Supplementary Material*

Ghasemiesfe M, Ravi D, Vali M, Korenstein D, Arjomandi M, Frank J, et al. Marijuana use, respiratory symptoms, and pulmonary function. A systematic review and meta-analysis. Ann Intern Med. 2018. doi:10.7326/M18-0522

* This supplementary material was provided by the authors to give readers further details on their article. The material was reviewed but not copyedited.

Supplement Part 1. SEARCH STRATEGIES

DATABASES/WEBSITES:

PubMed
EMBASE
PsycINFO
MEDLINE
Cochrane Library

PubMed

Date Searched: April 12, 2017; First Update: September 30, 2017; Second Update: April 30, 2018

Mesh terms		
Marijuana OR Marihuana OR Tetrahydrocannabinol OR Cannabinoid	AND	bronchial disease OR respiratory function test OR hemoptysis OR pulmonary hypertension OR interstitial lung diseases OR obstructive lung diseases OR lung injury OR pulmonary atelectasis OR pulmonary edema OR pulmonary embolism OR pulmonary eosinophilia OR pulmonary fibrosis OR pulmonary veno occlusive disease OR adult respiratory distress syndrome OR hospitalization OR survival rate OR respiration disorders OR pleural diseases OR respiratory tract infections OR respiratory hypersensitivity OR respiratory tract neoplasm OR respiratory care units OR respiratory signs and symptoms

#	Searches	Results
#8	Search #7	927
#7	#6 AND (("1973/01/01"[PDAT]: "2018/04/30"[PDAT])	927
#6	#5 AND ("humans"[MeSH Terms]	956
#5	#4 OR #3 AND English[lang]	1,138
#4	#1 AND #2	1,265
#3	(("cannabis"[MeSH Terms] OR "cannabis"[All Fields] OR "marijuana"[All Fields]) OR ("cannabis"[MeSH Terms] OR "cannabis"[All Fields] OR "marihuana"[All Fields]) OR ("dronabinol"[MeSH Terms] OR "dronabinol"[All Fields] OR "tetrahydrocannabinol"[All Fields]) OR ("cannabinoids"[MeSH Terms] OR "cannabinoids"[All Fields] OR "cannabinoid"[All Fields])) AND (("bronchial diseases"[MeSH Terms] OR ("bronchial"[All Fields] AND "diseases"[All Fields]) OR "bronchial diseases"[All Fields] OR ("bronchial"[All Fields] AND "disease"[All Fields]) OR "bronchial disease"[All Fields]) OR ("respiratory function tests"[MeSH Terms] OR ("respiratory"[All Fields] AND "function"[All Fields] AND "tests"[All Fields]) OR "respiratory function tests"[All Fields] OR ("respiratory"[All Fields] AND "function"[All Fields] AND "test"[All Fields]) OR "respiratory function test"[All Fields]) OR ("haemoptysis"[All Fields] OR "hemoptysis"[MeSH Terms] OR "hemoptysis"[All Fields]) OR ("hypertension, pulmonary"[MeSH Terms] OR ("hypertension"[All Fields] AND "pulmonary"[All Fields]) OR "pulmonary	1,857,391

	hypertension"[All Fields] OR ("pulmonary"[All Fields] AND "hypertension"[All Fields])) OR ("lung diseases, interstitial"[MeSH Terms] OR ("lung"[All Fields] AND "diseases"[All Fields] AND "interstitial"[All Fields]) OR "interstitial lung diseases"[All Fields] OR ("interstitial"[All Fields] AND "lung"[All Fields] AND "diseases"[All Fields])) OR ("lung diseases, obstructive"[MeSH Terms] OR ("lung"[All Fields] AND "diseases"[All Fields] AND "obstructive"[All Fields]) OR "obstructive lung diseases"[All Fields] OR ("obstructive"[All Fields] AND "lung"[All Fields] AND "diseases"[All Fields])) OR ("lung injury"[MeSH Terms] OR ("lung"[All Fields] AND "injury"[All Fields]) OR "lung injury"[All Fields]) OR ("pulmonary atelectasis"[MeSH Terms] OR ("pulmonary"[All Fields] AND "atelectasis"[All Fields]) OR "pulmonary atelectasis"[All Fields]) OR ("pulmonary oedema"[All Fields] OR "pulmonary edema"[MeSH Terms] OR ("pulmonary"[All Fields] AND "edema"[All Fields]) OR "pulmonary edema"[All Fields]) OR ("pulmonary embolism"[MeSH Terms] OR ("pulmonary"[All Fields] AND "embolism"[All Fields]) OR "pulmonary embolism"[All Fields]) OR ("pulmonary eosinophilia"[MeSH Terms] OR ("pulmonary"[All Fields] AND "eosinophilia"[All Fields]) OR "pulmonary eosinophilia"[All Fields]) OR ("pulmonary fibrosis"[MeSH Terms] OR ("pulmonary"[All Fields] AND "fibrosis"[All Fields]) OR "pulmonary fibrosis"[All Fields]) OR ("pulmonary veno-occlusive disease"[MeSH Terms] OR ("pulmonary"[All Fields] AND "veno-occlusive"[All Fields] AND "disease"[All Fields]) OR "pulmonary veno-occlusive disease"[All Fields] OR ("pulmonary"[All Fields] AND "veno"[All Fields] AND "occlusive"[All Fields] AND "disease"[All Fields]) OR "pulmonary veno occlusive disease"[All Fields]) OR ("respiratory distress syndrome, adult"[MeSH Terms] OR ("respiratory"[All Fields] AND "distress"[All Fields] AND "syndrome"[All Fields] AND "adult"[All Fields]) OR "adult respiratory distress syndrome"[All Fields] OR ("adult"[All Fields] AND "respiratory"[All Fields] AND "distress"[All Fields] AND "syndrome"[All Fields])) OR ("hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields]) OR ("survival rate"[MeSH Terms] OR ("survival"[All Fields] AND "rate"[All Fields]) OR "survival rate"[All Fields]) OR ("respiration disorders"[MeSH Terms] OR ("respiration"[All Fields] AND "disorders"[All Fields]) OR "respiration disorders"[All Fields]) OR ("pleural diseases"[MeSH Terms] OR ("pleural"[All Fields] AND "diseases"[All Fields]) OR "pleural diseases"[All Fields]) OR ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields]) OR ("respiratory hypersensitivity"[MeSH Terms] OR ("respiratory"[All Fields] AND "hypersensitivity"[All Fields]) OR "respiratory hypersensitivity"[All Fields]) OR ("respiratory tract neoplasms"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "neoplasms"[All Fields]) OR "respiratory tract neoplasms"[All Fields]) OR ("respiratory care units"[MeSH Terms] OR ("respiratory"[All Fields] AND "care"[All Fields] AND "units"[All Fields]) OR "respiratory care units"[All Fields]) OR (respiratory[All Fields] AND ("signs and symptoms"[MeSH Terms] OR ("signs"[All Fields] AND "symptoms"[All Fields]) OR "signs and symptoms"[All Fields])))	
#2	("bronchial diseases"[MeSH Terms] OR ("bronchial"[All Fields] AND "diseases"[All Fields]) OR "bronchial diseases"[All Fields] OR ("bronchial"[All Fields] AND "disease"[All Fields]) OR "bronchial disease"[All Fields]) OR ("respiratory function tests"[MeSH Terms] OR ("respiratory"[All Fields] AND "function"[All Fields] AND "tests"[All Fields]) OR "respiratory function tests"[All Fields] OR ("respiratory"[All Fields] AND "function"[All Fields] AND "test"[All Fields]) OR "respiratory function test"[All Fields]) OR ("haemoptysis"[All Fields] OR "hemoptysis"[MeSH Terms] OR "hemoptysis"[All Fields]) OR ("hypertension, pulmonary"[MeSH Terms] OR ("hypertension"[All Fields] AND "pulmonary"[All Fields]) OR "pulmonary hypertension"[All Fields] OR ("pulmonary"[All Fields] AND "hypertension"[All Fields])) OR ("lung diseases, interstitial"[MeSH Terms] OR ("lung"[All Fields] AND "diseases"[All Fields] AND "interstitial"[All Fields]) OR "interstitial lung diseases"[All Fields] OR ("interstitial"[All Fields] AND "lung"[All Fields] AND "diseases"[All Fields])) OR ("lung diseases, obstructive"[MeSH Terms] OR ("lung"[All Fields] AND "diseases"[All Fields] AND "obstructive"[All Fields]) OR "obstructive lung diseases"[All Fields] OR ("obstructive"[All Fields] AND "lung"[All Fields] AND "diseases"[All Fields])) OR ("lung injury"[MeSH Terms] OR ("lung"[All Fields] AND "injury"[All Fields]) OR "lung injury"[All Fields]) OR ("pulmonary atelectasis"[MeSH Terms] OR ("pulmonary"[All Fields] AND "atelectasis"[All Fields]) OR "pulmonary atelectasis"[All Fields]) OR ("pulmonary oedema"[All Fields] OR "pulmonary edema"[MeSH Terms] OR ("pulmonary"[All Fields] AND "edema"[All Fields]) OR "pulmonary edema"[All Fields]) OR ("pulmonary embolism"[MeSH Terms] OR ("pulmonary"[All Fields] AND "embolism"[All Fields]) OR "pulmonary embolism"[All Fields]) OR ("pulmonary eosinophilia"[MeSH Terms]	1,874,131

	OR ("pulmonary"[All Fields] AND "eosinophilia"[All Fields]) OR "pulmonary eosinophilia"[All Fields]) OR ("pulmonary fibrosis"[MeSH Terms] OR ("pulmonary"[All Fields] AND "fibrosis"[All Fields]) OR "pulmonary fibrosis"[All Fields]) OR ("pulmonary veno-occlusive disease"[MeSH Terms] OR ("pulmonary"[All Fields] AND "veno-occlusive"[All Fields] AND "disease"[All Fields]) OR "pulmonary veno-occlusive disease"[All Fields] OR ("pulmonary"[All Fields] AND "veno"[All Fields] AND "occlusive"[All Fields] AND "disease"[All Fields]) OR "pulmonary veno occlusive disease"[All Fields]) OR ("respiratory distress syndrome, adult"[MeSH Terms] OR ("respiratory"[All Fields] AND "distress"[All Fields] AND "syndrome"[All Fields] AND "adult"[All Fields]) OR "adult respiratory distress syndrome"[All Fields] OR ("adult"[All Fields] AND "respiratory"[All Fields] AND "distress"[All Fields] AND "syndrome"[All Fields])) OR ("hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields]) OR ("survival rate"[MeSH Terms] OR ("survival"[All Fields] AND "rate"[All Fields]) OR "survival rate"[All Fields]) OR ("respiration disorders"[MeSH Terms] OR ("respiration"[All Fields] AND "disorders"[All Fields]) OR "respiration disorders"[All Fields]) OR ("pleural diseases"[MeSH Terms] OR ("pleural"[All Fields] AND "diseases"[All Fields]) OR "pleural diseases"[All Fields]) OR ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields]) OR ("respiratory hypersensitivity"[MeSH Terms] OR ("respiratory"[All Fields] AND "hypersensitivity"[All Fields]) OR "respiratory hypersensitivity"[All Fields]) OR ("respiratory tract neoplasms"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "neoplasms"[All Fields]) OR "respiratory tract neoplasms"[All Fields]) OR ("respiratory care units"[MeSH Terms] OR ("respiratory"[All Fields] AND "care"[All Fields] AND "units"[All Fields]) OR "respiratory care units"[All Fields]) OR (respiratory[All Fields] AND ("signs and symptoms"[MeSH Terms] OR ("signs"[All Fields] AND "symptoms"[All Fields]) OR "signs and symptoms"[All Fields]))	
#1	(("cannabis"[MeSH Terms] OR "cannabis"[All Fields] OR "marijuana"[All Fields]) OR ("cannabis"[MeSH Terms] OR "cannabis"[All Fields] OR "marihuana"[All Fields]) OR ("dronabinol"[MeSH Terms] OR "dronabinol"[All Fields] OR "tetrahydrocannabinol"[All Fields]) OR ("cannabinoids"[MeSH Terms] OR "cannabinoids"[All Fields] OR "cannabinoid"[All Fields]))	44,108

EMBASE

Date Searched: April 12, 2017; First Update: September 30, 2017; Second Update: April 30, 2018

