The aging CF patient - challenges for the clinical pharmacist

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איגוד סיסטיק פיברוזיס בישראל
לתת מכל הנשימה
CF

בית החולים
אדמונד וליli ספרא
לילדים
המרכז הרפואי ע"ש ח.שיבא, תל השומר
בית החולים של המדינה

מרכז שניידר לרפואת ילדים בישראל
مركز شنايدر لطب الأطفال في اسرائيل
Schneider Children's Medical Center of Israel


Ceyston
Ceyston

Clinical case 1 – Introduction

- MV, a 56 Year old patient
- Diagnosed during childhood as asthmatic
- The father of 2 daughters with CF
- CF was diagnosed in 2006 (age of 47)
- G542X / 5T
- Pancreatic sufficient
- 1.88 m, 103 kg (BMI = 29 kg / m^2)
- Latest FEV_1 – 77%

MV – Problem list

- ABPA (Allergic broncho-pulmonary aspergillosis)
- Recurrent sinusitis
- GERD (gastro-esophageal reflux disease)
- Dyslipidemia
- Anxiety
- During the last year: pneumothorax, renal failure
- Latest HbA1c – 6.2%

MV - Chronic medications

1. Inh. Sol. Sodium chloride 6% (Mucoclear) - 4ml x 2 / day
2. Amp. Colistin (Coliracin) 1 million units (inhaled) x 2 / day
3. Cap omeprazole (Omepradex) 40 mg - 1 x 1 / day
4. Inh. Beclomethasone 100 microgram (Qvar) - 2 x 2 / day
5. Inh. Pwd. Formoterol / beclomethasone (Symbicort) 160 / 4.5 - 1 x 2 / day
6. Inh. Salbutamol (Ventolin) 100 microgram – SOS
7. Tab Rosuvastatin (Stator) 40 mg – 1 x 1 / day
8. Tab escitalopram (Cipralex) 10 mg – 1 x 1 / day

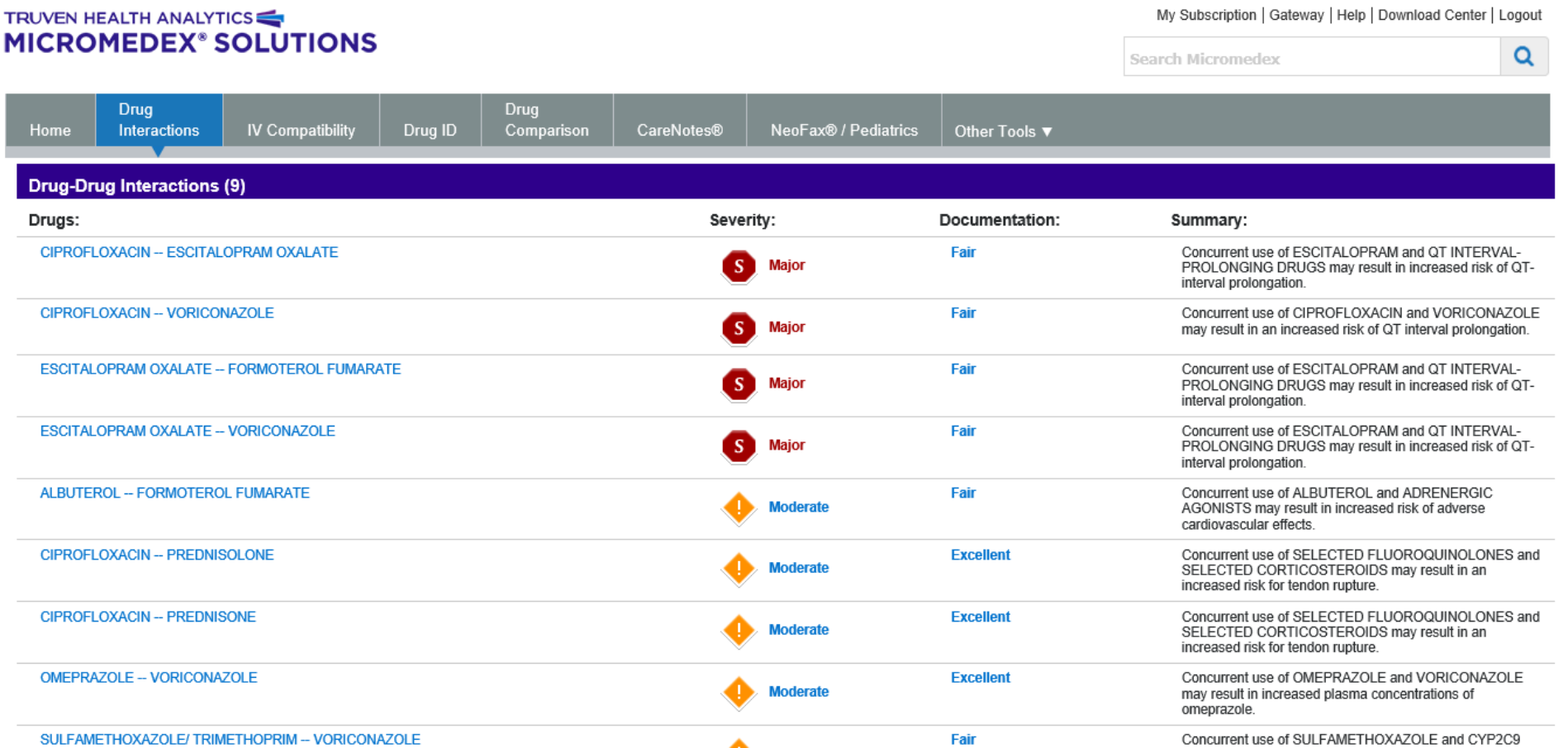
- November 2014 - Referred to the Clinic with an exacerbation, associated with his ABPA
- **What would you prescribe him?**

- Prednisone (40 mg / day for 3 day & tapering down)

MV - Treatment

- January 2015 – clinical worsening with a lot of coughs and chest pain. FEV_1 declined to 38%
- 107 kg (BMI – 30 kg / m^2)
- Diet
- Pulse steroids (methyl prednisolone 1 gr / day x 3 days)
- Voriconazole 200 mg x 2 day

- ECG – normal sinus rhythm
- Tapering down SSRI



MV - Treatment

- February - clinical improvement, with FEV_1 returning almost to baseline (72%)
- Redness in the face
- ECG: QT elevation, within the norm
- SSRI was stopped
- March - clinical deterioration, with FEV_1 decline to 54%,
- Blushing, feeling of fever
- Voriconazole switched to itraconazole 200 mg x 2 / day

MV - Treatment

- April - hemoptysis
- Tranexamic acid, Ciprofloxacin, TMP/ SMX, prednisone
- May - clinically better, FEV_1 64%
- Tapering down of steroids, Tranexamic acid stopped
- July - fever, muscle pains, light headedness
- Pulse steroids reduced to 800 mg x 1 / day
- Tingling in hands
- Switched itraconazole with amphotericin B inhalations

