

Setting Up a Multi-National Trial: Lessons Learned in the TIDES study

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How the Study Began: European CF Meeting in Crete, 2005!



Ask an interesting, focused question



- 1. Anecdotal evidence & single center studies indicated that patients and parents may have elevated symptoms of depression & anxiety
- 2. We spent 2 years planning the study at ECFS & NACF; getting buy-in and ideas from others
- 3. We created a website with the protocol, ethics submission, measures, and database
- 4. We found people who were committed to the research and could *do a lot with very little*
- I wrote a grant to CFF and then passed it on to other investigators



TIDES

The International Depression / Anxiety Epidemiological Study

• Overview

Documents

• Updates

• Contacts

IRB Templates

Measures

Presentations

Data Dictionary

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Research Protocol

- Full Grant Proposal 
- Short Ethics Proposal 

Consent & Assent Forms

- English
- Spanish

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Specific Aims

- *Aim 1:* To estimate the prevalence of depression and anxiety in patients with CF ages 12 through adulthood & parent caregivers of children with CF birth to 18
- *Aim 2:* To identify risk factors associated with symptoms of depression and anxiety
- *Aim 3:* To evaluate how depression and anxiety are associated with health outcomes (FEV_1 and BMI%/BMI) currently and in the future

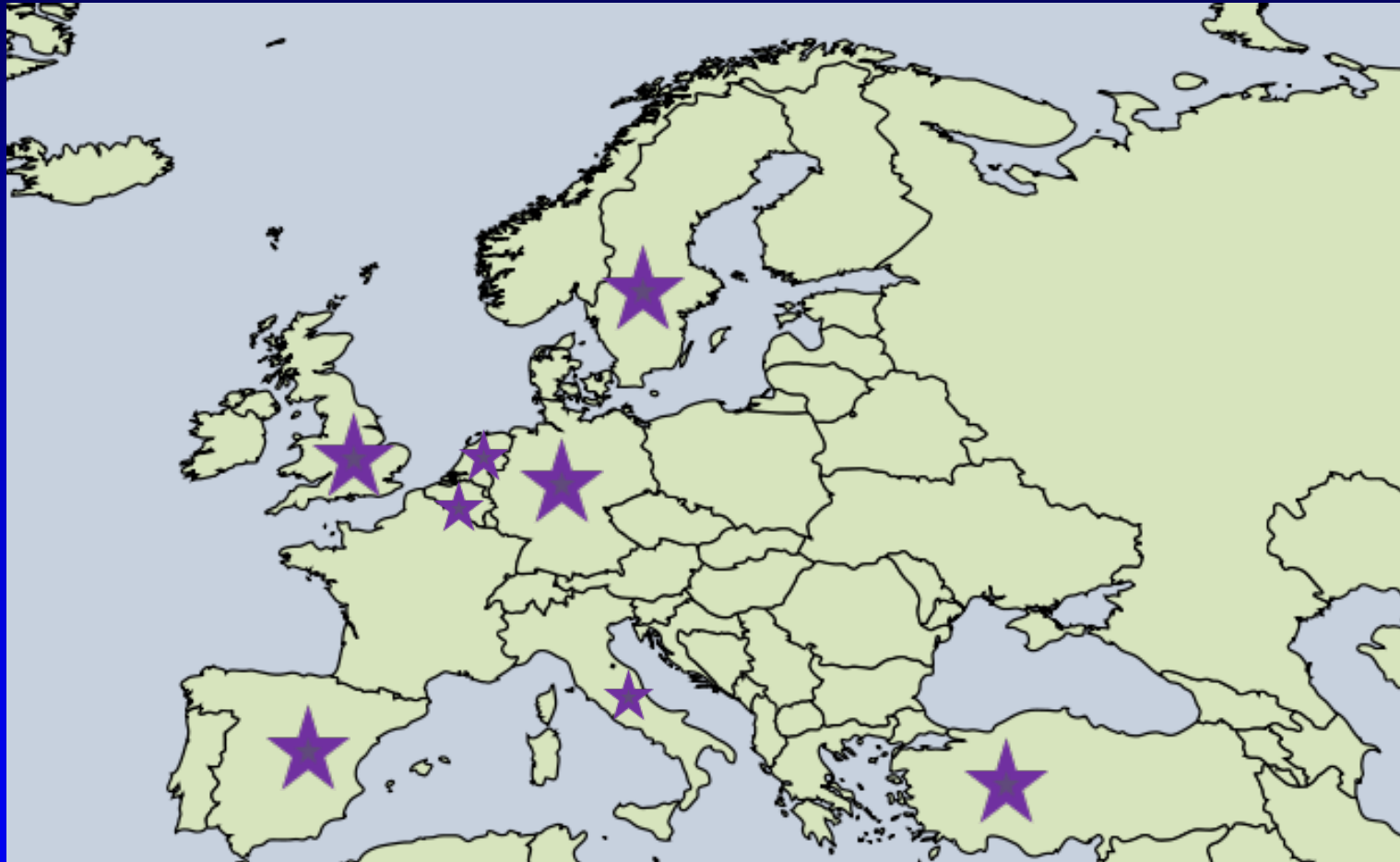
Methods

- Two brief screening measures of depression & anxiety (5 minutes each) were administered in clinic by a social worker or psychologist
 - Hospital Anxiety Depression Scale (HADS)
 - Center for Epidemiological Studies-Depression (CES-D)
- Patients and parents also completed a background/ medical information form, verified by chart review

Participating European Countries

N = 8

+ US = 9!!