#	Searches	Results
#1	'marijuana':ab,ti OR 'marihuana':ab,ti OR 'tetrahydrocannabinol':ab,ti OR 'cannabinoid':ab,ti	35,031
#2	#1 AND [1973-2018]/py	34,435
#3	'respiratory function tests':ab,ti OR 'airway resistance':ab,ti OR 'blood gas analysis':ab,ti OR 'bronchial provocation tests':ab,ti OR 'capnography':ab,ti OR 'exercise test':ab,ti OR 'lung compliance':ab,ti OR 'pulmonary gas exchange':ab,ti OR 'spirometry':ab,ti OR 'pulmonary ventilation':ab,ti	65,445
#4	#3 AND [1973-2018]/py	64,138
#5	'bronchial diseases':ab,ti OR 'asthma':ab,ti OR 'bronchial hyperreactivity':ab,ti OR 'bronchitis':ab,ti	214,063
#6	#5 AND [1973-2018]/py	204,421
#7	'hemoptysis':ab,ti OR 'pulmonary hypertension':ab,ti	60,508
#8	#7 AND [1973-2018]/py	58,780

#9	'lung diseases interstitial':ab,ti OR 'alveolitis extrinsic allergic':ab,ti OR 'idiopathic interstitial pneumonias':ab,ti OR 'idiopathic pulmonary fibrosis':ab,ti OR 'pneumoconiosis':ab,ti	15,810
#10	#9 AND [1973-2018]/py	14,759
#11	'lung diseases, obstructive':ab,ti OR 'pulmonary emphysema':ab,ti	4,566
#12	#11 AND [1973-2018]/py	3,378
#13	'lung injury':ab,ti OR 'pulmonary atelectasis':ab,ti OR 'pulmonary edema':ab,ti OR 'pulmonary embolism':ab,ti OR 'pulmonary eosinophilia':ab,ti OR 'pulmonary fibrosis':ab,ti OR 'pulmonary veno occlusive disease':ab,ti OR 'adult respiratory distress syndrome':ab,ti	119,873
#14	#13 AND [1973-2018]/py	116,505
#15	'hospitalization':ab,ti OR 'survival rate':ab,ti	268,971
#16	#15 AND [1973-2018]/py	268,706
#17	'respiration disorders':ab,ti OR 'apnea':ab,ti OR 'sleep apnea syndromes':ab,ti OR 'dyspnea, paroxysmal':ab,ti OR 'cough':ab,ti OR 'dyspnea':ab,ti OR 'hoarseness':ab,ti OR 'hyperventilation':ab,ti OR 'respiratory aspiration':ab,ti OR 'respiratory distress syndrome, adult':ab,ti OR 'respiratory insufficiency':ab,ti OR 'hypoventilation':ab,ti OR 'laryngismus':ab,ti OR 'tachypnea':ab,ti	189,801
#18	#17 AND [1973-2018]/py	184,983
#19	'pleural diseases':ab,ti OR 'empyema, pleural':ab,ti OR 'hemopneumothorax':ab,ti OR 'hemothorax':ab,ti OR 'hydropneumothorax':ab,ti OR 'hydrothorax':ab,ti OR 'pleural effusion':ab,ti OR 'malignant pleural neoplasms':ab,ti OR 'pleuropneumonia':ab,ti OR 'pneumothorax':ab,ti	56,826
#20	#19 AND [1973-2018]/py	52,850
#21	(((((((respiratory AND ('tract'/exp OR tract) AND ('infections'/exp OR infections) OR 'bronchitis'/exp OR bronchitis OR common) AND ('cold'/exp OR cold) OR influenza,) AND ('human'/exp OR human) OR 'laryngitis'/exp OR laryngitis OR 'lung'/exp OR lung) AND ('abscess'/exp OR abscess) OR 'lung'/exp OR lung) AND diseases, AND fungal OR aspergillosis,) AND allergic AND bronchopulmonary OR 'lung'/exp OR lung) AND diseases, AND parasitic OR 'pharyngitis'/exp OR pharyngitis OR 'nasopharyngitis'/exp OR nasopharyngitis OR 'pleuropneumonia'/exp OR pleuropneumonia OR 'pneumonia'/exp OR pneumonia OR 'bronchopneumonia'/exp OR bronchopneumonia OR 'rhinitis'/exp OR rhinitis OR severe) AND acute AND respiratory AND ('syndrome'/exp OR syndrome) OR 'sinusitis'/exp OR sinusitis OR 'epiglottitis'/exp OR epiglottitis OR 'tracheitis'/exp OR tracheitis	75,779
#22	#21 AND [1973-2018]/py	72,361
#23	(respiratory AND ('hypersensitivity'/exp OR hypersensitivity) OR respiratory) AND ('care'/exp OR care) AND units	10,237
#24	#23 AND [1973-2018]/py	10,225
#25	((((((((((respiratory AND ('tract'/exp OR tract) AND ('neoplasm'/exp OR neoplasm) OR laryngeal) AND ('neoplasms'/exp OR neoplasms) OR 'lung'/exp OR lung) AND ('neoplasms'/exp OR neoplasms) OR bronchial) AND ('neoplasms'/exp OR neoplasms) OR multiple) AND pulmonary AND nodules OR pancoast) AND ('syndrome'/exp OR syndrome) OR pulmonary) AND sclerosing AND ('hemangioma'/exp OR hemangioma) OR 'nose'/exp OR nose) AND ('neoplasms'/exp OR neoplasms) OR paranasal) AND ('sinus'/exp OR sinus) AND ('neoplasms'/exp OR neoplasms) OR pleural) AND ('neoplasms'/exp OR neoplasms) OR pleural) AND ('effusion'/exp OR effusion) OR malignant) AND tracheal AND ('neoplasms'/exp OR neoplasms)	1,136
#26	#25 AND [1973-2018]/py	1,123
#27	((((signs AND symptoms, AND respiratory OR 'apnea'/exp OR apnea OR 'cheyne stokes') AND ('respiration'/exp OR respiration) OR 'cough'/exp OR cough OR 'dyspnea'/exp OR dyspnea OR dyspnea,) AND paroxysmal OR 'hemoptysis'/exp OR hemoptysis OR 'hoarseness'/exp OR hoarseness OR 'hypercapnia'/exp OR hypercapnia OR 'hyperoxia'/exp OR hyperoxia OR 'hyperventilation'/exp OR	36,686

	hyperventilation OR 'hypocapnia'/exp OR hypocapnia OR 'hypoventilation'/exp OR hypoventilation OR 'hypoxia'/exp OR hypoxia OR 'mouth'/exp OR mouth) AND ('breathing'/exp OR breathing) OR respiratory) AND ('sounds'/exp OR sounds) OR 'snoring'/exp OR snoring OR 'sneezing'/exp OR sneezing OR 'tachypnea'/exp OR tachypnea	
#28	#27 AND [1973-2018]/py	36,547
#29	#1 AND #3 AND #5 AND #7 AND #9 AND #11 AND #13 AND #15 AND #17 AND #19 AND #21 AND #23 AND #25 AND #27	0
#30	#29 AND [1973-2018]/py	0
#31	#30 AND 'human'/de NOT 'nonhuman'/de	0
#32	#31 AND 'English (language)'	0
#33	('marijuana':ab,ti OR 'marihuana':ab,ti OR 'tetrahydrocannabinol':ab,ti OR 'cannabinoid':ab,ti) AND ('bronchial disease':ab,ti OR 'respiratory function test':ab,ti OR 'hemoptysis':ab,ti OR 'pulmonary hypertension':ab,ti OR 'interstitial lung diseases':ab,ti OR 'obstructive lung diseases':ab,ti OR 'lung injury':ab,ti OR 'pulmonary atelectasis':ab,ti OR 'pulmonary edema':ab,ti OR 'pulmonary embolism':ab,ti OR 'pulmonary eosinophilia':ab,ti OR 'pulmonary fibrosis':ab,ti OR 'pulmonary veno occlusive disease':ab,ti OR 'adult respiratory distress syndrome':ab,ti OR 'hospitalization':ab,ti OR 'survival rate':ab,ti OR 'respiration disorders':ab,ti OR 'pleural diseases':ab,ti OR 'respiratory tract infections':ab,ti OR 'respiratory hypersensitivity':ab,ti OR 'respiratory tract neoplasm':ab,ti OR 'respiratory care units':ab,ti OR 'respiratory signs':ab,ti) AND 'symptoms':ab,ti	100
#34	#33 AND [1973-2018]/py	100
#35	limit 34 to human	2
#36	limit 35 to English language	2
#37	limit 2 to human	3,778
#38	limit 2 to English language	151

PsycINFO

Date Searched: April 12, 2017; First Update: September 30, 2017; Second Update: April 30, 2018

#	Searches	Results
1	ab(marijuana OR marihuana OR tetrahydrocannabinol OR cannabinoid)	13,876
2	1 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	13,462
3	ab(respiratory function tests OR airway resistance OR blood gas analysis OR bronchial provocation tests OR capnography OR exercise test OR lung compliance OR pulmonary gas exchange OR spirometry OR pulmonary ventilation)	8,928
4	3 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	8,325
5	ab(bronchial diseases OR asthma OR bronchial hyperreactivity OR bronchitis)	6,782
6	5 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	6,405
7	ab(hemoptysis OR pulmonary hypertension)	489
8	7 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	481
9	ab(lung diseases interstitial OR alveolitis extrinsic allergic OR idiopathic interstitial pneumonias OR idiopathic pulmonary fibrosis OR	76

	pneumoconiosis)	
10	lung diseases obstructive OR pulmonary emphysema therapy	1,253
11	ab(lung injury OR pulmonary atelectasis OR pulmonary edema OR pulmonary embolism OR pulmonary eosinophilia OR pulmonary fibrosis OR pulmonary veno occlusive disease OR adult respiratory distress syndrome	1,447
12	9 AND 10 AND 11 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	13
13	ab(hospitalization OR survival rate	50,454
14	ab(respiration disorders OR apnea OR sleep apnea syndromes OR dyspnea paroxysmal OR cough OR dyspnea OR hoarseness OR hyperventilation OR respiratory aspiration OR respiratory distress syndrome adult OR respiratory insufficiency OR hypoventilation OR laryngismus OR tachypnea	13,604
15	ab(pleural diseases OR empyema pleural OR hemopneumothorax OR hemothorax OR hydropneumothorax OR hydrothorax OR pleural effusion OR malignant pleural neoplasms OR pleuropneumonia OR pneumothorax	189
16	13 AND 14 AND 15 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	3
17	ab(respiratory tract infections OR bronchitis OR common cold OR cold OR influenza human OR laryngitis OR lung OR lung abscess OR lung diseases, fungal OR aspergillosis allergic bronchopulmonary OR lung diseases parasitic OR pharyngitis OR pharyngitis OR nasopharyngitis OR nasopharyngitis OR pleuropneumonia OR pleuropneumonia OR pneumonia OR pneumonia OR bronchopneumonia OR bronchopneumonia OR rhinitis OR rhinitis OR severe acute respiratory syndrome OR syndrome OR sinusitis OR sinusitis OR epiglottitis OR epiglottitis OR tracheitis OR tracheitis	169,970
18	ab(respiratory hypersensitivity OR respiratory care units)	1,012
19	17 AND 18 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	397
20	ab(respiratory neoplasm OR laryngeal neoplasms OR lung neoplasms OR bronchial neoplasms OR multiple pulmonary nodules OR pancoast syndrome OR pulmonary sclerosing OR hemangioma OR nose neoplasms OR paranasal sinus neoplasms OR pleural neoplasms OR pleural effusion tracheal neoplasms	3,651
21	ab(signs symptoms respiratory OR apnea OR cheyne stokes respiration OR cough OR dyspnea OR dyspnea OR dyspnea paroxysmal OR hemoptysis OR hemoptysis OR hoarseness OR hoarseness OR hypercapnia OR hypercapnia OR hyperoxia OR hyperoxia OR hyperventilation OR hyperventilation OR hypocapnia OR hypocapnia OR hypoventilation OR hypoventilation OR hypoxia OR hypoxia OR mouth OR mouth breathing OR breathing OR respiratory sounds OR sounds OR snoring OR snoring OR sneezing OR sneezing OR tachypnea OR tachypnea	84,278
22	20 AND 21 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	245
23	2 AND 4 AND Limit to human AND English	37
24	2 AND 6 AND Limit to human AND English	22
25	2 AND 8 AND Limit to human AND English	0
26	1 AND 9 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	0
27	1 AND 10 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	3
28	1 AND 11 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	5
29	1 AND 13 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	195
30	1 AND 14 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	32
31	1 AND 15 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	1
32	1 AND 17 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	821
33	1 AND 18 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	0

34	1 AND 20 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	12
35	1 AND 21 AND Limit to human AND English AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	115

MEDLINE

Date Searched: April 12, 2017; First Update: September 30, 2017; Second Update: April 30, 2018

