Ageing and Co-morbidities in CF

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Cystic Fibrosis
Fibrose kystique
Canada

w/o limits

Disclosures

- Vertex Pharmaceuticals – consulting fees for CF Annual Program, speaking fees for educational events

- Viatris – travel funds to attend CF conference
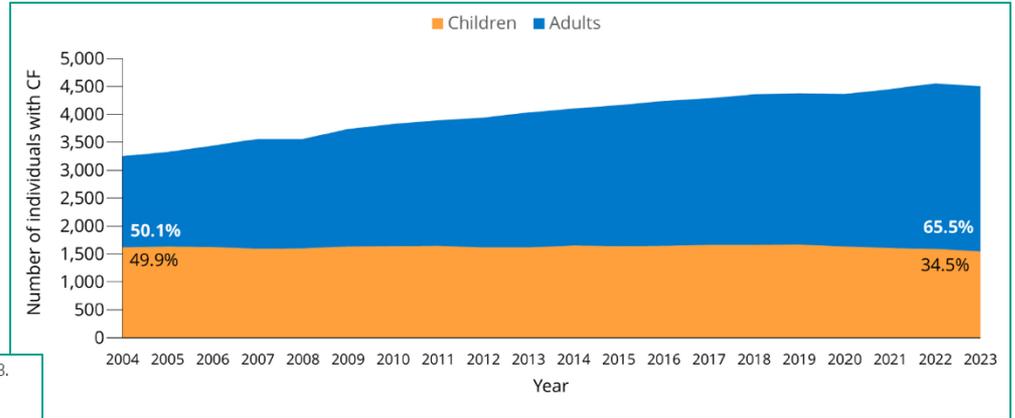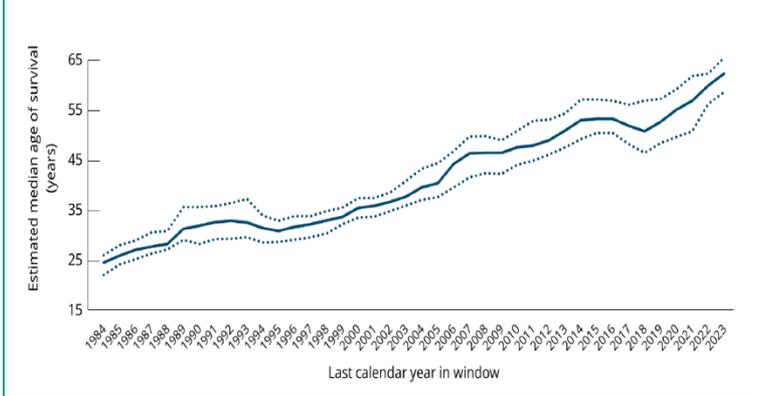
Canadian CF Registry

