The Natural History of Undiagnosed Celiac Disease: A Retrospective Study

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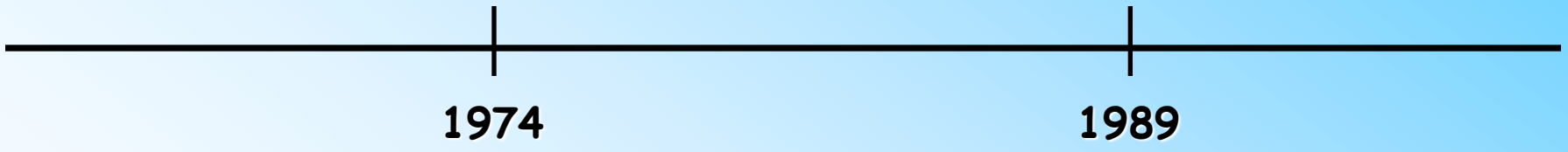
Current CD Knowledge

- Considered the most common autoimmune disease in North America and Europe
- CD shows a prevalence of 0.5 - 1% in the general population
- People are born with CD?
- Trend of prevalence is unknown
  - ↑ diagnosis due to ↑ awareness
  - ↑ in prevalence like other autoimmune diseases
- Comorbidity
  - Untreated celiac disease leads to comorbidity
  - Genes for celiac disease are linked to other diseases

Samples

	Clue I	Clue II
Total	11,653	22,888
Odyssey	8,394	8,394
Our Study	4,351	3,511



- The CLUE Campaigns came from the slogan

  "Give us a CLUE to Cancer"

- Brief histories, blood samples and a detailed heath questionnaires were obtained on all participants

Aims

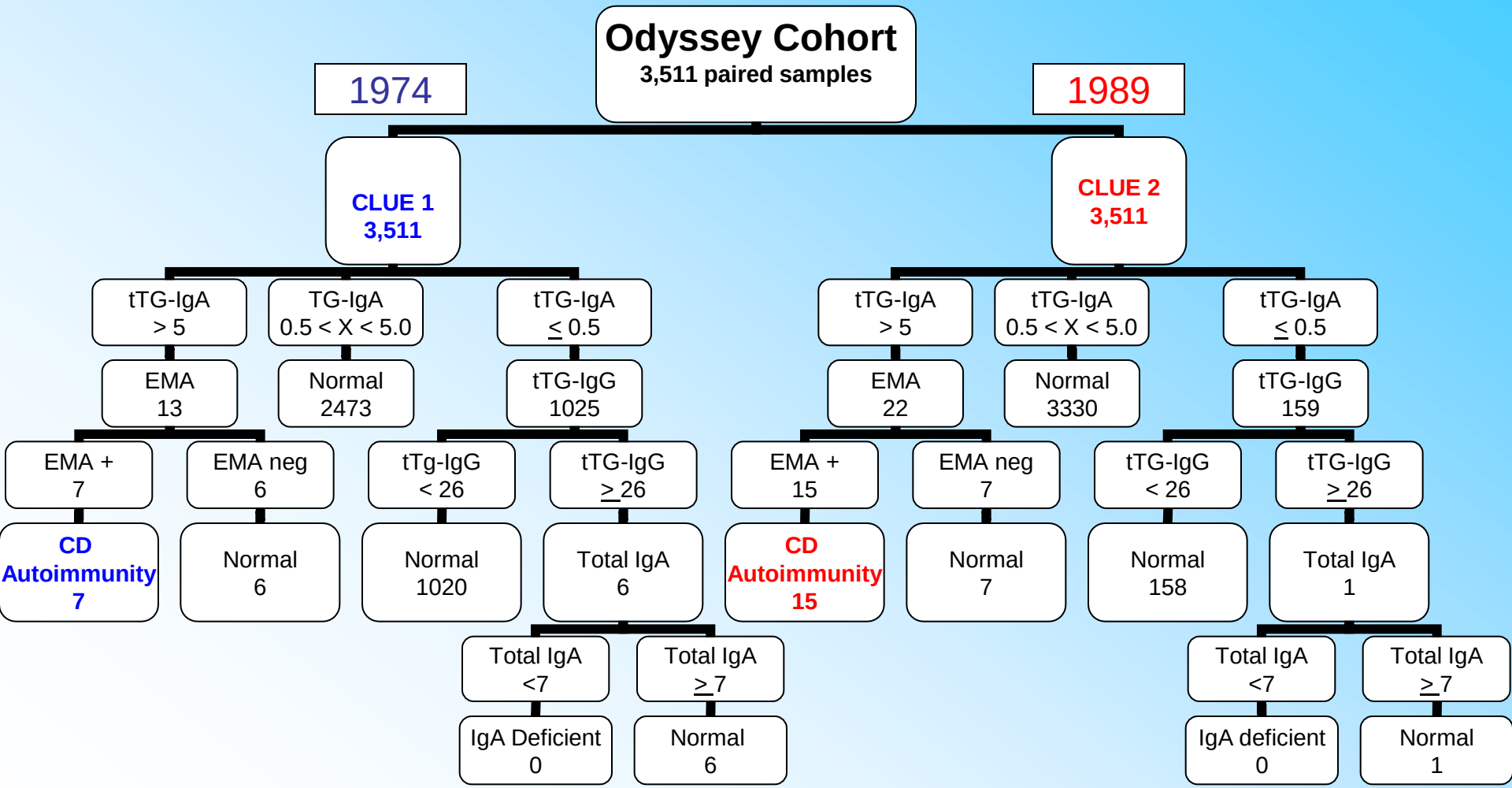
- To uncover the natural history of untreated Celiac Disease in a single large cohort