#	Searches	Results
1	(("cannabis"[MeSH Terms] OR "cannabis"[All Fields] OR "marijuana"[All Fields]) OR ("cannabis"[MeSH Terms] OR "cannabis"[All Fields] OR "marihuana"[All Fields]) OR ("dronabinol"[MeSH Terms] OR "dronabinol"[All Fields] OR "tetrahydrocannabinol"[All Fields]) OR ("cannabinoids"[MeSH Terms] OR "cannabinoids"[All Fields] OR "cannabinoid"[All Fields])) AND (("bronchial diseases"[MeSH Terms] OR ("bronchial"[All Fields] AND "diseases"[All Fields]) OR "bronchial diseases"[All Fields] OR ("bronchial"[All Fields] AND "disease"[All Fields]) OR "bronchial disease"[All Fields]) OR ("respiratory function tests"[MeSH Terms] OR ("respiratory"[All Fields] AND "function"[All Fields] AND "tests"[All Fields]) OR "respiratory function tests"[All Fields] OR ("respiratory"[All Fields] AND "function"[All Fields] AND "test"[All Fields]) OR "respiratory function test"[All Fields]) OR ("haemoptysis"[All Fields] OR "hemoptysis"[MeSH Terms] OR "hemoptysis"[All Fields]) OR ("hypertension, pulmonary"[MeSH Terms] OR ("hypertension"[All Fields] AND "pulmonary"[All Fields]) OR "pulmonary hypertension"[All Fields] OR ("pulmonary"[All Fields] AND "hypertension"[All Fields])) OR ("lung diseases, interstitial"[MeSH Terms] OR ("lung"[All Fields] AND "diseases"[All Fields] AND "interstitial"[All Fields]) OR "interstitial lung diseases"[All Fields] OR ("interstitial"[All Fields] AND "lung"[All Fields] AND "diseases"[All Fields])) OR ("lung diseases, obstructive"[MeSH Terms] OR ("lung"[All Fields] AND "diseases"[All Fields] AND "obstructive"[All Fields]) OR "obstructive lung diseases"[All Fields] OR ("obstructive"[All Fields] AND "lung"[All Fields] AND "diseases"[All Fields])) OR ("lung injury"[MeSH Terms] OR ("lung"[All Fields] AND "injury"[All Fields]) OR "lung injury"[All Fields]) OR ("pulmonary atelectasis"[MeSH Terms] OR ("pulmonary"[All Fields] AND "atelectasis"[All Fields]) OR "pulmonary atelectasis"[All Fields]) OR ("pulmonary oedema"[All Fields] OR "pulmonary edema"[MeSH Terms] OR ("pulmonary"[All Fields] AND "edema"[All Fields]) OR "pulmonary edema"[All Fields]) OR ("pulmonary embolism"[MeSH Terms] OR ("pulmonary"[All Fields] AND "embolism"[All Fields]) OR "pulmonary embolism"[All Fields]) OR ("pulmonary eosinophilia"[MeSH Terms] OR ("pulmonary"[All Fields] AND "eosinophilia"[All Fields]) OR "pulmonary eosinophilia"[All Fields]) OR ("pulmonary fibrosis"[MeSH Terms] OR ("pulmonary"[All Fields] AND "fibrosis"[All Fields]) OR "pulmonary fibrosis"[All Fields]) OR ("pulmonary veno-occlusive disease"[MeSH Terms] OR ("pulmonary"[All Fields] AND "veno-occlusive"[All Fields] AND "disease"[All Fields]) OR "pulmonary veno-occlusive disease"[All Fields] OR ("pulmonary"[All Fields] AND "veno"[All Fields] AND "occlusive"[All Fields] AND "disease"[All Fields]) OR "pulmonary veno occlusive disease"[All Fields]) OR ("respiratory distress syndrome, adult"[MeSH Terms] OR ("respiratory"[All Fields] AND "distress"[All Fields] AND "syndrome"[All Fields] AND "adult"[All Fields]) OR "adult respiratory distress syndrome"[All Fields] OR ("adult"[All Fields] AND "respiratory"[All Fields] AND "distress"[All Fields] AND "syndrome"[All Fields])) OR ("hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields]) OR ("survival rate"[MeSH Terms] OR ("survival"[All Fields] AND "rate"[All Fields]) OR "survival rate"[All Fields]) OR ("respiration disorders"[MeSH Terms] OR ("respiration"[All Fields] AND "disorders"[All Fields]) OR "respiration disorders"[All Fields]) OR ("pleural diseases"[MeSH Terms] OR ("pleural"[All Fields] AND "diseases"[All Fields]) OR "pleural diseases"[All Fields]) OR ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR	1,212

	"respiratory tract infections"[All Fields]) OR ("respiratory hypersensitivity"[MeSH Terms] OR ("respiratory"[All Fields] AND "hypersensitivity"[All Fields]) OR "respiratory hypersensitivity"[All Fields]) OR ("respiratory tract neoplasms"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "neoplasms"[All Fields]) OR "respiratory tract neoplasms"[All Fields]) OR ("respiratory care units"[MeSH Terms] OR ("respiratory"[All Fields] AND "care"[All Fields] AND "units"[All Fields]) OR "respiratory care units"[All Fields]) OR (respiratory[All Fields] AND ("signs and symptoms"[MeSH Terms] OR ("signs"[All Fields] AND "symptoms"[All Fields]) OR "signs and symptoms"[All Fields]))) AND medline[sb]	
2	1 AND (("1973/01/01"[PDAT] : "2018/04/30"[PDAT])	1,171
3	Limit 2 to human	1042
4	Limit 3 to English	927

Cochrane Library

Date Searched: April 12, 2017; First Update: September 30, 2017; Second Update: April 30, 2018

#	Searches	
1	Marijuana OR Marihuana OR Tetrahydrocannabinol OR Cannabinoid AND bronchial disease OR respiratory function test OR hemoptysis OR pulmonary hypertension OR interstitial lung diseases OR obstructive lung diseases OR lung injury OR pulmonary atelectasis OR pulmonary edema OR pulmonary embolism OR pulmonary eosinophilia OR pulmonary fibrosis OR pulmonary veno occlusive disease OR adult respiratory distress syndrome OR hospitalization OR survival rate OR respiration disorders OR pleural diseases OR respiratory tract infections OR respiratory hypersensitivity OR respiratory tract neoplasm OR respiratory care units OR respiratory signs and symptoms	6,249
2	1 AND [Jan 1973- April 2018]	6,249
3	2 AND human	5,827
4	3 AND English	2,403
5	4 AND Cochrane reviews (Protocols only), Trials, Methods Studies, Technology assessments, Economic Evaluations and Cochrane Groups AND NOT Cochrane reviews (Reviews)	180

Supplement Part 2. STUDY SELECTION

Inclusion and Exclusion criteria and process

1. Does the intervention or exposure consist of cannabis variants including plant based marijuana, marihuana in any form (smoking, vapor, edible, or extract) or tetrahydrocannabinol (THC) extract?

   No -> STOP. Excluded (Not relevant to topic)
   Yes -> Proceed to 2.

2. Is the article about "synthetic" cannabis, THC or marijuana?

   No -> STOP. Excluded (Not relevant to topic)
   Yes -> Proceed to 3.

3. Is the article of any following study designs or publication types?

   - Case report
   - Case series study
   - Review article
   - Opinion/Editorial
   - In-vitro and animal study

   No -> Proceed to 4.
   Yes-> STOP. Excluded (Excluded study design or publication type)

4. Is the article published in English?

   No -> STOP. Excluded (Excluded study language)
   Yes-> Proceed to 5.

5. Are most the study subjects younger than age 12?

   No -> Proceed to 6
   Yes -> STOP. Excluded

6. Does cumulative exposure to marijuana greater than or equal to 30 days?

No -> STOP. Excluded
Yes -> Proceed to 7

7. Do studies report outcomes follow acute exposure in a laboratory setting?

Yes -> STOP. Excluded
No -> Proceed to 8

8. Do studies contain sample size less than ten subject?

Yes -> STOP. Excluded
No -> Proceed to 9

9. Does the study report any of the following outcomes? The list below includes outcomes of interest:

- Pulmonary function - airway resistance, bronchial provocation tests, capnography, exercise test, lung compliance, lung volume measurements, maximal respiratory pressures, whole body plethysmography, pulmonary gas exchange, pulmonary diffusing capacity, ventilation-perfusion ratio, pulmonary ventilation, spirometry, broncho spirometry, work of breathing

- Respiratory disease outcomes - hemoptysis, pulmonary hypertension, lung abscess, fungal lung diseases, interstitial lung diseases, obstructive lung diseases, parasitic lung disease, lung injury, pneumonia, pulmonary atelectasis, pulmonary edema, pulmonary embolism, pulmonary eosinophilia, pulmonary fibrosis, pulmonary veno-occlusive disease, adult respiratory distress syndrome, pleural disease, respiratory tract infection, respiratory hypersensitivity, respiratory tract neoplasm

- Respiratory tract neoplasms - laryngeal neoplasm, lung neoplasm, bronchial neoplasm, multiple pulmonary nodules, Pancoast syndrome, pulmonary sclerosing hemangioma, nose neoplasm, paranasal sinus neoplasm, pleural neoplasm, pleural effusion, malignant, tracheal neoplasm

- Respiratory signs and symptoms include - apnea, cough, dyspnea, hemoptysis, hoarseness, hypercapnia, hyperoxia, hyperventilation, hypocapnia, hypoventilation, mouth breathing, respiratory sounds, snoring, sneezing, tachypnea

No -> STOP. Excluded
Yes -> Proceed to 10.

10. Does the study design a randomized clinical trial, clinical trial, interventional study, case-control, prospective cohort study, retrospective cohort study, cross-sectional, cross-sectional cohort or case crossover study?

No -> STOP. Excluded
Yes -> STOP. Included

Supplement Part 3: QUALITY ASSESSMENT CRITERIA AND RISK OF BIAS ASSESSMENT

Observational studies: criteria based on the Newcastle-Ottawa scale

Representativeness of the exposed cohort

1 = truly representative of the average patient in the community

1 = somewhat representative of the average patient in the community

0 = selected group of users (e.g., nurses, volunteers)

0 = no description of the derivation of the cohort

Selection of the non-exposed cohort Enter 0 or 1:

1 = drawn from the same community as the exposed cohort

0 = drawn from a different source

0 = no description of the derivation of the non-exposed cohort

Ascertainment of exposure Enter 0 or 1:

1 = biological test (e.g., blood/urine)

1 = structured interview

1 = written self-report that characterizes dose (current or cumulative)

0 = written self-report without quantification of exposure

0 = no description

Precision of Exposure Dose Ascertainment

1 = amount and time

0 = no information about amount and time

Ascertainment of exposure done prospectively or retrospectively

1 = Prospectively

0 = Retrospectively

Demonstration that outcome of interest was not present at start of study, or baseline assessment

1= yes

0 = no

Adjustment for confounding (rendering comparability of cohorts on the basis of the design or analysis)

1 = study accounts/controls for some confounders

2 = complete adjustment for confounders and all relevant baseline characteristics.

0 = no adjustment for potential confounders

Assessment of outcome Enter 0 or 1:

1 = objective measure

1 = validated self-report measures

0 = no information or non-validated measures

Was follow-up long enough for outcomes to occur?

1 = yes (need to define adequate follow-up period for outcome of interest)
0 = no
Adequacy of follow-up of cohorts Enter 0 or 1:
1 = complete follow-up; all subjects accounted for.
1 = subjects lost to follow-up unlikely to introduce bias; small number (less than 20 %) lost, or description was provided of those lost.
0 = follow-up rate < 80% and no description of those lost.
0 = no statement

Case Control Studies: Observational studies: criteria based on the Newcastle-Ottawa scale

Selection

1) Is the case definition adequate?
a) yes, with independent validation
b) yes, e.g. record linkage or based on self-reports
c) no description

2) Representativeness of the cases
a) consecutive or obviously representative series of cases
b) potential for selection biases or not stated

3) Selection of Controls
a) community controls
b) hospital controls
c) no description

4) Definition of Controls
a) no history of disease (endpoint)
b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
a) study controls for tobacco
b) study controls for any additional factors (socioeconomic and socio-demographic factors, relevant baseline factors for outcome of interest)

Exposure

1) Ascertainment of exposure
a) secure record (e.g. surgical records)
b) structured interview where blind to case/control status
c) interview not blinded to case/control status
d) written self-report or medical record only

e) no description

2) Same method of ascertainment for cases and controls

a) yes

b) no

3) Non-Response rate

a) same rate for both groups

b) non-respondents described

c) rate different and no designation

Clinical Trials: Criteria based on the Cochrane risk of bias tool

Domain	Support for judgment
Random sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.
Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.
Blinding of participants and personnel. Assessments should be made for each main outcome (or class of outcomes).	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.
Blinding of outcome assessment. Assessments should be made for each main outcome (or class of outcomes).	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.
Incomplete outcome data. Assessments should be made for each main outcome (or class of outcomes).	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.
Selective reporting	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.
Other sources of bias	State any important concerns about bias not addressed in the other domains in the tool.

