>T3	0	0	LC, HC	Germany	GC-MS
Poli *et al.*, 2010 (12)	40	I-III	21	0	LC, HC	Italy	GC-MS
Kischkel *et al.*, 2010 (13)	31	>T2	0	4	LC, HC	Germany	GC-MS
Song *et al.*, 2010 (14)	43	I-IV	0	0	LC, HC	China	GC-MS
Tran *et al.*, 2010 (15)	16	NR	16	18	LC, HC	China	Electronic Nose
Buszewski *et al.*, 2011 (16)	115	NR	NR	NR	LC, HC	Poland	GC-MS
Rudnicka *et al.*, 2011 (17)	23	NR	21	6	LC, HC	Poland	GC-TOF/MS
Ulanowska *et al.*, 2011 (18)	137	NR	NR	57	LC, HC	Poland	GC-MS
Buszewski *et al.*, 2012 (19)	29	NR	NR	NR	LC, HC	Poland	GC-TOF/MS
Filipiak *et al.*, 2014 (20)	36	I-IV	NR	NR	LC, HC	Austria	GC-MS
Gi *et al.*, 2014 (21)	NR	NR	NR	NR	LC, HC	Korea	GC-MS
Ma *et al.*, 2014 (22)	13	III-IV	5	16	LC, HC	China	NR
Phillips *et al.*, 2015 (23)	172	NR	NR	0	LC, HC	USA	GC-MS
Ligor *et al.*, 2015 (24)	123	III-IV	109	11	LC, HC	Austria	GC-MS
Gasparri *et al.*, 2016 (25)	70	I-IV	27	31	LC, HC	Italy	Electronic Nose
Itoh *et al.*, 2016 (26)	107	I-IV	NR	NR	LC, HC	Japan	GC-MS
Sakumura *et al.*, 2017 (27)	107	I-IV	47	5	LC, HC	Japan	GC-MS
Cai, *et al.*, 2017 (28)	57	NR	22	25	LC, HC	China	Electronic Nose
Chang *et al.*, 2018 (29)	37	I-IV	9	4	LC, HC	Korea	Metal oxide gas sensors
Huang *et al.*, 2018 (30)	56	I-IV	2	25	LC, HC	China	Electronic Nose
Yu *et al.*, 2018 (31)	6	NR	NR	NR	LC, HC	China	NR
Li *et al.*, 2019 (32)	389	NR	NR	NR	LC, HC	China	GC-MS

Appendix 2 (*continued*)

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Appendix 2 (*continued*)

Study	Information of patients						Analysis Platform
	Patients With Lung Cancer, No.	Cancer Stage	Smoker In Cancer	Smoker In Control	Groups	Setting	
Pesesse *et al.*, 2019 (33)	15	NR	3	1	LC, HC	Belgium	TD-GC × GC-TOFMS
Rudnicka *et al.*, 2019 (34)	108	I-IV	49	13	LC, HC	Poland	GC-MS
Chen *et al.*, 2020 (35)	48	NR	NR	NR	LC, HC	China	Electronic Nose
Gashimova *et al.*, 2020 (36)	75	T1-T4	25	12	LC, HC	Russia	GC-MS
Koureas *et al.*, 2020 (37)	51	NR	8	20	LC, HC	Greece	GC-MS
Li *et al.*, 2020 (38)	115	NR	NR	10	LC, HC	China	Electronic Nose
Saidi *et al.*, 2020 (39)	32	NR	2	3	LC, HC	Morocco	GC/QTOF/MS, Electronic Nose
Chen *et al.*, 2021 (40)	90	III, IV	63	75	LC, HC	China	Electronic Nose
Gashimova *et al.*, 2021 (41)	40	T1-T4	7	7	LC, HC	Russia	GC-MS, Electronic Nose
Koureas *et al.*, 2021 (42)	49	NR	NR	NR	LC, HC	Greece	GC-MS
Lee *et al.*, 2021 (43)	31	Mixed	NR	NR	LC, HC	Korea	Electronic Nose
Li *et al.*, 2021 (44)	6	NR	NR	NR	LC, HC	China	Q-TOF-MS
Liu *et al.*, 2021 (45)	46	NR	27	11	LC, HC	China	Electronic Nose
Liu *et al.*, 2021 (46)	102	NR	NR	NR	LC, HC	China	Electronic Nose
Long *et al.*, 2021 (47)	116	I-IV	100	106	LC, HC	China	GC-MS
Xia *et al.*, 2021 (48)	10	NR	NR	NR	LC, HC	China	NR
Zou *et al.*, 2021 (49)	60	I-IV	32	112	LC, HC	China	GC-MS
Tsou *et al.*, 2021 (50)	148	I-IV	9	0	LC, HC	China	SIFT-MS
Gashimova *et al.*, 2022 (51)	110	T1-T4	22	127	LC, HC	Russia	GC-MS
Larracy *et al.*, 2022 (52)	62	NR	12	6	LC, HC	Canada	CRDS
Wang *et al.*, 2022 (53)	157	I-III	12	NR	LC, HC	China	HPPI-TOFMS
Hao *et al.*, 2023 (54)	6	NR	NR	NR	LC, HC	China	GC-MS
Temerdashev *et al.*, 2023 (55)	112	I-IV	22	17	LC, HC	Russia	GC-MS
Li *et al.*, 2017 (56)	24	NR	19	4, 10	LC, PD, HC	China	Electronic Nose
Chen *et al.*, 2005 (57)	20	NR	NR	NR	LC, CB, HC	China	Electronic Nose
Poli *et al.*, 2005 (58)	36	I-II	2	1, 0	LC, COPD, HC	Italy	GC-MS
Mazzone *et al.*, 2007 (59)	49	I-IV	27	6, 0, 5, 0, 14	LC, COPD, IPF, PAH, S, HC	USA	Colorimetric sensor array
Dragonieri *et al.*, 2009 (60)	10	I-III	2	6, 0	LC, COPD, HC	The Netherlands	Electronic Nose
D'Amico *et al.*, 2010 (61)	28	NR	NR	NR	LC, PD, HC	Italy	GC-MS
Mazzone *et al.*, 2012 (62)	92	I-IV	25	28	LC, RLC	USA	Colorimetric sensor array
Santonico *et al.*, 2012 (63)	20	NR	7	NR	LC, BTS	Italy	Electronic Nose
Wang *et al.*, 2012 (64)	88	I-IV	55	35, 41	LC, BPD, HC	China	GC-MS
Broza *et al.*, 2013 (65)	12	I-II	5	2	LC, BPD	Israel	GC-MS

