

# CF Newborn Screening: What is best for Israel, and where do we stand in 2015?

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Pictures from: NHS document: A Laboratory Guide to Newborn Screening in the UK for Cystic fibrosis

# BENEFITS of CF NBS

**‘early diagnosis enables early treatment’**

- ↑ survival
- ↓ lung damage, chronic *P. aeruginosa*
- ↓ hospital care.
- ↑ nutrition:
- ↓ parental stress due to delayed diagnosis
- FUTURE: New therapies in presymptomatic phases

# Why is there no CF NBS in Israel?

- Because we are leaders in prenatal genetic screening for CF, since 1999
- Fully subsidized since 2008
- Thought CF newborns might almost disappear

Original Article

# The impact of a national population carrier screening program on cystic fibrosis birth rate and age at diagnosis: Implications for newborn screening☆☆☆

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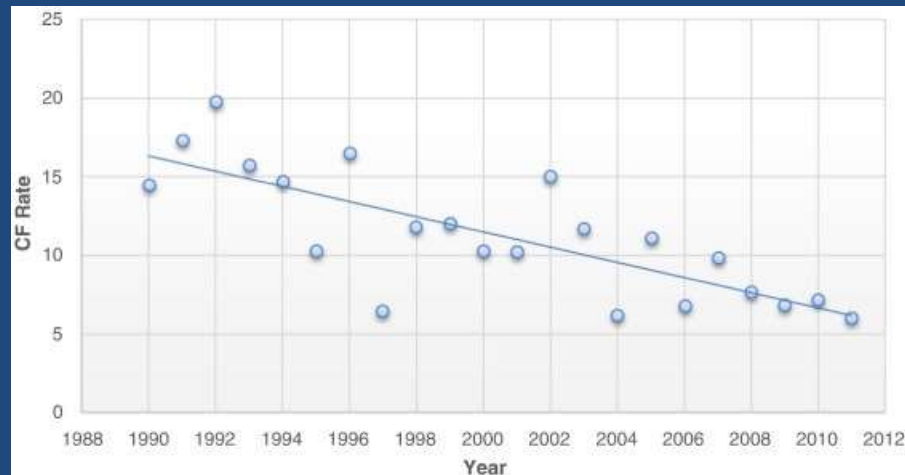
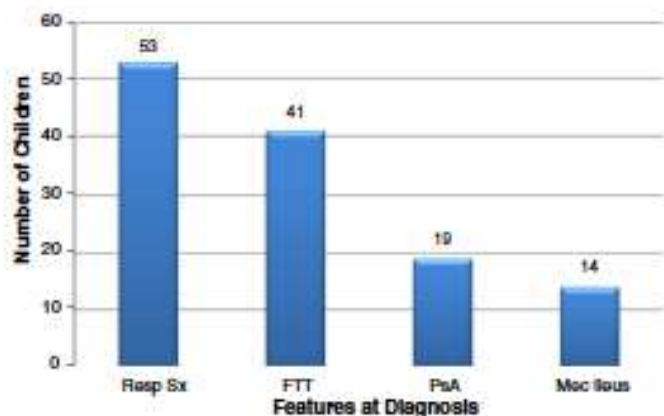
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# Impact of NBS on US CF Registry Data

- 2010- nationwide NBS screening

	2000	2012	
Wt %	19	32	p<001
Ht %	27	39	p<.001
Wt/Ht %	43	51	p <.001
+ PA	35	15	p <.001
+ SA	45	52%	p <.002