Table 1: Risk of Bias Assessment in Cohort and Cross-sectional Studies

Criteria	Macleod et al, 2015 (25) (cross-sectional)	Tan et al, 2009 (22) (cross-sectional)	Tashkin et al, 1980 (33) (cross-sectional)	Hancox et al, 2015 (16) (prospective)
Representativeness of the exposed cohort	1 – Participants were recruited from consecutive patients attending the Muirhouse Medical Group clinic.	1 – Adults 40 and older living in the health service delivery area of Vancouver Canada contacted by random digit dialing.	1 – Regular marijuana smokers were recruited through newspaper advertisements at the University of California at Los Angeles	1 – Participants from Dunedin Multidisciplinary Health and Development Study
Selection of the nonexposed Cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	0 – Matched subjects selected but unclear how the control subjects were identified	1 – Unexposed selected from same cohort
Ascertainment of Exposure	1 – Structured questionnaire used to ascertain exposure	1 – Conducted sampling in 2 stages, Structured questionnaire (7-item) used to ascertain exposure	0 – Inadequate description on how exposure was ascertained. In addition, no exposure assessment in controls	1 – Structured questionnaire used to ascertain exposure multiple times
Precision of Exposure Dose Ascertainment	1 – Responders reported periods of regular cannabis use, the main type of cannabis used during these periods, the mode of use, the terms of number of joints smoked, and the frequency of this use. Adults who used one cannabis joint per day for at least 1 year with self-reported were recruited as cases.	1 – Subjects asked, ever smoked pot/marijuana? age of first started, did they use in the past year, age stopped, if not stopped average over the entire time that joints/week, how many joints per week did they smoke, in an average week how many days they smoke, how many years have they smoked, also performed spirometric testing before and after administration of a bronchodilator.	0 – Inadequate description of how exposure dose was ascertained.	1 – Exposure was measured five times (year 18, 21, 26, 32, 38) Subjects asked, "how many times, they had used marijuana in the previous year. They divided the cohort to frequent cannabis users (≥ 52 times at least weekly on average over the previous year) and infrequent or occasional users (≤ 52 times). Changes between two consecutive assessments were classified to "nonusers", "quitters", "starters" and "continuing users".
Ascertainment of exposure done prospectively or retrospectively	0 – Retrospectively assessed	0 – Unclear	1 – Prospectively assessed	1-Prospectively assessed multiple times (baseline and years 18, 21, 26, 32, 38)
Demonstration that outcome of interest was not present at start of study, or baseline assessment	1 – Participants were excluded with known bronchiectasis, asthma, cystic fibrosis, and tuberculosis, and persons with significant occupational exposure known to be hazardous to the lungs.	2 – N/A	1 –Individuals with a history of asthma or other chronic lung disease, recent upper respiratory tract infection or employment in occupations were excluded.	1 – Adjusted for age, tobacco smoking, asthma and sex.
Adjustment for Confounding	1 – Adjusted for age, sex, deprivation, and tobacco pack-years.	2 – Adjusted for age, sex, ethnic background, body mass index, education, asthma and other	0 – Participants were matches for age, sex, height, quantity and duration of tobacco smoking. But no	1 – Adjusted for current and cumulative (pack-years) tobacco smoking, sex, body mass index, and

		comorbidities (i.e., heart disease, hypertension, stroke, diabetes and tuberculosis) and tobacco.	adjustment for tobacco.	asthma diagnosis.
Assessment of outcome	1- Self-reported respiratory symptoms (Cough, Phlegm, Wheeze, Dyspnea) using the NHANES III† questionnaire and spirometric testing in accordance with ATS guidelines, measurement of prevalence of COPD	1 – Spirometric test measurement of COPD* or self-report of respiratory symptoms suggestive of COPD* (Cough, Phlegm, Wheeze, Dyspnea)	1 – Self-report questionnaire of respiratory symptoms from the National Heart and Lung Institute and spirometric measurement	1 – Self-reported respiratory symptoms (Cough, Phlegm, Wheeze, Dyspnea) and Objective assessment, spirometry has been measured multiple times.
Was follow-up long enough for outcomes to occur?	N/A cross-sectional	N/A cross-sectional	N/A cross-sectional	1 – Followed from birth to 38 years. (Cannabis smoking history was obtained at ages 18, 21, 26, 32 and 38).
Adequacy of follow-up of cohorts	N/A cross-sectional	N/A cross-sectional	N/A cross-sectional	1-Adequate f/u
Comments on study quality	**High ROB –** Cross-sectional study with adequate adjustment for key confounders, while assessment of exposure was detailed, the analysis did not incorporate this data, cannabis and tobacco users were combined in the analysis. The data reporting could have been more transparent. The study demonstrated that compared to only smoking tobacco combined marijuana and tobacco use caused more symptoms.	**Low ROB** – Marijuana use was quantified. There was adequate adjustment for key confounders. Results were classified to no smoking (reference), marijuana smoking only, cigarette smoking only, and an interaction term of smoking marijuana and tobacco concurrently. The only limitations result from the low overall cumulative marijuana exposure in the sample; therefore, not generalizable to daily users.	**High ROB** – Cross-sectional study with matched subjects. Exposure assessment was simplistic with no exposure assessment in controls. No sample size justification to determine if sample size adequate for this investigation.	**Low ROB** – Large scale well designed study that collected exposure data multiple times but marijuana use was not quantified. Results did not report on marijuana only smokers.

*COPD - Chronic Obstructive Pulmonary Disease

†NHANES III - third National Health and Nutrition Examination Survey

Table 1: Risk of Bias Assessment in Cohort and Cross-sectional Studies *(continued)*

Criteria	Fligiel et al, 1997 (26) (cross-sectional)	Hancox et al, 2010 (29) (prospective)	Taylor et al, 2000 (23) (prospective)	Tashkin et al, 1997 (31) (prospective)
Representative-ness of the exposed cohort	1 – Participants from an ongoing longitudinal cohort study (recruited from the Los Angeles metropolitan area using newspaper and radio announcements and from the staff of UCLA Medical Center)	1 – Participants from Dunedin Multidisciplinary Health and Development Study (population based cohort)	1 – Participants from Dunedin Multidisciplinary Health and Development Study (population based cohort)	1- Participants were recruited from the Los Angeles metropolitan area using newspaper and radio announcements
Selection of the non-exposed Cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed from the same cohort
Ascertainment of Exposure	1 – Structured questionnaire used to ascertain exposure	1 – Structured questionnaire used to ascertain exposure multiple times	1 – Structured questionnaire used to ascertain exposure multiple times	1 – Structured questionnaire used to ascertain exposure multiple times
Precision of Exposure Dose Ascertainment	1 – Adults who had current smoking history of an average of ≥10 joints per week for ≥5 years were recruited as cases.	1 – Exposure was measured four times (year 18, 21, 26,32) Subjects asked, "how many times, they had used marijuana in the previous year.	1 – Exposure was measured two times (year 18, 21) and was evaluated through the lens of cannabis dependence. Cannabis dependence was assessed by a series of questions. Those who were cannabis dependent used cannabis 230 times in the past year. In contrast those who were not dependent used it 40 times in the past year.	1 – Exposure was measured two times, Subjects asked about amount of use.
Ascertainment of exposure done prospectively or retrospectively	1-Prospectively assessed	1-Prospectively assessed multiple times (baseline and years 18, 21, 26, 32)	1 – Prospectively assessed multiple times (baseline and years 18, 21)	1 – prospectively assessed multiple times (baseline and ≥ 1 yr.)
Demonstration that outcome of interest was not present at start of study, or baseline assessment	1 – Participants were excluded if they were IV drug abuser ≥6 times per lifetime, smoking of other illicit substances ≥20 times per lifetime, a recent (within 3 weeks) upper or lower respiratory tract infection, or a history of chronic lung disease (e.g., asthma, interstitial lung disease), previous or active tuberculosis, pneumonia within the past year, or significant occupational exposure to dust or fumes.	1 – Adjusted for baseline characteristics	1– Adjusted for baseline characteristics	1 – Participants were excluded who reported current or previous intravenous drug use or smoking of other illicit substances (e.g., crack, cocaine, phencyclidine, methamphetamine, heroin, and opium) more than 12 times in their lives or within the previous 6 mo. and who had significant occupational exposures to substances potentially hazardous to respiratory health, or with

				a history of chronic respiratory illness.
Adjustment for Confounding	1 – Participants were matched for age and the sample was divided into non-smokers, marijuana only smokers, tobacco only smokers and tobacco-marijuana smokers.	1 – Adjusted for age and height at age 15 and 32 and adjusted for use of the other substance.	1 – Adjusted for tobacco use and respiratory symptoms.	1 – Results were reported on men, female and MS*, MTS, TS and NS, separately.
Assessment of outcome	1- Self-reported respiratory symptoms (Cough, Phlegm, Wheeze) and spirometric measurement and mucosal biopsy.	1 – Objective assessment, spirometry has been measured at each assessment.	1 – Self-reported respiratory symptoms (Cough, Phlegm, Wheeze, Dyspnea) and Objective assessment, spirometry has been measured multiple times.	1 – Self-reported respiratory symptoms and spirometric measurement multiple times and mucosal biopsy.
Was follow-up long enough for outcomes to occur?	N/A- cross-sectional	1 – Followed from birth to 38 years. (Cannabis smoking history was obtained at ages 18, 21, 26 and 32).	1- Followed from birth to 21 years. (Cannabis smoking history was obtained at ages 18, 21).	1 – Follow up period of 8 years.
Adequacy of follow-up of cohorts	N/A cross-sectional	1-Adequate f/u	1-Adequate f/u	1-Adequate f/u
Comments on study quality	**Low ROB –** Marijuana use was quantified. There was adequate adjustment for key confounders. Internally valid cross-sectional study.	**Low ROB** – Well-designed study that collected exposure data multiple times and quantified it. Baseline characteristics and key confounders adjusted for in their analysis. Results were classified to smokers of tobacco only, cannabis non-tobacco users, cannabis tobacco users.	**Low ROB** – Large scale well designed study that collected exposure data multiple times. Baseline characteristics and key confounders adjusted for in their analysis. Results were classified to smokers of tobacco only, cannabis dependence non-tobacco users, cannabis dependence tobacco users, and non-smokers of either substance. The main limitation of this study is that the cannabis dependent group was small.	**Low ROB** – Well-designed study that collected exposure data multiple times and quantified it. Baseline characteristics and key confounders adjusted for in their analysis. Results were classified to smokers of tobacco only, smokers of cannabis only, smokers of cannabis and tobacco, and non-smokers of either substance. However, the sample was relatively young with a mean age of 33 at cohort inception.

*MS-Marijuana Smoker, MTS-Marijuana Tobacco Smoker, TS-Tobacco Smoker, NS-Non-smoker

Table 1: Risk of Bias Assessment in Cohort and Cross-sectional Studies *(continued)*

Criteria	Tashkin et al, 1993 (36) (cross-sectional)	Tashkin et al, 2012 (17) (prospective)	Brook et al, 2008 (35) (prospective)	Taylor et al, 2002 (30) (prospective)
Representative-ness of the exposed cohort	1 – Participants from an ongoing longitudinal cohort study (recruited from the Los Angeles metropolitan area using newspaper and radio and from the staff of UCLA Medical Center)	1 – Participants recruited from the Los Angeles metropolitan area using newspaper and radio announcements	1 – Random sample of children living in two upstate New York counties	1 – Participants from Dunedin Multidisciplinary Health and Development Study
Selection of the nonexposed Cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort
Ascertainment of Exposure	1 – Structured questionnaire used to ascertain exposure	1 – Structured questionnaire used to ascertain exposure multiple times (2 to 9 visits)	1 – Structured questionnaire used to ascertain exposure multiple times	1 – Structured questionnaire used to ascertain exposure multiple times
Precision of Exposure Dose Ascertainment	1 – Adults who smoked MJ at least 10 joints per week or the equivalent of marijuana for at least 5 yr., with self-reported history were recruited as cases	1 – Exposure was measured 2 to 9 times, Subjects asked about amount of use.	1 – Exposure was measured four times (year 14, 16, 22,27). Subjects asked, how frequently the participants used marijuana, how often they used marijuana ever, over the past two, five, and five years.	1 – Exposure was measured three times (year 18, 21, 26). The number of occasions on which they used cannabis in the preceding 12 months was assessed.
Ascertainment of exposure done prospectively or retrospectively	1 – Prospectively assessed	1 – Prospectively assessed	1 – prospectively assessed multiple times	1 – Prospectively assessed multiple times (baseline and years 18, 21, 26)
Demonstration that outcome of interest was not present at start of study, or baseline assessment	1 – Participants were excluded if they had intravenous illicit drugs use (> two times/lifetime); smoking of substances other than cannabis or tobacco (> 12 times/lifetime or within 6 months of the study); significant occupational exposure to hazardous dusts or fumes; a history of chronic respiratory disease, including asthma or chronic bronchitis since childhood; and previous chest surgery.	1– Participants were excluded if they had current or previous intravenous drug abuse; smoking of other illicit substances (e.g., crack, cocaine, PCP, methamphetamine, heroin or opium) >12 times per lifetime or within the previous 6 months; history of chronic respiratory illness; or significant occupational exposures to substances.	1 – Measures adjusted for included the following: age, gender, major depressive disorder in adolescence, parental education and income, mother's marijuana use, and maternal report of child's aggression at baseline	1– Adjusted for baseline characteristics
Adjustment for Confounding	1 – Results were reported on men, female and MS*, CS, MCS, MTS, TS, TCS, MTCS and NS separately.	1 – Adjusted for age, gender and tobacco.	0 – No adjustment for tobacco use.	1 – Adjusted for potential confounding factors (age, tobacco smoking and weight)
Assessment of outcome	1 –Objective assessment, spirometry/methacholine challenge	1 – Self-reported respiratory symptoms (Cough, Phlegm,	0 – Outcomes vague "respiratory problems"	1 –Objective assessment, spirometry has been measured two times.