- To investigate the changes in the prevalence of CD in the US over time

Methods

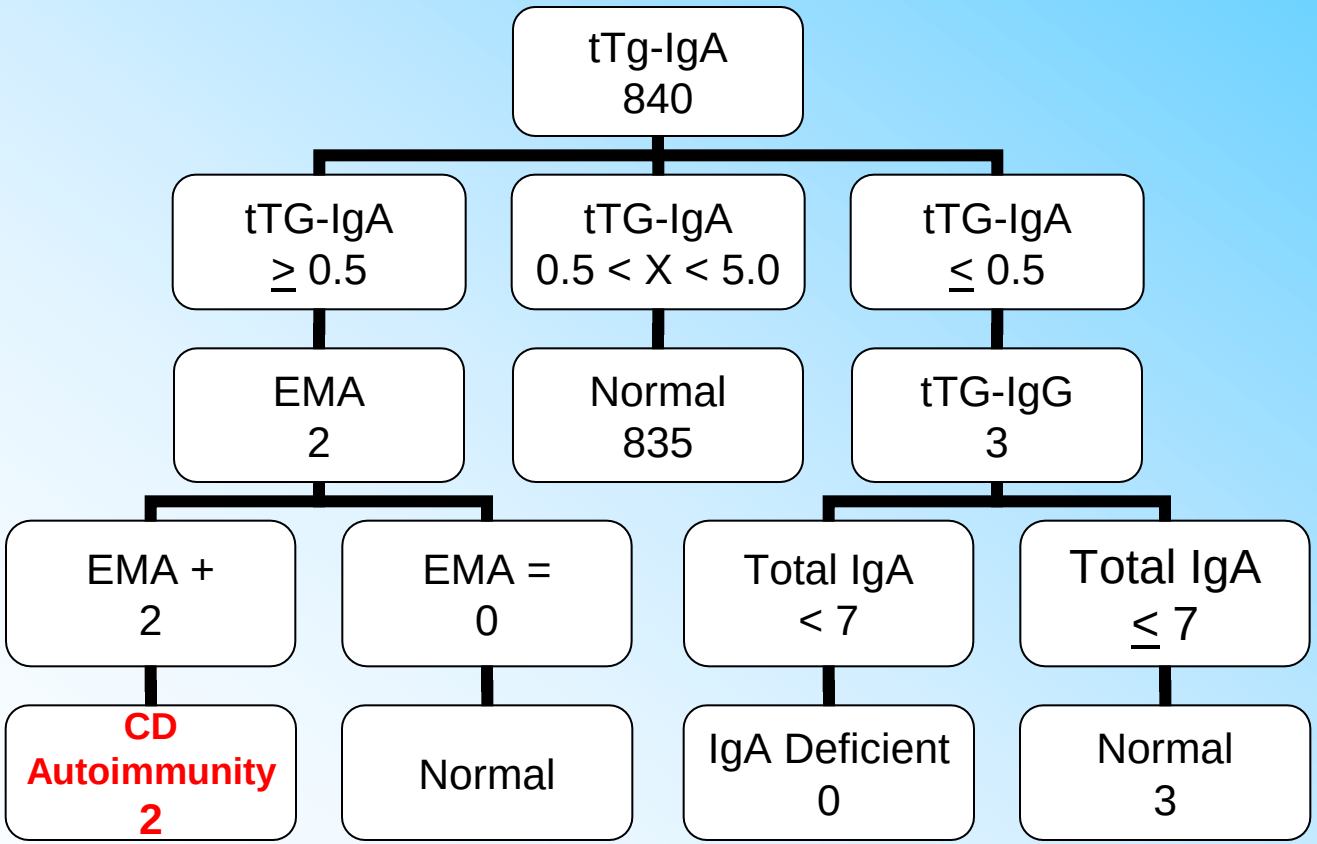
- Samples were initially screened for human anti-tissue transglutaminase-IgA antibodies (tTg-IgA)
- Positive tTg-IgA samples were screened for anti-endomysial antibodies (EMA)
- To detect any possible celiac in the cohort that may have a total IgA deficiency:
  - All tTG-IgA < 0.5 AU were screened with human anti-tissue transglutaminase-IgG antibodies (tTg-IgG)
  - Total serum IgA's were done on samples that were positive for tTG-IgG.

Results


Odyssey Cohort
3,511 paired samples
1974
1989
CLUE 1
3,511
CLUE 2
3,511
tTG-IgA
> 5
TG-IgA
0.5 < X < 5.0
tTG-IgA
≤ 0.5
tTG-IgA
> 5
tTG-IgA
0.5 < X < 5.0
tTG-IgA
≤ 0.5
EMA
13
Normal
2473
tTG-IgG
1025
EMA
22
Normal
3330
tTG-IgG
159
EMA +
7
EMA neg
6
tTg-IgG
< 26
tTG-IgG
≥ 26
EMA +
15
EMA neg
7
tTG-IgG
< 26
tTG-IgG
≥ 26
CD
Autoimmunity
7
Normal
6
Normal
1020
Total IgA
6
CD
Autoimmunity
15
Normal
7
Normal
158
Total IgA
1
Total IgA
<7
Total IgA
≥ 7
Total IgA
<7
Total IgA
≥ 7
IgA Deficient
0
Normal
6
IgA deficient
0
Normal
1