Children ■ Adults

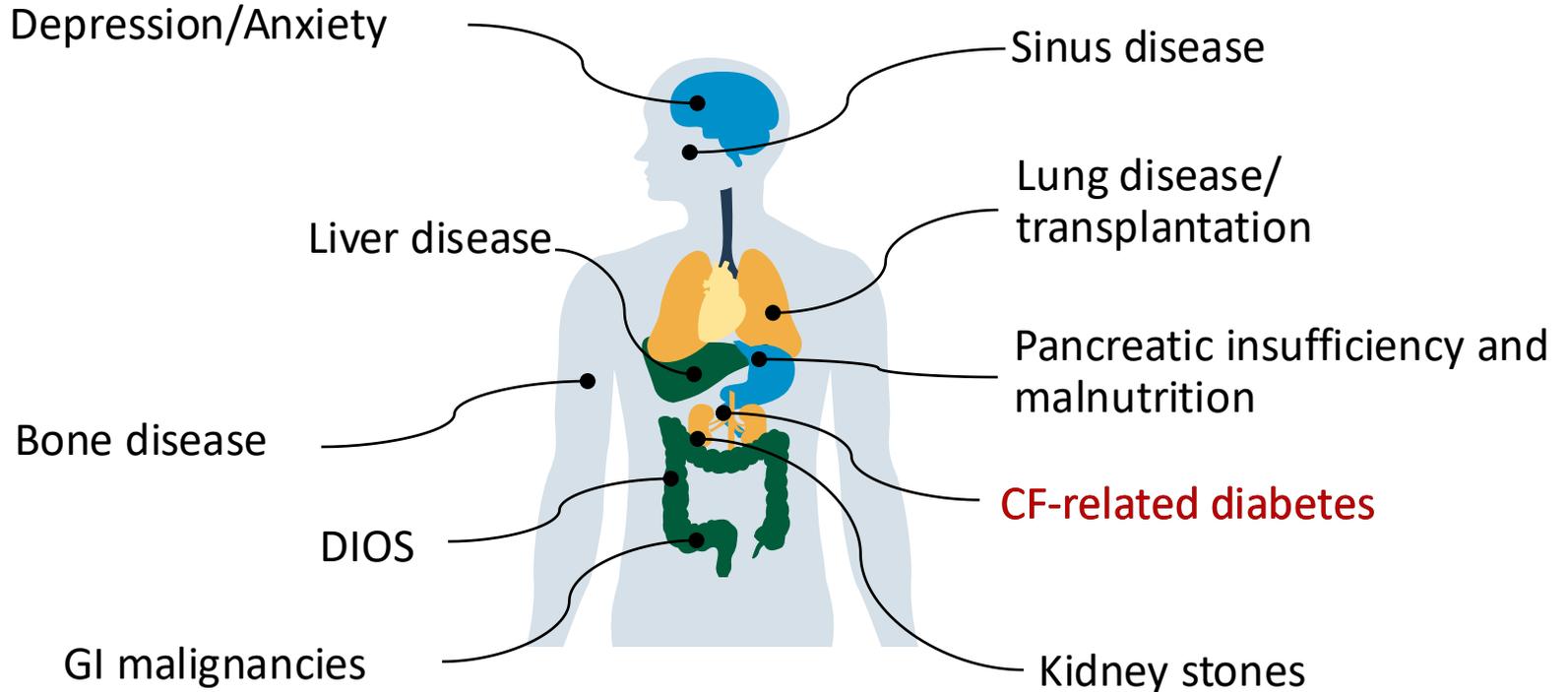**Figure 42** Estimated median age of survival for a moving 5-year window with 95% confidence intervals, 1984 to 2023.

Combination of better survival and living well into adulthood

The Canadian Cystic Fibrosis Registry 2023 Annual Data Report.

