



## *I percorsi per affrontare la genitorialità in Fibrosi Cistica*

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SCDO Pneumologia

Fibrosi Cistica- settore adulti .



11° Forum italiano sulla Fibrosi Cistica

Le nuove sfide per la comunità FC  
Riflessioni sui cambiamenti nelle cure e nel vissuto con la malattia

SAVE - the - DATE

forum 2023  
7 | 8 ottobre 2023 Parma | streaming on fibrosicistica.it  
Hotel Parma e Congressi



LIFC  
Lega Italiana  
Fibrosi Cistica

Parma 8 ottobre 2023

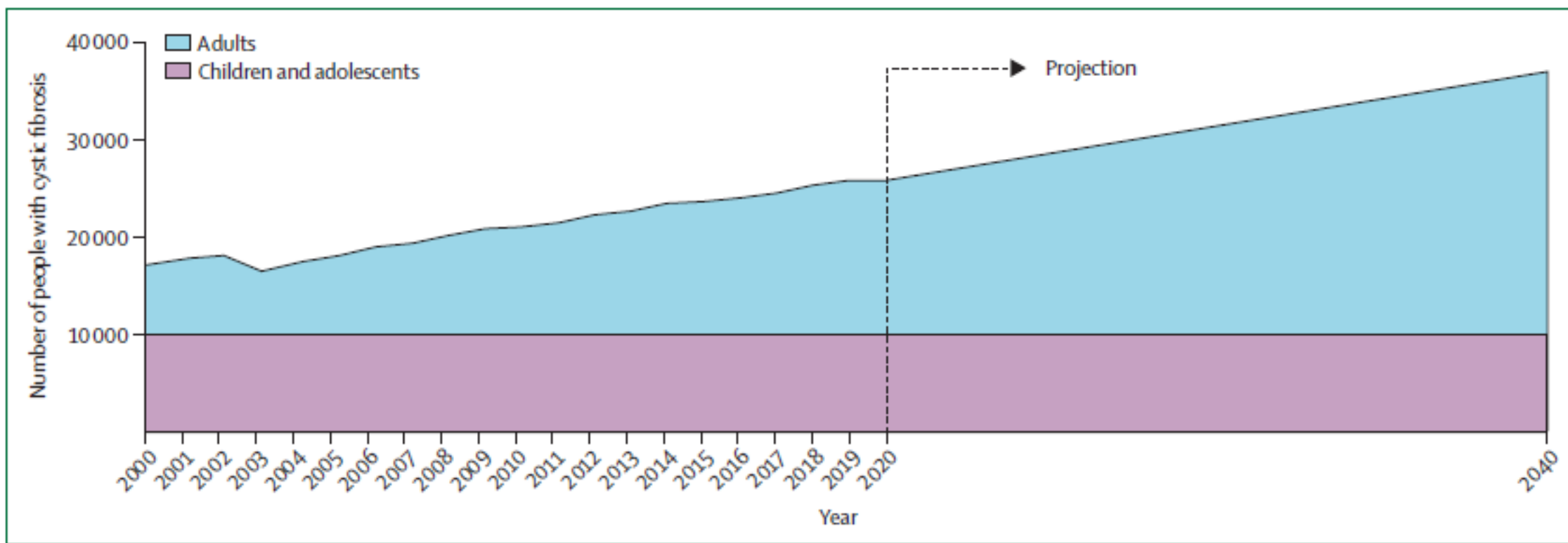
## *disclosure*

- ✧ Site PI on clinical studies for Vertex, Zambon, Novartis, Chiesi
- ✧ Participation in advisory boards for Vertex, Novartis, Chiesi



# Understanding and addressing the needs of people with cystic fibrosis in the era of CFTR modulator therapy

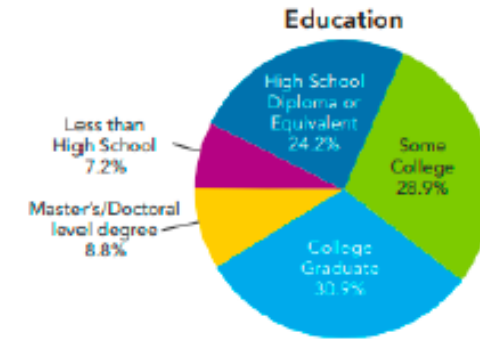
Lancet Respir Med 2023;  
11: 916-31



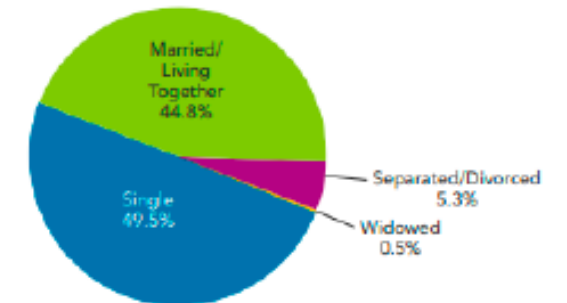
Change in the proportion of children (<18 years) and adults (≥18 years) in the cystic fibrosis population in the USA, based on data from the Cystic Fibrosis Foundation Patient Registry Annual Data Report 2021,<sup>24</sup> with projected change up to 2040. Data presented at the 2022 North American Cystic Fibrosis Conference, Plenary 3.