Appendix 2 (*continued*)

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Appendix 2 (*continued*)

Study	Information of patients						Analysis Platform
	Patients With Lung Cancer, No.	Cancer Stage	Smoker In Cancer	Smoker In Control	Groups	Setting	
Bousamra *et al.*, 2014 (66)	107	0, I, or II	44	12, 45	LC, BPD, HC	NR	NR
Fu *et al.*, 2014 (67)	97	I-IV	NR	NR	LC, BPN, HC	USA	NR
Zou *et al.*, 2014 (68)	79	I-IV	15	12, 9	LC, BPD, HC	China	GC-MS
Capuano *et al.*, 2015 (69)	20	NR	6	5	LC, PD	Italy	GC-MS, Electronic Nose
Li *et al.*, 2015 (70)	85	I-IV or unknown	45	10, 45	LC, BPN, HC	USA	FT-ICR-MS
Schumer *et al.*, 2015 (71)	156	0-IV	69	25, 73	LC, BPN, HC	USA	Silicon chip-MS
Tan *et al.*, 2016 (72)	12	II-IV	2	1, 0	LC, COPD, HC	Malaysia	Alkane sensor
Callol-Sanchez *et al.*, 2017 (73)	81	I-IV	50	34, 30	LC, COPD, HC	Spain	TD-GC-MS
Kistenev *et al.*, 2017 (74)	9	T2-T4	8	10	LC, COPD, HC	Russia	NR
Shlomi *et al.*, 2017 (75)	89	I-IV	72	24	LC, BPN	Israel	Electronic Nose
Wang *et al.*, 2018 (76)	233	NR	102	41, 69	LC, BPD, HC	China	GC-MS
Zuo *et al.*, 2019 (77)	41	≥IIIA	23	5, 18	LC, LI, HC	China	EESI-MS
Binson *et al.*, 2021 (78)	40	I-IV	0	28, 10	LC, COPD, HC	India	Electronic Nose
Binson *et al.*, 2021 (79)	51	NR	4	8, 3	LC, COPD, HC	India	Electronic Nose
Binson *et al.*, 2021 (80)	32	NR	3	6, 33	LC, COPD, HC	India	Electronic Nose
Binson *et al.*, 2021 (81)	48	I-IV	1	4, 10, 21	LC, COPD, Asthma, HC	India	Electronic Nose
Chen *et al.*, 2021 (82)	160	I-IV	33	12, 73	LC, BPN, HC	China	TD-GC-MS
Marzorati *et al.*, 2021 (83)	40	I-III	14	21	LC, RLC	Italy	Electronic Nose
Monedeiro *et al.*, 2021 (84)	16	NR	3	2, 2	LC, COPD, HC	Poland	GC-MS
Zhao *et al.*, 2021 (85)	84	NR	NR	NR	LC, COPD, HC	China	Electronic Nose
Rai *et al.*, 2022 (86)	156	0-II	149	113	LC, BPN, HC	USA	FT-ICR-MS
Wei *et al.*, 2022 (87)	92	NR	45	5, 5	LC, BPD, HC	China	CRDS
Smirnova *et al.*, 2022 (88)	88	I	NR	NR	LC, BPD	USA	GC-MS
Ding *et al.*, 2023 (89)	88	I-III	0	0	LC, BPN	China	HPPI-TOFMS