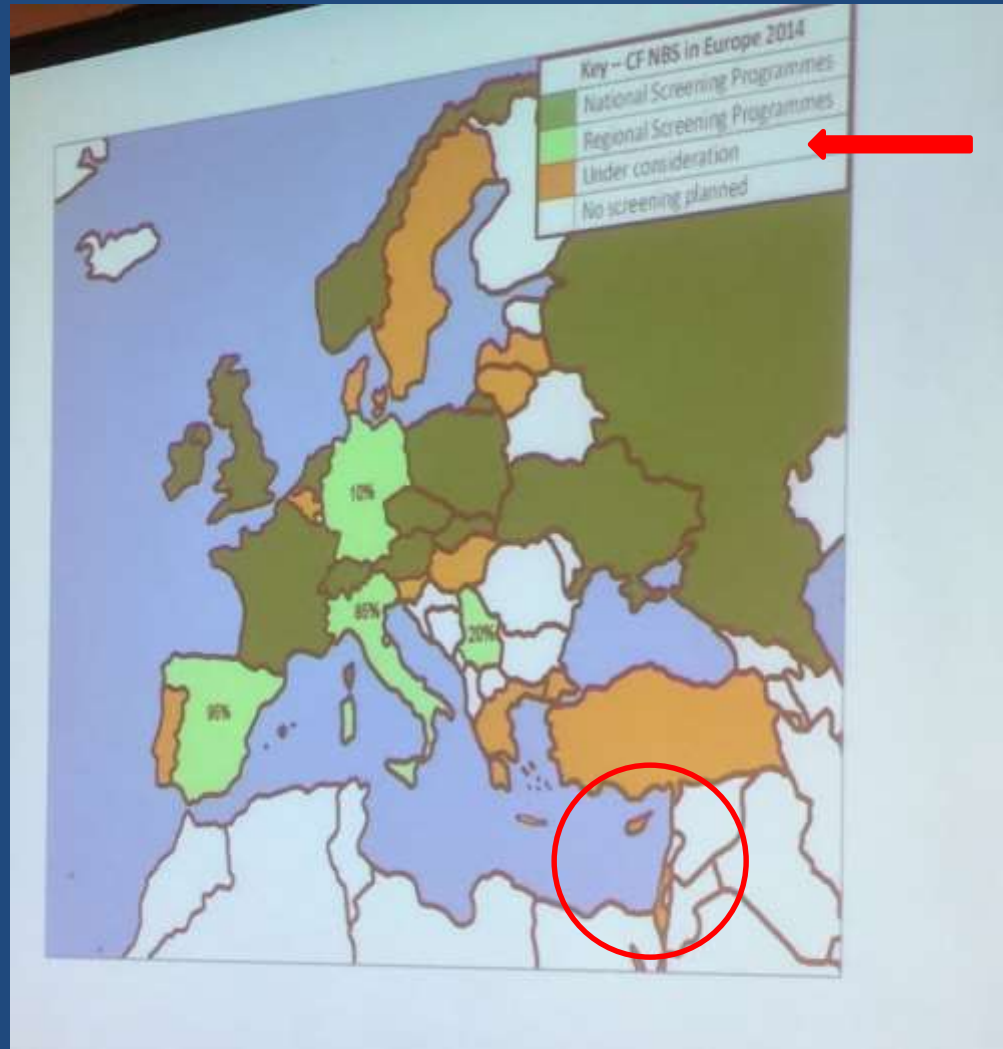
# Reasons for Diagnosis CFF patient registry\*

	2002 (%)	2012 (%) < 1 y	2012 (%) all patients
Respiratory symptoms	45.0	2.7	16.7
Failure to thrive/malnutrition	28.1	6.1	8.8
Meconium ileus	15.1	13.6	10.2
Family history	15.3	10.2	10.9
Newborn screening	12.8	82.4	61.4