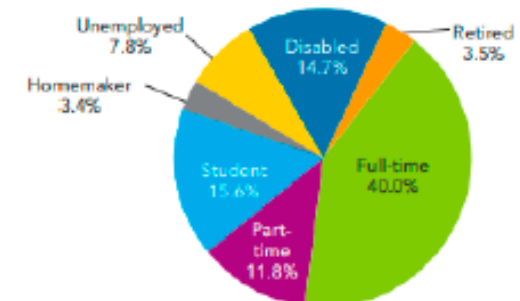
### Socioeconomic Characteristics of Adults 18 Years and Older with CF, 2021



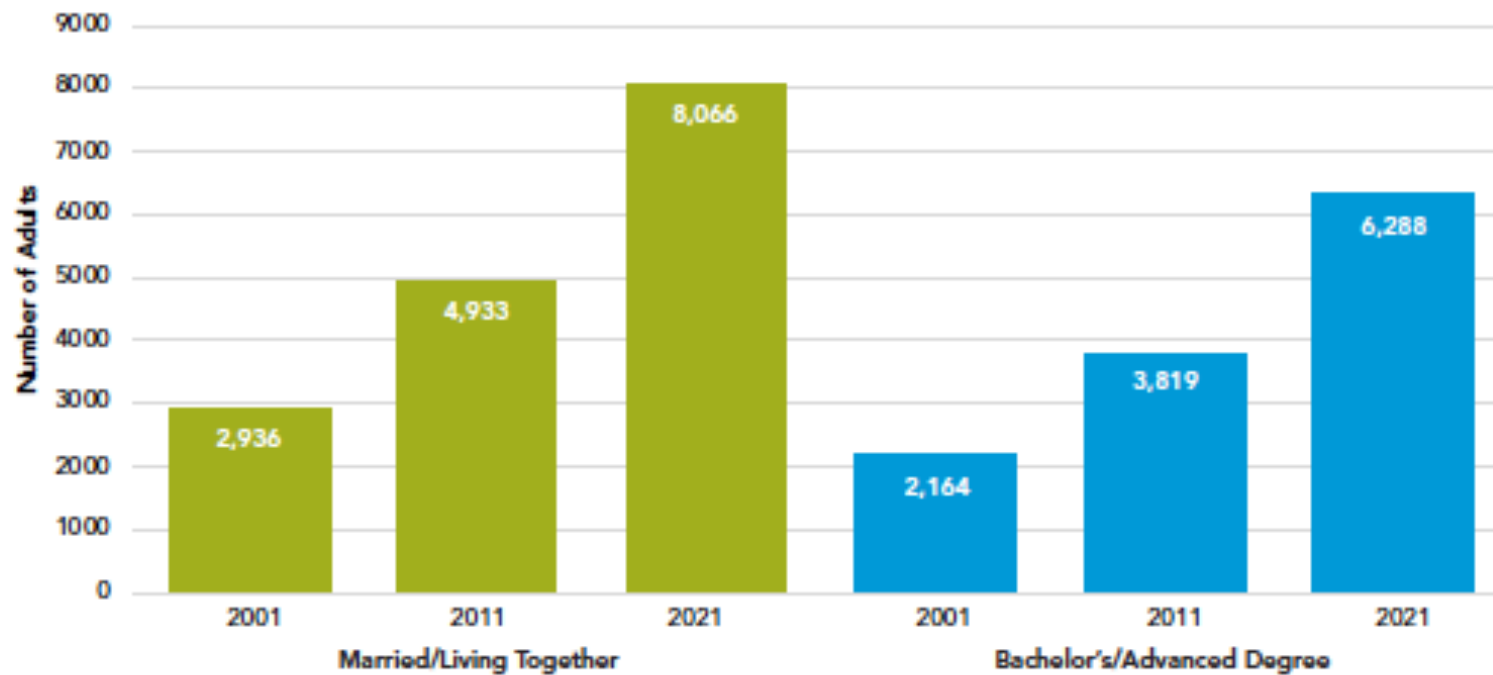
#### Marital Status



#### Employment



### Characteristics of Adults with CF, 2001, 2011, 2021



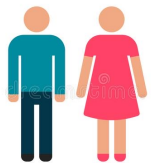
# Reproductive Health (ReH)

- Reproductive health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity, in all matters relating to the reproductive system and to its functions and processes.
- Reproductive health implies that people are able to have a *satisfying and safe sex life* and that they **have the capability to reproduce and the freedom to decide if, when and how often to do so.**