References are showed in Appendix 5. LC: lung cancer, HC: healthy control, BPN: benign pulmonary nodules, USA: United States of America, COPD: chronic obstructive pulmonary disease, S: sarcoidosis, RLC: have a risk for developing lung cancer, BPD: benign pulmonary disease, LI: lung infection, PD: pulmonary disease, BTS: benign tracheal stenosis, CB: chronic bronchitis, IPF: idiopathic pulmonary fibrosis, PAH: pulmonary arterial hypertension, NR: not report, MS: mass spectrometry; GC-MS: gas chromatography-mass spectrometry, PTR-MS: proton transfer reaction mass spectrometry, IMS: ion mobility spectrometry, Q-TOF-MS: quadrupole time-of-flight mass spectrometry, TD-GC-MS: thermal desorption-gas chromatography-mass spectrometry, SIFT-MS: selected ion flow tube-mass spectrometry, FT-ICR-MS: fourier transform ion cyclotron resonance mass spectrometry, CRDS: cavity ringdown spectroscopy, EESI-MS: extractive electrospray extraction ionization mass spectrometry, HPPI-TOFMS: high-pressure photon ionization time-of-flight mass spectrometry; GC-TOF/MS: gas chromatography-time of flight mass spectrometry; TD-GC × GC-TOFMS: thermal desorption-comprehensive two-dimensional gas chromatography-time of flight mass spectrometry; GC/QTOF/MS: gas chromatography-quadrupole-time of flight mass spectrometry.

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The Newcastle-Ottawa Quality Assessment Scale scores in the included studies

Study	Selection				Comparability	Outcome		Score
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of the exposure (risk factor)		Assessment of the outcome	Statistical test	
Bajtarevic *et al.*, 2009 (6)	★	★	★	★	★	★	★	7
Binson *et al.*, 2021 (78)	★		★	★	★★	★		6
Binson *et al.*, 2021 (79)	★		★	★	★	★	★	6
Binson *et al.*, 2021 (80)	★		★	★	★	★	★	6
Binson *et al.*, 2021 (81)	★		★	★	★★	★	★	7
Bousamra *et al.*, 2014 (66)	★	★	★	★★	★	★	★	8
Broza *et al.*, 2013 (65)	★	★	★	★	★	★	★	7
Buszewski *et al.*, 2012 (19)	★		★	★	★	★	★	6
Buszewski *et al.*, 2011 (16)	★	★	★	★	★	★	★	7
Cai, *et al.*, 2017 (28)	★		★	★	★	★	★	6
Callol-Sanchez *et al.*, 2017 (73)	★	★	★	★	★	★	★	7
Capuano *et al.*, 2015 (69)	★		★	★	★	★	★	6
Chang *et al.*, 2018 (29)	★	★		★	★	★	★	6
Chen *et al.*, 2021 (40)	★	★	★	★★	★★	★	★	9
Chen *et al.*, 2020 (35)	★		★	★	★	★	★	6
Chen *et al.*, 2005 (57)	★		★	★	★	★	★	6
Chen *et al.*, 2021 (82)	★	★	★	★	★★	★	★	8
D'Amico *et al.*, 2010 (61)	★	★	★	★	★	★	★	7
Ding *et al.*,2023 (89)	★	★	★	★	★★	★	★	8
Dragonieri *et al.*, 2009 (60)	★	★	★	★	★	★	★	7
Filipiak *et al.*, 2014 (20)	★		★		★	★	★	5
Fu *et al.*, 2014 (67)	★	★	★	★	★	★	★	7
Fuchs *et al.*, 2010 (11)	★	★	★	★★	★	★	★	8
Gashimova *et al.*, 2020 (36)	★	★	★	★	★	★	★	7
Gashimova *et al.*, 2021 (41)	★		★	★	★	★	★	6
Gashimova *et al.*, 2022 (51)	★	★	★	★	★★	★	★	8
Gaspar *et al.*, 2009 (7)	★		★	★	★	★	★	6
Gasparri *et al.*, 2016 (25)	★	★	★	★	★	★	★	7
Gi *et al.*, 2014 (21)	★		★	★	★		★	5
Hao *et al.*, 2023 (54)	★		★	★	★	★	★	6
Huang *et al.*, 2018 (30)	★	★	★	★★	★	★	★	8
Itoh *et al.*, 2016 (26)	★	★	★	★	★	★	★	7
Kischkel *et al.*, 2010 (13)	★		★	★	★	★	★	6

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Study	Selection				Comparability	Outcome		Score
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of the exposure (risk factor)		Assessment of the outcome	Statistical test	
Kistenev *et al.*, 2017 (74)	★		★	★	★	★	★	6
Koureas *et al.*, 2021 (42)	★		★	★	★	★	★	6
Koureas *et al.*, 2020 (37)	★	★	★	★	★	★	★	7
Larracy *et al.*, 2022 (52)	★	★	★	★	★		★	6
Lee *et al.*, 2021 (43)	★		★	★★	★	★	★	7
Li *et al.*, 2015 (70)	★	★	★	★★	★	★	★	8
Li *et al.*, 2019 (32)	★	★	★	★★	★★	★	★	9
Li *et al.*, 2020 (38)	★	★	★	★	★★	★	★	8
Li *et al.*, 2021 (44)	★			★	★	★	★	5
Ligor *et al.*, 2009 (8)	★		★	★	★	★	★	6
Ligor *et al.*, 2015 (24)	★	★	★	★	★	★	★	7
Liu *et al.*, 2021 (45)	★		★	★★	★	★	★	7
Liu *et al.*, 2021 (46)	★	★	★	★	★	★	★	7
Long *et al.*, 2021 (47)	★	★	★	★	★★	★	★	8
Ma *et al.*, 2014 (22)	★		★	★	★	★	★	6
Marzorati *et al.*, 2021 (83)	★		★	★★	★	★	★	7
Mazzone *et al.*, 2007 (59)	★		★	★	★	★	★	6
Mazzone *et al.*, 2012 (62)	★	★	★	★	★	★	★	7
Monedeiro *et al.*, 2021 (84)	★		★	★	★	★	★	6
Peng *et al.*, 2009 (9)	★		★	★	★	★	★	6
Pesesse *et al.*, 2019 (33)	★	★	★	★	★	★★	★	8
Phillips *et al.*, 1999 (1)	★		★	★★	★	★	★	7
Phillips *et al.*, 2007 (3)	★	★	★	★	★★	★	★	8
Phillips *et al.*, 2008 (5)	★	★	★	★	★	★★	★	8
Poli *et al.*, 2005 (58)	★		★	★	★	★	★	6
Poli *et al.*, 2010 (12)	★		★	★★	★	★	★	7
Rai *et al.*, 2022 (86)	★	★	★	★★	★	★	★	8
Rudnicka *et al.*, 2019 (34)	★	★	★	★	★	★	★	7
Rudnicka *et al.*, 2011 (17)	★	★	★	★	★	★	★	7
Saidi *et al.*, 2020 (39)	★		★	★★	★	★★	★	8
Sakumura *et al.*, 2017 (27)	★	★	★	★	★	★	★	7
Santonico *et al.*, 2012 (63)	★		★	★	★	★	★	6

