XXII CONGRESSO NAZIONALE SOCIETÀ ITALIANA DI TABACCOLOGIA



15-16 OTTOBRE 2026 - LECCE
Officine Cantelmo

NUOVI PRODOTTI, VECCHIE DIPENDENZE: IL TABAGISMO NELL'ERA DELLA NICOTINA GLOBALE

Patologie di genere fumo-correlate

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Università di Foggia
Scienze Mediche e Chirurgiche

Policlinico Foggia
ospedaliero-universitario

GISeG
Gruppo Italiano Salute e Genere

SIP IRS
SOCIETÀ ITALIANA DI PNEUMOLOGIA
Task Force Medicina di Genere

Agenda

- Differenze di genere nelle malattie respiratorie: dallo sviluppo embrionale all'età adulta

- Fattori che aumentano il rischio di patologie respiratorie nella donna: il ruolo del fumo di sigaretta

- Implicazioni cliniche del fumo di sigaretta

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L'influenza del genere in pneumologia è un campo di interesse crescente negli ultimi 20 anni

[Education and Clinical Practice CHEST Reviews]

CHEST

2022

Sex and Gender in Lung Disease and Sleep Disorders

A State-of-the-Art Review

Amik Sodhi, MBBS, MPH; Margaret Pisani, MD; Marilyn K. Glassberg, MD; Ghada Bourjeily, MD; and Carolyn D'Ambrosio, MD

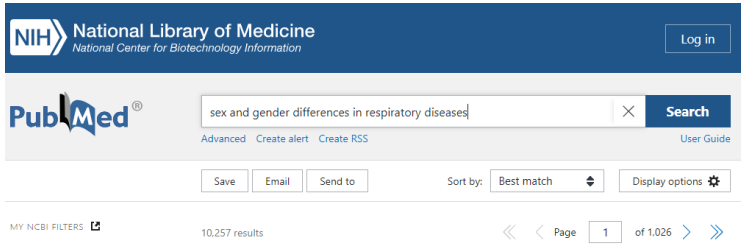
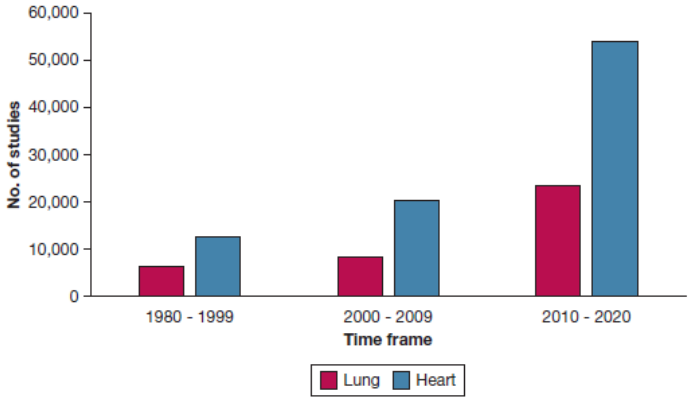
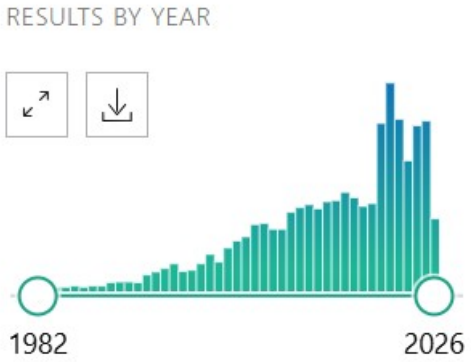
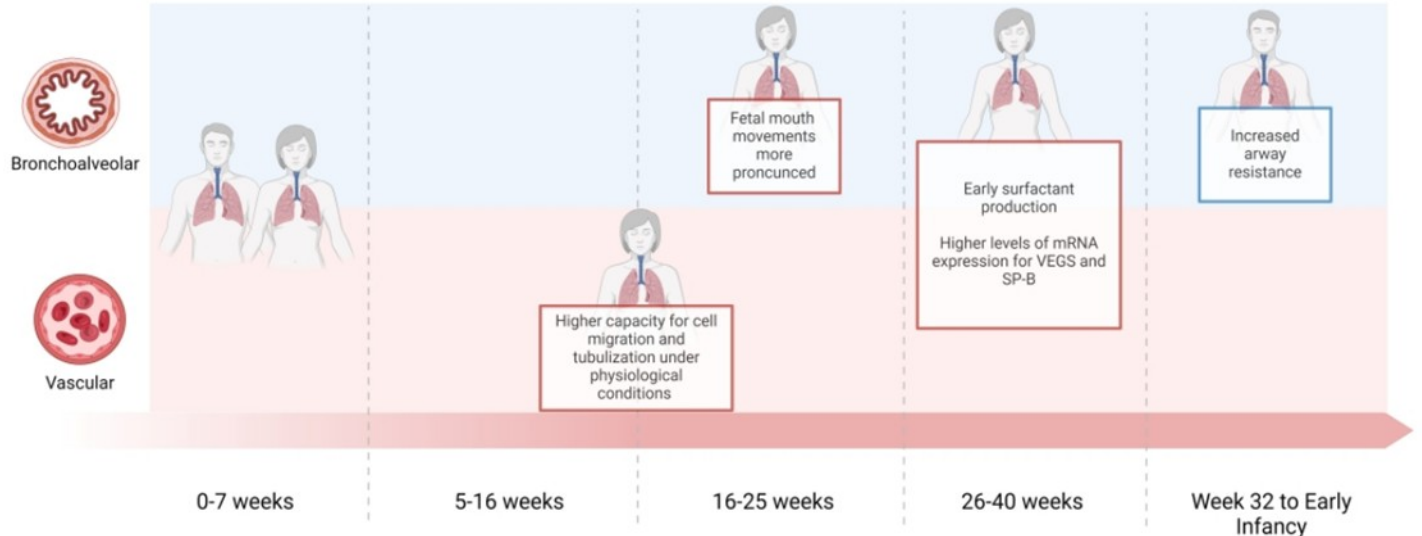


Figure 1 – *Bar graph showing studies indexed in PubMed over the time frame using the search terms "lung and (sex or gender)" and "heart and (sex or gender)."*





Sex and gender differences during the lung lifespan : unveiling a pivotal impact



Fase Embrionale

Fetal growth and breathing movements are detected earlier in the female fetus. AMH delays branching by promoting apoptosis in males.

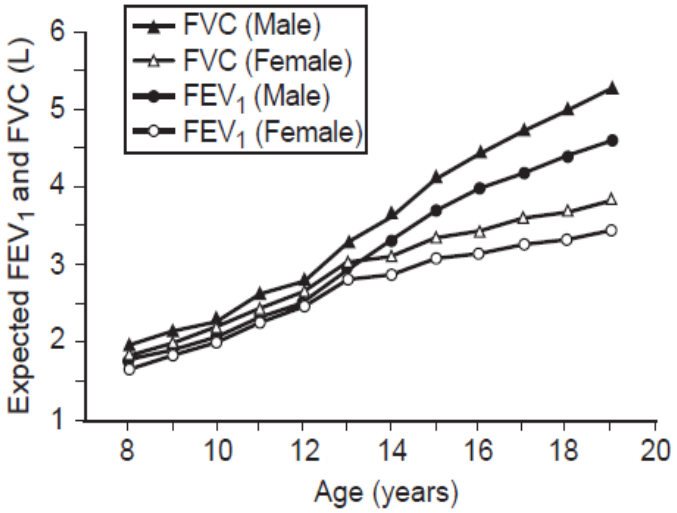
Surfactant secretion and phospholipid maturation are inhibited in males (androgens) and promoted in females (estrogens).

Fase Alveolare

Faster alveolarization in females. Higher flow rate per lung volume, but smaller lung size in girls. Better response to surfactant therapy in female newborns with RDS. FEV1 peaks earlier in females than males.