- Both man and female with CF face many sexual and reproductive health concerns



OMS



# Sexual and reproductive health in cystic fibrosis: a life-course perspective

Katherine B Frayman, Susan M Sawyer

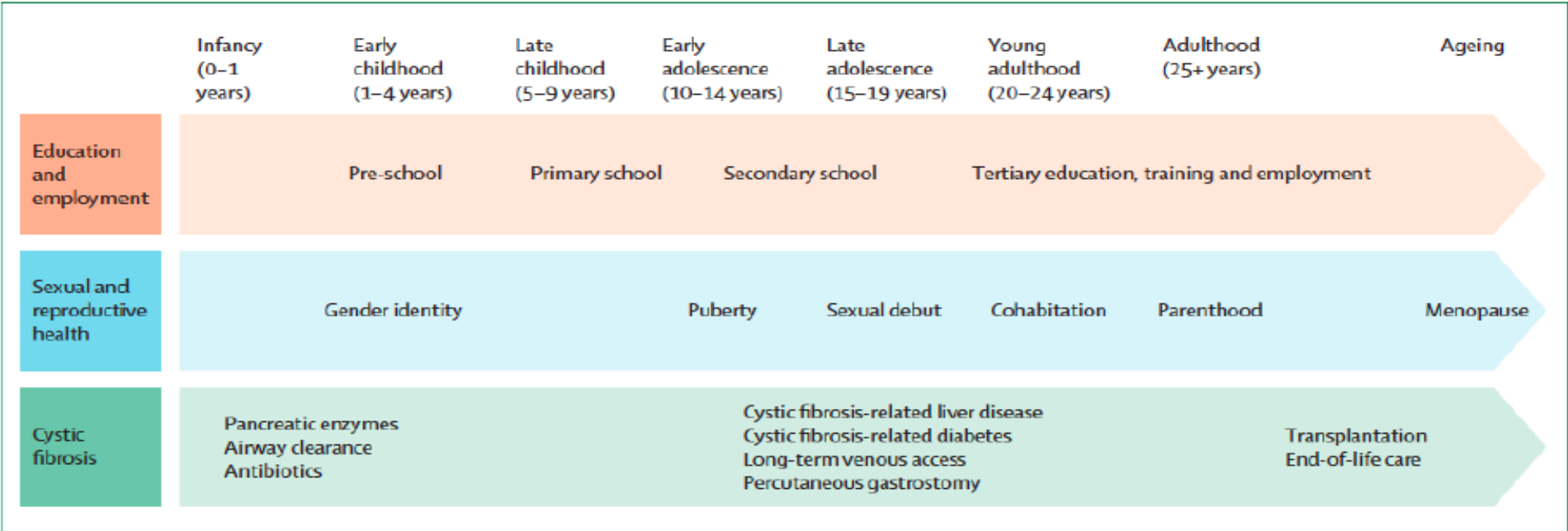


Figure 1: Developmental milestones

# Optimizing sexual and reproductive health across the lifespan in people with cystic fibrosis

*Pediatric Pulmonology*. 2022;57:S89–S100.

proactive approach

**TABLE 2** Sexual and reproductive health model of health assessment over the lifespan for CF care providers and collaborating care providers

Adolescence	Adulthood	Late adulthood
Assess pubertal development, hormones, and hypogonadism		
Openly discuss gender identity and sexual preferences		
Discuss fertility and contraception		
Counsel on STI prevention		
	Discuss sexual functioning; address any concerns	
	Discuss parenthood and reproductive options	
	Evaluate urinary incontinence	
		Evaluate peri-menopause symptoms

Abbreviation: STI, sexually transmitted infection.



# Cystic Fibrosis supporting your decisions

Can I have a baby?

What if my partner is a carrier of CF?

Will pregnancy affect my partner's health?

Will our baby have CF?

What if I need antibiotics during pregnancy?

Can I be a biological dad?

I've had a transplant, is it safe to have a baby?

Should I have a...



[cysticfibrosis.org.uk](http://cysticfibrosis.org.uk)

Thinking of starting a family?

2016





# *genitorialità...percorso... prospettiva*

**la consapevolezza  
di se'**

**la consapevolezza  
del proprio stato di  
salute**

**fertilità ed FC per  
l'uomo e la donna  
affetti**

**l'incontro con l'altro**

**la disclosure sulla  
propria malattia**

**la progettualità**

**La FC si trasmette**

**I portatori sani di  
mutazione del  
gene CFTR**

**la genetica della  
coppia – il rischio  
di trasmissione**

**possibilità di genitorialità biologica**

*percorsi # per l'uomo e la donna*

**gravidanza e FC**

**la pianificazione**

**procreazione  
spontanea**

**procreazione  
assistita**

**L'essere genitori... con la FC**

**saper delegare – rete di aiuto**



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Review Article



## How do cystic fibrosis patients experience parenthood? A systematic review

Journal of Health Psychology  
2021, Vol. 26(1) 60–81  
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DOI: 10.1177/1359105320916539  
[journals.sagepub.com/home/hpq](https://journals.sagepub.com/home/hpq)



Anne Jacob<sup>1</sup> , Jonathan Journiac<sup>1</sup>, Lotte Fischer<sup>1,2</sup>,  
Lisa Astrologo<sup>3</sup> and Cécile Flahault<sup>1,4,5</sup>

...Parenthood requires an important **reorganisation of daily life in order to remain capable of self and childcare.**

Cystic fibrosis patients have a positive outlook on parenthood. ...



# Sexual and Reproductive Health (SRH) in Male wCF



# SRH in Male wCF

- 98% infertile because of surgically uncorrectable obstructive azospermia related to CBAVD
- 2% fertile
- Men with CF do produce sperm and testicular histology is normal

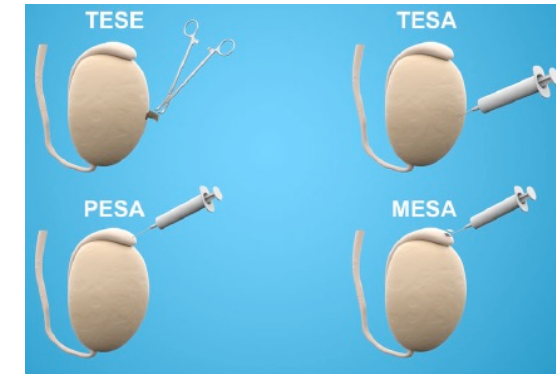
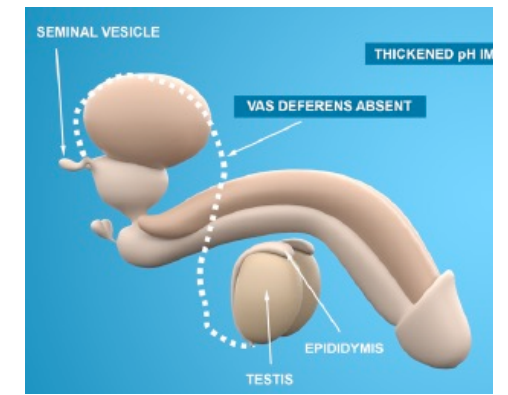
- ✓ Routine semen analysis recommended for all in late adolescence  
(*low volume acid ejaculate, azospermia*)