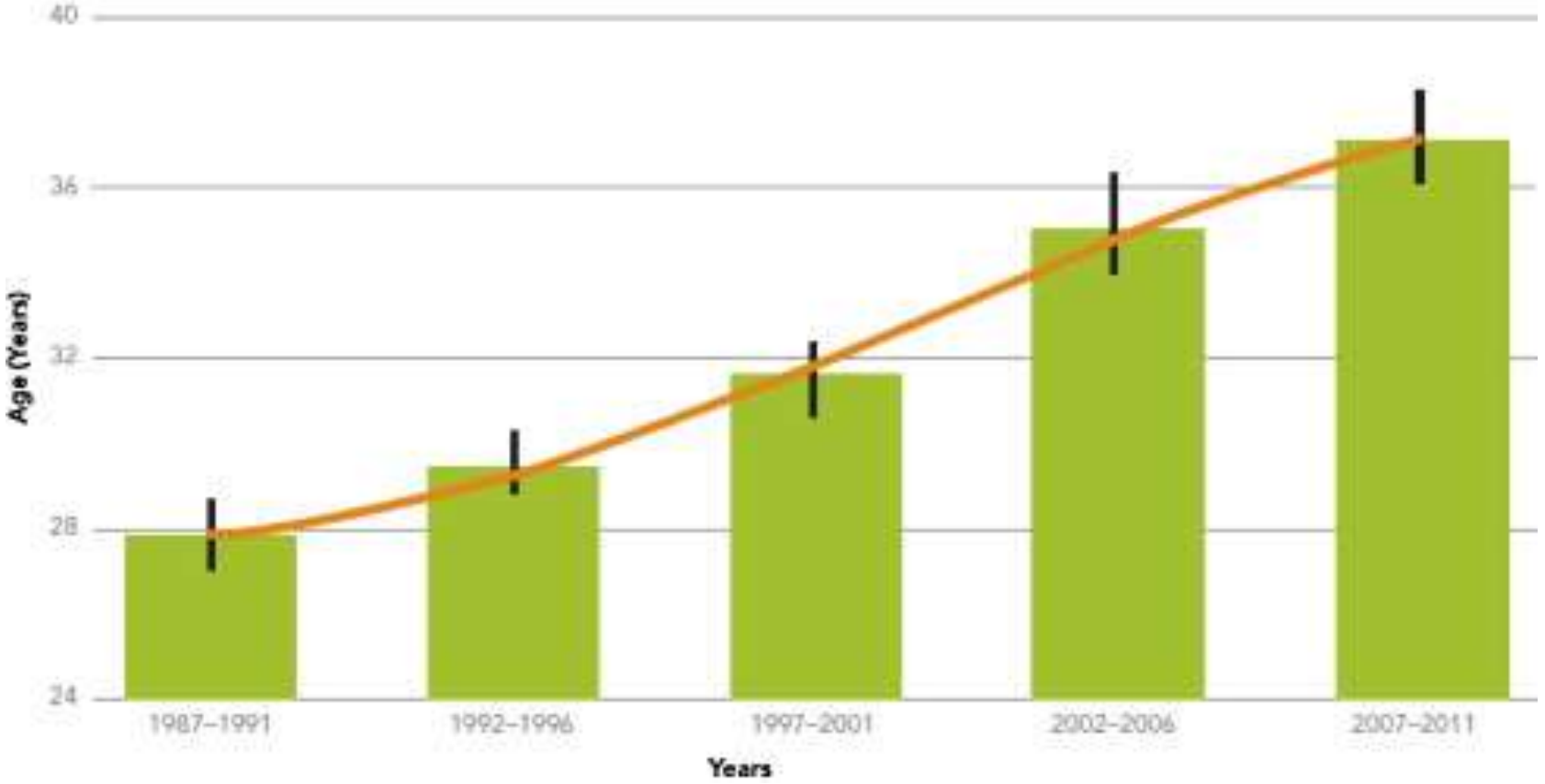
MV - Treatment

- August – FEV_1 = 75%
- ABPA is still active
- Diabetes, overweight
- Option - omalizumab as steroid sparing
- Anxiety

- October – FEV_1 = 81%
- No oral steroids or antibiotics

תאריך בדיקה	מדבקה	תוצאה	יחידת מידה	ערכי ייחוס	תוצאה גרפית
30/09/2015 09:16	227795	126 ↑	IU/ml	0-100	
09/08/2015 09:27	223858	213 ↑	IU/ml	0-100	
22/07/2015 14:37	222085	324 ↑	IU/ml	0-100	
19/04/2015 14:31	211943	648 ↑	IU/ml	0-100	
13/04/2015 11:39	211159	686 ↑	IU/ml	0-100	
25/03/2015 13:33	209667	468 ↑	IU/ml	0-100	
22/02/2015 09:29	206099	729 ↑	IU/ml	0-100	
21/01/2015 13:09	202496	1260 ↑	IU/ml	0-100	
27/11/2014 09:04	235978	1170 ↑	IU/ml	0-100	
07/08/2014 09:14	224955	428 ↑	IU/ml	0-100	
24/09/2013 10:00	229268	335 ↑	IU/ml	0-100	
14/07/2013 09:22	221677	369 ↑	IU/ml	0-100	
02/08/2012 08:06	222282	315 ↑	IU/ml	0-100	
10/10/2011 00:00	224441	564 ↑	IU/ml	0-100	