https://www.cysticfibrosis.ca/our-programs/cf-registry/reports-other-resources

Living longer with known complications: Classic CF

Depression/Anxiety

Sinus disease

Liver disease

Lung disease/transplantation

Pancreatic insufficiency and malnutrition

Bone disease

CF-related diabetes

DIOS

GI malignancies

Kidney stones

Emerging complications

Micro- and macro vascular disease

HTN

Cardiac disease

Metabolic syndrome
Obesity

Chronic kidney disease

Menopause

Non-GI malignancies
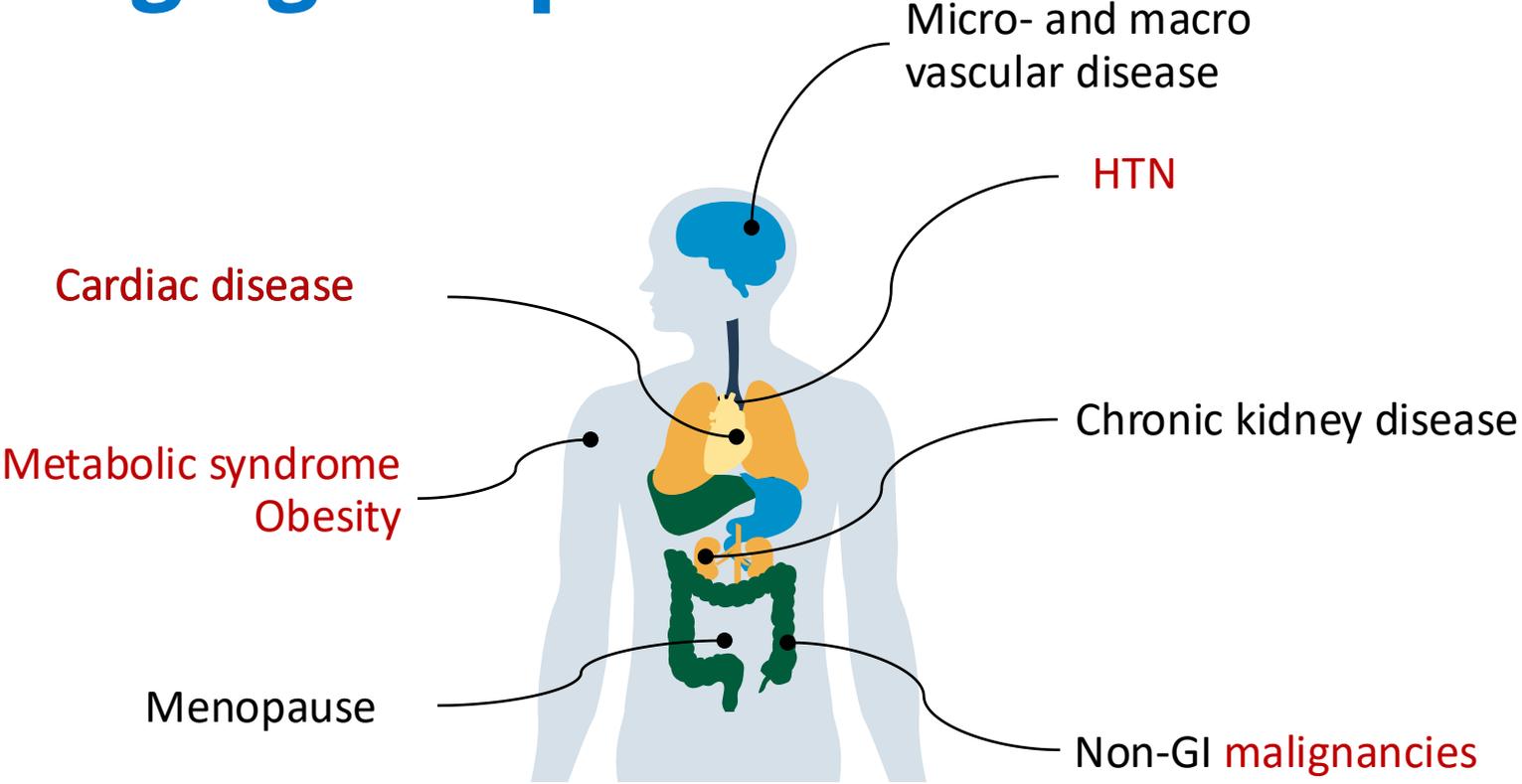
Unanticipated complications

Sleep disorders

Complex transplant candidates

Live longer with severe lung disease

More retransplants

Kidney transplant

Hepatic steatosis
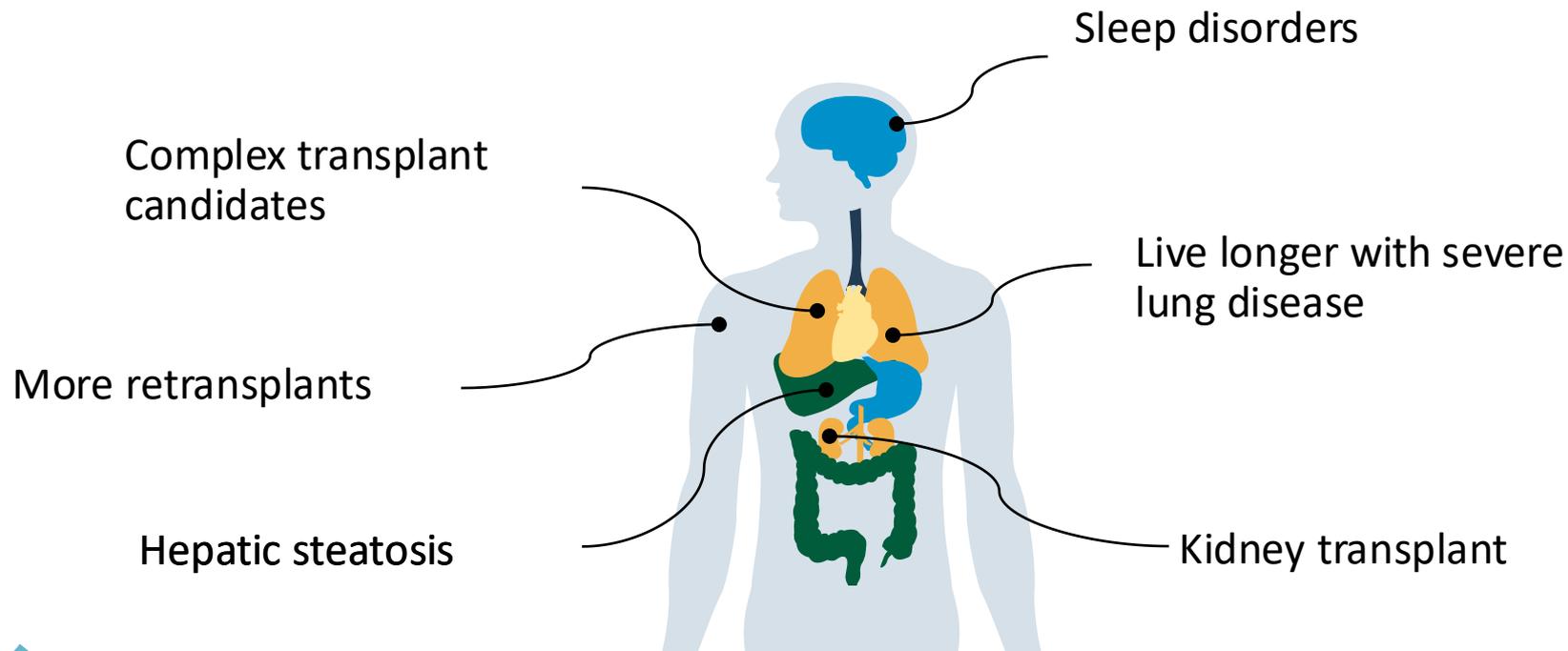
Cardiovascular disease and other conditions