(*continued*)

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(*continued*)

Study	Selection				Comparability	Outcome		Score
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of the exposure (risk factor)		Assessment of the outcome	Statistical test	
Schumer *et al.*, 2015 (71)	★	★	★	★	★	★	★	7
Shlomi *et al.*, 2017 (75)	★	★	★	★★	★		★	7
Smirnova *et al.*, 2022 (88)	★	★	★	★★	★	★	★	8
Song *et al.*, 2010 (14)	★		★	★	★★	★	★	7
Tan *et al.*, 2016 (72)	★		★	★	★	★	★	6
Temerdashev *et al.*, 2023 (55)	★	★	★	★★	★	★	★	8
Tran *et al.*, 2010 (15)	★		★	★	★	★	★	6
Tsou *et al.*, 2021 (50)	★	★	★	★★	★		★	7
Ulanowska *et al.*, 2011 (18)	★	★		★★	★	★	★	7
Wang *et al.*, 2018 (76)	★	★		★	★	★	★	6
Wang *et al.*, 2022 (53)	★	★	★	★	★★	★	★	8
Wang *et al.*, 2012 (64)	★	★	★	★	★	★	★	7
Wehinger *et al.*, 2007 (4)	★	★	★	★★	★		★	7
Wei *et al.*, 2022 (87)	★	★	★	★		★	★	6
Westhoff *et al.*, 2009 (10)			★	★	★	★	★	5
Xia *et al.*, 2021 (48)	★		★	★	★	★	★	6
Yu *et al.*, 2018 (31)	★		★	★	★	★	★	6
Yu *et al.*, 2005 (2)	★	★	★	★	★	★	★	7
Zhao *et al.*, 2021 (85)		★	★	★	★	★	★	6
Zou *et al.*, 2021 (49)	★	★	★	★★	★	★	★	8
Zou *et al.*, 2014 (68)	★	★	★	★★	★	★	★	8
Zuo *et al.*, 2019 (77)	★		★	★	★	★		5
Phillips *et al.*, 2015 (23)	★	★	★	★★	★	★	★	8
Li *et al.*, 2017 (56)	★		★	★	★	★	★	6

References are showed in Appendix 5.

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Appendix 3 Newcastle-Ottawa Quality Assessment Scale

(Adapted for cross-sectional studies)
Selection: (Maximum 5 stars)
1) Representativeness of the sample:
a) Truly representative of the average in the target population. * (all subjects or random sampling)
b) Somewhat representative of the average in the target population. * (non-random sampling)
c) Selected group of users.
d) No description of the sampling strategy.
2) Sample size:
a) Justified and satisfactory. *
b) Not justified.
3) Non-respondents:
a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. *
b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.
c) No description of the response rate or the characteristics of the responders and the non-responders.
4) Ascertainment of the exposure (risk factor):
a) Validated measurement tool. **
b) Non-validated measurement tool, but the tool is available or described.*
c) No description of the measurement tool.
Comparability: (Maximum 2 stars)
1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.
a) The study controls for the most important factor (select one). *
b) The study control for any additional factor. *
Outcome: (Maximum 3 stars)
1) Assessment of the outcome:
a) Independent blind assessment. **
b) Record linkage. **
c) Self report. *
d) No description.
2) Statistical test:
a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *
b) The statistical test is not appropriate, not described or incomplete.

