



Children's Hospital Colorado

Celiac Disease: is it time for mass screening yet?



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Conflicts and disclosure

- I have no conflicts of interest to disclose

Celiac Disease (CD) is not rare at all

- US population – overall 1% prevalence
- Higher in Europe – Finland – 2%
- In children born during the Swedish “Celiac Epidemic” of 1984-1996 – 3% of all 12 year olds
- Incidence is rising

Should we be performing mass screening for Celiac Disease?

- CD is common
- There is a large number of cases that remain undiagnosed
- Untreated CD may lead to complications
- The screening test is simple and safe

Many questions remain unanswered however...

Who does NASPGHAN currently recommend for CD screening?

- Groups with a higher risk for CD
 - Type 1 diabetes

Targeted screening based just on just risk factors would miss most CD cases!

- Turner Syndrome
- William Syndrome
- Selective IgA deficiency
- First degree relatives with celiac disease

Who do we typically test? ...those with symptoms:

Targeted screening based just on symptoms would miss about ½ of all CD cases

- **Subclinical CD:** CD that is below the threshold of clinical detection
- **Asymptomatic CD:** no signs or symptoms

HLA-DQ2 and DQ8 are the major genes for CD

- **DQ2** is seen in about 90% of all CD
- **DQ8** is seen in about 8-10% of all CD
- Without either of these genes, risk of CD is extremely low
- Having DQ2 or DQ8 \neq CD, it just means there is a risk

40% of the general population is at risk for CD

Distribution of HLA genotypes in a representative Denver cohort
(31,881 who consented to screening)

	*HLA distribution (%)
DQ2/DQ2	1.1
DQ2/DQ8	2.3
DQ2/X	17.1
DQ8/DQ8	2.2
DQ8/X	17.3
X/X	60.0