		Wheeze) and Objective assessment, spirometry has been measured multiple times.		
Was follow-up long enough for outcomes to occur?	1 – Follow up period of 5 years.	1 – Follow up period over a mean of 9.8 years.	1 – Follow up period of 8 years	1- Followed from birth to 26 years. (Cannabis smoking history was obtained at ages 18, 21, 26).
Adequacy of follow-up of cohorts	1-Adequate f/u	0-loss of a third of the cohort to follow-up	1-Adequate f/u	1-Adequate f/u
Comments on study quality	**Low ROB** – Marijuana use was quantified. There was adequate adjustment for key confounders.	**Moderate ROB** – Exposure data was collected multiple times. Results were classified to smokers of tobacco only, smokers of MJ only, smokers of MJ and tobacco, and non-smokers of either substance. However, the original study had 446 participants, this study has 299. There is significant loss to follow up.	**High ROB** – Large cohort with long follow-up period. Inadequate adjustment for key confounders.	**Moderate ROB** – Large scale well designed study that collected exposure data multiple times. Baseline characteristics and key confounders adjusted for in their analysis. The main limitation of this study is that the cannabis dependent group was small. Results were not classified to smokers of tobacco only, smokers of MJ only, smokers of MJ and tobacco, and non-smokers of either substance.

* MS-Marijuana Smoker, CS-Cocaine Smoker, MCS-Marijuana Cocaine Smoker, MTS-Marijuana Tobacco Smoker, TS-Tobacco Smoker, TCS-Tobacco Cocaine Smoker, MTCS-Marijuana Tobacco Cocaine Smoker, NS-Non-smoker

Table 1: Risk of Bias Assessment in Cohort and Cross-sectional Studies *(continued)*

Criteria	Pletcher et al, 2012 (28) (prospective)	Polen et al, 1993 (34) (prospective)	Moore et al, 2005 (19) (cross-sectional)	Bloom et al, 1987 (20) (cross-sectional)	Morris et al, 2018 (27) (cross-sectional)
Representative-ness of the exposed cohort	1 – Participants from the CARDIA* study	1 – Subjects were selected from the Kaiser Permanente Medical Care Program at two centers	1 – Subjects selected from NHANES III†	1 – Subjects selected from sample of households Tucson, Arizona	1 – Subjects were selected from SPIROMICS an ongoing multicenter prospective observational study. Patients were recruited at university medical centers
Selection of the nonexposed Cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort
Ascertainment of Exposure	1 – Structured questionnaire used to ascertain exposure multiple times	1 – Structured questionnaire used to ascertain exposure multiple times but not well described.	1 – Structured questionnaire used to ascertain exposure	0– Structured questionnaire used to ascertain exposure but marijuana use status not clearly ascertained.	1 – Structured questionnaire used to ascertain exposure

Precision of Exposure Dose Ascertainment	1 – Exposure was measured six times (smoking behavior, secondhand smoke exposure, height, and waist circumference) (Pulmonary function testing was performed at years 0, 2, 5, 10, and 20). Current intensity of marijuana use (episodes in the last 30 days) and total lifetime exposure to marijuana joints in joint-years assessed at each examination.	1 – Adults who smoked MJ (marijuana smokers who never smoked tobacco) more than six times in their lifetimes and who were current users were recruited as cases.	1 – Subjects asked a range of general health regarding marijuana and tobacco use, a physician's exam, and a spirometry component. Subjects asked ever using marijuana, ''About how many times in your lifetime have you used marijuana,'' if yes; ''1 or 2 times,'' ''3 to 10 times,'' ''11 to 99 times,'' and ''100 or more times.'' lifetime users were also asked, ''During the past month, on how many days did you use marijuana?''. Current marijuana use was defined as self-reported 100+ lifetime uses and at least 1 day of use in the past month.	0 – Exposure was quantified by questions about the duration and intensity of non-tobacco cigarette smoking but never clearly clarified if this referred to marijuana use.	1 – Marijuana use was categorized into current (use in the past 30 days), and former (use over 30 days ago) users and compared to never users. Those with a history of marijuana use estimated the number of bowls or joint equivalents smoked per week and how many years the participant had smoked marijuana. Joint years were categorized into <10, 10-20, and >20 joint-year history and compared to those who reported zero joint years.
Ascertainment of exposure done prospectively or retrospectively	1– Prospectively assessed	1 – Prospectively assessed	1 – Prospectively assessed	0 – Retrospectively assessed	0 – Retrospectively assessed
Demonstration that outcome of interest was not present at start of study, or baseline assessment	1 – Matched for equal numbers of "black, not Hispanic" and "white, not Hispanic" men and women, Height and waist circumference, socioeconomic status, Secondhand smoke exposure in hours per week, Asthma was self-reported at each examination; average annual city-specific levels of airborne particulate matter less than 10 microns and less than 2.5 microns in size around the 4 CARDIA study centers from the Environmental	1 – Matched for sex, age (birth year), race (Asian, African American, white), and index multiphasic health checkup date (within a month).	N/A cross-sectional	1 – Predicted values were based on the subject's age, sex, and height using prediction equations derived from asymptomatic, non-diseased, non-smoking subjects in this population.	1– Marijuana users in this group were known to have normal lung function at enrollment. Because of this recruitment bias, never tobacco-smoking controls were excluded from the analysis. The study therefore only examines the health effects of marijuana use among current or former tobacco users.

	Protection Agency.				
Adjustment for Confounding	1 – Adjusted for year, center and center-year (their interaction), race-sex category, education, and asthma; cubic splines for age, height, waist circumference, secondhand smoke exposure, and exposure to airborne particulate matter less than 10 microns and less than 2.5 microns in size; and interactions between the age spline variables and race-sex, asthma, waist spline variables, and height spline variables.	1 –Demographic and social characteristics, medical history, health habits, the use of tobacco and alcohol were queried. Adjusted for sex, age, race, educational level, marital status, and alcohol consumption.	1 – The analysis of controlling for gender, age, current asthma, and tobacco cigarettes used per day. They excluded patients with asthma. They did not exclude patients with COPD‡/Emphysema or other respiratory conditions.	1 – Results were categorized by tobacco smoking status and were reported on never smoked either tobacco or non-tobacco cigarettes, current tobacco smoking, current smokers of non-tobacco cigarettes, current smokers of both, separately. No adjustment for other variables.	1 – Adjusted for gender, race, height, age, current tobacco smoking status, and pack years.
Assessment of outcome	1 – Objective assessment, spirometry has been measured multiple times.	1 – Self-reported non-specific respiratory symptoms	1 – Self-reported respiratory symptoms (cough, phlegm, wheeze, dyspnea) and objective assessment by spirometry	1 – Self-reported respiratory symptoms (cough, phlegm, wheeze, dyspnea) and objective assessment by spirometry	1 – Self-reported respiratory symptoms (cough, wheeze) and objective assessment by spirometry
Was follow-up long enough for outcomes to occur?	1 – Follow up period of 20 years.	1 – Follow up period of 8 years.	N/A cross-sectional	N/A cross-sectional	N/A cross-sectional
Adequacy of follow-up of cohorts	1-Adequate f/u	1-Adequate f/u	N/A cross-sectional	N/A cross-sectional	N/A cross-sectional
Comments on study quality	**Low ROB** – Large scale well designed study that collected exposure data	**Low ROB** – Baseline characteristics and key confounders adjusted for in	**Moderate ROB** – Cross-sectional study with adequate assessment of	**Moderate ROB** – Unclear what is meant by non-tobacco user, authors noted	**Low ROB** – Cross-sectional study with adequate assessment of marijuana

	multiple times. Baseline characteristics and key confounders adjusted for in their analysis. Results were classified to current and lifetime marijuana and tobacco smokers. However, overall exposure among participants was minimal. Generalizability limited to infrequent users.	their analysis. Some details of methods are unclear but it seems that baseline detail on marijuana use was collected. Results were on marijuana only smokers. Study generalizable to insured populations with limited exposure.	marijuana exposure and adjustment for key confounders. Many of the marijuana smokers were also tobacco smokers. The data from marijuana only users are not reported separately.	most of the population was marijuana users but did ask participants what form of "non-tobacco" cigarettes was used.	exposure and adjustment for confounders. While the study was well done it is only examines the health effects of marijuana among current or former tobacco users.

* CARDIA - Coronary Artery Risk Development in Young Adults Study

† NHANES III - third National Health and Nutrition Examination Survey

‡COPD-Chronic Obstructive Pulmonary Disease

Table 1: Risk of Bias Assessment in Cohort and Cross-sectional Studies *(continued)*

Criteria	Aldington et al, 2007 (18) (cross-sectional)	Tashkin et al, 1987 (21) (cross-sectional)	Tashkin et al, 1988 (37) (cross-sectional)	Kempker et al, 2015 (32) (cross-sectional)	Sherrill et al, 1991 (24) (prospective)
Representative-ness of the exposed cohort	1 – Participants recruited from the Wellington Respiratory Survey and the Greater Wellington area through newspaper and radio	1 – Participants recruited from the Los Angeles metropolitan area using newspaper and radio	1 – Participants recruited from the Los Angeles metropolitan area using newspaper and radios	1 – Subjects selected from NHANES *	1 – Subjects selected from four consecutive surveys of Tucson longitudinal study
Selection of the nonexposed Cohort	0 – Unexposed were from electoral registry	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort	1 – Unexposed selected from same cohort
Ascertainment of Exposure	1 – Structured questionnaire used to ascertain exposure	1 – Structured questionnaire used to ascertain exposure	1 – Structured questionnaire used to ascertain exposure	1 – Structured questionnaire used to ascertain exposure	0– Structured questionnaire used to ascertain exposure but marijuana use status not clearly ascertained
Precision of Exposure Dose Ascertainment	1 – Adults who had lifetime exposure of at least 5 joint-years of cannabis with self-reported history recruited as cases. Subjects were asked about smoking history, passive smoking exposure, respiratory symptoms, family history, occupation and known respiratory illnesses.	1 – Adults who smoked at least 10 joints per week or the equivalent of marijuana for at least 5 yr. were recruited as cases. Subjects asked about respiratory symptoms, general health, residence and occupational history, socioeconomic status, and current and history of tobacco and	1 – Adults who smoked on the average, at least five marijuana cigarettes (joints) or the equivalent per week for at least five years with self-reported history recruited as cases. Subjects asked about respiratory and general health, physician-diagnosed illness, lifetime	1 – Exposure was quantified by the frequency of use in the past 30 days and the cumulative, lifetime exposure.	0 – Exposure was quantified by questions about the duration and intensity of non-tobacco cigarette smoking but never clearly clarified if this referred to marijuana use.