Participating Centers in US

N = 45 CF Centers

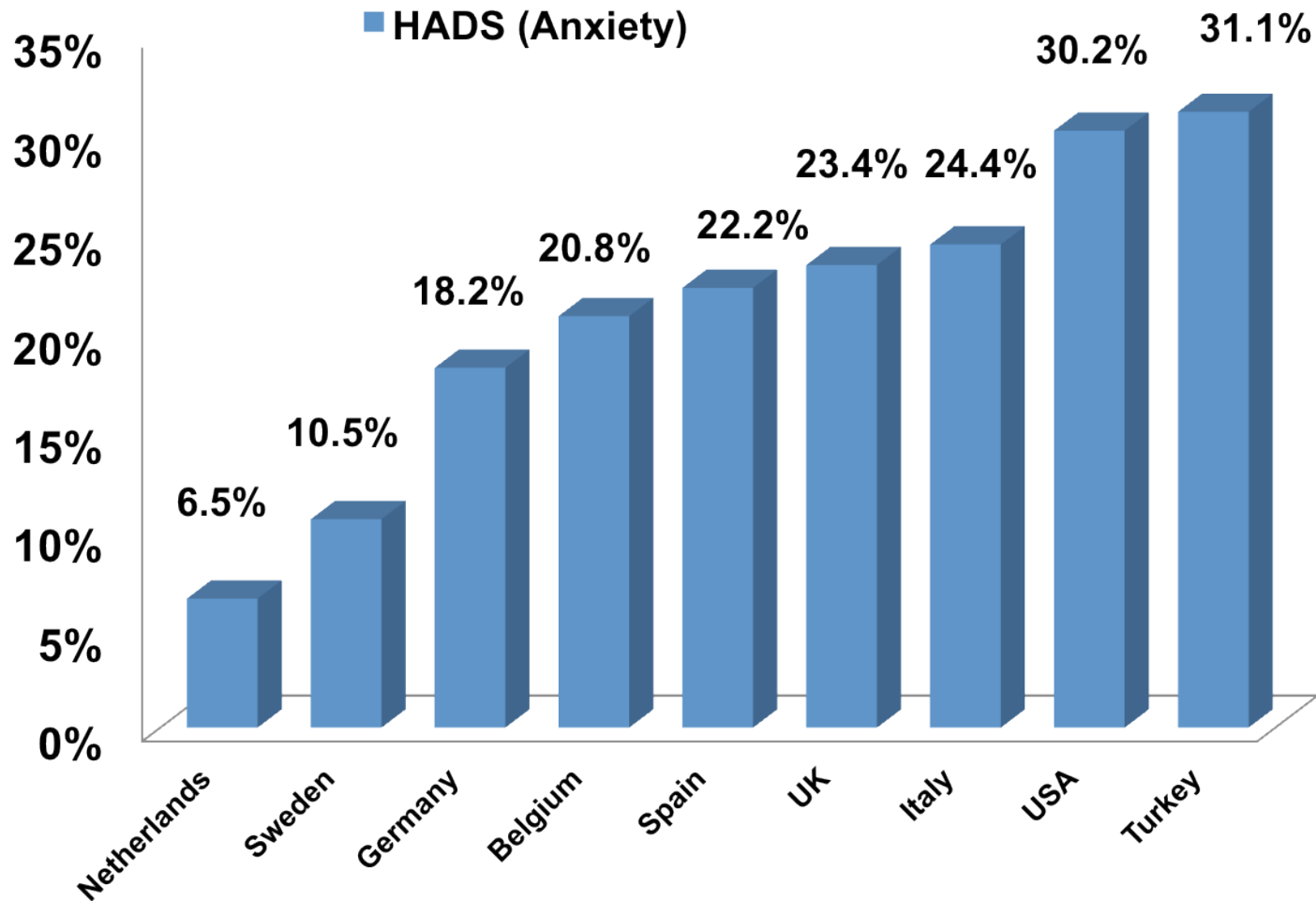


Patient Demographics

Total N = 6023

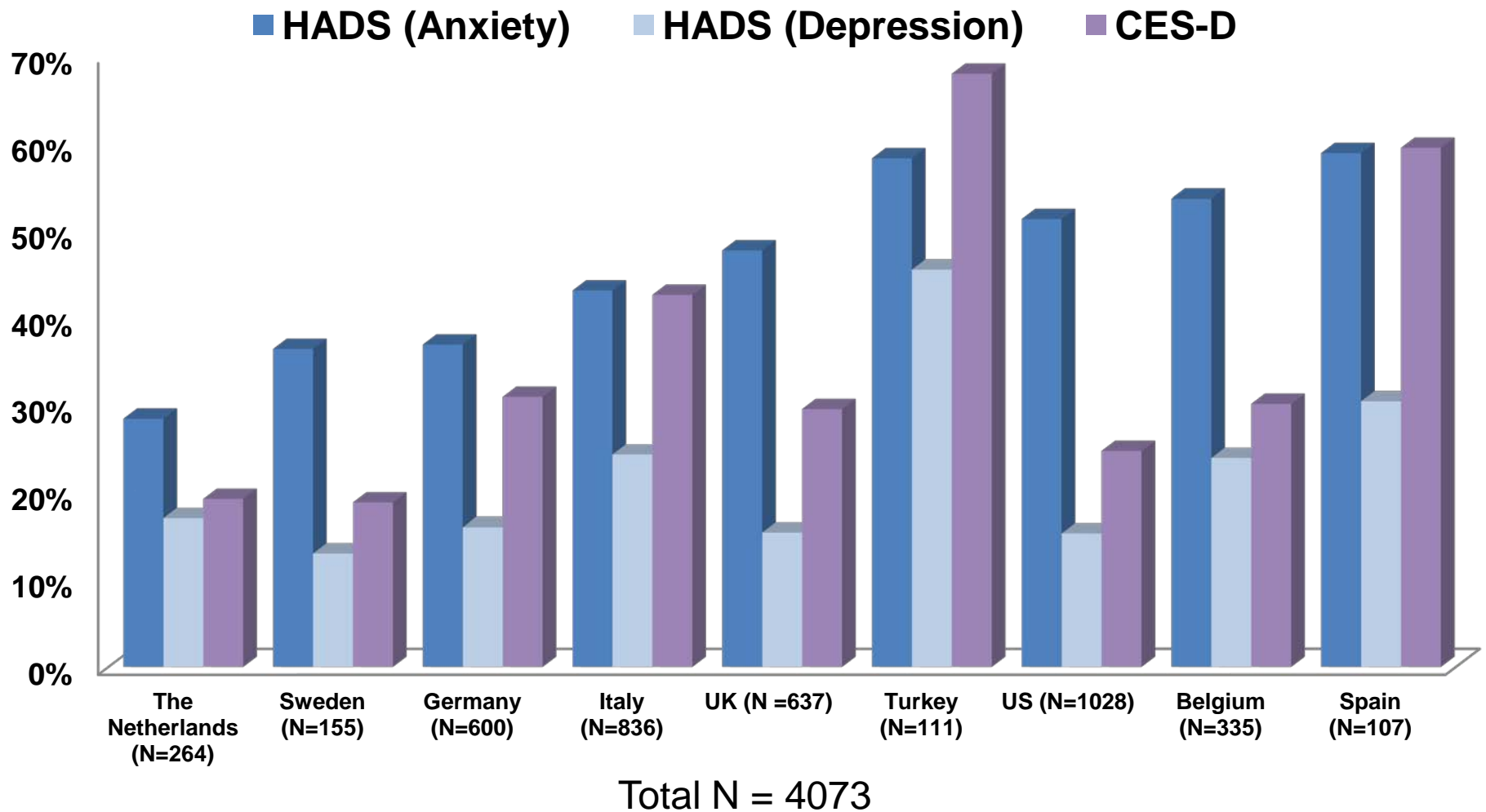
Country	N	Age	Age Range	FEV ₁ %	BMI
Belgium	417	25.9	13-69	71.8	20.7
Germany	683	23.4	13-65	67.4	20.0
Italy	753	24.4	12-70	74.3	20.5
Netherlands	509	27.7	13-69	66.6	21.4
Spain	269	26.0	13-53	64.8	21.4
Sweden	166	26.9	13-70	75.1	21.8
Turkey	34	16.8	13-29	71.5	20.1
UK	2033	27.6	13-78	62.9	22.1
US	1159	25.3	12-73	67.9	21.8