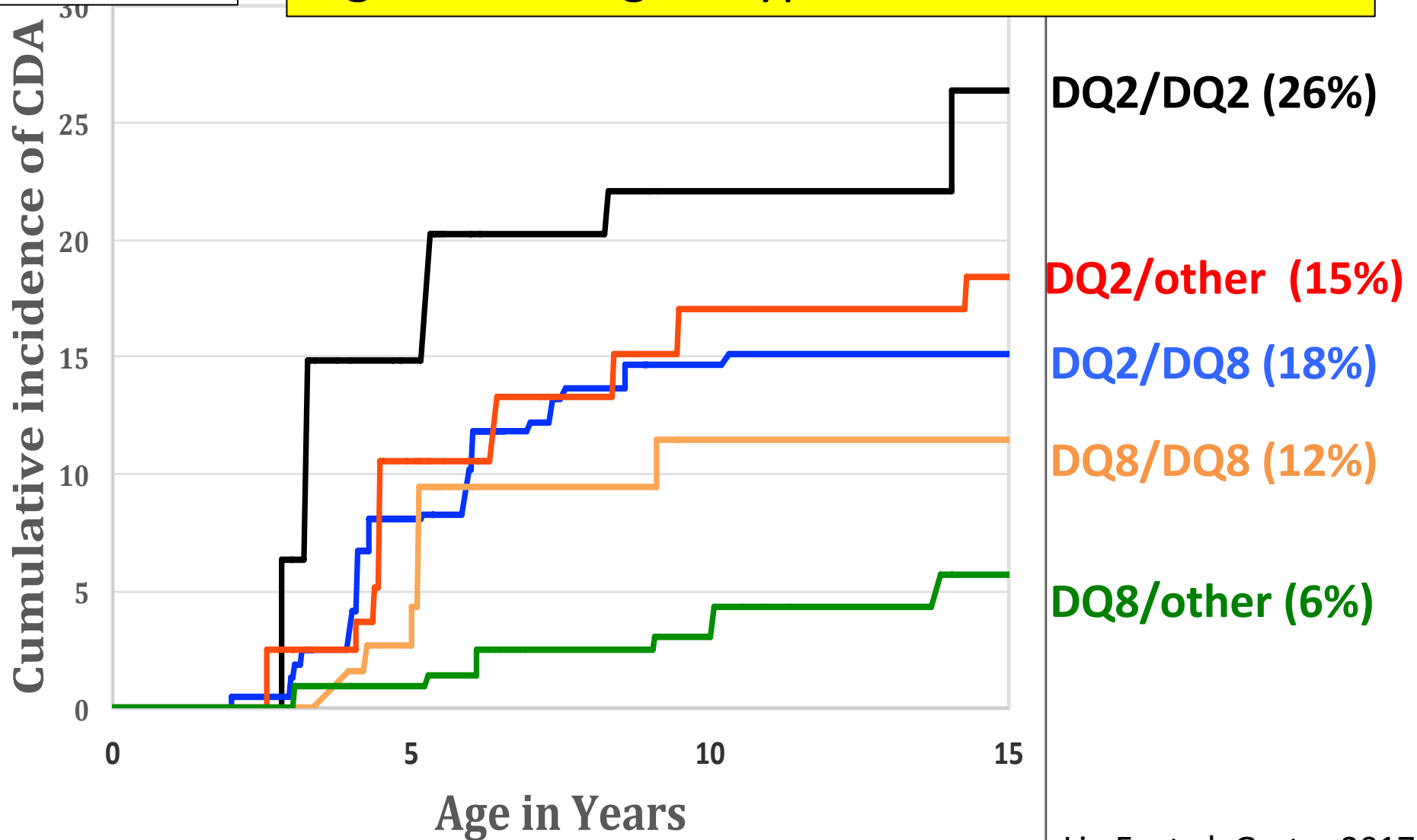
} 40%

(*X = not DQ2 or DQ8)

Liu, Gastro 2017, data from Diabetes Autoimmunity Study of the Young (DAISY)