Prevalence, risk factors and outcomes of cardiac disease in cystic fibrosis: a multinational retrospective cohort study

Freddy Frost [1,2], Dilip Nazareth [2,3], Laurent Fauchier [4], Dennis Wat [2,3], James Shelley [5], Philip Austin [6], Martin J. Walshaw [2,3] and Gregory Y.H. Lip [1,7]

Objective

- To investigate cardiac disease in CF using multisource patient data registries
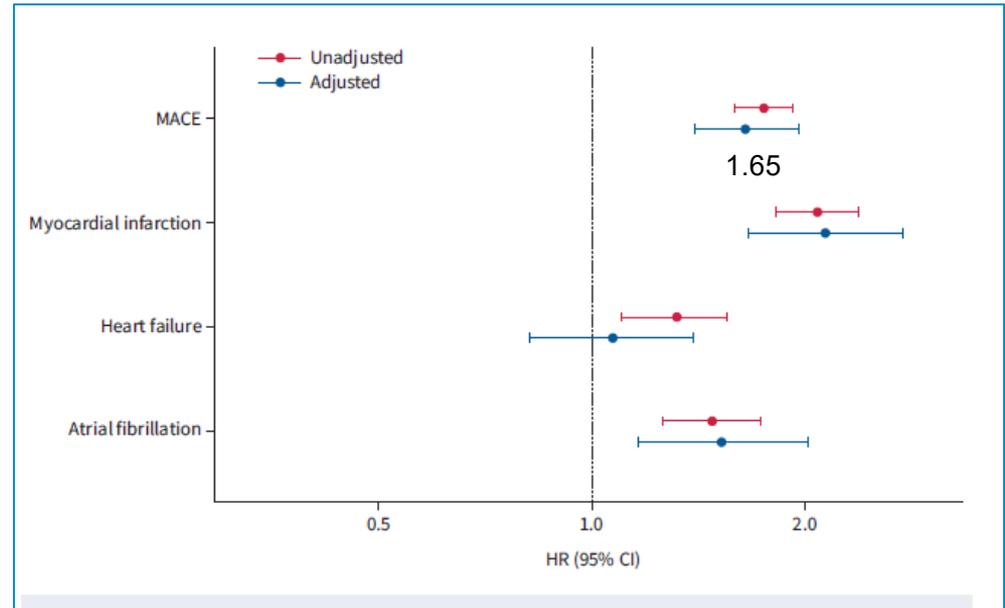
Design

- Adults, 2016-2020

- Data sources:
  - UK CF Registry
    - Data on ~12 000 PwCF
  - TriNetX
    - Health administrative data; 70 healthcare organizations

Frost et al., *ERJ*, 2023

Cardiovascular outcomes

Prevalence: 6.9% TriNetX, 1.6% in UK CF Registry

CF vs. General Population

(TriNetX data; adjusted for cardiac risk factors)