CFF Patient Registry, 2002 and 2012 Annual Data report

\*Not mutually exclusive

# CF EUROPEAN NBS MAP: There is hope!

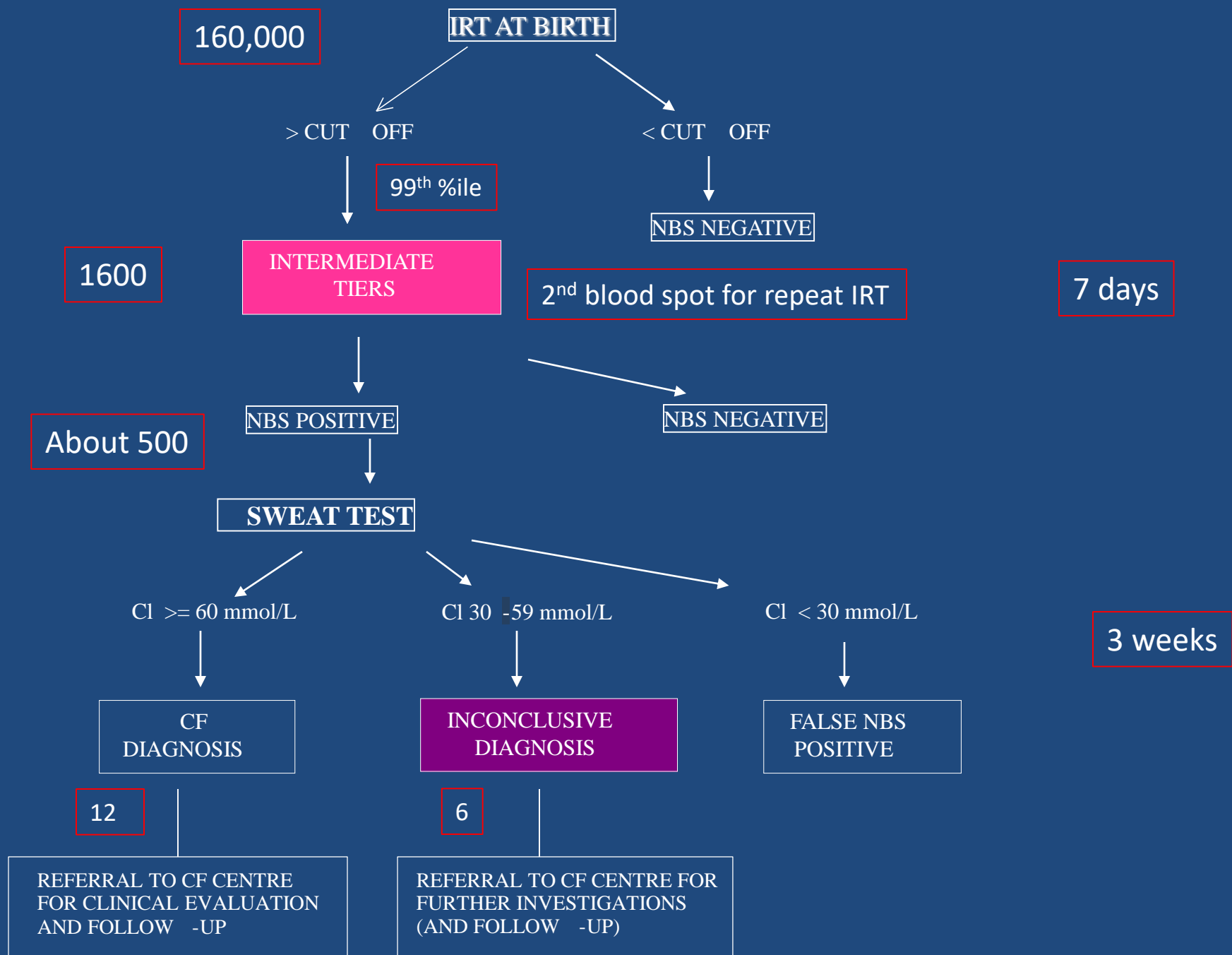


# CF NBS in Israel: Recent developments

- Recent developments:
  - Dr. Ami Zinger new Health Ministry Geneticist
    - Strongly involved with CF genetics in Israel
    - Protagonist of population carrier screening [as was Dr. Zlotogora before him]
    - Would like DNA in NBS but recognizes legal barrier regarding informed consent
  - Dr. Shlomo Almashanu, NBS Lab director
    - very supportive and helpful regarding setting up CF NBS
    - Not prepared to institute PAP till fully commercial system with positive and negative controls
  - Meeting of the above with CF center directors to discuss the exact proposed algorithm of CF NBS