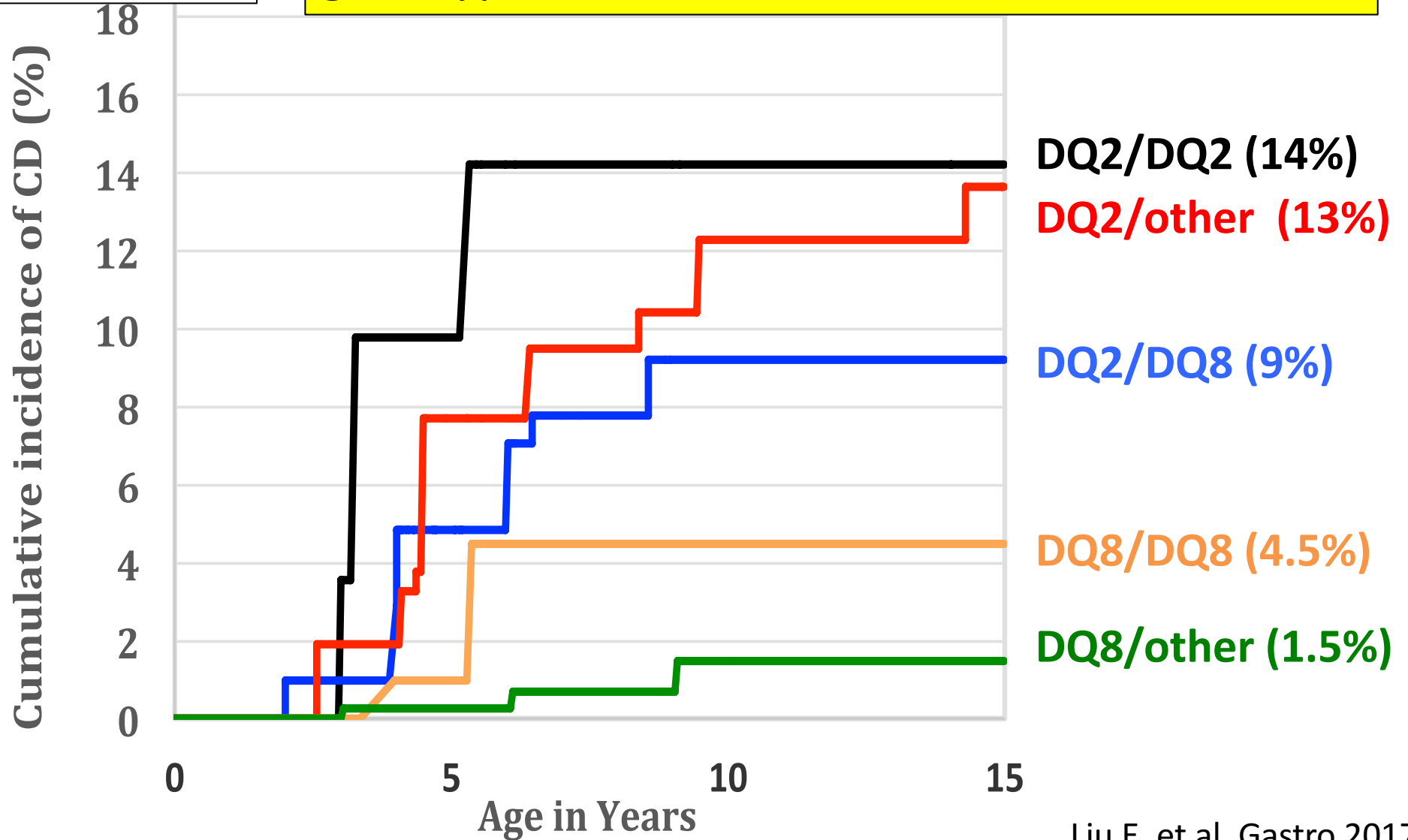


Development of tTG antibodies: 15 year follow-up of 1339 Colorado children with high-risk HLA genotypes