MACE: major adverse cardiac events

Frost et al., *ERJ*, 2023

Older & Wiser: Aging in cystic fibrosis study Objectives

1. Rate of non-pulmonary emerging co-morbidities (CVD, CKD and stones, malignancy)

2. Quantify the rate of age-related cancer screening (mammography, colonoscopy, Pap smear)
   a. Is this influenced by the presence of a primary care provider

3. Compare rates of emerging conditions and screening rates in pwCF to the non-CF population

Creating the linked dataset capitalizing on strengths of both

CF-specific data

ER Inpatient

Outpatient

Specialty databases

Probabilistic linkage

Ontario CF Database

94% Linkage Rate

Rates of emerging complications

	Non-transplant cohort (n=16,437,035)		Transplant cohort (n=1,473)	
Cardiovascular disease				
Chronic kidney disease				
Symptomatic kidney stones				
Cancer				

<u>Definitions</u>:
CVD: hospital admission for MI, stroke, heart failure; ER visit with diagnosis of cardiac or vascular disease; CABG, stents;
Sensitivity analysis: HTN, valvular disease, acute coronary syndrome, MI, arrhythmia, arterial disease, heart failure
CKD: based on lab work to calculate GFR
Symptomatic kidney stones: ER or hospitalization for stone or required urologic intervention
Cancer: any type

Arya et al, *Annals ATS*, 2025

Rates of emerging complications

	Non-transplant cohort (n=16,437,035)		Transplant cohort (n=1,473)	
	CF (N=1,435)		CF (N=208)	
Cardiovascular disease	24.5 (21.5-28.0)		115.3 (88.6-149.9)	
Chronic kidney disease	3.7 (2.7-5.2)		631.4 (501.4-795.5)	
Symptomatic kidney stones	7.4 (6.1-9.0)		14.2 (8.6-23.3)	
Cancer	5.8 (4.5-7.6)		35.9 (22.7-54.0)	

*Rates are per 1000 person/years

- Rates are **higher** in **transplant** vs. non-transplant cohort in CF

Arya et al, *Annals ATS*, 2025

Rates of emerging complications

	Non-transplant cohort (n=16,437,035)		Transplant cohort (n=1,473)
	CF (N=1,435)	non-CF (N=16,435,600)	
Cardiovascular disease	**24.5 (21.5-28.0)**	8.4 (8.3-8.4)	
Chronic kidney disease	**3.7 (2.7-5.2)**	1.8 (1.8-1.8)	
Symptomatic kidney stones	**7.4 (6.1-9.0)**	2.5 (2.5-2.5)	
Cancer	**5.8 (4.5-7.6)**	3.0 (3.0-3.0)	

*Rates are per 1000 person/years

- Rates are **higher in transplant** vs. non-transplant cohort in CF
- Rates **higher** in the **CF** vs. non-CF in **non-transplant** cohort

Arya et al, *Annals ATS*, 2025

Rates of emerging complications

	Non-transplant cohort (n=16,437,035)		Transplant cohort (n=1,473)	
			CF (N=208)	non-CF (N=1,265)
Cardiovascular disease			**115.3 (88.6-149.9)**	121.9 (113.0-132.6)
Chronic kidney disease			**631.4 (501.4-795.5)**	365.9 (338.8-395.1)
Symptomatic kidney stones			**14.2 (8.6-23.3)**	10.4 (8.1-13.3)
Cancer			**35.9 (22.7-54.0)**	28.1 (24.1-32.8)

*Rates are per 1000 person/years

- Rates are **higher in transplant** vs. non-transplant cohort in CF
- Rates **higher** in the **CF** vs. non-CF in **non-transplant** cohort
- Similar rates in the transplant cohort (CF vs. non-CF)

Arya et al, *Annals ATS*, 2025

Age of emerging complications

	Cardiovascular disease		Chronic Kidney Disease		Symptomatic Kidney Stones		Cancer	
	CF	*Non-CF*	*CF*	*Non-CF*	*CF*	*Non-CF*	*CF*	*Non-CF*
Non-transplanted	33 (24-47)	65 (53-77)	37 (29-52)	76 (68-83)	31 (25-39)	51 (39-62)	47 (30-56)	67 (57-76)
Transplanted	35 (28-45)	63 (56-68)	32 (27-41)	63 (57-68)	32 (27-39)	63 (56-70)	37 (31-48)	67 (60-71)

Median age at outcome:

~20 years earlier in pre-transplant CF

~30 years earlier in the post-transplant CF

vs. Non CF cohort

Arya et al, *Annals ATS*, 2025

What about cancer screening?