Tondo et al. Eur Respir Rev. 2024

Growth pattern in FEV1 and FVC in normal subjects



Xuan W et al. Am J Respir Crit Care Med

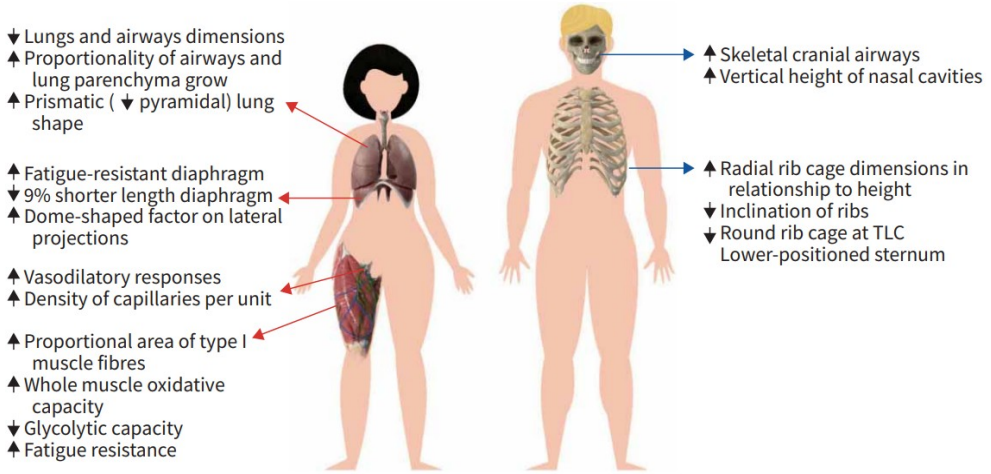


FIGURE 2 A simplified conceptual model to summarise the main sex differences in lung, airways, ribcage and skeletal muscles. ↓: lower than the other sex; ↑: higher than the other sex. TLC: total lung capacity.

LoMauro A, Aliverti A. Eur Respir Rev 2021

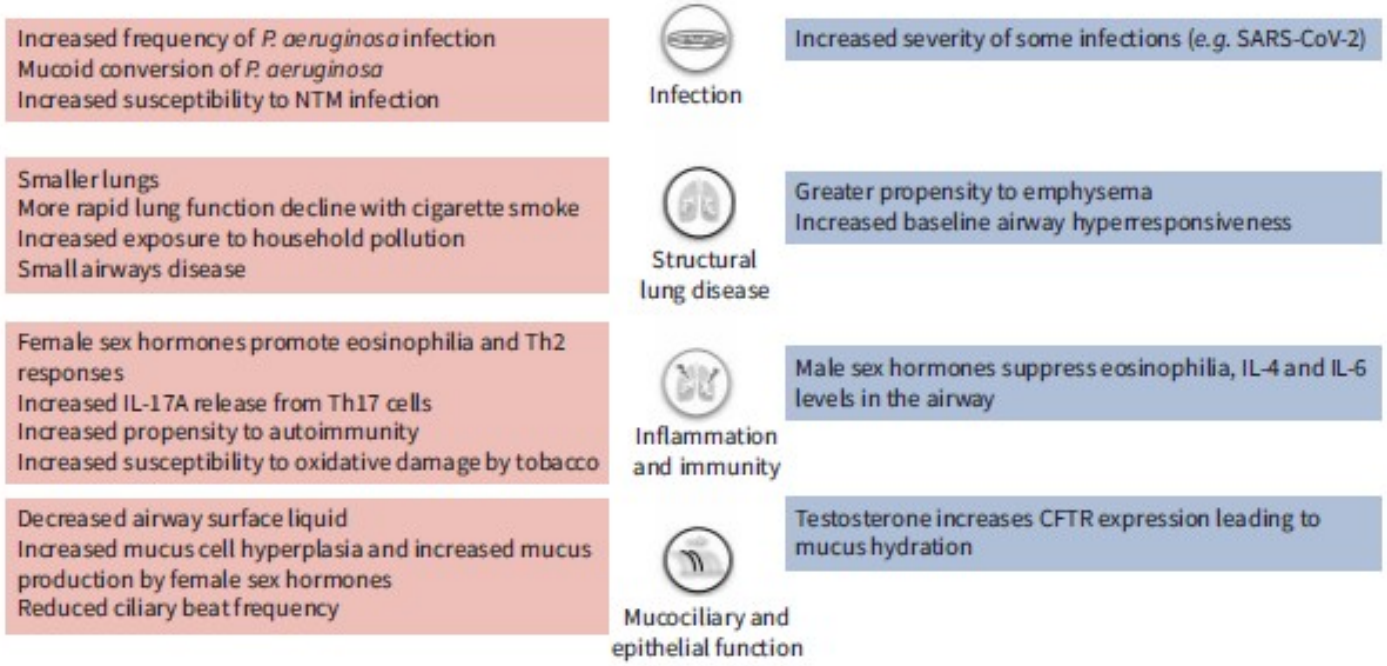


FIGURE 2 Postulated mechanisms by sex for chronic lung disease. Pink: female; blue: male. CFTR: cystic fibrosis transmembrane conductance regulator; IL: interleukin; NTM: non-tuberculous mycobacteria; *P. aeruginosa*: *Pseudomonas aeruginosa*; SARS-CoV-2: severe acute respiratory syndrome-coronavirus-2.

Somayaji R, Chalmers JD. Just breathe: a review of sex and gender in chronic lung disease. Eur Respir Rev 2022

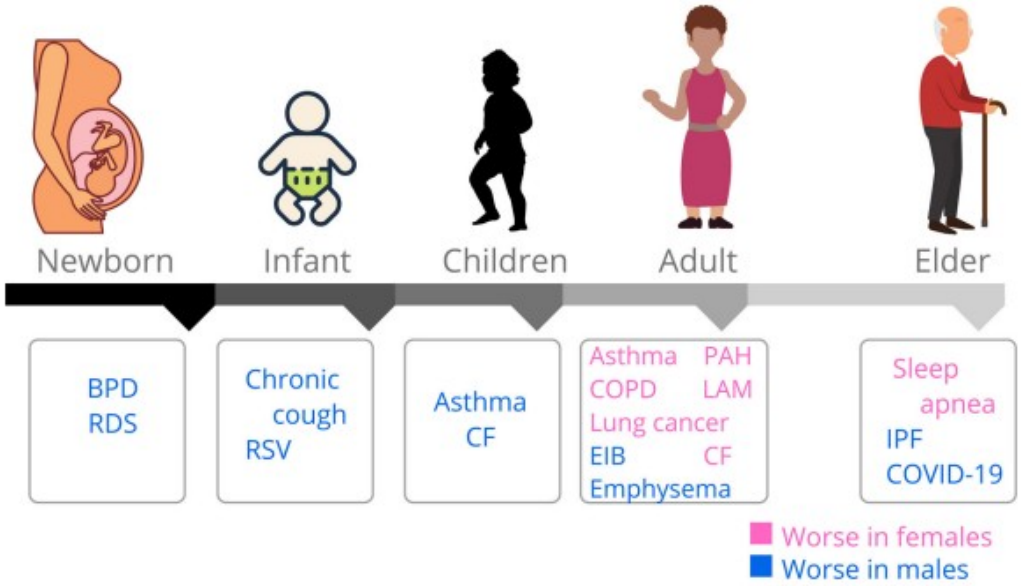


Fig. 1. Sex differences in lung disease progression across lifespan.
There are sex differences in the prevalence of several lung diseases across the lifespan. In pink are lung diseases that are more prevalent in females than males (blue). (Abbreviations-BPD: Bronchopulmonary dysplasia; RDS: Respiratory distress syndrome; RSV: Respiratory syncytial virus; CF: Cystic fibrosis; PAH: Pulmonary arterial hypertension; COPD: Chronic obstructive pulmonary disease; LAM: Lymphangioleiomyomatosis; EIB: Exercise-induced bronchoconstriction; IPF: Idiopathic pulmonary fibrosis; COVID-19: Coronavirus disease 2019)

Silveyra P, et al. Sex and Gender Differences in Lung Disease. Adv Exp Med Biol. 2021