# Setting up NBS in Israel

- Which method?
  - IRT/IRT –requires 2<sup>nd</sup> blood spot. System exists today
    - Therefore, the most suitable system for Israel at present
  - IRT/DNA/± next generation sequencing. In use in 90% of NBS programs world wide. However, problematic in Israel because of informed consent required for genetic testing
  - IRT/PAP/DNA – no standardized commercial kit for PAP



# False Negative NBS Results CANNOT Be Avoided

- Expect about 1/year
- Many reasons:
  - Missed and unsatisfactory blood specimens
  - Biological and timing factors
  - Mislabeling of Guthrie cards
  - Laboratory errors

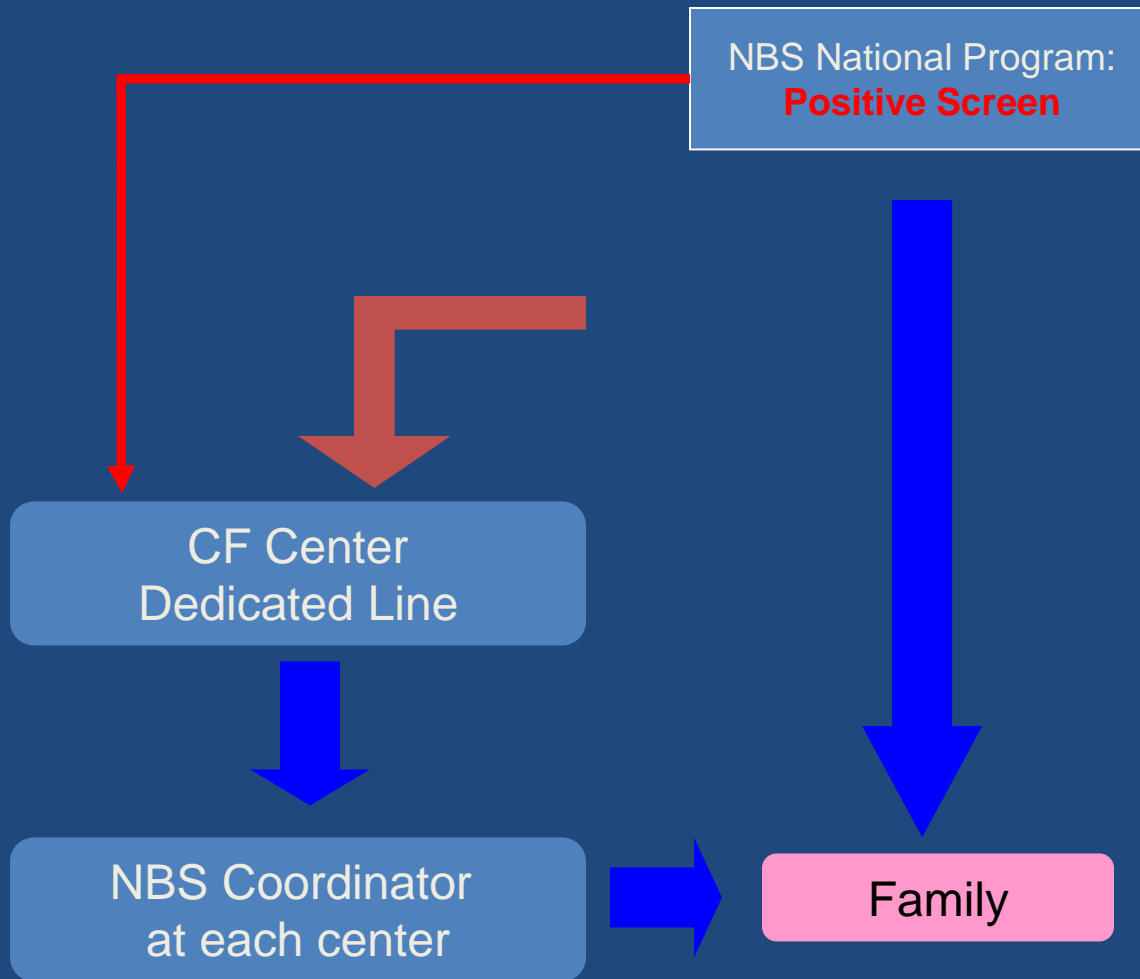
**\*THEREFORE, VIGILANCE MUST BE MAINTAINED**  
And order sweat test if suspect clinically