Adolescent Anxiety: % Above Cut-off



All Caregivers: Above Clinical Cutoff

N = 4,073



Our Amazing Success!

We screened 6023 patients, ages 12 to 78!

We screened 4073 parents of children with CF ages 0 to 18!

Even more remarkable in a rare disease

Our findings revealed high rates of depression and anxiety in both patients and parents

How did we pull this off?

- We involved many members of the multidisciplinary team (nurses, social workers, psychologists)
- We continued to build consensus on the aims and methods; introduced new people to the study as turn-over occurred
- We had annual “progress report” meetings at ECFS and NACF to present our data and progress---to keep up enthusiasm!
- The study design and measures were relatively simple and doable
- We emailed and communicated regularly with countries and PIs

Issues Not Anticipated

- **Who would enter the data in each country?**
- **Who would clean the database once completed and answer queries?**
- **Ethical rules about data transfer**
 - ❖ **Almost blocked inclusion of the UK data**
 - ❖ **Delayed receipt of the data until 4 weeks before ECFS!**

Mistakes We Made—But It's OK!

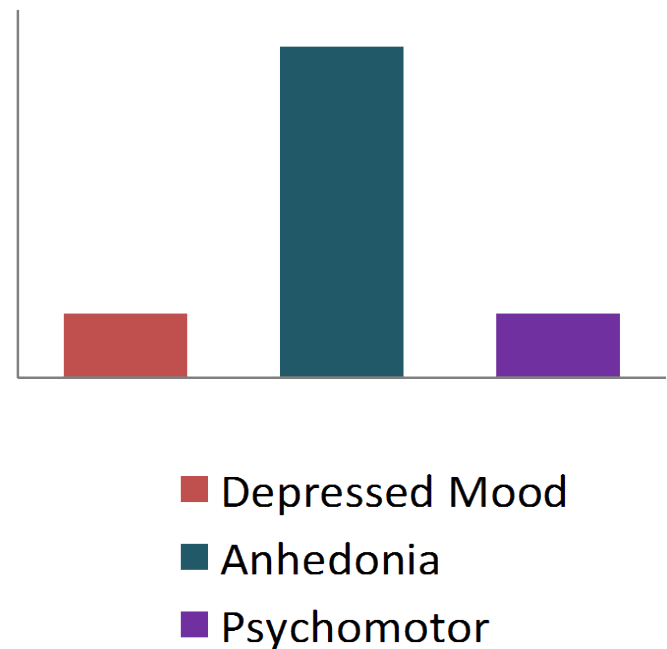
- Europeans wanted to use the HADS as a screener for anxiety and depression
- This instrument has not been used in the US
- We compromised and many countries administered *both* the HADS and the CES-D
- In every study, there are things you would do differently *next time*
- *Research is an iterative process*