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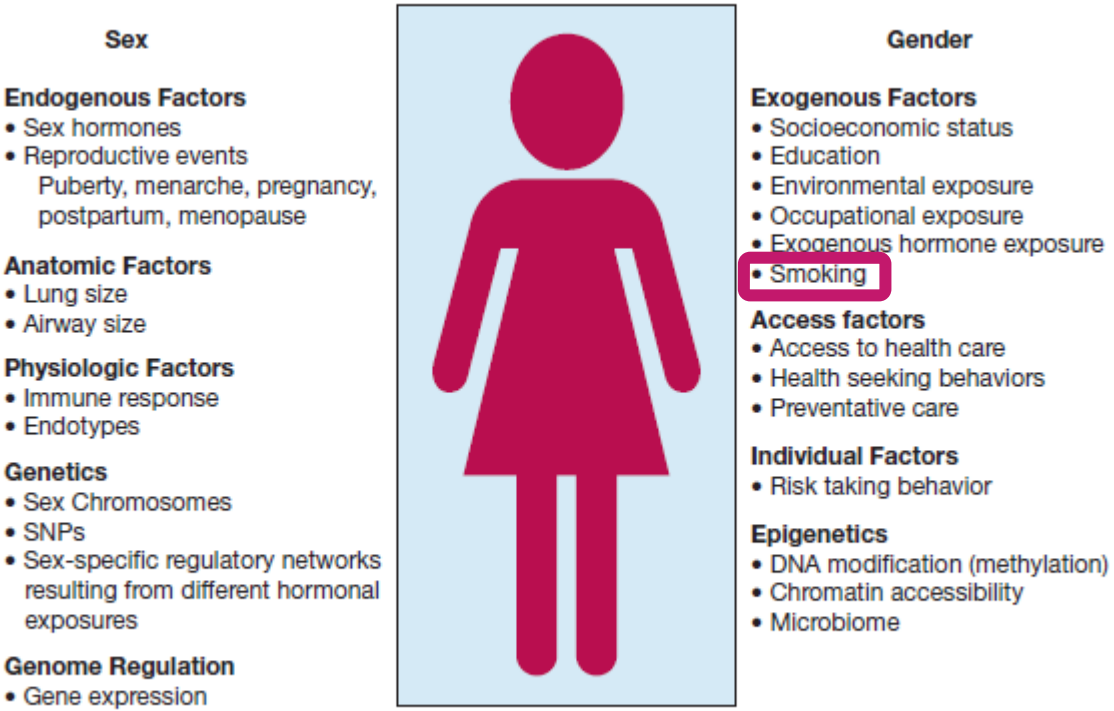
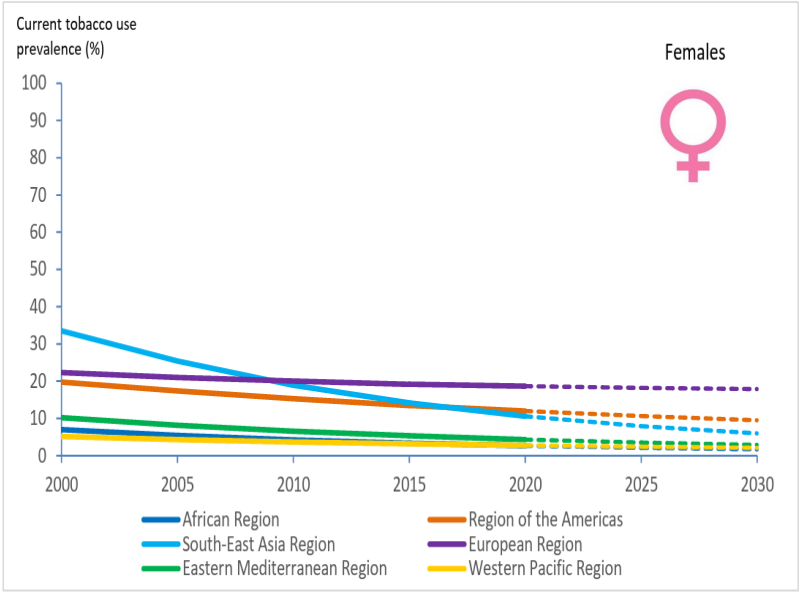
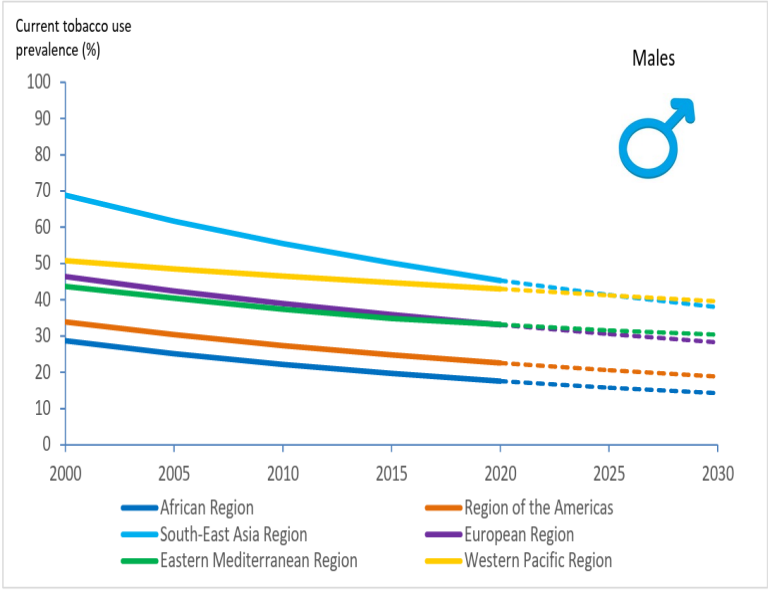


Figure 3 – *Diagram showing the domains through which sex and gender impact respiratory disease. Sex and gender also interact with each other at various points of development, diagnosis, and management of respiratory diseases.*

Sodhi A Chest 2022





WHO global report on trends in prevalence of tobacco use 2000–2030

….e in Italia?

Istituto Superiore di Sanità
EpiCentro - L'epidemiologia per la sanità pubblica

Non Fumatori: 35,3 milioni 68,5%	**Ex Fumatori:** 5,7 milioni 11,0%	**Fumatori:** **10,5 milioni** **20,5%**
Uomini: 15,2 milioni 61,2%	**Uomini:** 3,4 milioni 13,7%	**Uomini:** 6,3 milioni **25,1%**
Donne: 20,0 milioni 75,3%	**Donne:** 2,2 milioni 8,4%	**Donne:** 4,4 milioni **16,3%**

OSSFAD – Indagine DOXA-ISS 2023

Fonte: Istituto Superiore di Sanità (ISS), *Rapporto Nazionale sul Tabagismo 2023*

Survey: metodologia e campionamento

POPOLAZIONE

Studenti 11-13 anni residenti in Italia

Studenti 14-17 anni residenti in Italia

METODOLOGIA CAMPIONAMENTO

Modello *Probability Proportional to Size* (PPS) a tre stadi

- ✓ 1 stadio: **selezione dei comuni** con stratificazione per dimensione (meno di 100.000, tra 100.000 e 200.000 e oltre 200.000) e macroarea geografica (Nord-ovest, nord-est, centro, meridione, isole)
- ✓ 2 stadio: **selezione delle scuole**
- ✓ 3 stadio: **selezione delle classi** (prime, seconde e terze)

Il campione garantisce la rappresentatività della popolazione degli studenti 11-13 anni residenti in Italia

Modello *Probability Proportional to Size* (PPS) a tre stadi

- ✓ 1 stadio: **selezione dei comuni** con stratificazione per dimensione (meno di 100.000, tra 100.000 e 200.000 e oltre 200.000) e macroarea geografica (Nord-ovest, nord-est, centro, meridione, isole)
- ✓ 2 stadio: **selezione delle scuole** con stratificazione per tipologia (licei, istituti professionali, istituti tecnici, istituti d'arte)
- ✓ 3 stadio: **selezione delle classi** (prime, seconde, terze e quarte)