If man choose to pursue biologic parenthood -after confirmation of infertility- sperm extraction (possibility of semen cryopreservation), and subsequent ICSI and IVF (PMA).

. MESA/E or TESA/E with ICSI has been reported to result in pregnancy rates of 30.35% per cycle.

Hormonal ovarian stimulation and ovocytes retrieval needed in female partner  
(risk for Ovarian Hyperstimulation Syndrome)

Success rate depends also on maternal age (<35 yrs success rate of a live birth 46-48%)



J Cystic Fibr 2019; 18:S105-S100  
J Cystic Fibr 2022; 21: 657-661  
Curr Opin Pulm Med 2020; 26:685-695



# CFTR modulators and fertility in Male wCF



No reports of improved fertility in Male wCF with CFTR modulators

Pediatr Pulmonol  
2022; 57;S75-S88

Case reports describe self resolving testicular pain in 7 pts after starting ETI therapy

J Cystic Fibr  
2020;19; e39-e41

In G551D homozygous ferret exposed in utero throughout pregnancy to ivacaftor has been described rescue of the vas deferens and epididymis

SCI Trans Med  
2019; 11 eeau7531

The impact of modulators on fertility rescue or prevention non evaluated in human

Pediatr Pulmonol  
2022; 57;S75-S88

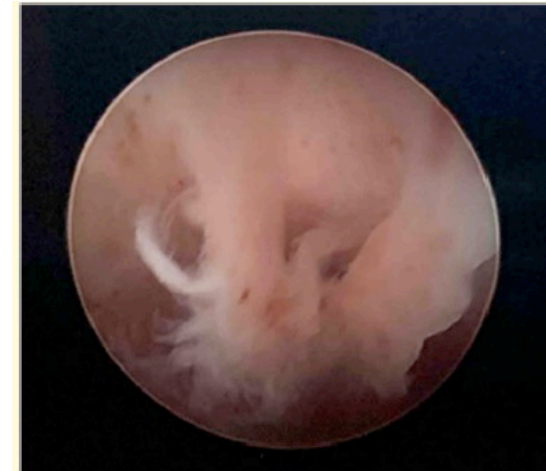
Males who wish to completely avoid exposure of sperm to CFTR modulators must discontinue modulators for the life of an average sperm, approximately 80 days before semen extraction

Pediatr Pulmonol  
2022; 57;S75-S88

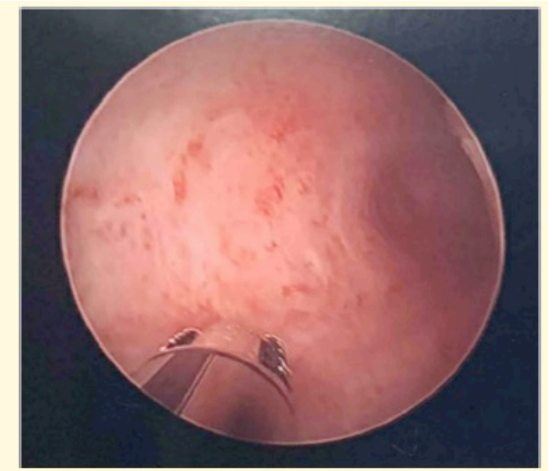
# SRH in Female wCF



- ✓ high proportion of FwCF experience **multifactorial subfertility/infertility** (35% vs 5.15% in general population)
  - delayed puberty/increased anovulatory cycles/ reduced ovarian reserve
  - nutritional deficiencies
  - thick acidic female reproductive tract mucus (physical barrier to sperm entrance into the uterus and impairment sperm capacitation)
  -
- ✓ **CFTR modulators improve FwCF fertility** → discuss the potential role of modulators on fertility in every FwCF of reproductive age before they begin treatment
- increasing number of pregnancies in last years
- contraception's counseling



(A)



(B)

# La gravidanza nella donna con FC

Costruzione di un progetto operativo individualizzato per una adeguata pianificazione

Il bilancio sulla propria salute (FEV1%, PAP, stato nutrizionale, diabete)  
"criteri di rischio"

La stabilità clinica

L'ottimizzazione del trattamento

L'adeguamento terapeutico



Intensificazione del follow up e delle cure

L'esclusione-correzione di complicanze

Equipe multidisciplinare esperta



# Reproductive Counseling and Care in Cystic Fibrosis: A Multidisciplinary Approach for a New Therapeutic Era

Julie McGlynn<sup>1</sup>, Joan K. DeCelie-Germana<sup>2</sup>, Catherine Kier<sup>3</sup>  and Elinor Langfelder-Schwind<sup>4,\*</sup> 

*Life* 2023, 13, 1545



Clinical support and care team for a pregnant woman with CF.