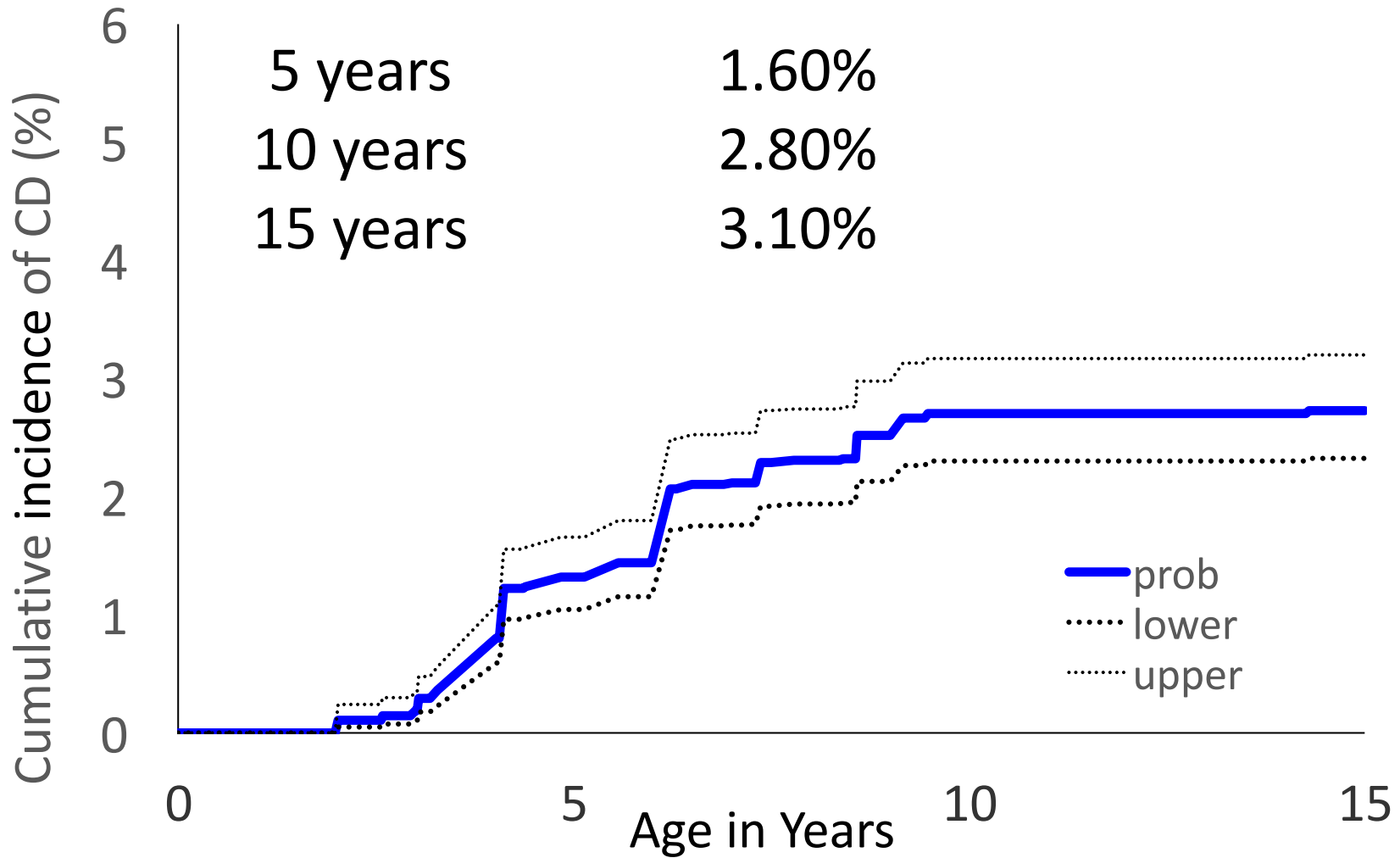


Development of CD: 15 year follow-up of 1339 Colorado children with high-risk HLA genotypes





Estimated cumulative incidence of celiac disease in the Denver general population



Conclusions from this study

- All you need is HLA-DQ2 or DQ8 to develop CD
 - Even without a family history
 - Even without having symptoms
- Not all with DQ2 or DQ8 will develop CD
- Development of CD occurs quickly in childhood.
- The rate of CD development slows down after age 10
- Up to 5% of Colorado adolescents will develop tTG antibodies at some point.
 - Not everyone with tTG antibodies will have CD
- There appears to be an increased incidence of CD in the Denver general population in adolescents (3%)
 - Similar to reports in Finland (2%) and Sweden (3%)

If we were to do general population screening for CD...

- Either done by first performing HLA gene testing.
 - Then screen only those with a genetic risk

OR

- Mass screening for everyone

Either approach may require multiple time points for screening for CD

What's the holdup then for doing mass screening?

1. In someone who is asymptomatic, are we causing any harm?
 - In screening (causing anxiety, depression)
 - In diagnosing (unnecessary biopsies)
 - In treating (affecting quality of life)
2. Is there benefit if they are asymptomatic?
 - (Are we actually improving health)
3. Is it cost effective to do general population screening for CD?

Screening for Celiac Disease

US Preventive Services Task Force Recommendation Statement

- The USPSTF found inadequate evidence
 - on the accuracy of screening for celiac disease
 - on the potential benefits and harms of screening vs not screening
 - for targeted vs universal screening
 - for the potential benefits and harms of treatment of screen-detected celiac disease.

Call for more studies

- To understand the effects of a gluten-free diet in asymptomatic CD
- To better understand the natural history of asymptomatic CD
- To understand the positive/negative impact of screening for CD

FREE SCREENING TYPE 1 DIABETES AND CELIAC DISEASE Autoimmunity Screening for Kids (ASK)

Eligibility criteria include:

- Children 2-17 years of age
- Live in the Denver metro area
- Not diagnosed with Type 1 Diabetes
- Consent by parent or legal guardian



Just ASK....

303.724.1275

www.ASKhealth.org

Approved by the Colorado Multiple IRB #14-0553 Marian Rewers, MD, PhD



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- ▶ ASK is a free population screening initiative for early type 1 diabetes (T1D) and celiac disease (CD) for ages 2-17
- ▶ ASK is funded by the Juvenile Diabetes Research Foundation (JDRF) and Helmsley Charitable Trust (HCT)
- ▶ Goal is to screen 55k children over the next 3 years

Approved by the Colorado Multiple IRB
#14-0553 Marian Rewers, MD, PhD



- The purpose of ASK is to test the feasibility of mass screening for type 1 diabetes and CD
- To date, 1,808 screened
 - 55 are tTG+ (3%)
 - 26 have high tTG+ levels (1.4%)



- Will be able to study the impact on children and families of finding out they are tTG+ (especially asymptomatic)
- There will be a follow-up study to look at outcomes of tTG+ children:
 - Can study the natural history of asymptomatic tTG+ children
 - Can look at quality of life in tTG+ children
 - Can look at costs associated with mass screening

Summary

- There are a lot of reasons why we should consider mass screening for CD
- We need to learn more about the potential benefits and harms of doing mass screening
- The ASK study (and will be doing mass screening in Denver to start to address these questions