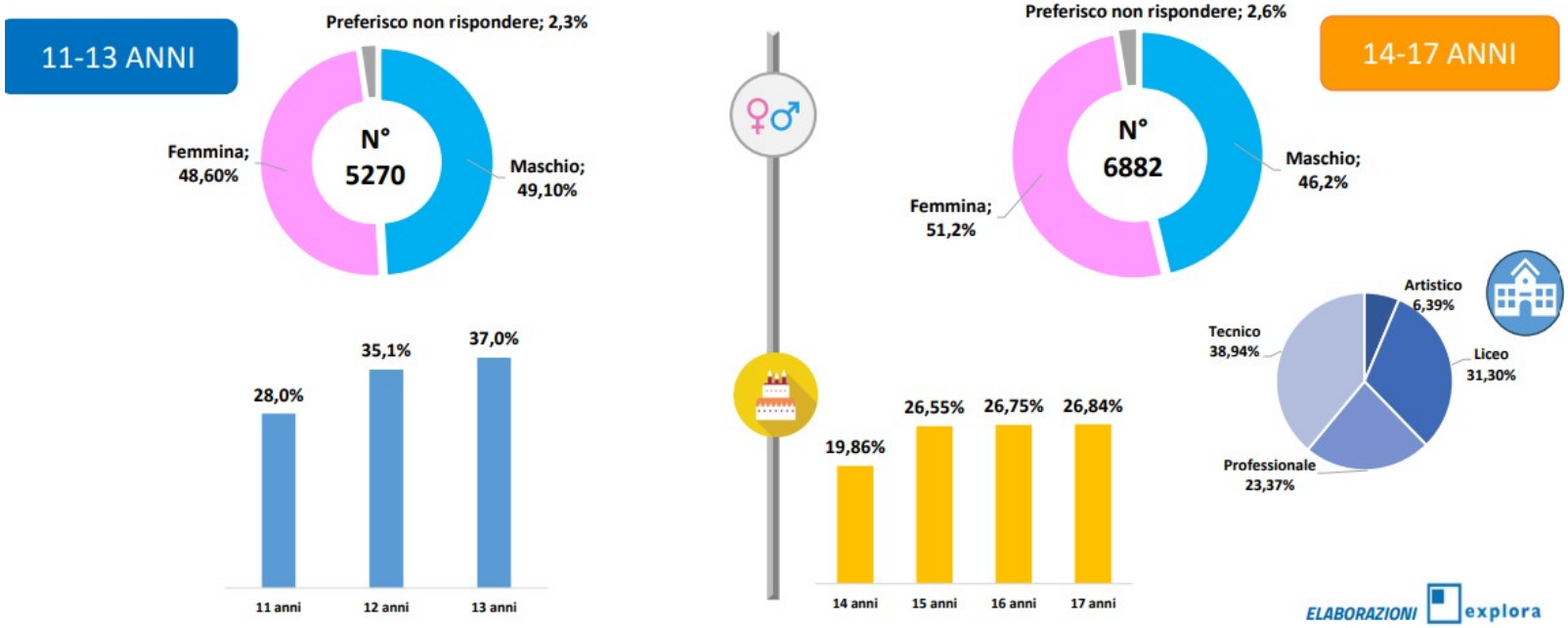
Il campione garantisce la rappresentatività della popolazione degli studenti 14-17 anni residenti in Italia

METODOLOGIA INDAGINE

Somministrazione in modalità *Computer Assisted Web Interview* (CAWI)

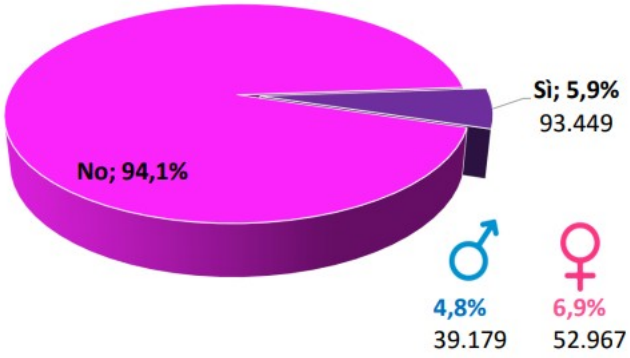
Somministrazione in modalità *Computer Assisted Web Interview* (CAWI)

Caratteristiche del campione

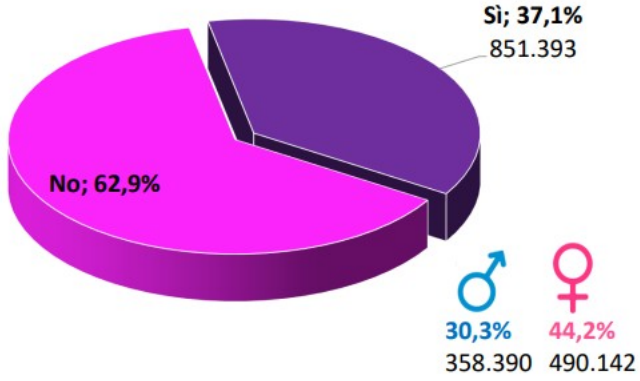


PREVALENZA CONSUMATORI PRODOTTI CONTENENTI TABACCO O NICOTINA - SIGARETTE TRADIZIONALI, HTP, E-CIG (ultimi 30gg)

11-13 ANNI



14-17 ANNI



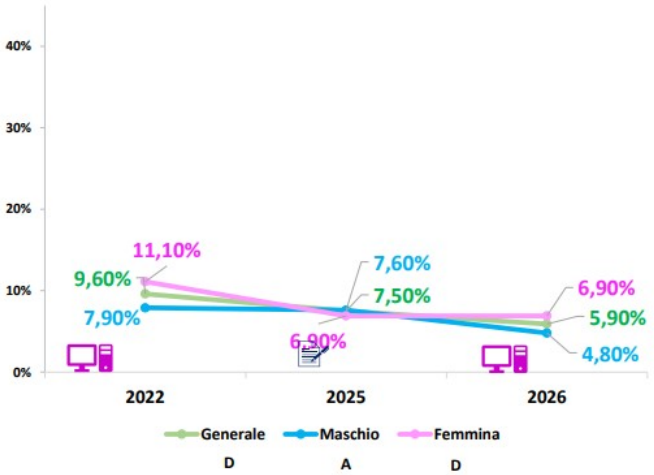
ELABORAZIONI explora

ISTITUTO SUPERIORE DI SANITÀ
CENTRO NAZIONALE DIPENDENZE E DOPING

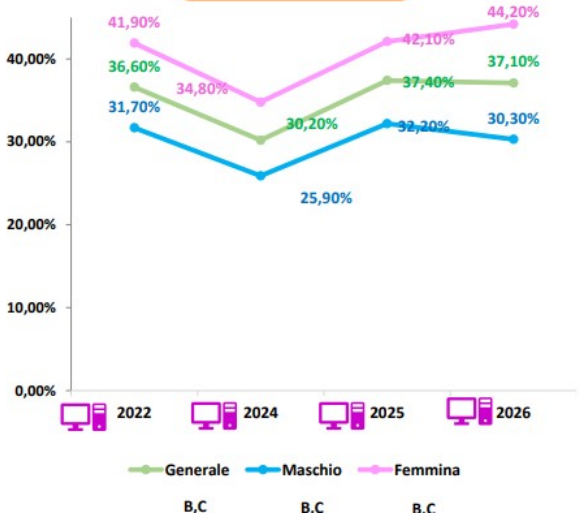
2026

PREVALENZA CONSUMATORI PRODOTTI CONTENENTI TABACCO O NICOTINA - SIGARETTE TRADIZIONALI, HTP, E-CIG (ultimi 30gg)