# Working groups required:

- Method optimization: IRT lab
- Method optimization: 2<sup>nd</sup> blood spot acquisition –
  - Finding families and infant rapidly. System in place already
- Sweat testing coordination – NBS CF trained nurse
  - Which CF center should be referred to?
    - By hospital of birth? Region of residence? Preference?
    - MUST BE PLANNED AHEAD OF NBS PROGRAM INITIATION
  - Family notification
  - Need practice in neonatal sweat testing with few QNS
  - Need to set up answer within 1-2 days (chloride, not conductance)
  - Need to correct refunding or count as day hospitalization (includes counselling session as well)
- Managing diagnosed patients: true CF (about 12/y);
- CF screening positive, inconclusive diagnosis (about 6/y)

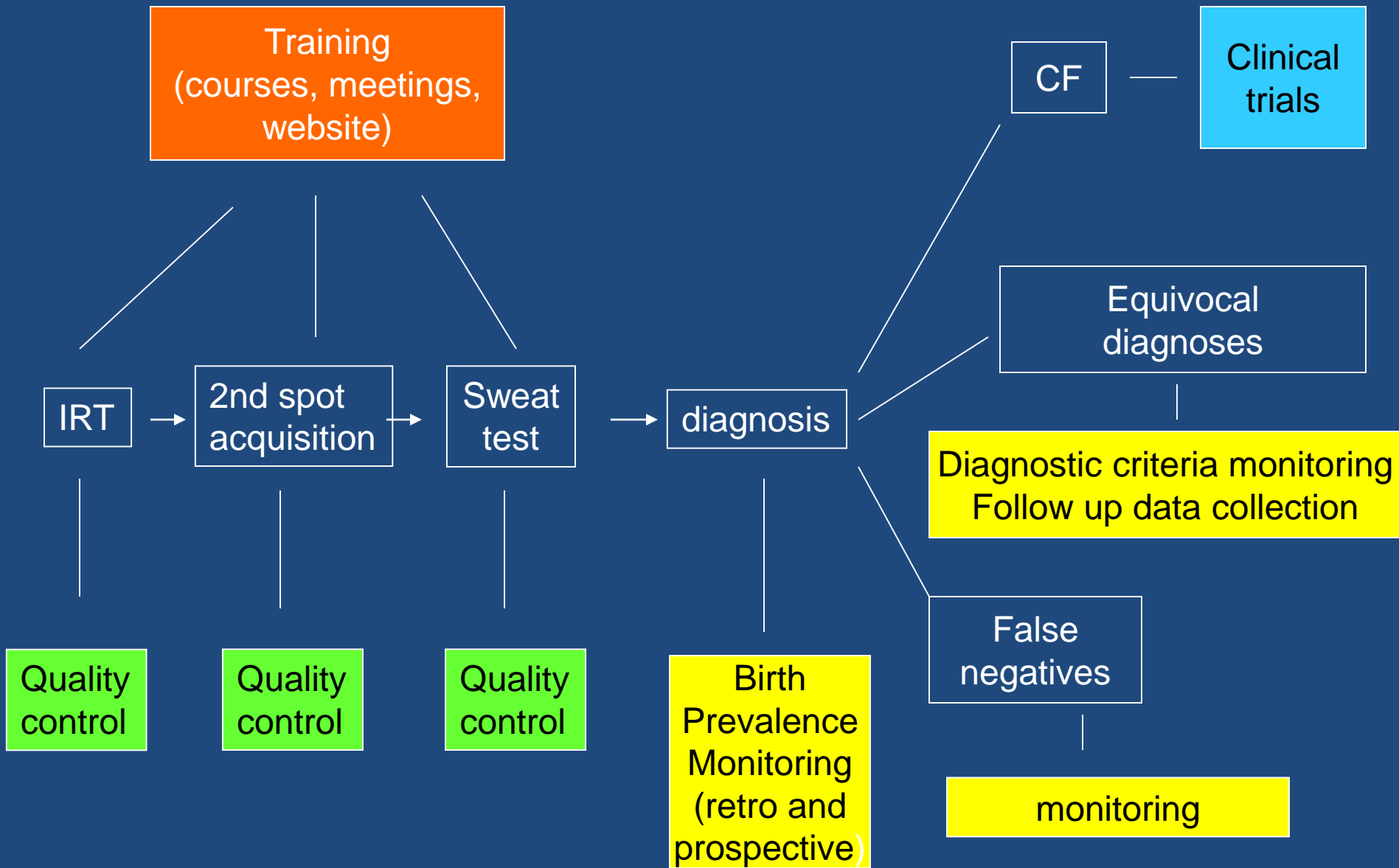
# Immunoreactive trypsin (IRT) assay (ng/ml)