CF - from a childhood disease to a chronic condition



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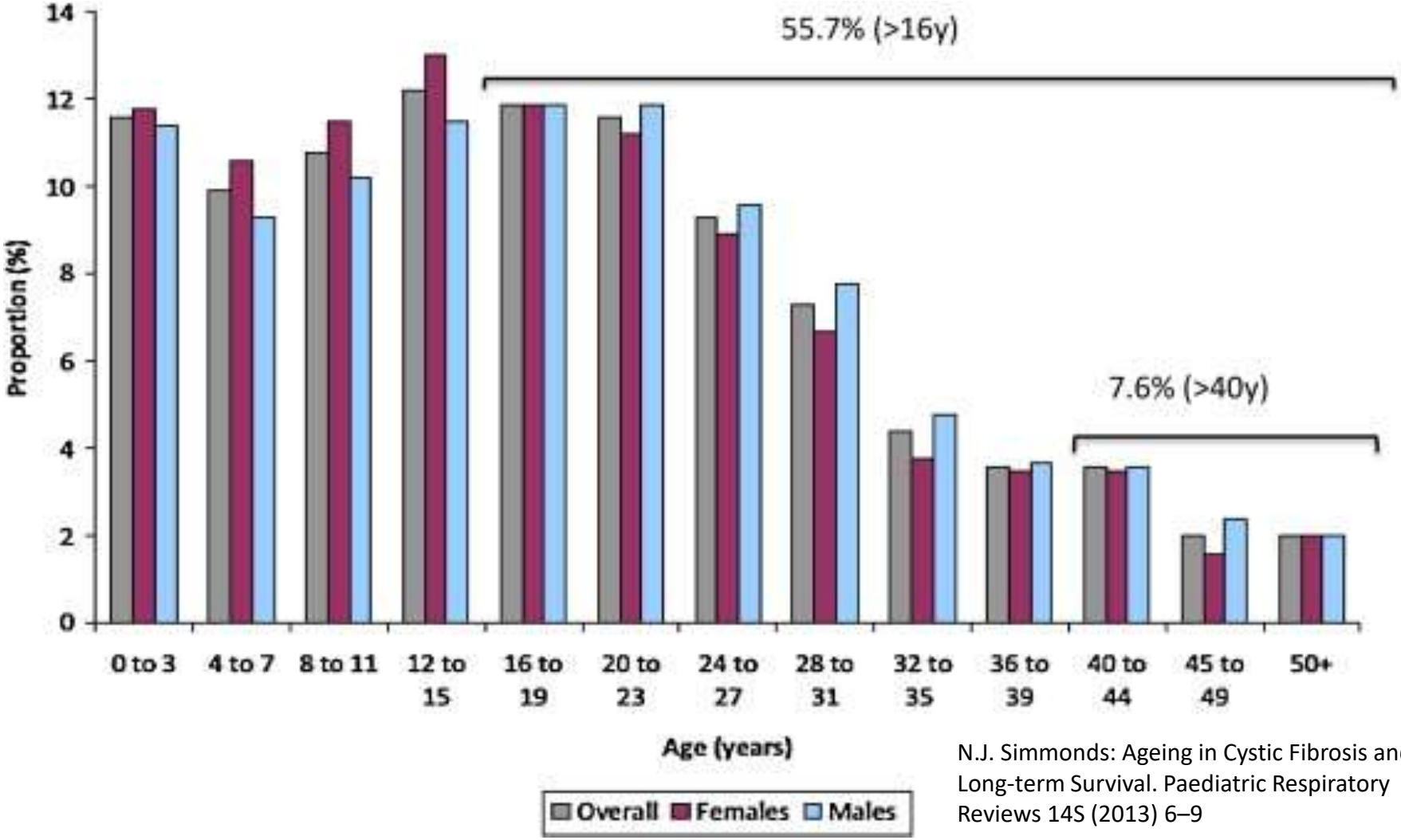
A demographic change in the proportion of patients over 18



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Age and the Israeli CF population

- 572 CF patients are registered in Israel
- Average age: 22.94 years
- 361 (63.11%) are over 18 years old
- 58 (10.13%) are over 40 years old
- 34 (58.62%) are treated in Safra & Schneider's CF centers

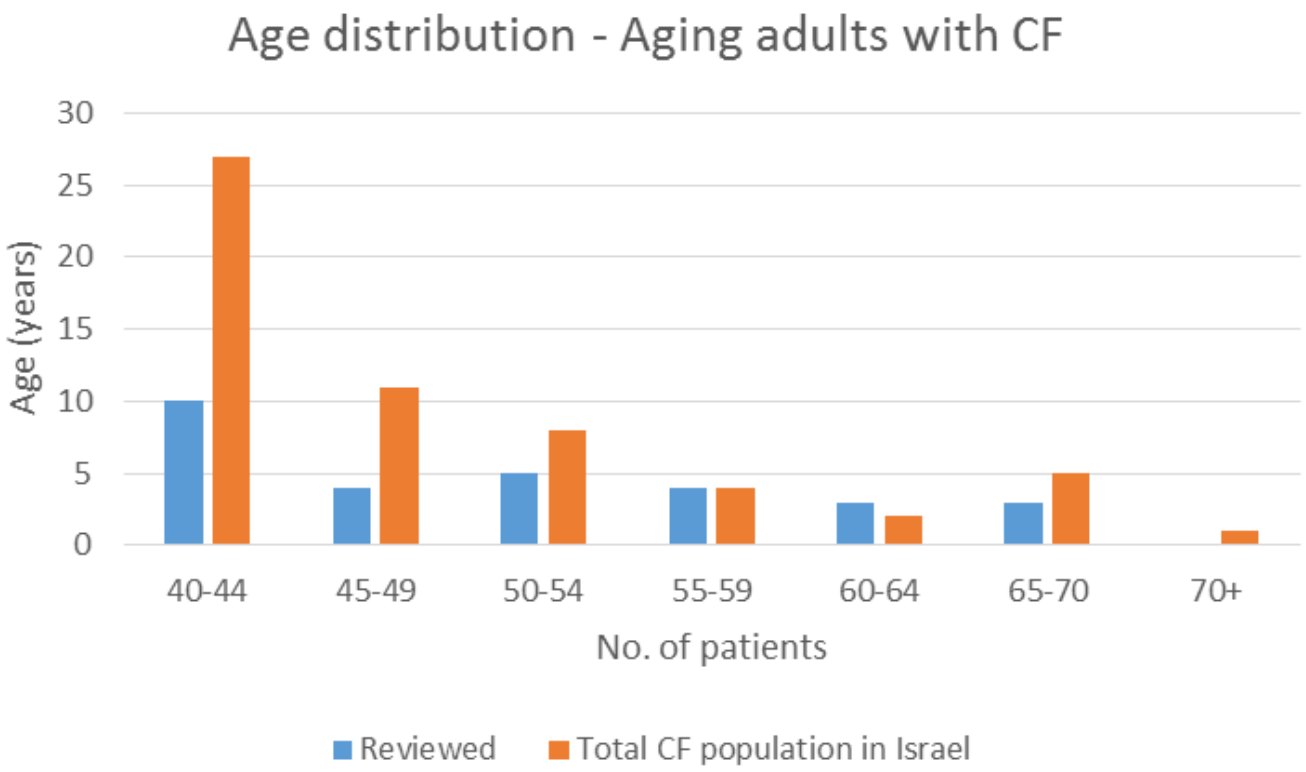
Method

Included: All patients over 40 years visited Safra / Schneider's CF centers
Excluded: lung transplant / death / lost of follow up

Medical records reviewed for:

- Mutations
- Age of diagnosis
- Pancreatic in/ sufficiency
- Diabetes
- Osteopenia / osteoporosis
- BMI
- Latest FEV_1
- Pathogens
- No. of chronic medications
- Other medical conditions
- Parenting