		alcohol use and use of marijuana and other illicit drugs.	and current drug use. occupational exposures, education and residence.		
Ascertainment of exposure done prospectively or retrospectively	0 – Retrospectively assessed	0 – Retrospectively assessed	0 – Retrospectively assessed	1 – Prospectively assessed	0 – Retrospectively assessed
Demonstration that outcome of interest was not present at start of study, or baseline assessment	1 – Subjects were excluded if they had chronic lung disease (such as asthma, chronic bronchitis or cystic fibrosis) before the age of 16, were pregnant, were heterozygous or homozygous for a1-antitrypsin deficiency, used a substance of abuse other than cannabis, tobacco and alcohol >12 times in their lifetime.	1 – Subjects were excluded if they were current or previous users of other illicit substances; occupational exposure (e.g., sandblasting, asbestos exposure); or a history of chronic respiratory disease (e.g., asthma, chronic bronchitis or bronchiectasis since childhood, cystic fibrosis, tuberculosis, or kyphoscoliosis) or chest surgery.	1– Subjects were excluded if they used intravenous use of illicit drugs (>2times/lifetime); smoking of substances other than cannabis or tobacco (>12 times/lifetime or within six months of study); occupational exposure to hazardous dusts or fumes; a history of chronic respiratory disease, including asthma or chronic bronchitis since childhood; and previous chest surgery.	1 – Matched for tobacco exposure, age, race, sex, economic status, and history of asthma, emphysema, and chronic bronchitis.	1– Adjusted for baseline characteristics
Adjustment for Confounding	1 – Adjusted for age, sex, height, family history, passive smoking, ethnicity, atopy and years of working in an at-risk occupation.	2 –Adjusted mean values of lung function from analysis of covariance with age and height as covariates are presented for men and women separately. Also, adjustment for anemia and carboxyhemoglobinemia. Results were reported on men, female and MS†, MTS separately.	1 – Results were reported on MS†, MTS, TS, and NS separately.	1 – Adjusted for sex, age, height, race and tobacco.	1 – Adjusted for age, gender and tobacco smoking.
Assessment of outcome	1- Self-reported respiratory symptoms (Cough, Wheeze, Dyspnea), spirometric measurement of chronic bronchitis, asthma and using CT scan report of two radiologists.	1 – Self-reported respiratory symptoms (Cough, Sputum, Wheeze), spirometric measurement of Pulmonary function	1 – Spirometric measurement of Pulmonary function	1 – Objective assessment by spirometry	1 – Self-reported respiratory symptoms (Cough, Sputum, Wheeze) and objective assessment by spirometry

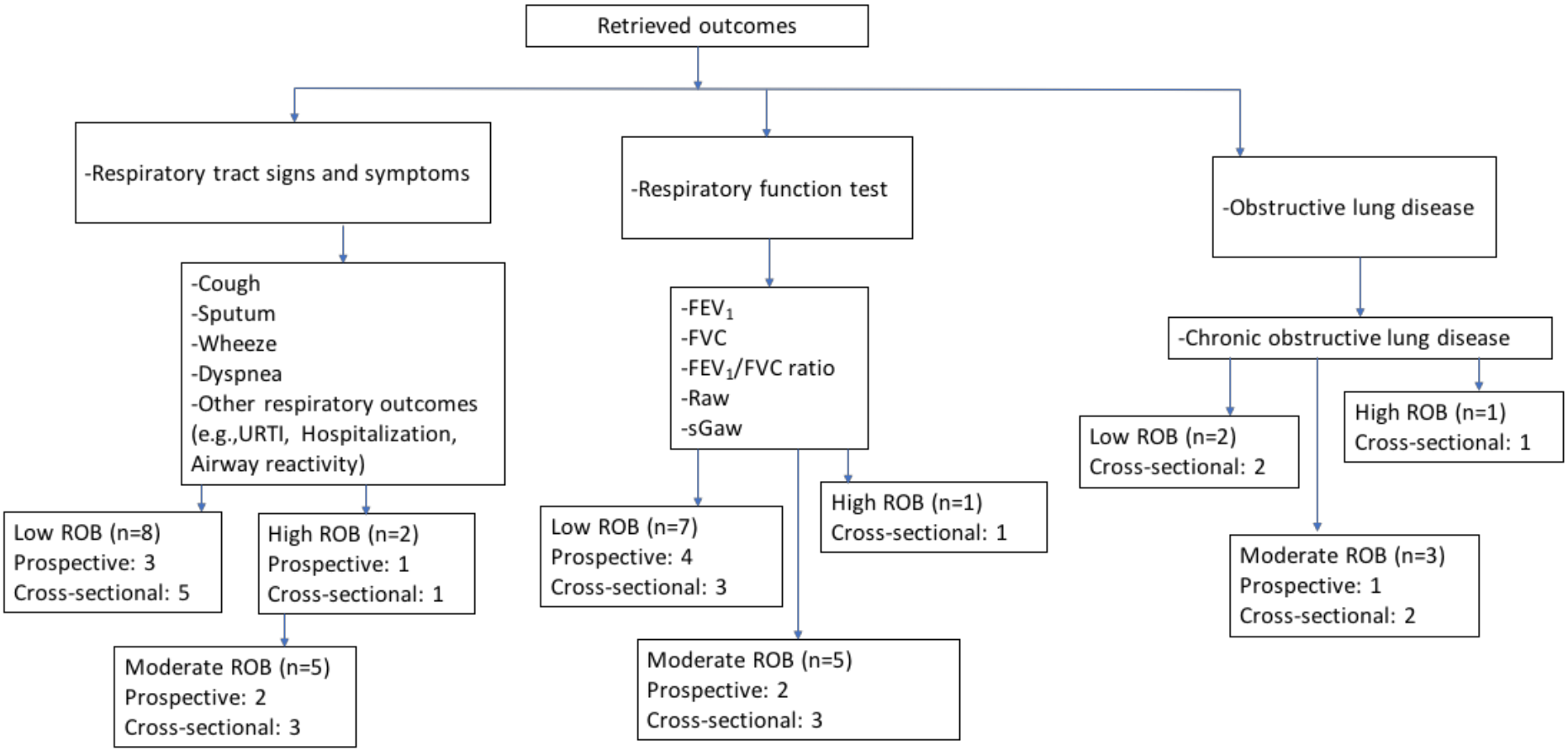
Was follow-up long enough for outcomes to occur?	N/A cross-sectional	N/A cross-sectional	N/A cross-sectional	N/A cross-sectional	1 – Follow up period of 6 years.
Adequacy of follow-up of cohorts	N/A cross-sectional	N/A cross-sectional	N/A cross-sectional	N/A cross-sectional	1-Adequate f/u
Comments on study quality	**Moderate ROB –** Sample recruitment was not necessarily representative and smokers and non-smokers were not from the same population. Marijuana use was quantified. There was adequate adjustment for key confounders. Results were classified to smokers of tobacco only, smokers of MJ only, smokers of MJ and tobacco, and non-smokers of either substance.	**Low ROB –** Marijuana use was quantified. There was adequate adjustment for key confounders. Results were classified to smokers of tobacco only, smokers of MJ only, smokers of MJ and tobacco, and non-smokers of either substance.	**Low ROB** – Marijuana use was quantified Results were classified to smokers of tobacco only, smokers of MJ only, smokers of MJ and tobacco, and non-smokers of either substance.	**Low ROB** – Cross-sectional study with adequate adjustment for key confounders. Large sample of users. Lifetime exposure assessment. Larger sample of marijuana users than most studies.	**Moderate ROB** – Unclear how the participants interpreted "non -tobacco users" authors noted most of the population was marijuana users but did ask participants what constituted a "non-tobacco" cigarette.

* NHANES - National Health and Nutrition Examination Survey

†MS-Marijuana Smoker, MTS-Marijuana Tobacco Smoker, TS-Tobacco Smoker, NS-Non-smoker

Supplement Part 4. Meta-analysis

Figure 1: Flow diagram of outcomes and Risk of Bias identified in the review



- URTI-Upper Respiratory Tract Infection; FEV_1-Forced Expiratory Volume in one second; FVC-Forced Vital Capacity; Raw-Airway Resistance; sGaw-Specific Airway Conductance; ROB-Risk of Bias
- Nine papers had multiple outcomes.

Table 2: Studies that examined exposure to marijuana and development of respiratory tract symptoms

Study, Year Design	Study Population	Sample Size, n	Age (years)	Average of MJ exposure	% of MJ only, users	Confounders and baseline variables	Adjustment	Outcome Examined	Follow -up	Result in Study	Risk of Bias	Funding source
Morris et al, 2018 (27), Cross-sectional	Participants from SPIROMICS	2,304	40-80	30.15±68.5 joint-years	Not specified	1.Age 2.Gender 3.Race 4.Height 5.Tobacco	Adequate	1.Cough 2.Wheeze	NA	• Among current or former MJ smokers, smoking MJ was not associated with cough and wheezing compared to never MJ smokers after adjusting for covariates. • Among MJ smokers, smoking MJ (10-20, or > 20 joint-year) was associated with wheezing (OR=2.27, 95% CI 1.09-5.39; RR= 1.66, 95% CI 1.04-2.76) compared to never MJ smokers after adjusting for covariates.	Low	NHLBI
Hancox et al, 2015 (16), Prospective cohort	Volunteers from the Dunedin Birth cohort 1972-73	1,037	From birth till 38	Greater than 1 times per week for a year	Not specified	1.Gender 2.BMI 3.Tobacco 4.Asthma	Adequate	1.Cough 2.Sputum 3.Wheeze 4.Dyspnea	Followed from birth to 38 years	• Smoking cannabis was associated with morning cough (OR=1.97, 95% CI 1.57–2.48, p<0.001), sputum production (OR=2.31, 95% CI 1.83–2.91, p<0.001), and wheezing (OR=1.55, 95% CI 1.23–1.94, p<0.001) compared to non-smokers after adjusting for tobacco and other baseline variables. • Smoking cannabis was not associated with dyspnea (OR=1.23, 95% CI 0.97–1.56, p=0.086) compared to non-smokers after adjusting for tobacco and other baseline variables.	Low	UK MRC, US NIA, US NIMH, US NIDA, the Jacobs Foundation
Macleod et al, 2015 (25), Cross-sectional	Patients with tobacco or cannabis use	500	Mean: 37 MTS, 45 TS	Male: 104.5, Female: 53.2 joint-years	None	1.Age 2.Gender 3.Tobacco	Inadequate, unclear if all MJ smokers were also tobacco smokers, patients with respiratory disease or occupational exposure excluded	1.Cough 2.Sputum 3.Wheeze 4.Dyspnea	NA	• Smoking cannabis was associated with cough (0.3%, 95% CI=0.0 to 0.5, p=0.026), sputum production (0.4%, 95% CI 0.1-0.6, p=0.006), and dyspnea (0.2%, 95% CI 0.0-0.4, p=0.022) after adjusting for tobacco and other baseline differences. • Smoking cannabis was not associated with wheezing (0.2%, 95% CI –0.1-0.4, p=0.240) after adjusting for tobacco and other baseline differences.	High	Chief Scientist Office project grant
Tashkin et al, 2012 (17), Prospective cohort	Healthy MJ users	299	Mean: 33.4±6.4	3.0±0.4 joints per day for 9.8 years	27.4 % (82/299)	1.Age 2.Gender 3.Tobacco	Adequate, patients with illicit drug using, respiratory disease or occupational exposure excluded	1.Cough 2.Sputum 3.Wheeze	9.8 y	• Smoking MJ was associated with increased risk of cough (OR=2.5, 95% C.I 1.3-5.1, p = 0.009), sputum production (OR=7.7, 95% C.I 2.2-26.3, p < 0.001) and wheezing (OR=13.0, 95% C.I 4.4-43.6, p < 0.0001) compared to non-MJ smokers after adjusting for tobacco and other baseline differences.	Moderate	NIDA
Aldington et al, 2007 (18), Cross-sectional	Participants from WRS and GWA	339	WRS: 25-75 GWA: 18-70	54.2±75.3 joint-years	22.1 % (75/339)	1.Age 2.Gender 3.Height 4.Ethnicity 5.Tobacco 6.Occupational exposures 7.Family history of respiratory disease	Adequate, patients with illicit drug using, respiratory disease excluded	1.Cough 2.Wheeze 3.Dyspnea	NA	• Among cannabis-only smokers, smoking cannabis was associated with cough (OR=1.5, 95% CI 1.1-2.0), wheezing (OR 1.3, 95% CI 1.0-1.6) and dyspnea (OR=1.4, 95% CI 1.1-1.7) compared to non-smokers after adjusting for baseline differences.	Moderate	NZMH, HBMR, GlaxoSmithKline (UK)