11-13 ANNI



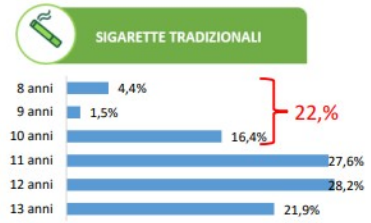
14-17 ANNI

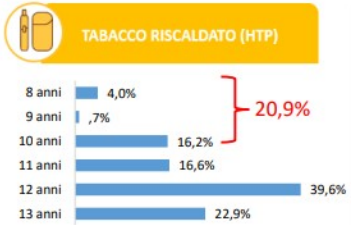


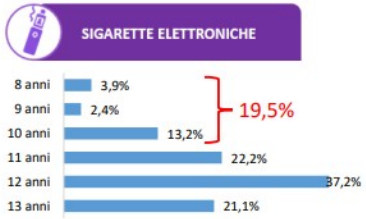
ISTITUTO SUPERIORE DI SANITÀ
CENTRO NAZIONALE
DIPENDENZE E DOPING

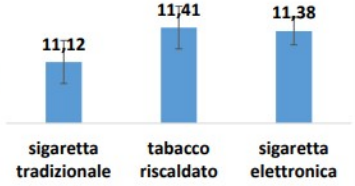
ETÀ PRIMO CONSUMO SIGARETTE TRADIZIONALI, HTP, E-CIG (ultimi 30 gg)

11-13 ANNI

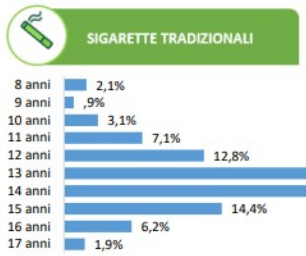


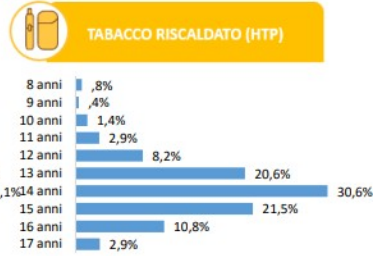


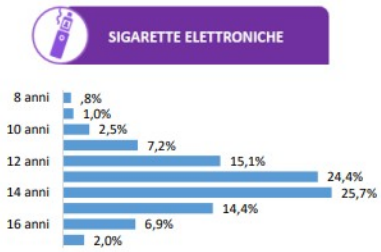


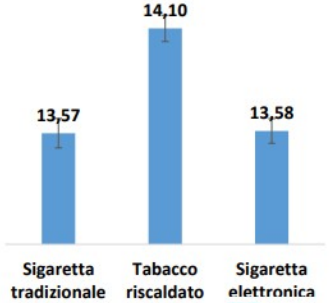


14-17 ANNI





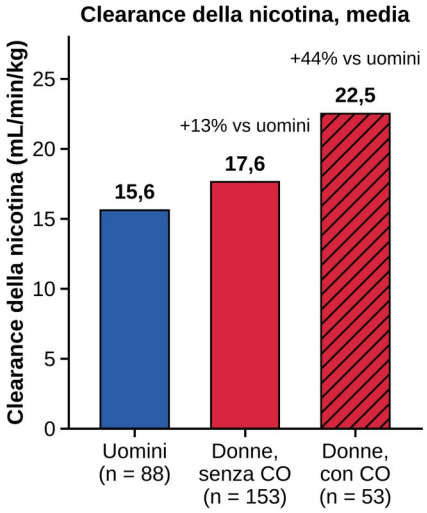




ELABORAZIONI explora

Differenze di sesso nella farmacologia della nicotina

Ambito	Donne vs uomini	Implicazione
Farmacocinetica	Clearance più rapida: +21% nelle donne, +44% con contraccettivi orali (induzione del CYP2A6 da parte degli estrogeni) [2]; ulteriore aumento in gravidanza [3]	Calo più rapido della nicotina; dose di NRT da rivalutare
Farmacodinamica	Minore sensibilità agli effetti discriminativi e titolazione meno precisa [1]; recettori β2*-nAChR aumentati nei fumatori maschi (+13–17%), non nelle donne [4]	Fumo meno guidato dalla nicotina nelle donne
Comportamento	Ruolo maggiore di stimoli ambientali, affettività negativa e controllo del peso [1]; progesterone associato a craving e astinenza [4]	Gestire umore, timore del peso e stimoli
Cessazione	Beneficio della NRT circa la metà rispetto agli uomini [5]; vareniclina più efficace nelle donne a 3–6 mesi, uguale a 12 mesi [6, 7]	Vareniclina da preferire nelle donne



1. Benowitz NL, Hatsukami D. Addict Biol 1998;3:383–404.
2. Benowitz NL, et al. Clin Pharmacol Ther 2006;79:480–8.
3. Dempsey D, et al. J Pharmacol Exp Ther 2002;301:594–8.
4. Cosgrove KP, et al. Arch Gen Psychiatry 2012;69:418–27.
5. Perkins KA, Scott J. Nicotine Tob Res 2008;10:1245–50.
6. McKee SA, et al. Nicotine Tob Res 2016;18:1002–11.
7. Smith PH, et al. Nicotine Tob Res 2017;19:273–81.

Tabaccologia 1-2019

Differenze di genere nell'abitudine al fumo e sue conseguenze

Liana Fattore



Prevalenza e frequenza: M>F
Sensibilità agli effetti gratificanti della nicotina: M>F
Intensità di craving: F>M
Rischio di ricadute: F>M
Rischi per la salute: F>M

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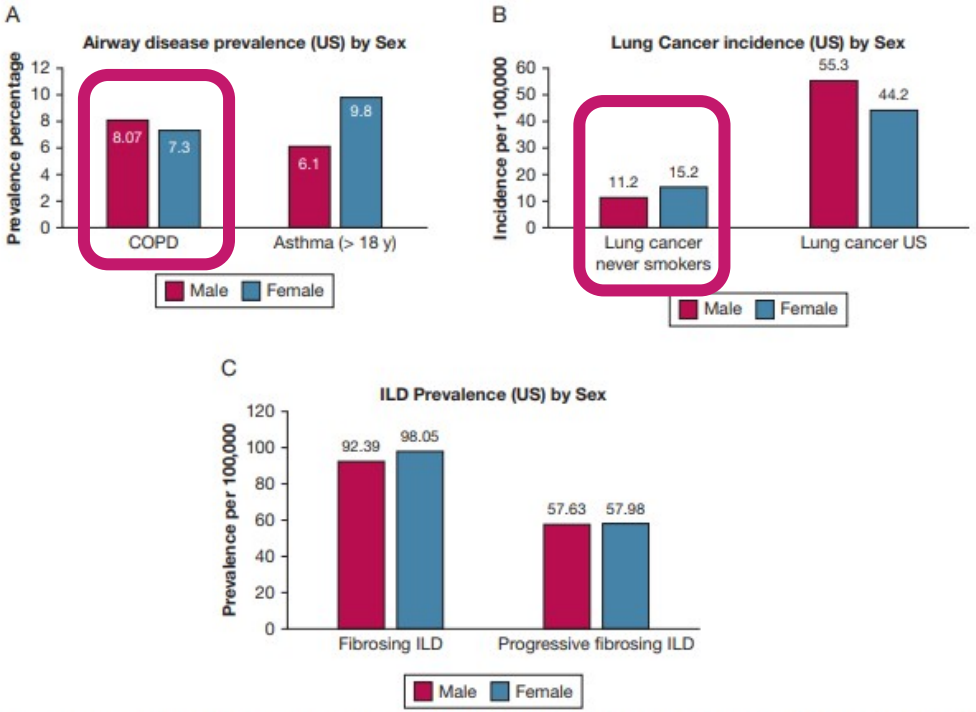


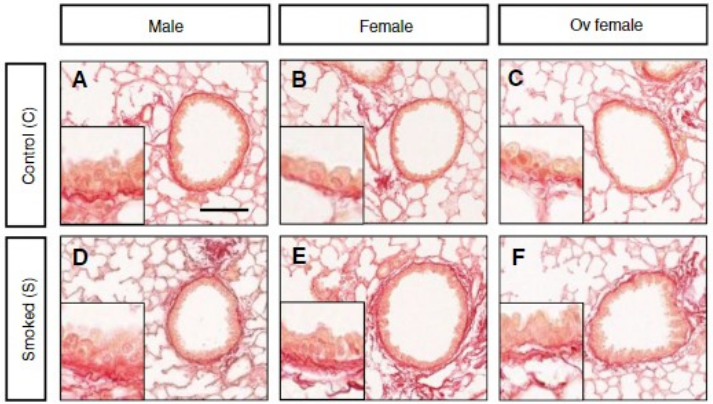
Figure 2 – *A-C, Bar graphs showing the prevalence of airway disease by sex (A), the prevalence of ILD by sex (B), and incidence of lung cancer by sex (C). ILD = interstitial lung disease.*

GENETIC:
The **contribution of the X chromosome** to COPD susceptibility is suggested by an increased risk of early onset COPD in females who smoke and also have a mother with COPD. The COPD Gene study therefore identified **female sex as a significant risk factor for early onset COPD.**

GREATER INFLAMMATORY RESPONSE:
An analysis of the proteome of bronchoalveolar lavage from females and males with COPD showing significant **differences including downregulation of the lysosomal pathway and upregulation of oxidative phosphorylation in females.**

An der Plaat DA et al. Age at menopause and lung function: a Mendelian randomisation study. Eur Respir J 2019; 54: 1802421
Barnes PJ et ak. Sex differences in chronic obstructive pulmonary disease mechanisms. Am J Respir Crit Care Med, 2016: 813–814

HORMONAL: Estrogen may contribute to declining lung function while testosterone may be protective, and therefore suggesting a contribution of sex hormones to the greater susceptibility of females to rapid FEV1 decline.