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Appendix 4 171 articles excluded after the full-text review

No.	Study, year	Main reason	Citations
1	Poli, 2008	Not published in full-text	Poli D, Goldoni M, Caglieri A, *et al.* Breath analysis in non small cell lung cancer patients after surgical tumour resection. Acta bio-medica : Atenei Parmensis 2008;79 Suppl 1:64-72
2	Umin, 2011	Not published in full-text	Umin. Ion Mobility Spectrometry in healthy and respiratory disease subjects. 2011
3	Umin, 2012	Not published in full-text	Umin. Detection of histological type and genetic mutation in lung cancer using ion mobility spectrometry. 2012
4	Ho, 2014	Not published in full-text	Ho KC, Seungho L, Kim D, *et al.* Preparation and characterization of the primary gas standards for isoprene. J Anal Sci Technol 2014;27:357-63
5	Mgwenya, 2018	Not published in full-text	Mgwenya TNZ. Polymer Nanocomposites-Based Sensors for the Detection of Lung Cancer Volatile Organic Biomarkers. 2018
6	Schallschmidt, 2015	Duplicate article	Schallschmidt K, Becker R, Zwaka H, *et al.* In vitro cultured lung cancer cells are not suitable for animal-based breath biomarker detection. J Breath Res 2015;9:027103
7	Bianchi, 2017	Duplicate article	Bianchi F, Riboni N, Carbognani P, *et al.* Solid-phase microextraction coupled to gas chromatography–mass spectrometry followed by multivariate data analysis for the identification of volatile organic compounds as possible biomarkers in lung cancer tissues. J Pharm Biomed Anal 2017;146:329-33
8	Cao, 2008	Articles published not in English	Cao MF, Chen X, Wang YQ, *et al.* A novel electronic nose for detection of lung cancer based on virtual SAW gas sensors array. Chin J Biomed Eng 2008;27:102-7
9	Liu, 2009	Articles published not in English	Liu H, Song G, Qin T, *et al.* Quantitative analysis of volatile biomarkers in breath of non-small cell lung cancer patients. Chin J Cancer Prev Treat 2009;16:1857-9
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Appendix 4 (*continued*)

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Appendix 4 (*continued*)

No.	Study, year	Main reason	Citations
35	Munoz-Lucas, 2013	Review, meta, letter, comment or conference abstract	Munoz-Lucas A, Wagner-Struwing C, Jareno-Esteban J, *et al.* Differences in volatile organic compounds (VOC) determined in exhaled breath in two populations of lung cancer (LC): With and without COPD. Eur Respir J 2013;42
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No.	Study, year	Main reason	Citations
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Appendix 4 (*continued*)

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Appendix 4 (*continued*)

No.	Study, year	Main reason	Citations
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122	Liu, 2011	No complete collection methods	Liu FL, Xiao P, Fang HL, *et al.* Single-walled carbon nanotube-based biosensors for the detection of volatile organic compounds of lung cancer. Physica E 2011;44:367-72.
123	Ehmann, 2012	No complete collection methods	Ehmann R, Boedeker E, Friedrich U, *et al.* Canine scent detection in the diagnosis of lung cancer: revisiting a puzzling phenomenon. Eur Respir J 2012;39:669-76.
124	Chatterjee, 2013	No complete collection methods	Chatterjee S, Castro M, Feller JF. An e-nose made of carbon nanotube based quantum resistive sensors for the detection of eighteen polar/nonpolar VOC biomarkers of lung cancer. J Mater Chem B 2013;1:4563-75.
125	Hou, 2013	No complete collection methods	Hou C, Lei J, Huo D, *et al.* Discrimination of Lung Cancer Related Volatile Organic Compounds with a Colorimetric Sensor Array. Anal Lett 2013;46:2048-59.
126	Handa, 2014	No complete collection methods	Handa H, Usuba A, Maddula S, *et al.* Exhaled Breath Analysis for Lung Cancer Detection Using Ion Mobility Spectrometry. PLoS One 2014;9.
127	Wang, 2014	No complete collection methods	Wang C, Dong R, Wang X, *et al.* Exhaled volatile organic compounds as lung cancer biomarkers during one-lung ventilation. Sci Rep 2014;4.
128	Wu, 2014	No complete collection methods	Wu Y, Huo D, Hou C, *et al.* Colorimetric Artificial Nose for Identification of Breath Volatile Organic Compounds of Patients with Lung Cancer. Chem Res Chin Univ 2014;30:572-7.
129	de Vries R, 2015	No complete collection methods	de Vries R, Brinkman P, van der Schee MP, *et al.* Integration of electronic nose technology with spirometry: validation of a new approach for exhaled breath analysis. J Breath Res 2015;9.
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131	Mazzone, 2015	No complete collection methods	Mazzone PJ, Wang XF, Lim S, *et al.* Progress in the development of volatile exhaled breath signatures of lung cancer. Ann Am Thorac Soc 2015;12:752-7.
132	Zhang, 2016	No complete collection methods	Zhang X-F, Zhang Z-W, He Y-L, *et al.* Sniffing lung cancer related biomarkers using an oxidized graphene SAW sensor. Front Phys 2016;11.
133	Chen, 2017	No complete collection methods	Chen X, Wang F, Lin L, *et al.* Association of Smoking with Metabolic Volatile Organic Compounds in Exhaled Breath. Int J Mol Sci 2017;18.
134	Kort, 2017	No complete collection methods	Kort S, Brusse-Keizer M, Gerritsen J-W, *et al.* Data analysis of electronic nose technology in lung cancer: generating prediction models by means of Aethena. J Breath Res 2017;11.
135	Li, 2017	No complete collection methods	Li Z, Xu C, Shu J, *et al.* Doping-assisted low-pressure photoionization mass spectrometry for the real-time detection of lung cancer-related volatile organic compounds. Talanta 2017;165:98-106.