						8.Passive smoking 9.Atopy						
Moore et al, 2005 (19), Cross-sectional*	NHANES III between 1988-1994	6,728	20-59	10.2±0.84 days in last month	1.4 % (94/6728)	1.Age 2.Gender 3.Tobacco	Adequate, patients with asthma excluded	1.Cough 2.Sputum 3.Wheeze 4.Dyspnea	NA	• Smoking MJ was associated with cough (OR=2.00, 95% CI 1.32-3.01, P=.001), sputum production (OR=1.89, 95% CI 1.35-2.66, P=.0005), and wheezing (OR= 2.98, 95% CI 2.05-4.34, P<0.0001) compared to non-smokers after adjusting for tobacco and other baseline variables. • Marijuana use was not associated with dyspnea (OR=1.29, 95% CI 0.81-2.03, P=0.26) compared to non-smokers after adjusting for tobacco and other baseline variables.	Moderate	National Training Award, NIDA, NCI
Taylor et al, 2000 (23), Prospective cohort	Volunteers from the Dunedin birth cohort 1972-73	943	From birth till 21	230 times in the past year	3 % (28/943)	1.Gender 2.Tobacco 3.Respiratory symptoms	Adequate	1.Cough 1.Sputum 2.Wheeze 3.Dyspnea	Followed from birth to 21 years	• Among cannabis-only smokers, smoking cannabis was not associated with increased risk of cough (OR=1.08, 95% CI 0.25–4.75), morning sputum production (OR=1.30, 95% CI 0.38–4.50), wheezing (OR=2.07, 95% 0.94–4.55), dyspnea (OR=0.61, 95% CI 0.14–2.65) and change in exercise tolerance (OR=1.45, 95% CI 0.65–3.23) compared to non-smokers compared to non-smokers after adjusting for baseline variables.	Low	NIMH, Health Research Council of New Zealand
Fligiel et al, 1997 (26), Cross-sectional	Healthy MJ users	241	Mean: 35.4 ±8.3	Greater than 10 joints per week for more than 5 years	16.6 % (40/241)	1.Age 2.Tobacco	Adequate, patients with illicit drug using, respiratory disease or occupational exposure excluded	1.Cough 2.Sputum 3.Wheeze	NA	• Among MJ-only smokers, smoking MJ was not associated with a higher frequency of chronic bronchitis symptoms (e.g. cough and sputum production) compared to non-smokers. • Marijuana use was associated with a higher prevalence of wheezing (p<0.05) compared to non-smokers.	Low	NIDA/ NIH
Sherrill et al, 1991 (24), Prospective †	Random cluster sample of households in Tucson (1972-1973)	1,802	15-60	Male: 4.0 Female: 5.0-5.5 MJ cigarettes per week	20% (242/1212)	1.Age 2.Gender 3.Tobacco	Adequate	1.Cough 2.Sputum 3.Wheeze	6 y	• Current MJ† smoking was associated with chronic cough (OR=1.73, 95% CI 1.21-2.47, 0.001<p<0.01), chronic sputum production (OR=1.53, 95% CI 1.08-2.18, 0.01<p<0.05) and wheezing (OR=2.01, 95% CI 1.50-2.70, P<0.001) compared to non-smokers after adjusting for tobacco and other baseline variables.	Moderate	NHLBI SCOR
Bloom et al, 1987 (20), Cross-sectional †	Random cluster sample of households in Tucson (1972-1973)	990	15-40	58.2 MJ cigarettes years	4 % (38/990)	1.Age 2.Gender 3.Height 4.Tobacco	Adequate	1.Cough 2.Sputum 3.Wheeze 4.Dyspnea	NA	• Among MJ-only smokers †, frequency or duration of MJ smoking was not associated with cough compared to non-smokers. • Among MJ-only smokers †, frequency or duration of MJ smoking was associated with sputum production (p=0025), wheezing (p=0 01), and attacks of dyspnea with wheezing (p<0.01) compared to non-smokers.	Moderate	NHLBI SCOR
Tashkin et al, 1987 (21), Cross-sectional ‡	Heavy MJ smokers and non-MJ smokers	446	25-49	50.4±4.6 joint-years	32.2 % (144/446)	1.Age 2.Gender 3.Height 4.Tobacco 5.Anemia 6.Carboxyhemoglobinemia	Adequate, patients with illicit drug using, respiratory disease or occupational exposure	1.Cough 2.Sputum 3.Wheeze 4.Dyspnea	NA	• Among MJ-only smokers, smoking MJ was associated with a higher prevalence of chronic cough (18 to 24%), sputum production (20 to 26%) and wheezing (25 to 37%) (p< 0.01, chi square) compared to non-smokers. • Among MJ-only smokers, smoking MJ was not associated with a higher prevalence of	Low	U.S. Public Health Service

							excluded			dyspnea compared to non-smokers.		

BMI- Body Mass Index; HBMR-Hawke's Bay Medical Research; MDD-Major Depressive Disorder in adolescence; MJ-Marijuana; MS-Marijuana Smokers; MTS-Marijuana Tobacco Smoker; NA-not applicable; NCI-National Cancer Institute; NIDA-National Institute on Drug Abuse; NIA- National Institute on Aging; NIH- National institute of Health; NHLBI-National Heart, Lung, and Blood Institute; NHLBI SCOR-National Heart, Lung, and Blood Institute Specialized Center of Research; NZMH-New Zealand Ministry of Health; NS-Not Specified; TS-Tobacco Smoker; WRS- Wellington Respiratory Survey; GWA- Greater Wellington Area; US NIMH-US National Institute of Mental Health; UK MRC-UK Medical Research Council

*Not specified route of exposure.

†The term Non-Tobacco Cigarette was used in the paper instead of marijuana because of the illegality of marijuana use

‡We extracted adjusted risk ratio for these studies to use in the meta-analysis.

§All studies used structured questionnaire to assess MJ exposure and self-reported respiratory symptoms used to assess outcomes.

Table 3: Studies that examined exposure to marijuana and development of obstructive lung disease

Study Year Design	Study Population	Sample Size, n	Age (years)	Average of MJ exposure	% of MJ only, users	Confounders and baseline variables	Adjustment	Outcome Examined	Follow-up	Result in Study	Risk of Bias	Funding source
Morris et al, 2018 (27), Cross-sectional	Participants from SPIROMICS	2,304	40-80	30.15±68.5 joint-years	Not specified	1.Age 2.Gender 3.Race 4.Height 5.Tobacco	Adequate	1.Chronic bronchitis	NA	• Among current or former MJ smokers, smoking MJ was not associated with increased risk for chronic bronchitis (OR=0.87, 95% CI 0.59-1.31; OR=1.00, 95% CI 0.79-1.26) compared to never MJ smokers after adjusting for covariates.	Low	NHLBI
Macleod et al, 2015 (25), Cross-sectional‖	Patients with tobacco or cannabis use	500	Mean: 37 MTS, 45 TS	Male: 104.5, Female: 53.2 joint-years	None	1.Age 2.Gender 3.Tobacco	Inadequate, unclear if all MJ smokers were also tobacco smokers, patients with respiratory disease or occupational exposure excluded	1.COPD	NA	• Smoking cannabis was associated with increased prevalence of COPD with each additional joint-year (0.3%, 95% CI = 0.0 to 0.5) after adjusting **for** tobacco and other baseline differences.	High	Chief Scientist Office project grant
Tashkin et al, 2012 (17), Prospective cohort	Healthy MJ users	299	Mean: 33.4±6.4	3.0±0.4 joints per day for 9.8 years	27.4 % (82/299)	1.Age 2.Gender 3.Tobacco	Adequate, patients with illicit drug using, respiratory disease or occupational exposure excluded	1.Chronic bronchitis	9.8 y	• Smoking MJ was associated with increased risk of bronchitis episodes (OR=2.3, 95%CI 1.2-4.4 p= 0.0117) compared to non-MJ smokers after adjusting for tobacco and other baseline differences.	Moderate	NIDA
Tan et al, 2009 (22), Cross-sectional*,‖	Volunteers from BOLD study	864	Mean: 56.3	0.23 joint-years in their lifetimes	6.2 % (54/864)	1.Age 2.Gender 3.Height 4.Ethnicity 5.BMI 6.Tobacco 7.Asthma 8.Education 9.Comorbidities†	Adequate	1.COPD	NA	• Among MJ-only smokers, smoking MJ (more than 50 cigarette) was not statistically associated with COPD (OR=1.66, 95% CI 0.52–5.26) compared to non-smokers after adjusting for baseline variables.	Low	Educational grant
Aldington et al, 2007 (18), Cross-sectional	Participants from WRS and GWA	339	WRS: 25-75 GWA: 18-70	54.2±75.3 joint-years	22.1 % (75/339)	1.Age 2.Gender 3.Height 4.Ethnicity 5.Tobacco 6.Occupational exposures 7.Family history of respiratory disease 8.Passive smoking 9.Atopy	Adequate, patients with illicit drug using, respiratory disease excluded	1.Chronic bronchitis	NA	• Among cannabis-only smokers, smoking cannabis was associated with chronic bronchitis (OR=2.0 95%CI 1.4 - 2.7) compared to non-smokers after adjusting for baseline variables.	Moderate	NZMH, HBMR, GlaxoSmithKline (UK)

Moore et al, 2005 (19), Cross-sectional*	NHANES III between 1988-1994	6,728	20-59	10.2±0.84 days in last month	1.4 % (94/6728)	1.Age 2.Gender 3.Tobacco	Adequate, patients with asthma excluded	1.Chronic bronchitis	NA	• Smoking MJ was associated with chronic bronchitis (OR=2.17, 95% CI 1.11-4.26, P=.02) compared to non-smokers after adjusting for tobacco and other baseline variables.	Moderate	National Training Award, NIDA, NCI

BOLD-Burden of Obstructive Lung Disease; BMI- Body Mass Index; COPD-Chronic Obstructive Pulmonary Disease; HBMR-Hawke's Bay Medical Research; MJ-Marijuana; MTS-Marijuana Tobacco Smoker; NA-not applicable; NCI-National Cancer Institute; NIDA-National Institute on Drug Abuse; NZMH-New Zealand Ministry of Health; TS-Tobacco Smoker; WRS- Wellington Respiratory Survey; GWA- Greater Wellington Area; NHANES - National Health and Nutrition Examination Survey

*Not specified route of exposure

†Comorbidities (i.e., heart disease, hypertension, stroke, diabetes and tuberculosis).

‡All studies used structured questionnaire to assess MJ exposure

§ Self-reported respiratory symptoms and objective assessment by spirometry|| used to assess outcomes.

Table 4: Studies that examined exposure to marijuana and change in pulmonary function

Study Year Design	Study Population	Sample Size, n	Age (years)	Average of MJ exposure	% of MJ only, users	Confounders and baseline variables	Adjustment	Outcome Examined	Follow-up	Result in Study	Risk of Bias	Funding source
Morris et al, 2018 (27), Cross-sectional	Participants from SPIROMICS	2,304	40-80	30.15±68.5 joint-years	Not specified	1.Age 2.Gender 3.Race 4.Height 5.Tobacco	Adequate	1.FEV_1 2.FVC 3.FEV_1/FVC	NA	• Current and former MJ users had a higher percent predicted FEV1 (P<0.001, P<0.001), and FVC (p<0.001, P<0.001) compared to never MJ smokers after adjusting for tobacco and other variables. • Current MJ use resulted in a significant positive association with FEV1/FVC (P<0.001) compared to never MJ smokers after adjusting for covariates.	Low	NHLBI
Kempker et al, 2015 (32), Cross-sectional	NHANES from 2007–2008 and 2009–2010	6,723	18–59	15.8 joint-years	21.5 % (184/855)	1.Age 2.Gender 3.Race 4.Height 5.Tobacco	Adequate, patients matched for economic status, history of asthma, emphysema, and chronic bronchitis.	1.FEV_1 2.FVC 3.FEV_1/FVC	NA	• Each additional joint-year of smoking MJ was not associated with change in the mean percent predicted FEV_1 (0.02±0.02%, P = 0.4), an increase in FVC (0.07±0.02%, P = 0.004) and a decrease in FEV_1/FVC (-0.03 ± 0.01%; P = 0.02) compared to non-smokers after adjusting for tobacco and other variables. • Smoking MJ over a 20 joint-year period was associated with FEV_1/FVC <70% (OR=2.1; 95% CI 1.1–3.9, P= 0.02) compared to non-smokers after adjusting for tobacco and other baseline variables.	Low	NIH
Pletcher et al, 2012 (28), Prospective Cohort	Healthy adults at the enrollment	5,115	18-30	2-3 episodes per month	15.5 % (795/5115)	1.Age 2.Gender 3.Race 4.Height 5.Tobacco 6.Asthma 7.Education 8. Airborne particulate 9.Secondhand smoker 10.Waist circumference	Adequate	1.FEV_1 2.FVC	20 y	• Current (use in the last 30 days) smoking of MJ (more than 20 episode/30 day) was not associated with change in FEV_1 (−18 mL, 95% CI −42 to 6.1, p=0.32) compared to non-smokers. • Lifetime smoking of MJ (more than 10 joint-years) was associated with an increase in FEV_1 (36 mL, 95% CI, −6.5 to 79, p=0.049) compared to non-smokers. • Current smoking of MJ (more than 20 episodes/30d) was associated with an increase in FVC (20 ml, 95% CI -5.2 to 49, p=0.03) compared to non-smokers. • More than 10 joint-years use was associated with an increase in FVC (59 ml, 95% CI, 12-107, P=0.01) in MJ smokers compared to non-smokers after adjusting for tobacco use and other baseline variables.	Low	Industry-sponsored grants from GlaxoSmithKl-ine and Boehringer-Ingelheim