Tam A, et al. Sex Differences in Airway Remodeling in a Mouse Model of Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2016

Fattori che aumentano il rischio di BPCO nelle donne

Experimental studies suggest a **biological basis** for these differences that may relate to the effect of **sex hormones** and **anatomical differences** between males and females.

ANATOMICAL : smaller lungs and increased deposition of cigarette smoke in the airways. Since the surface area for deposition is smaller, the concentration of particles per unit of surface area will be greater.

TABLE 1] Anatomic and Physiological Differences Between the Sexes

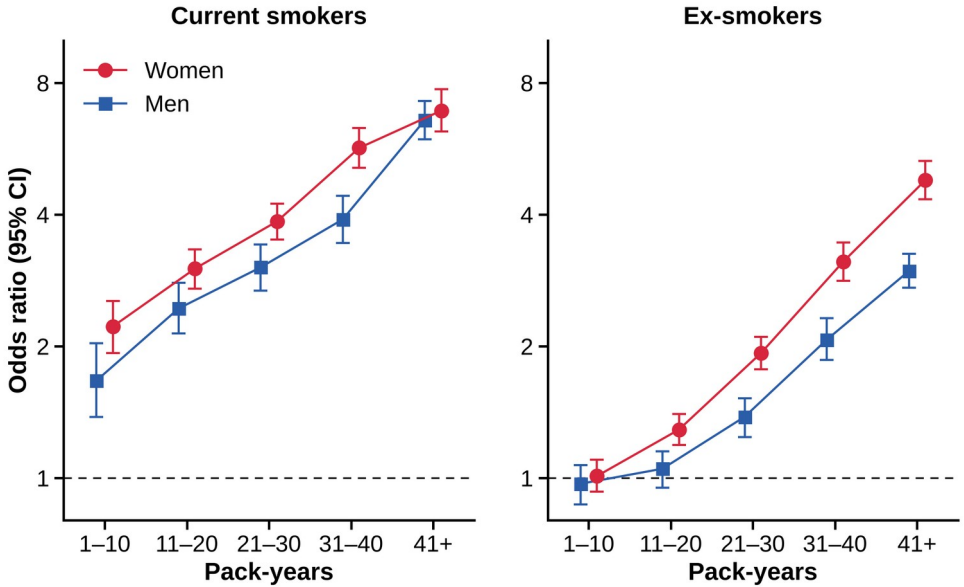
Lower in Women	Higher in Women	Equal in Both Sexes
TLC (corrected for height)	Expiratory flow limitation	Respiratory rate
Tidal volume (corrected for height), minute ventilation (corrected for height)	Resistive work of breathing	Viscoelastic work of breathing
Peak inspiratory flow (corrected for height), peak expiratory flow (corrected for height)	Dyspnea rating (for given minute ventilation)	No. of alveoli per unit volume
Airway size (height matched)	. . .	. . .
Tracheal diameter (matched for TLC)	. . .	. . .
Pharyngeal airway length	. . .	. . .

TLC = total lung capacity.

Sodhi A Chest 2022

Female smokers are at greater risk of airflow obstruction

- UK Biobank: 149,075 women and 100,252 men aged 40–69; airflow obstruction = FEV1/FVC below LLN
- At equal pack-years the risk is higher in women (sex × pack-years interaction P = 1.3×10^{-6} in current and 6.6×10^{-18} in ex-smokers)
- In ex-smokers, risk rises from about 10 pack-years in women vs 19 in men
- *Limitations: cross-sectional design, self-reported smoking; the gap closes at ≥41 pack-years in current smokers; the smaller benefit of quitting in women is not significant (P = 0.098)*



Amaral AFS, et al. Am J Respir Crit Care Med 2017;195:1226–35.

Analysis by sex distinction provides insight into how different risk factors affect the two sexes differently

RISK FACTORS	DISEASE (Feature)	WOMEN	MEN
Cigarette smoke	COPD (Functional decline – More dyspnea)		
	Lung cancer (Mortality)		
Second-hand smoke	COPD (Incidence)		
	Lung cancer (Incidence)		
Indoor pollution	COPD (Incidence)		
	Lung cancer (Incidence)		
Outdoor pollution	Asthma (Lack of control/Exacerbations)		
	Lung cancer (Incidence)		
Low socio-cultural level	COPD (Functional decline)		

whit permission of Meschi C

Sex differences in the characteristics of respiratory diseases related to risk factors
The green box shows the least presence of a pathological feature, the red box shows the greatest presence of a pathological feature.

LoMauro A, Aliverti A. Sex and gender in respiratory physiology. Eur Respir Rev. 2021;30(162):210038. doi:10.1183/16000617.0038-2021

Baldacci S, Maio S, Meschi C, et al. A narrative review of epidemiology and prevention of lung cancer: sex/gender differences? Precision Cancer Medicine. 2022;5(0). doi:10.21037/pcm-21-54

BMJ Open Respiratory Research

Gender, tobacco and chronic obstructive pulmonary disease: analysis of the 2020 National Health Interview Survey

Table 2 Tobacco product use by gender and COPD diagnosis in 2020 NHIS respondents aged ≥40 years

	Men		Women	
	No COPD	COPD diagnosis	No COPD	COPD diagnosis
	Weighted % (or weighted mean)	Weighted % (or weighted mean)	Weighted % (or weighted mean)	Weighted % (or weighted mean)
Cigarette use				
Never	55.5	14.3	66.9	26.4
Former	31.8	53.3	23.0	41.0
Current	12.7	32.4	10.1	32.5
Cigarettes per day*	(15.7)	(21.7)	(12.3)	(17.6)
Pack-year exposure†	(22.0)	(41.8)	(17.4)	(34.8)
Age at onset of smoking†				
<15	7.5	28.0	4.2	19.1
15–24	33.2	54.4	24.7	47.3
≥25	3.2	3.1	3.7	6.8
Other tobacco use				
Ever cigar	41.6	55.6	11.5	20.9
Ever pipe	18.2	35.1	3.9	7.8
Ever e-cigarette	10.3	19.7	8.3	26.4
Ever smokeless	18.9	25.5	1.9	4.6

*Among respondents who currently smoke cigarettes.
†Among respondents who have ever smoked >100 cigarettes in their lifetime.
COPD, chronic obstructive pulmonary disease; NHIS, National Health Interview Survey.