Appendix 4 (*continued*)

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Appendix 4 (*continued*)

No.	Study, year	Main reason	Citations
136	Liu, 2017	No complete collection methods	Liu L, Zhang D, Zhang Q, *et al.* Smartphone-based sensing system using ZnO and graphene modified electrodes for VOCs detection. Biosens Bioelectron 2017;93:94-101.
137	Nag, 2017	No complete collection methods	Nag S, Castro M, Choudhary V, *et al.* Sulfonated poly(ether ether ketone) [SPEEK] nanocomposites based on hybrid nanocarbons for the detection and discrimination of some lung cancer VOC biomarkers. J Mater Chem B 2017;5:348-59.
138	Oguma, 2017	No complete collection methods	Oguma T, Nagaoka T, Kurahashi M, *et al.* Clinical contributions of exhaled volatile organic compounds in the diagnosis of lung cancer. PLoS One 2017;12.
139	Saalberg, 2017	No complete collection methods	Saalberg Y, Bruhns H, Wolff M. Photoacoustic Spectroscopy for the Determination of Lung Cancer Biomarkers-A Preliminary Investigation. Sensors 2017;17.
140	Zhang, 2017	No complete collection methods	Zhang Z, Yu W, Wang J, *et al.* Ultrasensitive Surface-Enhanced Raman Scattering Sensor of Gaseous Aldehydes as Biomarkers of Lung Cancer on Dendritic Ag Nanocrystals. Anal Chem 2017;89:1416-20.
141	Gregis, 2018	No complete collection methods	Gregis G, Sanchez J-B, Bezyerkhyy I, *et al.* Detection and quantification of lung cancer biomarkers by a micro-analytical device using a single metal oxide-based gas sensor. Sensor Actuat B-Chem 2018;255:391-400.
142	Kort, 2018	No complete collection methods	Kort S, Tiggeloven MM, Brusse-Keizer M, *et al.* Multi-centre prospective study on diagnosing subtypes of lung cancer by exhaled-breath analysis. Lung Cancer 2018;125:223-9.
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145	Rocco, 2018	No complete collection methods	Rocco G. Every breath you take: The value of the electronic nose (e-nose) technology in the early detection of lung cancer. J Thorac Cardiovasc Surg 2018;155:2622-5.
146	Wan, 2018	No complete collection methods	Wan Q, Xu Y, Xiao H. Exhaled gas detection by Ir-doped CNT for primary diagnosis of lung cancer. AIP Adv 2018;8.
147	Zhao, 2018	No complete collection methods	Zhao G, Li M. Ni-doped MoS₂ biosensor: a promising candidate for early diagnosis of lung cancer by exhaled breathe analysis. Appl Phys A-Mater 2018;124.
148	Zhao, 2018	No complete collection methods	Zhao S, Lei J, Huo D, *et al.* A colorimetric detector for lung cancer related volatile organic compounds based on cross-response mechanism. Sensor Actuat B-Chem 2018;256:543-52.
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150	Zhong, 2018	No complete collection methods	Zhong X, Li D, Du W, *et al.* Rapid recognition of volatile organic compounds with colorimetric sensor arrays for lung cancer screening. Anal Bioanal Chem 2018 410:3671-81.
151	Kovalska, 2019	No complete collection methods	Kovalska E, Lesongeur P, Hogan BT, *et al.* Multi-layer graphene as a selective detector for future lung cancer biosensing platforms. Nanoscale 2019;11:2476-83.
152	Lu, 2019	No complete collection methods	Lu B, Fu L, Nie B, *et al.* A Novel Framework with High Diagnostic Sensitivity for Lung Cancer Detection by Electronic Nose. Sensors 2019;19.
153	Tirzite, 2019	No complete collection methods	Tirzite M, Bukovskis M, Strazda G, *et al.* Detection of lung cancer with electronic nose and logistic regression analysis. J Breath Res 2019;13.
154	Kononov, 2020	No complete collection methods	Kononov A, Korotetsky B, Jahatspanian I, *et al.* Online breath analysis using metal oxide semiconductor sensors (electronic nose) for diagnosis of lung cancer. J Breath Res 2020;14.
155	Kort, 2020	No complete collection methods	Kort S, Brusse-Keizer M, Gerritsen JW, *et al.* Improving lung cancer diagnosis by combining exhaled-breath data and clinical parameters. ERJ OPEN RESEARCH 2020;6.
156	Majidi, 2020	No complete collection methods	Majidi R, Nadafan M. Detection of exhaled gas by γ-graphyne and twin-graphene for early diagnosis of lung cancer: A density functional theory study. Phys Lett A 2020;384.
157	Xu, 2020	No complete collection methods	40. Xu Y, Jiang J, Bu H, *et al.* A dual-channel self-calibrating multi-parameter sensor for lung cancer-related exhaled marker rapid identification. Anal Methods 2020;12:620-9.
158	Zhang, 2020	No complete collection methods	Zhang X, Zhang Q, Wang X, *et al.* Structured sparse logistic regression with application to lung cancer prediction using breath volatile biomarkers. Stat Med 2020;39:955-67.
159	Mirzaei, 2021	No complete collection methods	Mirzaei M, Gulseren O, Rafienia M, *et al.* Nanocarbon-assisted biosensor for diagnosis of exhaled biomarkers of lung cancer: DFT approach. Eurasian Chemical Communications 2021;3:154-61.
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162	Zou, 2022	No complete collection methods	Zou Y, Hu Y, Jiang Z, *et al.* Exhaled metabolic markers and relevant dysregulated pathways of lung cancer: a pilot study. Ann Med 2022;54:790-802.
163	Li, 2023	No complete collection methods	Li L, Tian Z-W, Zhao W-H, *et al.* "Sniff"lung cancer biomarkers in breath using N-doped monolayer WS2: A theoretical feasibility. Appl Surf Sci 2023;614.
164	Liu, 2023	No complete collection methods	Liu L, Ru L, Tang H, *et al.* A multi-responsive Tb-doped MOF probe for highly specific breath volatile biomarker recognition of lung cancer. J Mater Chem C 2023;11:3059-69.
165	Mashhadbani, 2023	No complete collection methods	Mashhadbani M, Faizabadi E. Early detection of lung cancer biomarkers in exhaled breath by modified armchair stanene nanoribbons. PCCP 2023;25:3875-89.
166	Guirao, 2017	Use trained dogs to analysis VOCs	Guirao Montes A, Molins Lopez-Rodo L, Ramon Rodriguez I, *et al.* Lung cancer diagnosis by trained dogs. Eur J Cardiothorac Surg 2017;52:1206-10.
167	Fischer-Tenhagen, 2018	Use trained dogs to analysis VOCs	Fischer-Tenhagen C, Johnen D, Nehls I, *et al.* A Proof of Concept: Are Detection Dogs a Useful Tool to Verify Potential Biomarkers for Lung Cancer? Front Vet Sci 2018;5.
168	Guirao, 2019	Use trained dogs to analysis VOCs	Guirao A, Molins L, Ramon I, *et al.* Trained dogs can identify malignant solitary pulmonary nodules in exhaled gas. Lung Cancer 2019;135:230-3.
169	Mazzola, 2020	Use trained dogs to analysis VOCs	Mazzola SM, Pirrone F, Sedda G, *et al.* Two-step investigation of lung cancer detection by sniffer dogs. J Breath Res 2020;14.
170	Feil, 2021	Use trained dogs to analysis VOCs	Feil C, Staib F, Berger MR, *et al.* Sniffer dogs can identify lung cancer patients from breath and urine samples. BMC Cancer 2021;21.
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Appendix 5 89 articles included in full text