## Medical and obstetric complications among pregnant women with cystic fibrosis

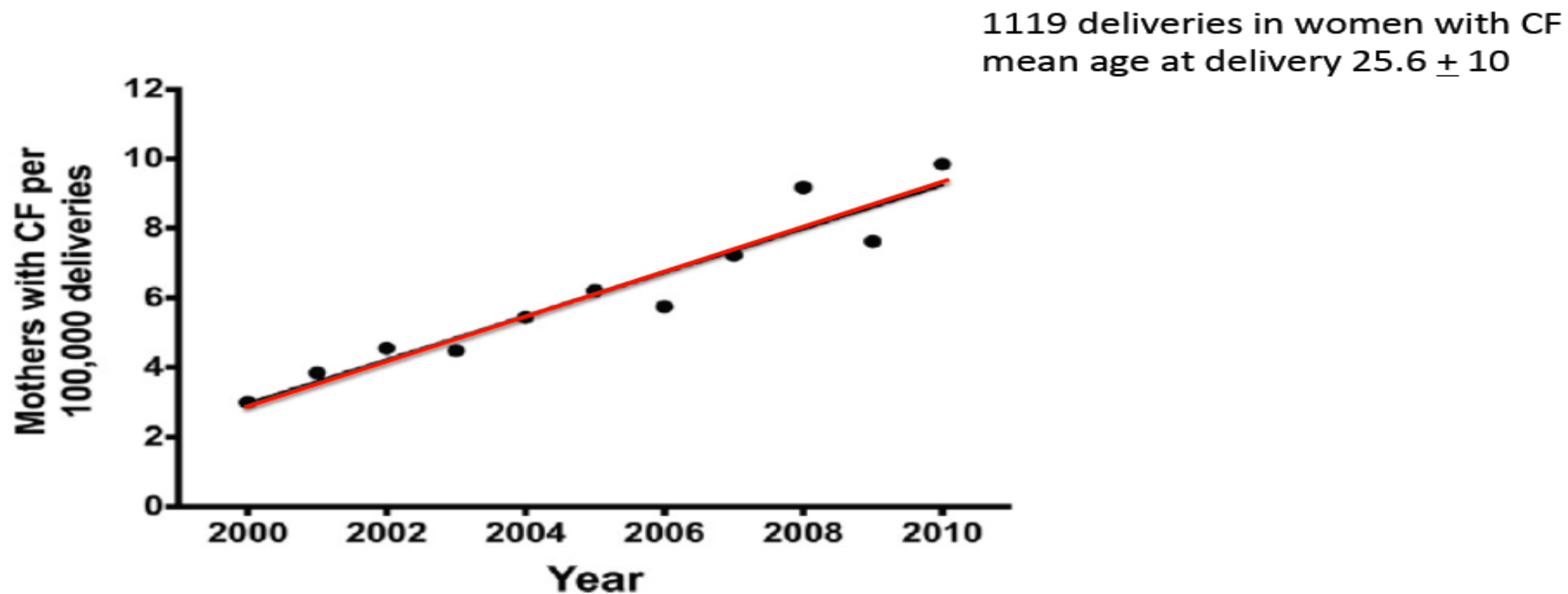




TABLE 4

**Obstetric events present at time of delivery among women with CF**

Condition, n (%) <sup>a</sup>	CF n = 1119	No CF n = 12,627,627	OR (95% CI)	P value
Cesarean delivery	351 (31.4)	4,041,005 (32.0)	1.0 (0.9–1.1)	.67
Operative vaginal delivery	100 (8.9)	792,143 (6.3)	1.5 (1.2–1.8)	.0002
Multiple gestation	39 (3.5)	267,193 (2.1)	1.7 (1.2–2.3)	.0013
GDM	148 (13.2)	714,940 (5.7)	2.5 (2.1–3.0)	< .0001
Preeclampsia, eclampsia, gest HTN	76 (6.8)	931,154 (7.4)	0.9 (0.7–1.1)	.48
Preterm labor	209 (18.7)	1,051,494 (8.3)	2.5 (2.2–2.9)	< .0001
Abruption	16 (1.4)	136,053 (1.1)	1.3 (0.8–2.2)	.22
Fetal growth restriction	29 (2.6)	271,882 (2.2)	1.2 (0.8–1.8)	.26
Postpartum hemorrhage	15 (1.3)	321,959 (2.5)	0.5 (0.3–0.9)	.012
Chorioamnionitis	36 (3.2)	323,531 (2.6)	1.3 (0.9–1.8)	.17

CF, cystic fibrosis; CI, confidence interval; GDM, gestational diabetes; gest HTN, gestational hypertension; NIS, Nationwide Inpatient Sample; OR, odds ratio.

<sup>a</sup> The NIS does not allow reporting the number of cases when the cell frequency is less than or equal to 10. There were 10 or fewer cases of fetal demise and placenta previa among women with CF.

Patel. Cystic fibrosis in pregnancy. *Am J Obstet Gynecol* 2015.