DSM-IV Criteria for Depression

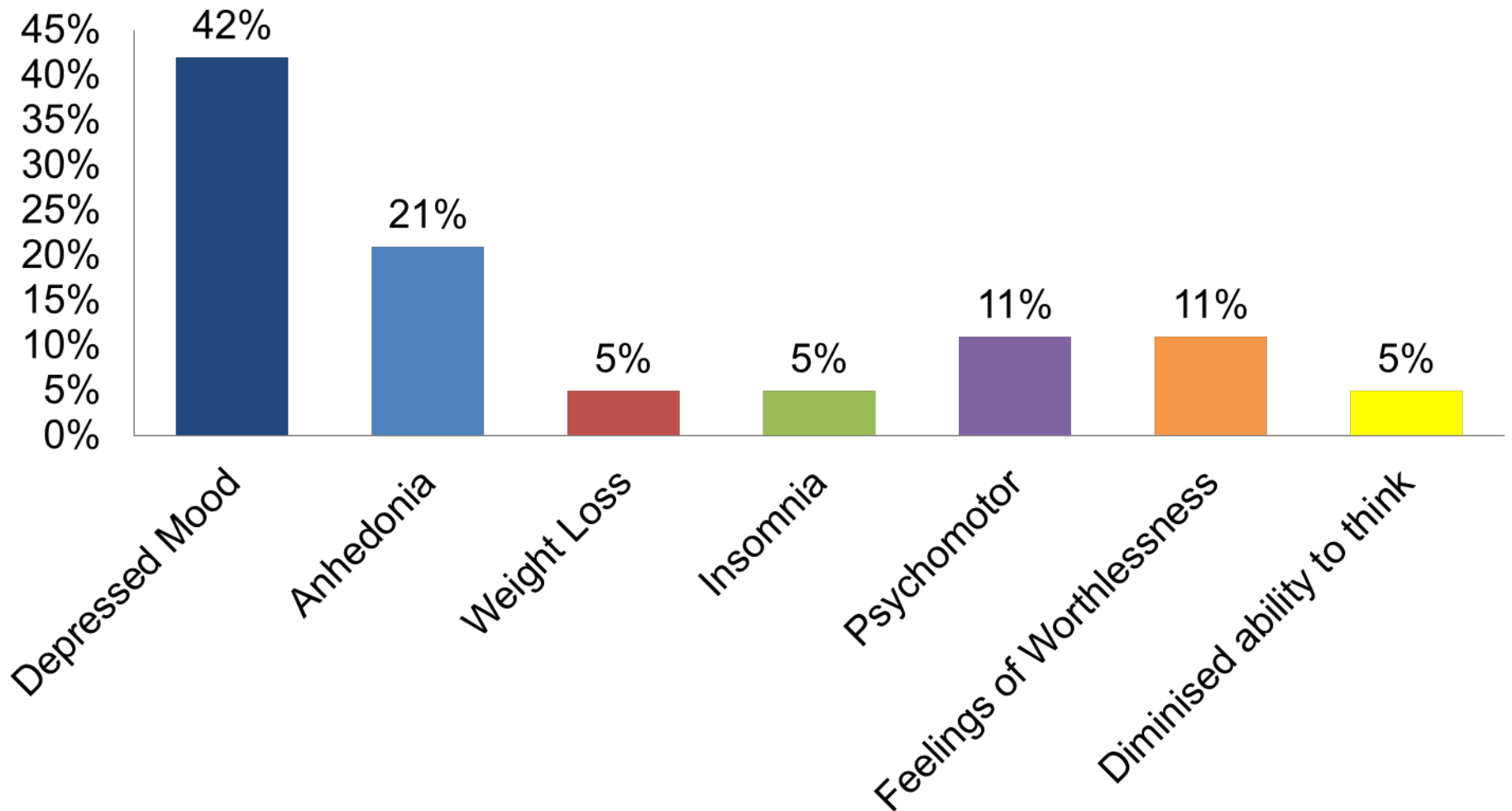
- 5 or more of the following within a two week period
 1. Depressed mood
 2. Anhedonia
 3. Significant weight loss
 4. Insomnia or hypersomnia
 5. Psychomotor agitation or retardation
 6. Fatigue
 7. Feelings of worthlessness
 8. Diminished ability to think
 9. Recurrent thoughts of death or suicide

HADS-Depression: Mostly Anhedonia

- I enjoy the things I used to enjoy
- I can laugh and see the funny side of things
- I feel cheerful
- I feel as if I am slowed down
- I have lost interest in my appearance
- I look forward with enjoyment of things
- I can enjoy a good book, radio or television program



CES-D: Cognitive Symptoms of Depression



Important Considerations

- Funding is important to cover the time of those collecting data
- We did this study on a “shoe string” with little \$; but having some funding was key
- Send quarterly newsletters to share information and progress
- Set up annual luncheons or coffee times to improve communication
- Decisions about authorship should be made early on; but it also depends on effort
- We now have momentum-- what question should we ask next?

Future Directions

- **Do something with the results!!**
- **Hold a consensus conference through ECFS and CFF to review the literature, our data, and agree on recommendations**
- **Perform annual screening with patients and parents**
- **Develop referral pathways to provide assistance**