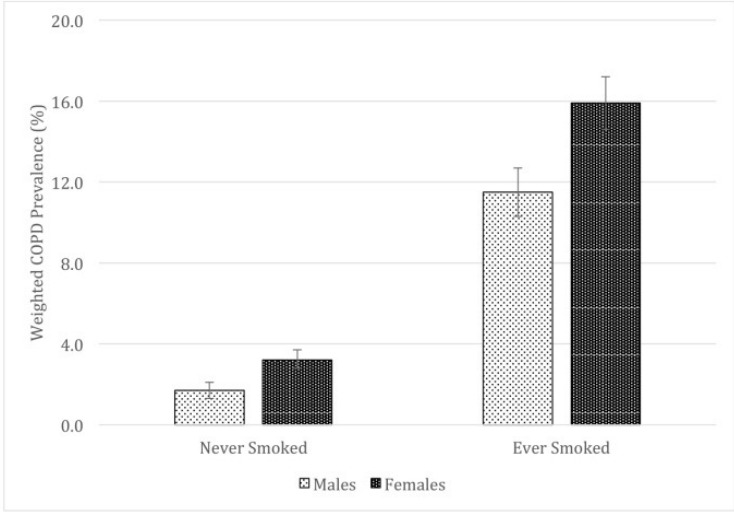


Table 3 Relative risk of COPD by cigarette use and gender among 2020 NHIS respondents aged ≥40 years overall and stratified by smoking status

		Relative risk			
	COPD prevalence	Unadjusted	Adjusted*	95% CI (adjusted)	P value (adjusted)
Male	6.5%	Ref	Ref	Ref	Ref
Female	7.8%	1.21	1.47	1.3 to 1.65	<0.001
Male, never smoked	1.7%	Ref	Ref	Ref	Ref
Female, never smoked	3.2%	1.88	1.63	1.22 to 2.15	<0.001
Male, ever smoked	11.5%	Ref	Ref	Ref	Ref
Female, ever smoked	15.9%	1.38	1.43	1.25 to 1.63	<0.001

*Adjusted for age, race, family poverty ratio, urban/rural county, pack-year cigarette exposure (per 10 pack-years), age started smoking and e-cigarette use. The overall model was further adjusted for smoking status.
COPD, chronic obstructive pulmonary disease; NHIS, National Health Interview Survey.

Steinberg AW, et al. BMJ Open Respir Res. 2025

Implicazioni cliniche delle differenze di genere in BPCO

frontiers in Medicine

MINI REVIEW
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Women's COPD

Maéva Zysman [1,2] and Chantal Raherison-Semjen [2,3]*

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TABLE 1 | Clinical presentation differentiating COPD expression among men and women.

	Women	Men
Lung function decline	++	+
Exacerbations	++	+
Breathlessness	++	+
Cough/sputum	+	++
Quality of life	↓↓	↓
Comorbidities	Anxiety, depression, osteoporosis	Cardiovascular diseases
Underdiagnosis of COPD	+++	++

COPD, Chronic Obstructive Pulmonary Disease. +: a little increased; ++: increased; +++: very increased; ↓: decreased.

Women and COPD: do we need more evidence?

Eur Respir Rev 2019; 28: 180055

Christophe Gut-Gobert[1], Arnaud Cavaillès[2], Adrien Dixmier[3], Stéphanie Guillot[4], Stéphane Jouneau[5,6], Christophe Leroyer[1], Sylvain Marchand-Adam[7], David Marquette[8], Jean-Claude Meurice[9], Nicolas Desvigne[10], Hugues Morel[3], Christine Person-Tacnet[11] and Chantal Raherison[12]

TABLE 1 Studies concerned with quality of life by sex in chronic obstructive pulmonary disease (COPD)

First author [ref.]	Country	Quality of life (tools used)	COPD stage	Females/males n	Results
De Torres [82]	Spain, single-centre	SGRQ	GOLD II, III	73/73	Quality of life more impaired in females Dyspnoea and arterial saturation: only factors associated with the SGRQ score, unlike males for whom exercise capacity, dyspnoea and comorbidities are found
Katsura [83]	Japan, single-centre	SGRQ–SF-36, Philadelphia Geriatric Center morale scale	GOLD II	39/117	SGRQ: highest score for activity, impact and total score among females compared with males SF-36 highest score on perceived health and health compared with 1 year ago for females/males
Kaptein [84]	Netherlands	Telephone or e-mail questionnaire: intimate physical contact scale (IPCS) or Respiratory Experiences with Sexuality Profiles (RESP)	COPD, asthma	55 patients (of whom 10 females and 15 males with COPD)	Reduced sexual activity in males and deterioration in quality of sex life More seldom occurrence in women
Rodríguez-González Moro [85]	Spain	SF-12 (used during consultations with pulmonologists and treating physician)	GOLD II, III	1786/1661	Quality of life more impaired in females, particularly concerning the mental and physical aspects of SF-12
Raherison [1]	France, multicentre	SGRQ, HADS, Q-MAT (for active smokers)	GOLD II, III, IV	247/183	Poorer anxiety and quality of life scores in females even though lung function impairment was less severe than in males

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Mini-Review

Sex and Gender Differences in Lung Cancer and Chronic Obstructive Lung Disease

Jill M. Siegfried,

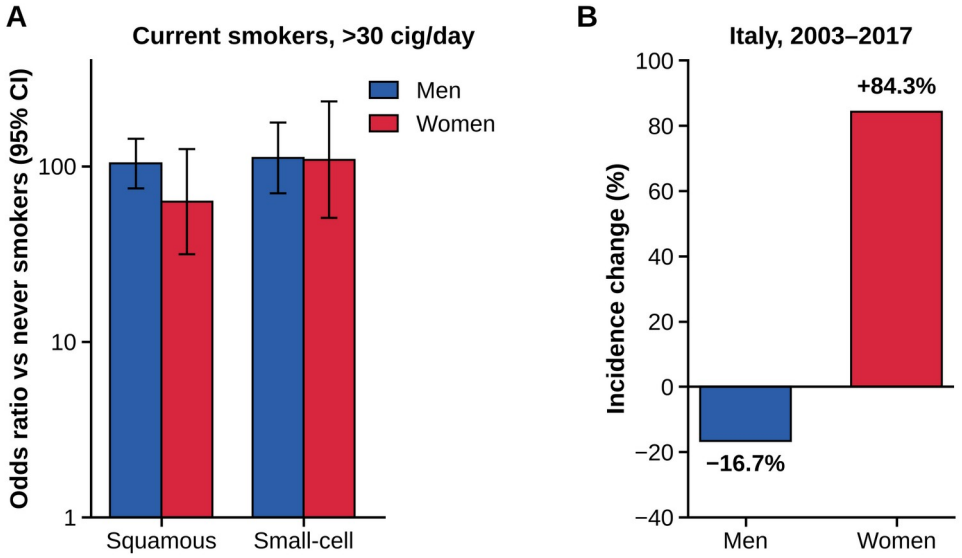
Table 1. Major sex and gender differences in lung cancer and COPD

Disease	Age at diagnosis	Tobacco exposure	Presentation	Outcomes
Lung Cancer	Diagnosis at an earlier average age in women (7) Higher incidence at age < 50 years in women (7) Increased incidence rate in premenopausal women (14)	20%-25% lower average pack-years at diagnosis in women (11, 12) Diagnosis in never smokers higher in women (7, 8, 16, 17)	Adenocarcinoma more frequent in women (18) Mutational patterns differ between women and men (19-21)	Overall survival better in women than men (22-24) Better response to chemotherapy in women (24) Women more likely to benefit from therapies targeting mutations found in never smokers (24) Premenopausal women have shorter survival than either postmenopausal women or men (25) Women diagnosed prior to age 45 have more aggressive disease (26)
COPD	Diagnosis at an earlier average age in women (9, 10) Higher incidence at age < 50 years in women (3, 9, 10)	20%-25% lower average pack-years at diagnosis in women (13, 15) Diagnosis in never smokers higher in women (3, 15)	Airway obstruction more likely than emphysema in women (27-30) Bronchitis more prominent in women (27, 28) Comorbidities such as depression and dyspnea more prominent in women, heart disease more prominent in men (4, 31, 32)	More rapid disease progression in women (2-4, 10) Risk of death from COPD higher for women than men with same smoking history (31-33)

The higher prevalence of COPD and lung cancer in females despite females smoking fewer cigarettes than males suggests that ***females may be more susceptible to the effects of cigarette smoke***. The contribution of non-cigarette risk factors to the global burden of COPD and lung cancer is large and growing. **The burden of indoor air pollutant exposure** such as biomass fuel falls disproportionately on females and consequently some studies show that **females account for up to two thirds of non-smoking COPD and lung cancer cases.**