- n = 29

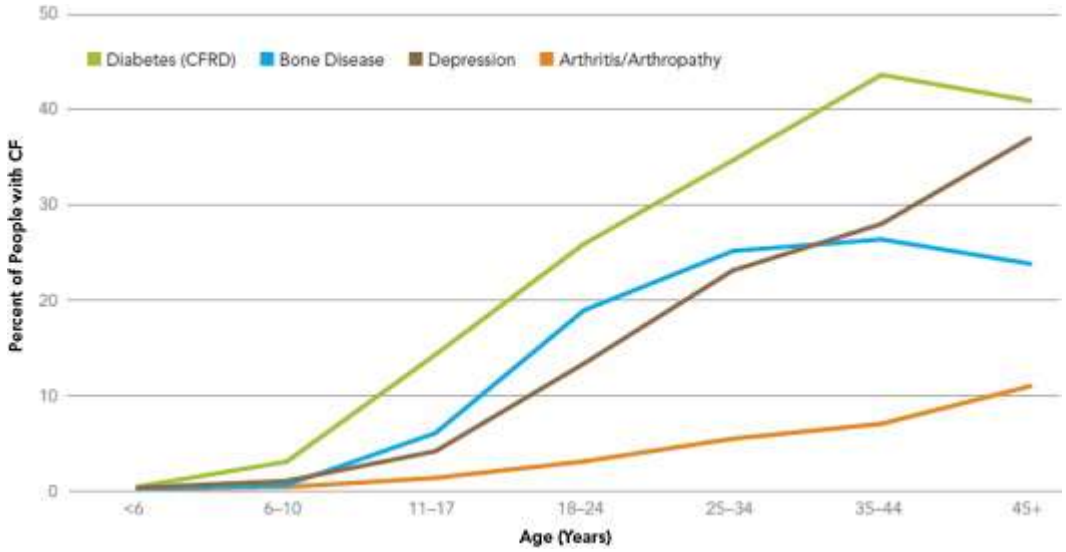


Medical issues in the aging CF population

- The improvement in survival brings the potential for a new set of medical and psychosocial issues
- Broadly, these can be considered as CFTR or non-CFTR related

Medical issues in the aging CF population - CFTR-related

- Longevity exposes organs to abnormal CFTR function for a longer duration
- Susceptible tissues might eventually develop a disease, manifested as new symptoms



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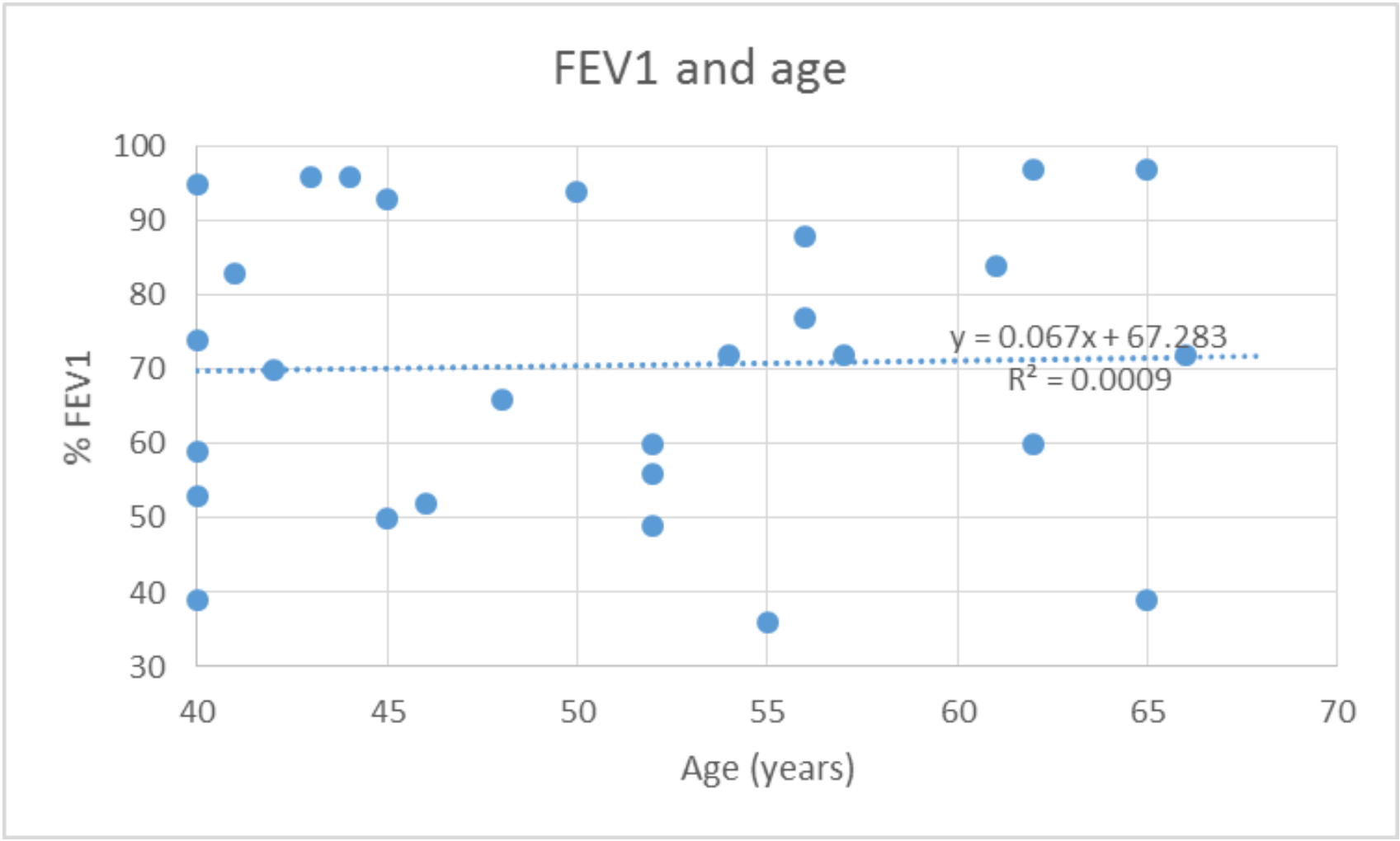
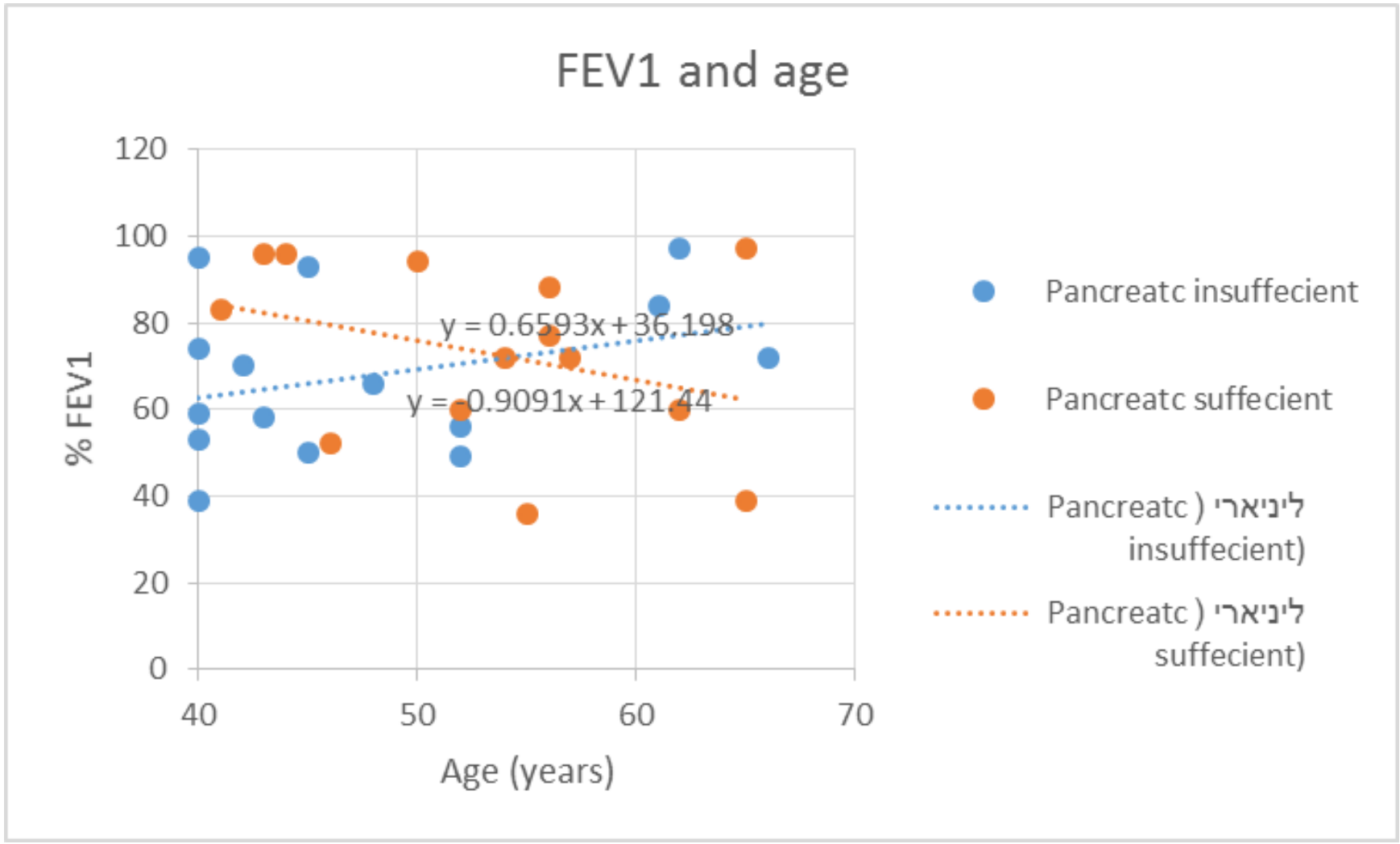