How well are we doing in completing cancer screening in pwCF?
Does having a family doctor influence the rate of cancer screening?
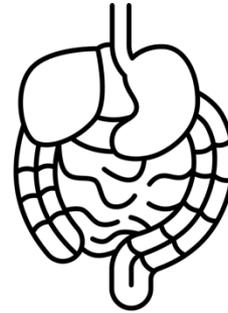
Methods

- Study period between 2012 and 2022 using linked dataset

- "Ever screened" within the age-appropriate time frame

mammography
breast cancer

Pap test
cervical cancer

colonoscopy
colon cancer

Stephenson et al, *J Cyst Fibros*, 2025

Cancer screening

How well are we doing in completing cancer screening for pwCF?

Table 1: Percent of completed age-appropriate cancer screening at least once in pwCF

	Breast cancer	Cervical cancer	Colorectal cancer (pre-transplant)	Colorectal cancer (post-transplant)
Percent screened	67.3%	59.3%	46.3%	50.7%

Not bad but room for improvement

Stephenson et al, *J Cyst Fibros*, 2025

Cancer screening

Does having a family doctor influence rates of cancer screening?

Table 2: Screening test in CF cohort comparing primary care provider (PCP) vs. no PCP involvement

	Rate Ratio	95% CI	p-value
Mammography	3.6	1.13-11.44	**0.03**
Pap smear	1.71	1.13-2.57	**0.01**
Colonoscopy (pre-tx)*	1.57	1.06-2.32	**0.03**
Colonoscopy (post-tx)*	0.89	0.38-2.08	0.89

*adjusted by sex
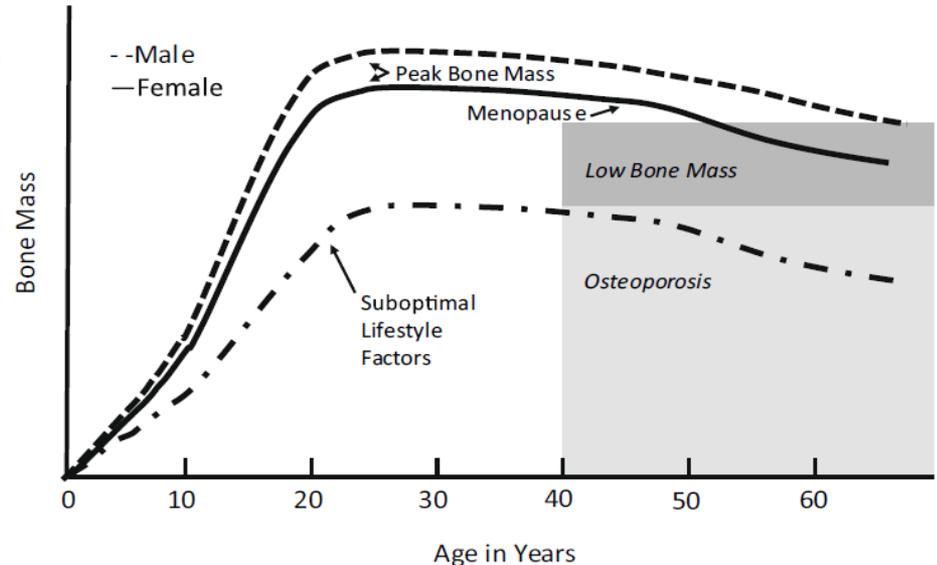
Stephenson et al, *J Cyst Fibros*, 2025

Bone Health

# Bone mineral density (BMD)

- In the healthy population, peak bone mass is generally reached by 20

- Bone loss does not occur until late adulthood

- Osteoporosis and fractures are known complications of CF
  - Pain, risk for PEx

- Changes in BMD over time unclear

Fig. 1 Bone mass across the lifespan with optimal and suboptimal lifestyle choices

Weaver CM et al. *Osteoporosis Int*. 2016 Apr;27(4):1281-1386.