No.	Study, year	Citations
1	Phillips, 1999	Phillips M, Gleeson K, Hughes JM, *et al.* Volatile organic compounds in breath as markers of lung cancer: a cross-sectional study. Lancet 1999;353:1930-3.
2	Yu, 2005	Yu H, Xu L, Wang P. Solid phase microextraction for analysis of alkanes and aromatic hydrocarbons in human breath. J Chromatogr B Analyt Technol Biomed Life Sci 2005;826:69-74.
3	Phillips, 2007	Phillips M, Altorki N, Austin JHM, *et al.* Prediction of lung cancer using volatile biomarkers in breath. Cancer Biomarkers 2007;3:95-109.
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6	Bajtarevic, 2009	Bajtarevic A, Ager C, Pienz M, *et al.* Noninvasive detection of lung cancer by analysis of exhaled breath. BMC Cancer 2009;9.
7	Gaspar, 2009	Gaspar EM, Lucena AF, Duro da Costa J, *et al.* Organic metabolites in exhaled human breath--a multivariate approach for identification of biomarkers in lung disorders. J chromatogr A 2009;1216:2749-56.
8	Ligor, 2009	Ligor M, Ligor T, Bajtarevic A, *et al.* Determination of volatile organic compounds in exhaled breath of patients with lung cancer using solid phase microextraction and gas chromatography mass spectrometry. Clin Chem Lab Med 2009;47:550-60.
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11	Fuchs, 2010	Fuchs P, Loeseken C, Schubert JK, *et al.* Breath gas aldehydes as biomarkers of lung cancer. Int J Cancer 2010;126:2663-70.
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13	Kischkel, 2010	Kischkel S, Miekisch W, Sawacki A, *et al.* Breath biomarkers for lung cancer detection and assessment of smoking related effects - confounding variables, influence of normalization and statistical algorithms. Clin Chim Acta 2010;411:1637-44.
14	Song, 2010	Song G, Qin T, Liu H, *et al.* Quantitative breath analysis of volatile organic compounds of lung cancer patients. Lung Cancer 2010;67:227-31.
15	Tran, 2010	Tran VH, Chan HP, Thurston M, *et al.* Breath Analysis of Lung Cancer Patients Using an Electronic Nose Detection System. IEEE Sens J 2010;10:1514-8.
16	Buszewski, 2011	Buszewski B, Ulanowska A, Kowalkowski T, *et al.* Investigation of lung cancer biomarkers by hyphenated separation techniques and chemometrics. Clin Chem Lab Med 2011;50:573-81.
17	Rudnicka, 2011	Rudnicka J, Kowalkowski T, Ligor T, *et al.* Determination of volatile organic compounds as biomarkers of lung cancer by SPME-GC-TOF/MS and chemometrics. J Chromatogr B Analyt Technol Biomed Life Sci 2011;879:3360-6.
18	Ulanowska, 2011	Ulanowska A, Kowalkowski T, Trawinska E, *et al.* The application of statistical methods using VOCs to identify patients with lung cancer. J Breath Res 2011;5.
19	Buszewski, 2012	Buszewski B, Ligor T, Jezierski T, *et al.* Identification of volatile lung cancer markers by gas chromatography-mass spectrometry: comparison with discrimination by canines. Anal Bioanal Chem 2012;404:141-6.
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22	Ma, 2014	Ma H, Li X, Chen J, *et al.* Analysis of human breath samples of lung cancer patients and healthy controls with solid-phase microextraction (SPME) and flow-modulated comprehensive two-dimensional gas chromatography (GC x GC). Anal Methods 2014;6:6841-9.
23	Phillips, 2015	Phillips M, Bauer TL, Cataneo RN, *et al.* Blinded Validation of Breath Biomarkers of Lung Cancer, a Potential Ancillary to Chest CT Screening. PLoS One 2015;10.
24	Ligor, 2015	Ligor T, Pater L, Buszewski B. Application of an artificial neural network model for selection of potential lung cancer biomarkers. J Breath Res 2015;9.
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28	Cai, 2017	Cai X, Chen L, Kang T, *et al.* A Prediction Model with a Combination of Variables for Diagnosis of Lung Cancer. Med Sci Monit 2017;23:5620-9.
29	Chang, 2018	Chang J-E, Lee D-S, Ban S-W, *et al.* Analysis of volatile organic compounds in exhaled breath for lung cancer diagnosis using a sensor system. Sensor Actuat B-Chem 2018;255:800-7.
30	Huang, 2018	Huang C-H, Zeng C, Wang Y-C, *et al.* A Study of Diagnostic Accuracy Using a Chemical Sensor Array and a Machine Learning Technique to Detect Lung Cancer. Sensors (Basel) 2018;18.
31	Yu, 2018	Yu L-Q, Wang L-Y, Su F-H, *et al.* A gate-opening controlled metal-organic framework for selective solid-phase microextraction of aldehydes from exhaled breath of lung cancer patients. Microchim Acta 2018;185.
32	Li, 2019	Li W, Dai W, Liu M, *et al.* VOC biomarkers identification and predictive model construction for lung cancer based on exhaled breath analysis: research protocol for an exploratory study. BMJ Open Sci 2019;9.
33	Pesesse, 2019	Pesesse R, Stefanuto PH, Schleich F, *et al.* Multimodal chemometric approach for the analysis of human exhaled breath in lung cancer patients by TD-GC×GC-TOFMS. J Chromatogr B Analyt Technol Biomed Life Sci 2019;1114-1115:146-53.
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Appendix 5 (*continued*)