TABLE 3

**Medical events present at time of delivery among women with CF**

Condition, n (%) <sup>a</sup>	CF n = 1119	No CF n = 12,627,627	OR (95% CI)	P value
Death	11 (1.0)	921 (0.007)	125 (67–233)	< .0001
Mechanical ventilation	25 (2.2)	9003 (0.07)	31.9 (21.4–47.5)	< .0001
Transfusion	20 (1.8)	131,684 (1.0)	1.7 (1.1–2.7)	.01
Pneumonia	75 (6.7)	13,150 (0.1)	68.7 (54.3–86.9)	< .0001
Acute respiratory failure	14 (1.2)	5450 (0.04)	29.6 (16.7–48.0)	< .0001
Acute renal failure	11 (1.0)	7075 (0.06)	16.4 (8.9–30.4)	< .0001
Composite CF outcome <sup>b</sup>	95 (8.5)	33,275 (0.26)	35.3 (28.6–43.5)	< .0001

CF, cystic fibrosis; CI, confidence interval; NIS, Nationwide Inpatient Sample; OR, odds ratio.

<sup>a</sup> The NIS does not allow for... fewer cases of myocardial infarction, pulmonary embolism, influenza among women with CF, sepsis, pneumonia, acute renal failure.

Patel. Cystic fibrosis in pregnancy.

**CONCLUSION:** Pregnant women with CF are more likely to die, require mechanical ventilation, and have infectious complications compared with women without CF, although the absolute risks are low and these events are relatively rare.

# Baseline Cystic fibrosis disease severity has an adverse impact on pregnancy and infant outcomes, but does not impact disease progression<sup>☆</sup>

Malena Cohen-Cymerknoh<sup>a,1,\*</sup>, Bar Gindi Reiss<sup>b,1</sup>, Joel Reiter<sup>a,1</sup>, Noah Lechtzin<sup>c</sup>, Joel Melo<sup>d</sup>, Gema Pérez<sup>d</sup>, Hannah Blau<sup>e</sup>, Huda Mussaffi<sup>e</sup>, Hagit Levine<sup>e</sup>, Lea Bentur<sup>f</sup>, Michal Gur<sup>f</sup>, Galit Livnat<sup>g</sup>, Javier Perez Miranda<sup>h</sup>, Eva Polverino<sup>h</sup>, Francesco Blasi<sup>i</sup>, Stefano Aliberti<sup>i</sup>, Micha Aviram<sup>j</sup>, Inbal Golan Tripto<sup>j</sup>, Elie Picard<sup>k</sup>, Michal Novoselsky<sup>l</sup>, Hagai Amsalem<sup>l</sup>, Drorith Hochner Celnikier<sup>l</sup>, Eitan Kerem<sup>a</sup>, Michal Shteinberg<sup>g</sup>

**Unplanned pregnancies following the  
introduction of  
elexacaftor/tezacaftor/ivacaftor therapy  
in women with Cystic Fibrosis**

*Archives of Gynecology and Obstetrics.* 2023; 308:1657-9

**Association between unplanned pregnancies  
and maternal exacerbations in Cystic Fibrosis**

*J Cystic Fibrosis.* 2023. doi.org/10.1016/j.jcf.2023.03.020

PEX + 26% in the unplanned group  
PEX – 16% in the planned group

## Impact of CFTR modulators on Female wCF fertility and pregnancy

### The Impact of Highly Effective Cystic Fibrosis Transmembrane Conductance Regulator Modulators on the Health of Female Subjects With CF

Accepted for publication January 31, 2023  
<https://doi.org/10.1016/j.clinthera.2023.01.016>

Clinical Therapeutics

the potential effect of HEMT **on fertility** should be discussed with every fwCF of reproductive age before they begin therapy

tremendous general and respiratory health benefits with HEMT  
occurrence of «withdrawal syndrome»

*ETI passes the placenta* (no teratogenicity or fetal toxicity in animal reproduction models) ETI concentration in cord blood are similar to those of maternal serum

J Pers Med 2012;11:418

-ETI during early pregnancy →

J Cyst Fibros 2020;19:521-526

-ETI throughout pregnancy →

Am J Obst Gynecol 2022;226:S393-4

-ETI during breastfeeding →

J Cyst Fibros 2020;19:521-526

**neonatal transient transaminitis**

**neonatal cataracts**

-CF fetus exposed to ETI during pregnancy and lactation → neonatal negative sweat test and pancreatic sufficiency at birth  
→ resolution of meconius ileo



# CFTR modulators in pregnancy

Modulator	Pregnancies/Modulator Used throughout Preg, (n)	Miscarriage	Prematurity	Fetal Complications		Maternal Complications	
				Related to Modulator*	Unknown/Not Related	Related to Modulator*	Unknown/Not Related
IVA	31/15	2	-	0	3	0	16
LUM/IVA	26/16	0	4	0	8	2	17
TEZ/IVA	7/5	1	-	0	2	0	5
ETI**	47/23	4	5	0	20 <sup>a</sup>	1	30 <sup>b</sup>

fetal multiple severe malformation  
forceps delivery  
intrauterine growth retardation  
large for gestational age  
Trisomy 16 with spontaneous miscarriage

cholestasis  
cholecystitis  
cholecystectomy

gestational diabetes  
gestational hypertension  
hemoptysis preeclampsia  
post partum depression  
seizures  
nephrolithiasis  
wound infection  
neck pain after epidural  
headache after epidural

## expert recommendation on CFTR modulators in pregnancy

### ERS/TSANZ Task Force Statement on the management of reproduction and pregnancy in women with airways diseases

*Eur Respir J* 2020; 55:

CFTR modulators	Pre/T1	T2/T3	Labour	Breastfeeding	Observations/considerations
Ivacaftor (B3) [-] Lumacaftor and ivacaftor (B3) [-] Tezacaftor and ivacaftor (B3) [-] Elexacaftor and tezacaftor and ivacaftor (B3) [-]		Probably safe			Limited data in humans [56–58]. No evidence of toxicity in animals at usual doses. Modulators are present in breast milk, although potential effects on the fetus are unknown. <u>Maternal benefit</u> may outweigh potential risk during pregnancy and/or breastfeeding, although exact risks are unknown.