What happens to BMD over the life course in CF?
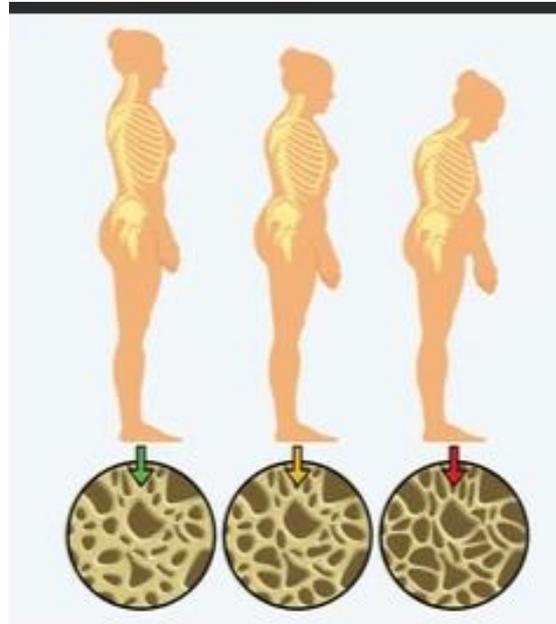
Design

- **Retrospective longitudinal cohort study**
  - **N=500 people with 1500 DEXA scans**

- **Inclusion Criteria:**
  - Adults with CF followed at St Michael's Hospital aged **25-48 years**
  - January 2000 and December 2021
  - ≥ 1 DEXA scan done on Lunar Prodigy machine

- **Exclusion Criteria:**
  - DEXA scans post-initiation of bisphosphonates, CFTR modulators or transplant
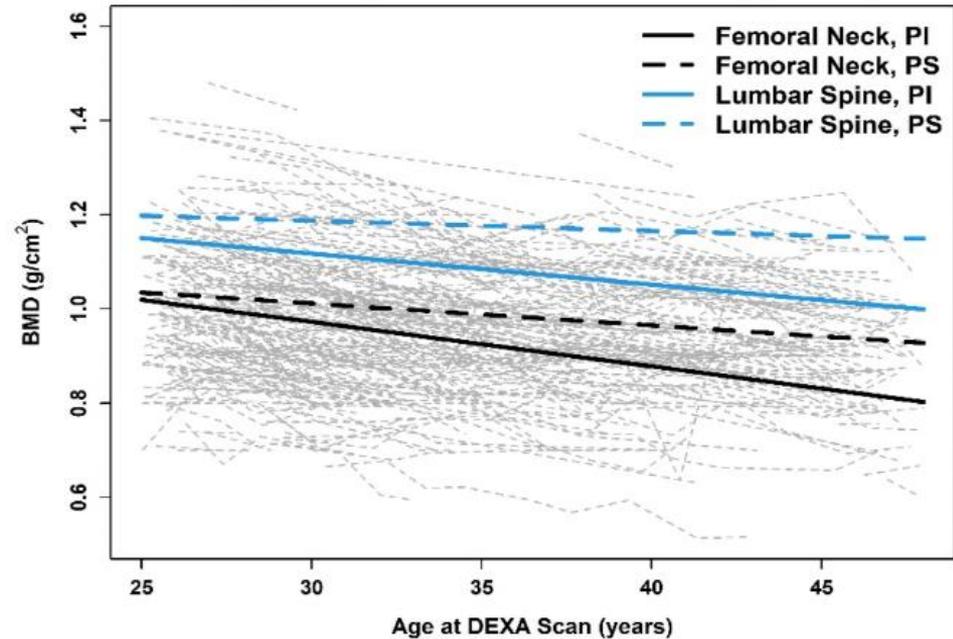
Results

Bone loss highest in pancreatic insufficient patients

Lumbar spine (PI):
-**13.1%** change between age 25 and age 48 y

Femoral neck (PI):
-**21.3%** change between age 25 and age 48 y

- Individuals with CF are losing bone during a period when we do not expect bone loss
- Magnitude of bone loss is comparable to older peri-menopausal women
- CF will be entering menopause with lower than expected BMD

Jad R et al, *J Bone Mineral Res*, 2024

Conclusions

High rates of emerging complications in pwCF

These are happening at earlier than expected ages

Screening for cancer are important to detect curable disease

Engagement of primary care physicians in the management of pwCF is even more critical now

Education of the CF community and subspecialists to ensure appropriate and timely care

Acknowledgements

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Patients and families who agree to participate in the Canadian CF Registry

Thank You.