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Appendix 5 (*continued*)

No.	Study, year	Citations
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39	Saidi, 2020	Saidi T, Moufid M, de Jesus Beleno-Saenz K, *et al.* Non-invasive prediction of lung cancer histological types through exhaled breath analysis by UV-irradiated electronic nose and GC/QTOF/MS. Sensor Actuat B-Chem 2020;311.
40	Chen, 2021	Chen K, Liu L, Nie B, *et al.* Recognizing lung cancer and stages using a self-developed electronic nose system. Comput Biol Med 2021;131.
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42	Koureas, 2021	Koureas M, Kalompatsios D, Amoutzias GD, *et al.* Comparison of Targeted and Untargeted Approaches in Breath Analysis for the Discrimination of Lung Cancer from Benign Pulmonary Diseases and Healthy Persons. Molecules (Basel, Switzerland) 2021;26.
43	Lee, 2021	Lee JM, Choi EJ, Chung JH, *et al.* A DNA-derived phage nose using machine learning and artificial neural processing for diagnosing lung cancer. Biosens Bioelectron 2021;194.
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60	Dragonieri, 2009	Dragonieri S, Annema JT, Schot R, *et al.* An electronic nose in the discrimination of patients with non-small cell lung cancer and COPD. Lung Cancer 2009;64:166-70.
61	D'Amico, 2010	D'Amico A, Pennazza G, Santonico M, *et al.* An investigation on electronic nose diagnosis of lung cancer. Lung Cancer 2010;68:170-6.
62	Mazzone, 2012	Mazzone PJ, Wang X-F, Xu Y, *et al.* Exhaled Breath Analysis with a Colorimetric Sensor Array for the Identification and Characterization of Lung Cancer. J Thorac Oncol 2012;7:137-42.
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Appendix 5 (*continued*)

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Appendix 5 (*continued*)

No.	Study, year	Citations
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68	Zou, 2014	Zou Y, Zhang X, Chen X, *et al.* Optimization of volatile markers of lung cancer to exclude interferences of non-malignant disease. Cancer Biomarkers 2014;14:371-9.
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70	Li, 2015	Li M, Yang D, Brock G, *et al.* Breath carbonyl compounds as biomarkers of lung cancer. Lung Cancer 2015;90:92-7.
71	Schumer, 2015	Schumer EM, Trivedi JR, van Berkel V, *et al.* High sensitivity for lung cancer detection using analysis of exhaled carbonyl compounds. J Thorac Cardiovasc Surg 2015;150:1517-22.
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https://dx.doi.org/https://dx.doi.org/10.21037/jtd-24-1001