### The Impact of Highly Effective Cystic Fibrosis Transmembrane Conductance Regulator Modulators on the Health of Female Subjects With CF

the decision to continue versus discontinue HEMT during pregnancy and lactation warrants a clear and comprehensive conversation between **provider and mother/partner** with ***informed shared decision-making***.

data support the need to consider infant monitoring with ***routine -liver function testing and -ophthalmologic examinations for cataracts***.

... careful in neonatal testing for CF

Clinical Therapeutics 2023

### Pregnancy in cystic fibrosis: Review of the literature and expert recommendations

Most common therapies used in the chronic treatment of CF.

Medication	Route of Administration	Considerations	Use in Pregnancy	Use in Lactation
CFTR modulators (ivacaftor, tezacaftor/ivacaftor, lumacaftor/ ivacaftor, elexacaftor/tezacaftor/ivacaftor)	Oral	No harm observed of individual components given in animal models, but human data is limited	Yes, if necessary for <u>mother's health</u>	Yes, if necessary for <u>mother's health</u>

# Impact of CFTR modulators on pregnancy and infant born to mothers with CF

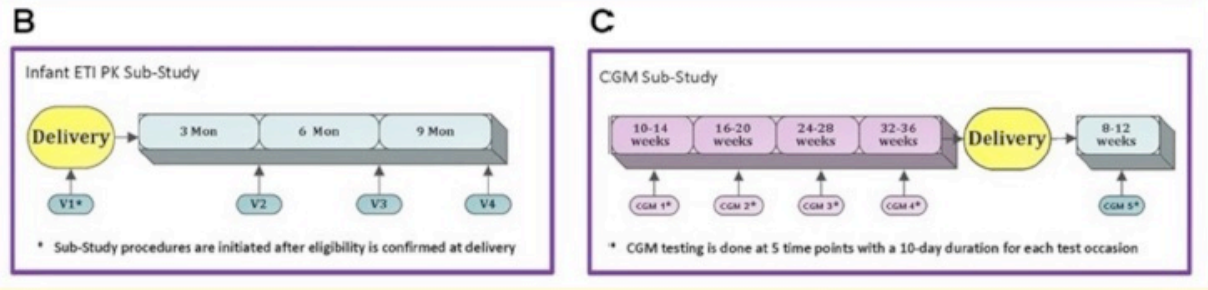
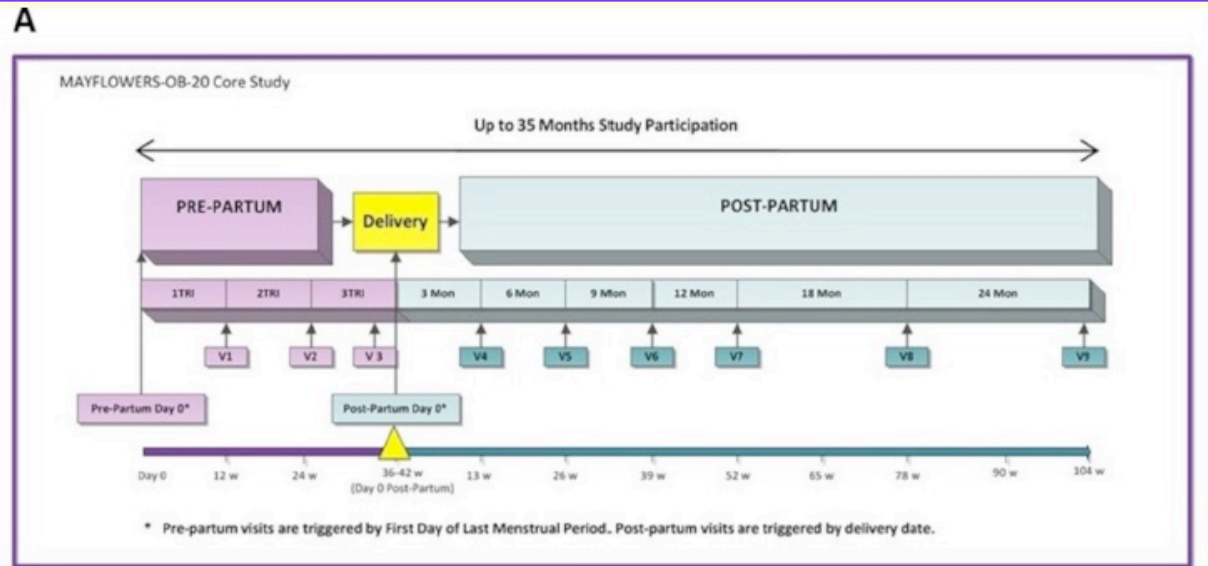
Open Access

Cystic fibrosis

BMJ Open  
Respiratory  
Research

## Prospectively evaluating maternal and fetal outcomes in the era of CFTR modulators: the MAYFLOWERS observational clinical trial study design

**longitudinal prospective** multicentre observational study  
40 US TDN CF centres  
CFF sponsored  
**2021-2025**  
aims to enroll 285 fwCF