- AutoDELFIA Neonatal IRT kit and immunoassay system
- fully integrate within the existing program
- Periodic multidisciplinary review of local policies for CF NBS



# Follow up responsibilities

- Sweat tests – about 500
  - (CF centers)
- Counselling and support
  - (Nurse – 1 position )
- Treatment – CF centers
  - True CF – 12/y
  - Indeterminate diagnosis ('metabolic syndrome') – 6/y
  - False negatives (missed CF – 2/y)



- After review may need to change resource allocations
- Organize a consortium of CF centers in partnership with the NBS Laboratory with 2 designated leaders – 1 in lab and 1 clinical

# Israel costs of care per CF patient

- Estimated at 10 million shekels over a life-time
- -includes: expensive drugs – Inhaled TOBI, Cayston, Pulmozyme, IV antibiotics, hospitalizations, home physiotherapy, lung transplant
- NBS would decrease costs by about 1/3 over a lifetime (**about 3 million shekels saving /patient**): less medications, physiotherapy, hospitalizations
- Dramatically improved quality of life for patient and family
- **About 12 patients born /year – save 36 million NIS/y**
- **Additional saving: sweat tests, 4000/y drop to 1000.y (300,000 NIS)**

# CF NBS costs: Personnel

- CF NBS nurse coordinator: 1 full time post nationally, probably best based at NBS lab – about 500 screen positive cases/year to coordinate to sweat tests
- Sweat test technician, disposables, materials – current staff
- Additional work load at CF centers, about 6/year screen positive, diagnosis indeterminate, follow up

# CF NBS costs: laboratory

Based on Prof. Joel Zlotogora estimates 2014: about 5 million shekels/year

Equipment: 820,000 NIS

Computerization: 100,000 NIS

Increased personnel: 700,000 NIS

Director of molecular tests, NBS-CF program: 50% position,

Lab director

Vice head of program

Annual costs: Kits: 2 million NIS – about 200,000 tests/year

May require new system for testing depending on Autodelphia or other technology:

Possible additional 1,200,000 NIS

# Summary: Recommendations for Israel\*

- CF NBS can be readily/effectively implemented in Israel with IRT/IRT and excellent CF centers.
- Transform to a balanced, cost effective public health strategy combining population/prenatal CF screening with IRT/IRT screening of newborns

When legally enabled, may consider converting to an IRT/DNA protocol

- Plan intensively for implementation, follow-up, quality assurance, and changing resource allocations
- Organize a consortium of CF centers in partnership with the NBS Laboratory with 2 designated leaders

In Israel:

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Michael Wilschanski

Eitan Kerem

All 6 Israeli CF Center physicians

Meir Mei-Zahav

Joel Zlotogora

Globally

Phil Farrell

Olaf Sommerberg

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Milan Macek

Kevin Southern

Ann Munck

THANK  
YOU!!