Hancox et al, 2010 (29), Prospective cohort	Volunteers from the Dunedin birth cohort 1972-73	1,037	From birth till 32	Not specified	Not specified	1.Age 2.Gender 3.Height 4.Tobacco 5.Illicit drugs	Adequate	1.FEV_1 2.FVC 3.FEV_1/FVC 4.Raw 5.sGaw		• Among cannabis-only smokers, smoking cannabis was not associated with a decrease in FEV_1 (CI 95% -16.0–19.0, p=0.867), or FEV_1/FVC (CI 95% -0.42–0.04, p=0.100) compared to non-smokers after adjusting for baseline variables. • Smoking cannabis was associated with a higher value for FVC (CI 95% -2.5–37.4, p=0.087), Raw (CI 95% 0.001–0.057, p= 0.042) and lower sGaw (CI 95% -11.8 to -1.7, p= 0.010) after adjusting for baseline variables.	Low	UK Medical Research Council, US NIMH, William T. Grant Foundation
Aldington et al, 2007 (18), Cross-sectional	Participants from WRS and GWA	339	WRS: 25-75 GWA: 18-70	54.2±75.3 joint-years	22.1 % (75/339)	1.Age 2.Gender 3.Height 4.Ethnicity 5.Tobacco 6.Occupational exposures 7.Family history of respiratory disease 8.Passive smoking 9.Atopy	Adequate patients with illicit drug using, respiratory disease excluded	1.FEV_1 2.FEV_1/FVC 3.sGaw	NA	• Among cannabis-only smokers, smoking cannabis was not associated with changes in FEV_1 (ETD†= –0.01, 95% CI–0.13 to 0.11) compared to non-smokers after adjusting for baseline variables. • Smoking cannabis was associated with a reduction in the FEV_1/FVC (ETD = –1.1, 95% CI–2.6 to 0. 1) and a reduction in sGaw (ETD = –0.12, 95% CI –0.21 to –0.03) compared to non-smokers after adjusting for baseline variables.	Moderate	New Zealand Ministry of Health, Hawke's Bay Medical Research, GlaxoSmithKline (UK)
Moore et al, 2005 (19), Cross-sectional*	NHANES III between 1988 and 1994	6,728	20-59	10.2±0.84 days in last month	1.4 % (94/6728)	1.Age 2.Gender 3.Tobacco	Adequate, patients with asthma excluded	1.FEV_1/FVC	NA	• Smoking MJ was not associated with a higher rate of FEV_1/FVC <70% (OR=1.01, 95% CI 0.51-1.94, P=.99) compared to non-smokers after adjusting for tobacco and other baseline variables.	Moderate	National Training Award, NIDA, NCI
Taylor et al, 2002 (30), Prospective cohort	Volunteers from the Dunedin birth cohort 1972-73	900	From birth till 26	Not specified	Not specified	1.Age 2.Weight 3.Tobacco	Adequate	1.FEV_1/VC	Followed from birth to 26 years	• Smoking cannabis was associated with a marginally significant negative effect on mean FEV_1/VC (P < 0.09) after controlling for potential confounding factors.	Moderate	NIMH
Taylor et al, 2000 (23), Prospective cohort	Volunteers from the Dunedin birth cohort 1972-73	943	From birth till 21	230 times in the past year	3 % (28/943)	1.Gender 2.Tobacco 3.Respiratory symptoms	Adequate	1.FEV_1/FVC	Followed from birth to 21 years	• FEV_1/FVC dropped below 80% for 36% of cannabis-only smokers compared to 20% for non-smokers (chi-sq =4.06, df= 1, p=0.04) after adjusting for tobacco and other baseline variables.	Low	NIMH, Health Research Council of New Zealand
Tashkin et al, 1997 (31), Prospective cohort	Healthy volunteers	394	25-49	Greater than 3.5 joints per day	33.2 % (131/394)	1.Tobacco	Adequate, patients with illicit drug using, respiratory disease or occupational exposure excluded	1.FEV_1	8 y	• Among MJ-only smokers, intermittent and continuing smoking of MJ was not associated with a reduction in FEV_1 (0.97 and 1.94 ml/year, respectively) compared to non-MJ smokers.	Low	NIH/NIDA
Sherrill et	Random cluster sample			Male: 4.0 Female:		1.Age 2.Gender				• Among current MJ smokers‡ a significant (p<0.01) reduction in		

al, 1991 (24), Prospective	of households in Tucson (1972-1973)	1,802	15-60	5.0-5.5 MJ cigarettes per week	20% (242/1212)	3.Tobacco	Adequate	1.FEV_1 2.FEV_1/FVC	6 y	pulmonary function was found after one year of follow up compared to non-smokers after adjusting for tobacco and other baseline variables.	Moderate	NHLBI SCOR
Bloom et al, 1987 (20), Cross-Sectional	Random cluster sample of households in Tucson (1972-1973)	990	15-40	58.2 MJ cigarette years	3.8 % (38/990)	1.Age 2.Gender 3.Height 4.Tobacco	Adequate	1.FEV_1 2.FEV_1/FVC	NA	• Among MJ-only smokers‡, smoking MJ was not associated with changes in FEV_1 and FEV_1/FVC compared to non-smokers after adjusting for baseline variables. • Current male MJ-only smokers had a significant decrease in the FEV_1/FVC ($p<0.05$) compared to non-smokers after adjusting for baseline variables.	Moderate	NHLBI SCOR
Tashkin et al, 1987 (21), Cross-sectional	Heavy MJ smokers and non-MJ smokers	446	25-49	50.4±4.6 joint-years	32.2 % (144/446)	1.Age 2.Gender 3.Height 4.Tobacco 5.Anemia 6.Carboxyhemoglobinemia	Adequate, patients with illicit drug using, respiratory disease or occupational exposure excluded	1.FEV_1 2.FVC 3.FEV_1/FVC 4.Raw 4.sGaw	NA	• Smoking MJ was not associated with the significant differences in pulmonary function tests compared to non-smokers or tobacco-only smokers after adjusting for baseline variables. • Among male MJ-only smokers, smoking MJ was associated with the significant worse values for Raw and sGaw ($p<0.03$) compared to non-smokers or tobacco-only smokers after adjusting for baseline variables.	Low	U.S. Public Health Service
Tashkin et al, 1980 (33), Cross-sectional §	Healthy MJ user volunteers	115	Mean: 24.1±0.31 users, 24.1±0.37 non-users	3 days per week for more than 2-5 years	43.5%	1.Age 2.Gender 3.Height 4.Tobacco	Inadequate adjustment for tobacco, patients with respiratory disease or occupational exposure excluded and matched for age, sex, and height.	1.FEV_1 2.FVC 3.Raw 4.sGaw	NA	• Smoking MJ was not associated with the significant differences in respiratory function test after adjusting for age and height compared to the control group ($P > 0.05$). • Smoking MJ was associated with a significant higher Raw ($P < 0.001$) and a significant lower sGaw ($P < 0.001$) compared to the control group. Results were not adjusted for tobacco.	High	NIDA, NIH, NIEHS

Raw-airway resistance; MJ-Marijuana; sGaw-specific airway conductance; NA-not applicable; NCI-National Cancer Institute; NIH- National institute of Health; NHLBI-National Heart, Lung, and Blood Institute; NHLBI SCOR-National Heart, Lung, and Blood Institute Specialized Center of Research; NIDA-National Institute on Drug Abuse; NIMH-National Institute of Mental Health; NIEHS-National Institute of Environmental Health Science; NHLD-National heart and lung Institute; NHANES - National Health and Nutrition Examination Survey; WRS- Wellington Respiratory Survey; GWA- Greater Wellington Area; NS-Non-Smoker

*Not Specified route of exposure

† ETD-Estimate of Difference

‡They used "Non-Tobacco Cigarette" smoking in the paper instead of marijuana with the reason of illegality of marijuana use.

§ All studies used structured questionnaire to assess MJ exposure except § and objective assessment by spirometry used to assess outcomes.

Table 5: Studies that examined exposure to marijuana and development of other respiratory outcomes

Study Year Design	Study Population	Sample Size, n	Age (years)	Average of MJ exposure	% of MJ only, users	Confounders and baseline variables	Adjustment	Outcome Examined	Follow-up	Result in Study	Risk of Bias	Funding source
Brook et al, 2008 (35), Prospective Cohort	MJ users	749	Mean *: 14.05 ± 2.8^{T2}, 16.7 ± 2.8^{T3}, 22.0 ± 2.8^{T4}, 27.0 ± 2.8^{T5}	Mean: 0.58 ± 1.2^{T2}, 0.76 ± 1.3^{T3}, 1.03 ± 1.4^{T4}, 0.95 ± 1.4^{T5}	Not specified	1.Age 2.Gender 3.Tobacco 4.MDD 5.Parental education and income 6.Maternal MJ use 7.Childhood aggression	Inadequate adjustment for tobacco	1.Non-specific respiratory illness	8 y	• Smoking MJ was associated with increased risk of respiratory problems † [(T2–T4) (A.O.R=1.44, 95% CI, 1.12–1.85, p <0.01)], [(T2–T5) (A.O.R=1.47, 95% CI, 1.16–1.87, p<0.01)]. Results were not adjusted for tobacco.	High	NIDA, NCI, Research Scientist Award from the NIDA
Polen et al, 1993 (34), Prospective Cohort	MJ users and controls	902	<25 - ≥35	Greater than 6 times in their lifetimes	50.1 % (452/902)	1.Age 2.Gender 3.Race 4.Tobacco 5.Educational level 6.Alcohol consumption	Adequate	1.Non-specific respiratory illness	8 y	• Among MJ-only smokers, smoking MJ was associated with small increased risk of outpatient visits for respiratory illnesses ‡ (RR=1.19, 95% CI=1.01-1.41) compared with non-smokers. • Smoking MJ was not associated with hospital admission (RR = 1.51, 95% CI 0.93-2.46) compared with non-smokers after adjusting for baseline variables.	Low	NIDA
Tashkin et al, 1993 (36), Cross-Sectional	Healthy MJ users	542	Mean: 34.8±6.8	Greater than 10 joints per week for more than 5 years	20.8 % (113/542)	1.Tobacco 2.Illicit drugs	Adequate, patients with illicit drug using, respiratory disease or occupational exposure excluded	1.FEV_1	NA	• Smoking MJ was not associated with changes in FEV_1 by methacholine challenge test with PC20<25 mg/ml among men (OR=1.59, 95% CI 0.72-3.51) and women (OR=1.56, 95% CI 0.51-4.83), and with PC20 < 5 mg/ml among men (OR=1.21, 95% CI 0.74-1.98) and women (OR=1.91, 95% CI 0.77-4.72) compared to non-smokers after adjusting for other substances.	Low	NIDA
Tashkin et al, 1988 (37), Cross-sectional	Heavy habitual users of marijuana	281	Mean: 34.9 MS, 34.5 MTS, 38.3 TS, 33.8 NS	Greater than 5 joints per week for more than 5 years	41.2 % (116/281)	1.Tobacco	Adequate, patients with illicit drug using, respiratory disease or occupational exposure excluded	1.FEV_1	NA	• Among MJ-only smokers, smoking MJ was not associated with decreased in FEV_1 (p=0.172) and airway hyperactivity following the maximal inhaled dose of methacholine compared to non-smokers.	Low	Not specified

MDD-Major Depressive Disorder in adolescence; MJ-Marijuana; MS-Marijuana Smokers; MTS-Marijuana Tobacco Smoker; NA-not applicable; NCI-National Cancer Institute; NIDA-National Institute on Drug Abuse; NS-Non-smokers; TS-Tobacco Smoker

*Time waves (Time 2–5 = T2–T5; 1983, 1985–1986, 1991–1993, and 1997)

†Respiratory illness was assessed by four items: sore throat or cold with fever; shortness of breath with light exercise; trouble with sinus congestion, runny nose, or sneezing; and colds.

‡Cold, flu, or Sore throat.
§ All studies used structured questionnaire to assess MJ exposure except § and objective assessment by spirometry used to assess outcomes.

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