### WHAT THIS STUDY ADDS

⇒ The Maternal and Fetal Outcomes in the Era of Modulators (MAYFLOWERS) is the first prospective study of pregnancy in CF. It will also provide the first prospectively collected data on infants born to mothers with CF, and include outcome data for mothers and infants for 2 years following pregnancy.

sub studies: infant ETI PK and maternal Continuous Glucose Monitoring

## FAMILY-BUILDING OPTIONS



## When a Parent has CF: Explaining Your Illness to Your Child



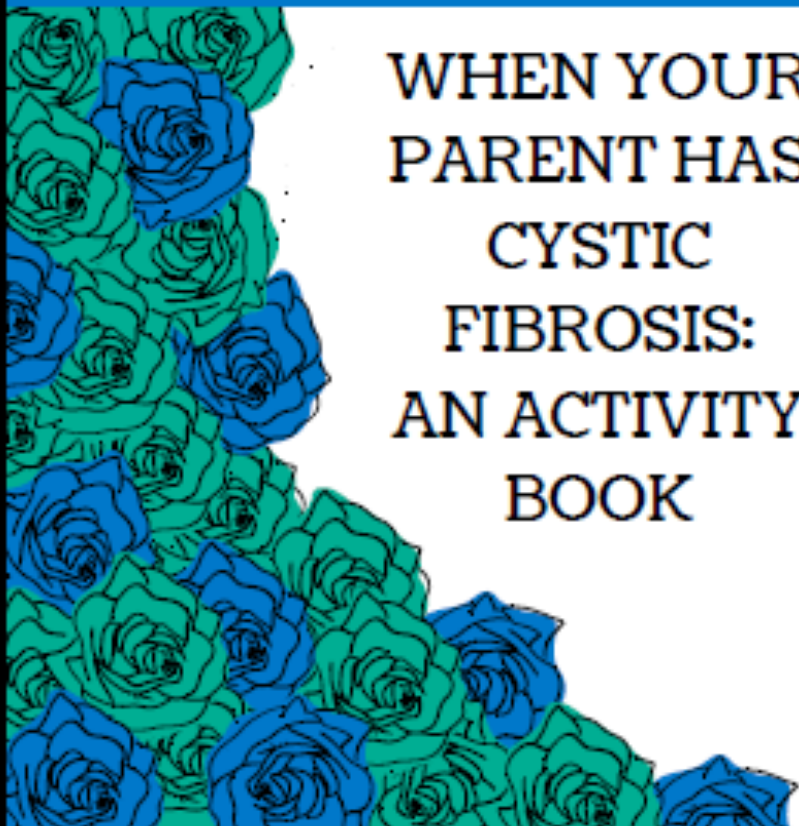
# PARENTING WHEN YOU HAVE CYSTIC FIBROSIS

A resource to help you succeed while being a parent and  
living with cystic fibrosis.



# KEEPIN' IT ROSY

## WHEN YOUR PARENT HAS CYSTIC FIBROSIS: AN ACTIVITY BOOK



## VISUAL SCHEDULES

Parent Instructions: Visual Schedules, or schedules in general, can help children feel more comfortable and safe by helping them know what to expect.

Some example situations where visual schedules might help young children are:

- When helping your children understand the amount of time/effort that is needed to dedicate to your medications and what they can do during this time
- When planning the daily routine when you are in the hospital or away for a day at CF Clinic

Example:

<p>First</p> <p>Mama's Medicine</p>	<p>Then</p> <p>Playground</p>
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## SCIENCE EXPERIMENT FOR PARENTS AND KIDS: HOW DO LUNGS WORK?

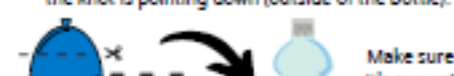
- Materials:**
- 1 clear empty plastic bottle, label removed
  - 2 balloons
  - 1 straw
  - Modeling clay/dough
  - Tape or elastic
  - Exacto knife or scissors



**1** Cut off bottom half of bottle.

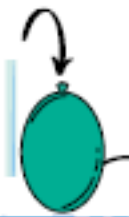


**2** Take 1 balloon: tie it (without blowing it up), cut off the bottom part of the balloon. Stretch this over the bottom (cut) part of the bottle so that the knot is pointing down (outside of the bottle).



Make sure

**3** Take the straw with tape



## WHAT DOES CF LOOK LIKE?

C F Z F E H B I I B Z E U U T B  
T Y F N G A B A C T E R I A N N  
M I S P H Y S I O T H E R A P Y  
U A N T I B I O T I C S N O I I  
C F K A I F T D O N T J E S E H  
O P S M Q C H I C C F Q X T N Y  
U E Y R I Y F P G P D O E O E M  
S Q C O U G H I N G O P R M B E  
R F T S R I I L B R C D C A U D  
N L V E U X S L D R T U I C L I  
O X Y G E N R S U C O M S H I C  
F O D C D O C A U N R S E W Z I  
N O K A T Z T P Y V G P I U E N  
E N Z Y M E S U O A Y S M S R E



COUGHING  
ANTIBIOTICS  
PHYSIOTHERAPY  
CYSTIC FIBROSIS  
LUNGS  
DOCTOR  
MUCOUS  
EXERCISE

PILLS  
X RAY  
BACTERIA  
OXYGEN  
NEBULIZER  
MEDICINE  
STOMACH  
ENZYMES





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forum 2023



grazie per  
l'attenzione

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