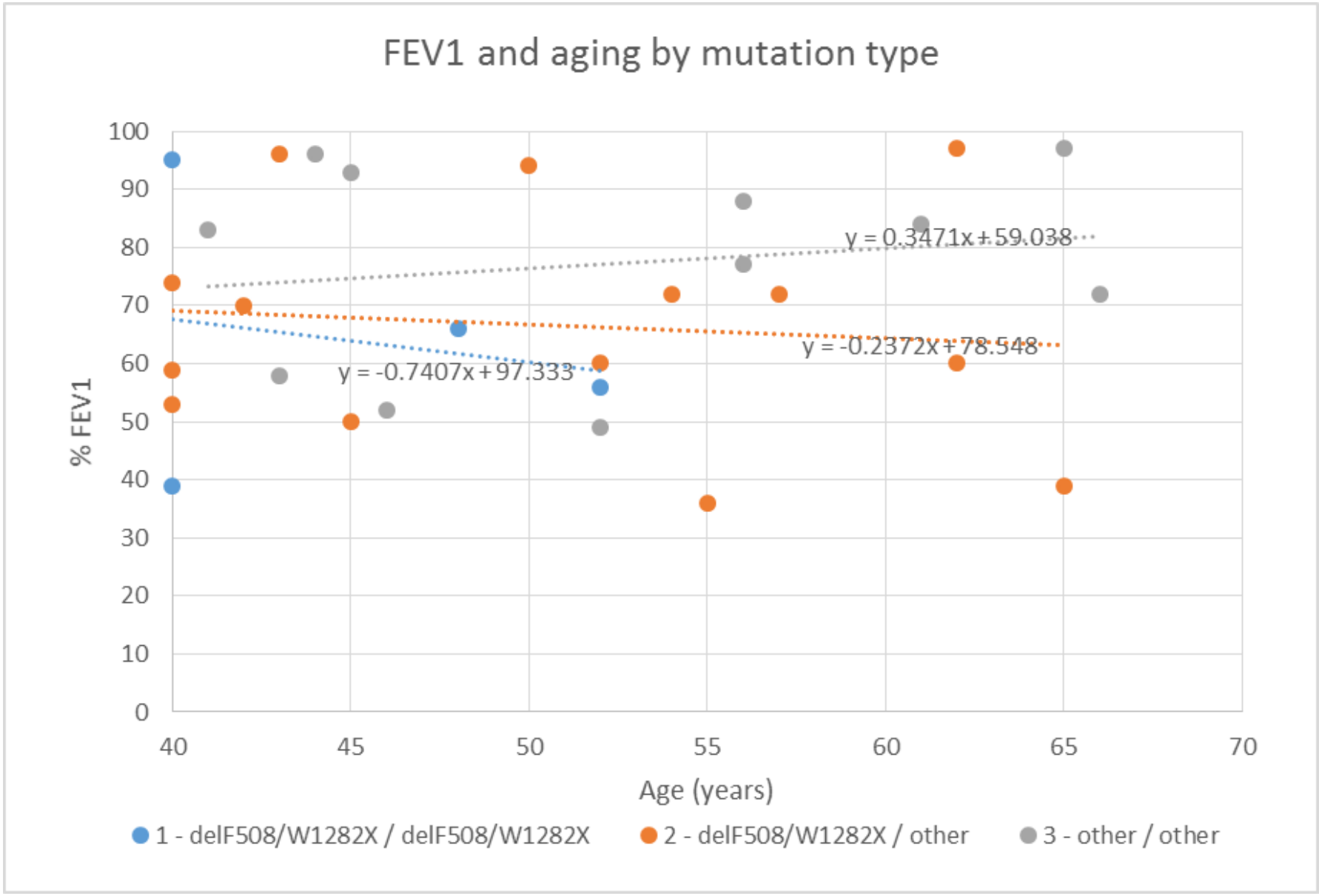
Average age: 50.67 years
Average FEV_1: 70.24%