Lung cancer: smoking risk by histotype and sex

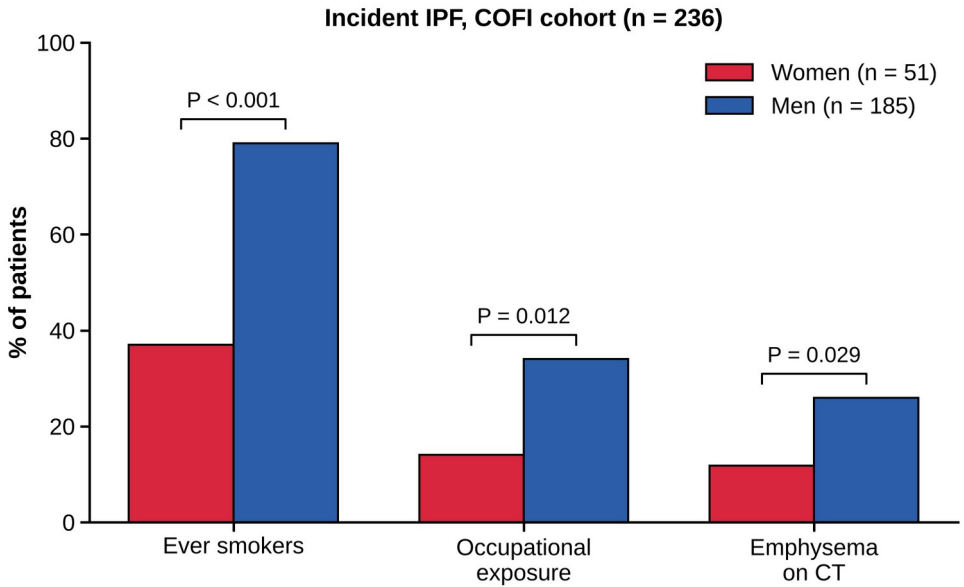
- Steepest dose–response for small-cell and squamous carcinoma (OR > 100 in heavy male smokers); adenocarcinoma lowest, yet the most frequent subtype in women and never smokers [1]
- No excess susceptibility in women: at equal dose HR 0.9 (0.8–0.9) vs men among current smokers (NIH-AARP, 463,837 adults); among never smokers HR 1.3 for women [2]
- Italy 2003–2017: incidence −16.7% in men, +84.3% in women [3]; in the EU, female mortality is now levelling at about 12.5/100,000 [4]
- *The rising burden in women reflects the female smoking epidemic, not greater biological susceptibility*



1. Pesch B, Kendzia B, Gustavsson P, et al. Int J Cancer 2012;131:1210–9.; 2. Freedman ND, Leitzmann MF, Hollenbeck AR, et al. Lancet Oncol 2008;9:649–56.; 3. AIOM, AIRTUM, et al. I numeri del cancro in Italia 2025. Roma; 2025.; 4. Santucci C, et al. Ann Oncol 2026;37:555–64.

Idiopathic pulmonary fibrosis: smoking and sex

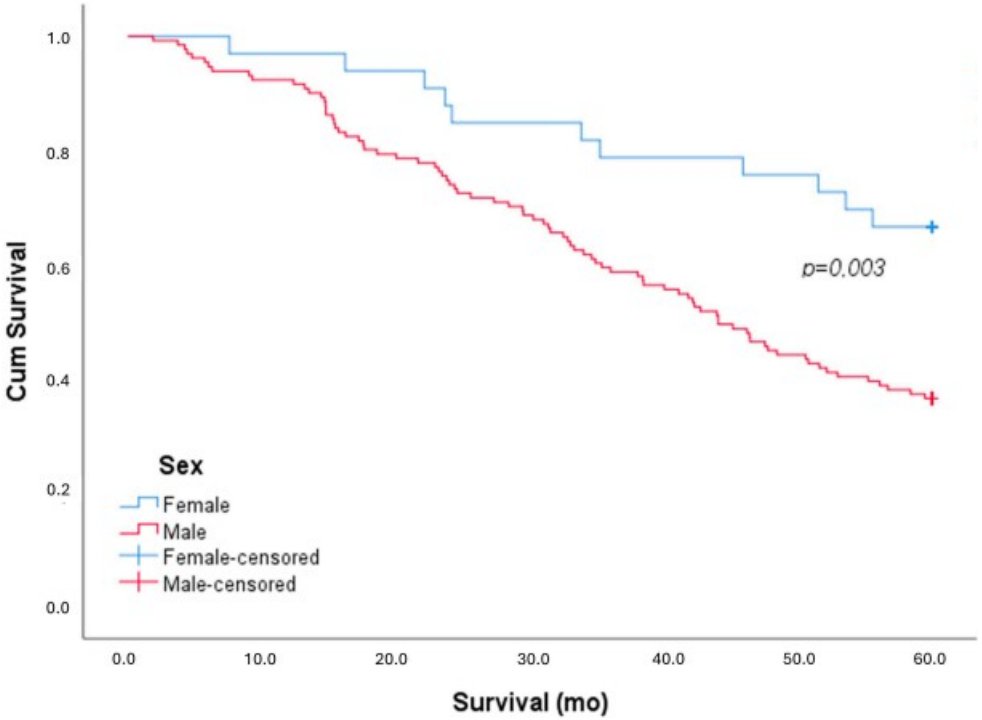
- Smoking is the main environmental risk factor: pooled OR 1.58 (1.27–1.97) for ever-smoking [1]; UK Biobank HR 2.12 (1.81–2.47), dose-dependent [2]
- IPF is male-predominant (78% men in the COFI cohort); women are mostly never smokers (63% vs 21%) [3]
- CPFE, the most smoking-related fibrotic phenotype: 60 of 61 patients were men, all smokers (mean 46 pack-years) [4]
- Adjusted survival does not differ by sex (HR women 0.85, 95% CI 0.58–1.25) [3]
- *Unlike COPD, no data show greater susceptibility in women; the male excess is plausibly driven by exposure*



1. Taskar VS, Coultas DB. Proc Am Thorac Soc 2006;3:293–8.; 2. Bellou V, Belbasis L, Evangelou E. Chest 2021;160:983–93.; 3. Sesé L, et al. Front Med (Lausanne) 2021;8:713698.; 4. Cottin V, et al. Eur Respir J 2005;26:586–93.

Gender Differences Are a Leading Factor in 5-Year Survival of Patients with Idiopathic Pulmonary Fibrosis over Antifibrotic Therapy Reduction

Pasquale Tondo [1,2,†], Giulia Scioscia [1,2,†], Cosimo C. De Pace [3], Fabiola Murgolo [1], Federica Maci [4], Giulia M. Stella [5,6], Dalila Pescatore [1], Maria Pia Foschino Barbaro [1] and Donato Lacedonia [1,2,*]



Sex, male	n = 131 (80%)
Exitus	M 83 (63%) F 11 (33%) P=0.002
Survival (mo)	M 40.8 ± 19.2 F 51.2 ± 15.6 P=0.005

Smoking habits OR 2.39 [95% CI 1.24–4.62]; p = 0.009
Male sex OR 3.36 [95% CI 1.5–7.5]; p = 0.003

Take-home messages

- Le differenze di genere nelle patologie respiratorie affondano le radici già dall'età embrionale.
- Tra i fattori di rischio nella donna, la maggiore suscettibilità al fumo di sigaretta ha un ruolo importante per quanto riguarda le diagnosi di BPCO e tumore nel polmone.
- Le differenze di genere nel tabagismo non sono solo quantitative, ma riguardano motivazioni, risposta psicologica, astinenza, efficacia del trattamento.
- Le donne possono avere maggiore difficoltà nella cessazione permanente se non ricevono un supporto adeguato.
- Le strategie anti-fumo devono incorporare la prospettiva di genere per essere efficaci e giuste.
- ***Proposte operative***: ricerca con dati aggiornati, disaggregati per genere, soprattutto su fasce d'età più giovani; campagne anti-fumo dedicate, supporti personalizzati, monitoraggio differenziato.

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Putting gender on the agenda

Biomedical research continues to use many more male subjects than females in both animal studies and human clinical trials. The unintended effect is to short-change women's health care.

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...grazie per l'attenzione!