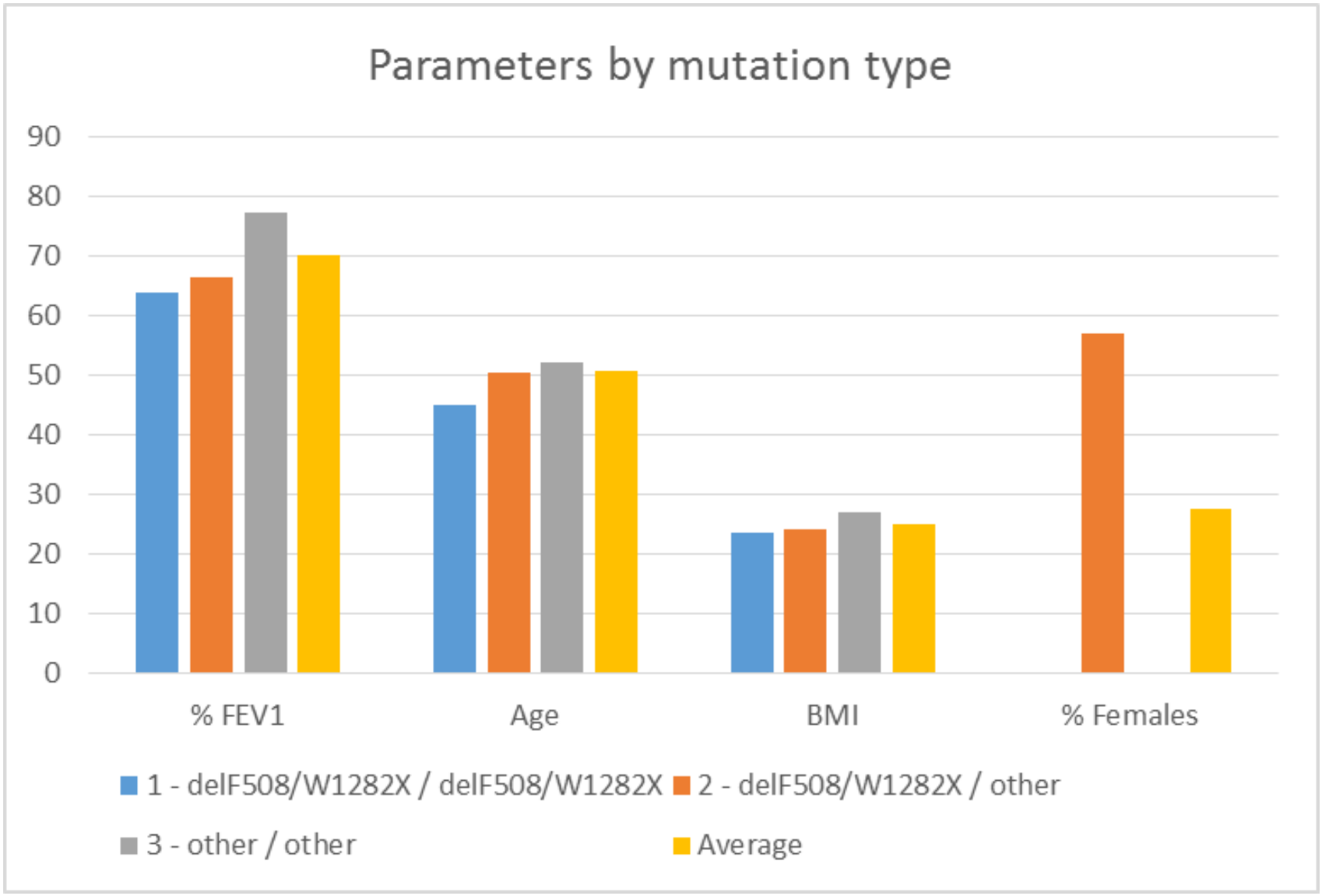
Med age: 50 years
Med FEV_1: 72%

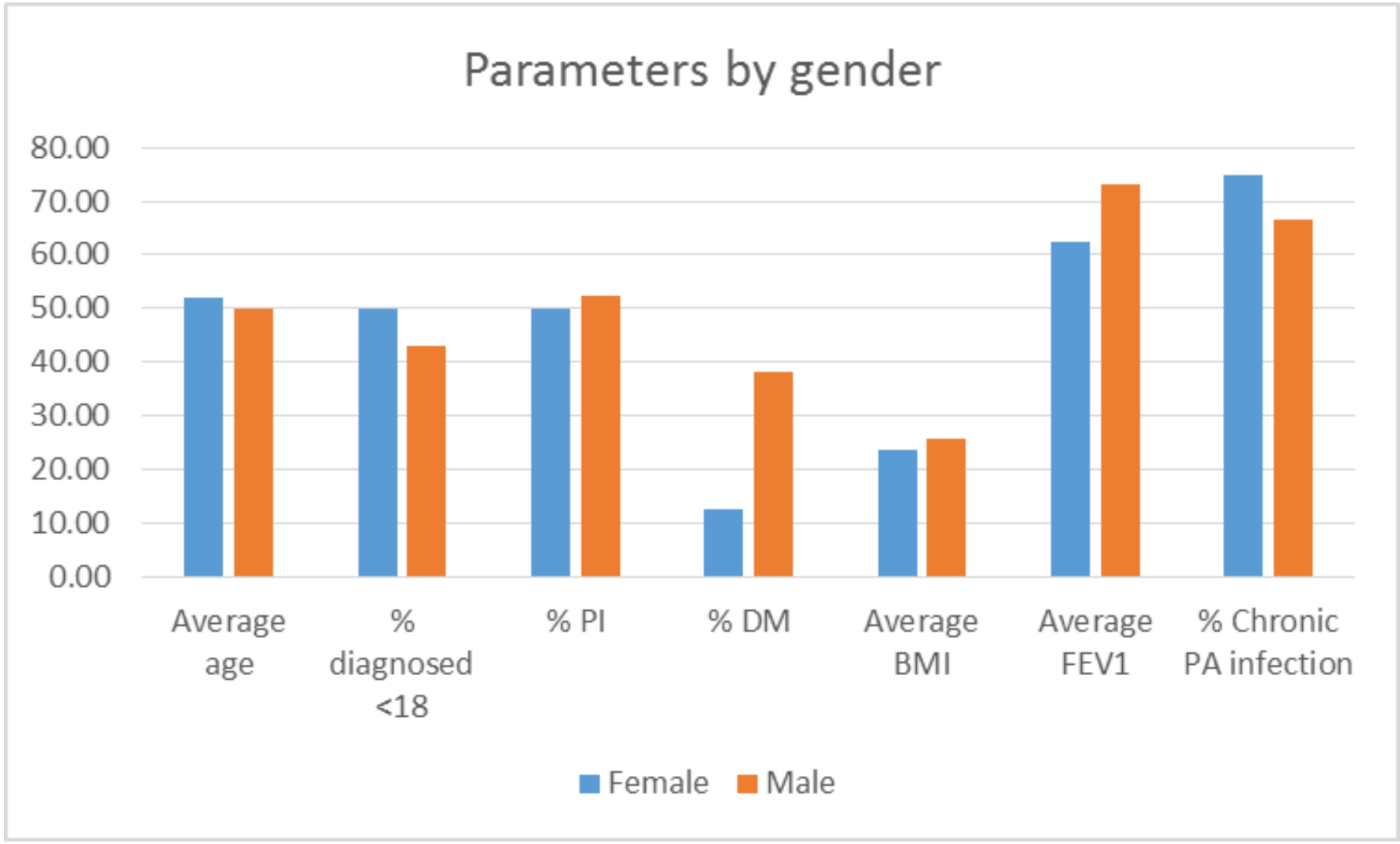


Average age PS: 53.28 years
Average age PI: 47.73 years

Average FEV_1 PS: 73%
Average FEV_1 PI: 67.66%

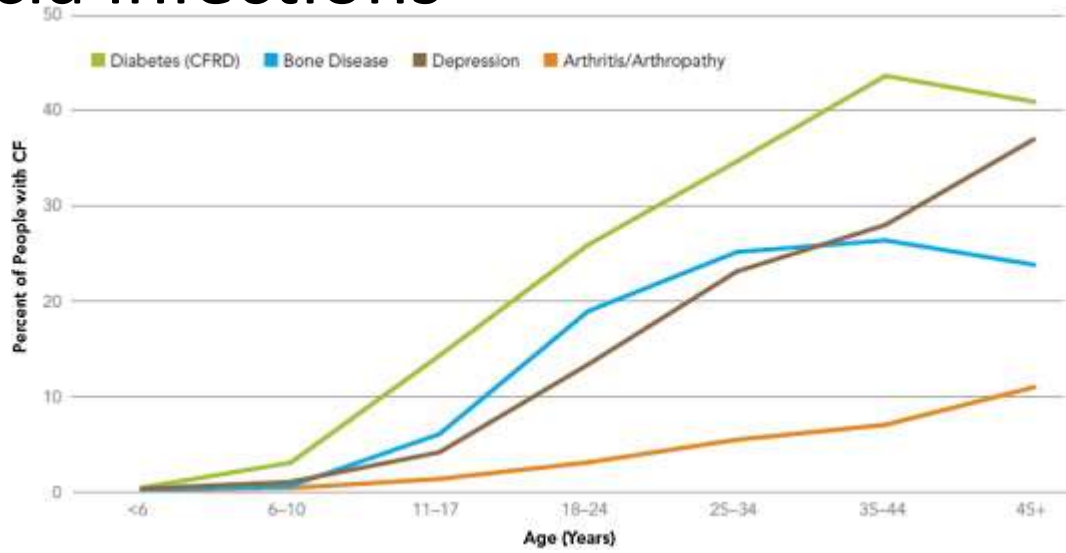

FEV1 and aging by mutation type
% FEV1
Age (years)
y = 0.3471x + 59.038
y = -0.2372x + 78.548
y = -0.7407x + 97.333
1 - delF508/W1282X / delF508/W1282X
2 - delF508/W1282X / other
3 - other / other


Parameters by mutation type
90
80
70
60
50
40
30
20
10
0
% FEV1
Age
BMI
% Females
1 - delF508/W1282X / delF508/W1282X
2 - delF508/W1282X / other
3 - other / other
Average


Parameters by gender
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
Average age
% diagnosed <18
% PI
% DM
Average BMI
Average FEV1
% Chronic PA infection
Female
Male

CFTR-related medical issues - Diabetes

- Has an age-dependent prevalence
- Associated with a decline in pulmonary function & nutrition
- An increase in Pseudomonas aeruginosa & Burkholdaria cepacia infections
- Increase in hospitalizations rate



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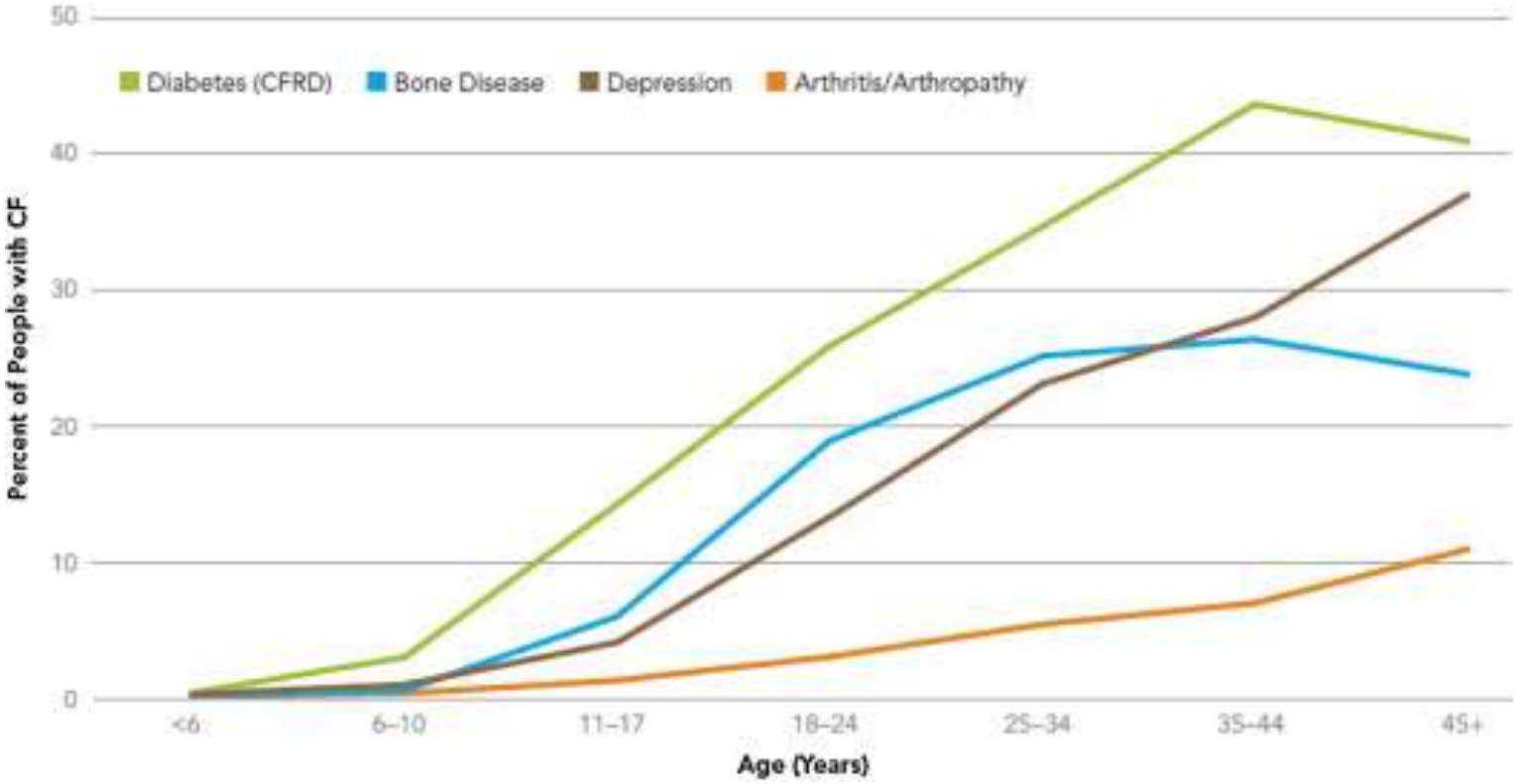
CFTR-related medical issues - Diabetes

- 9 patients (31%) of patients in Safra & Schneider are diagnosed with CFRDM



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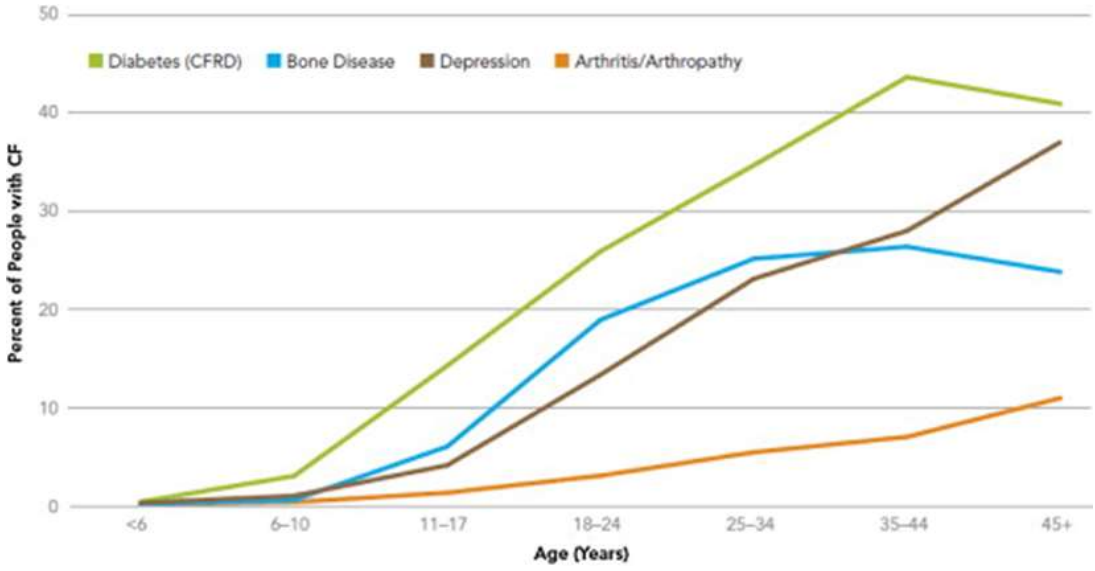
CFTR-related medical issues – Bone disease

- Bone mineral content (BMC) and bone mineral density (BMD) are usually normal in children with normal nutritional status and well preserved lung function
- Reduced BMD is common in adolescents and adults
- Adults have an increased risk of fracture compared to a healthy population of the same age and gender

I. Sermet-Gaudelusa et al: European cystic fibrosis bone mineralisation guidelines. Journal of Cystic Fibrosis. Volume 10 Supp 2 (2011) S16–S23

Bone disease – Risk factors

- Poor nutritional status
- Reduced levels of weight bearing activity
- Effect of CFTR dysfunction on bone cells
- A negative calcium balance
- Abnormal fatty acid status
- Glucocorticoid treatment
- Lung infection
- Vitamin D insufficiency
- Vitamin K insufficiency
- Hypogonadism
- Delayed puberty
- CF related diabetes



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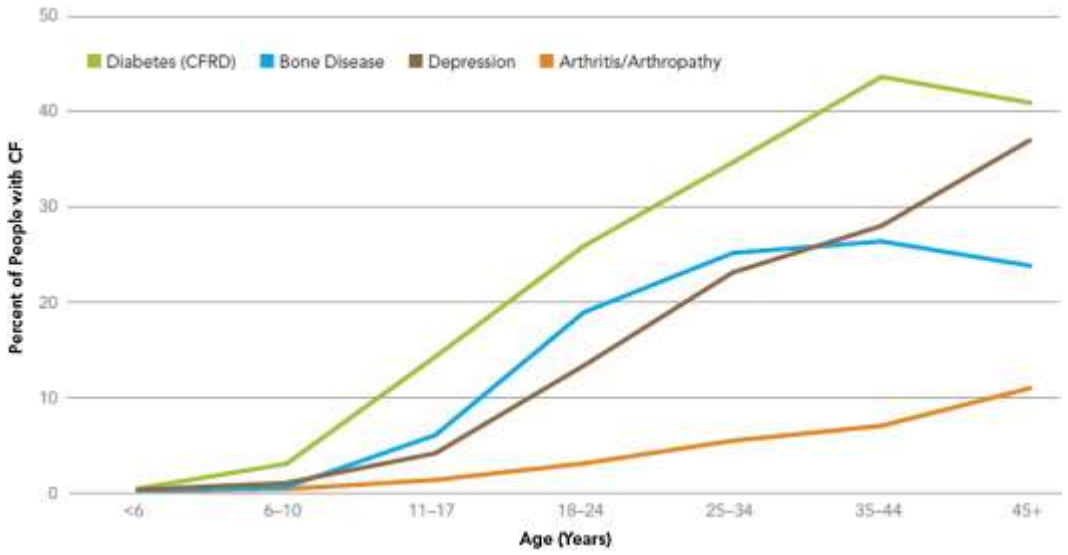
Medical issues in the aging CF population - CFTR-related

- Other CFTR-related age-associated conditions include:
  - Arthropathy
  - Large volume haemoptysis
  - Pneumothoraces
  - Chronic Pseudomonas aeruginosa colonization



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Medical issues in the aging CF population – non CFTR-related

- Non-CFTR-related Age-related complications of the general population
- intensifies the already burdensome treatment regimen
- Increasing the potential for drug-related interactions
- Historically, risk of cardiovascular disease had been estimated as very low in CF
- But, cases of myocardial infarction in pancreatic insufficient patients have been reported

Medical issues in the aging CF population – non CFTR-related

- Drug-related side effects are another important issue, as patients with CF live longer
- Aminoglycosides are used as anti bacterials and are instrumental in controlling disease
- Unfortunately, they might increase the incidence of renal and vestibulocochlear complications
- A large US registry study has reported of a three times elevated risk of gastro-intestinal tract cancers in CF
- The psychological stresses of living with a chronic condition
- Depression and other mental health issues often increase in adulthood
- Presumably, this might be due to increasing co-morbidities and personal responsibilities

Thanks

- Prof. Hannah Blau & the team of the Graub CF center, Schneider children's medical center of Israel
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