Results

840 deceased subjects after CLUE 1



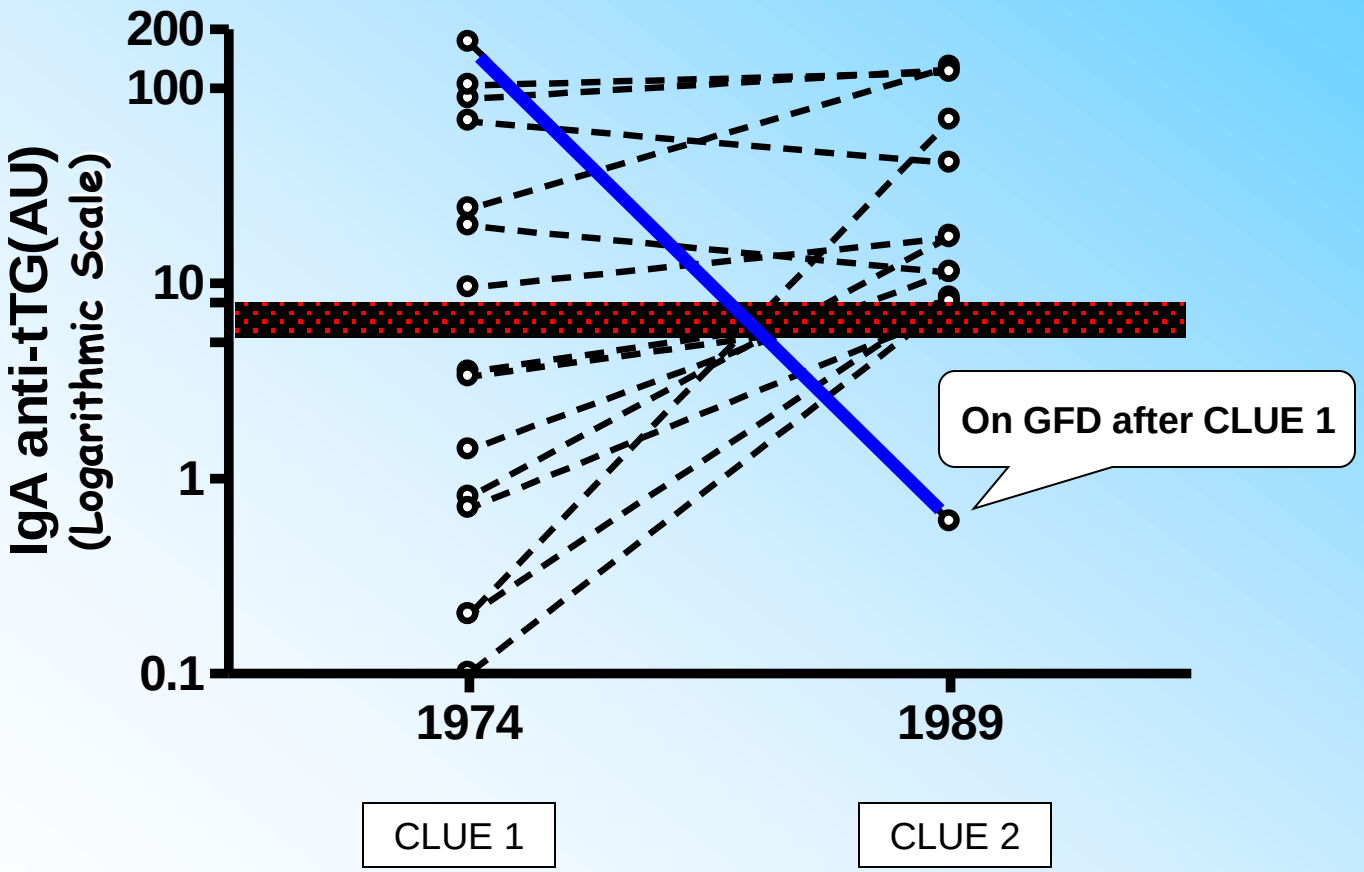
CD cases

			Age	CLUE 1 (1974)		CLUE 2 (1989)		
Case #	Race	Gender	CLUE 1	tTG-IgA	EMA	tTG-IgA	EMA	Clinical Findings
1	C	F	52	**19.6**	**>1:50**	**11.3**	**>1:50**	Osteoporosis
2	C	F	50	**24.0**	**>1:50**	**127.9**	**>1:50**	
3	C	F	32	**88.1**	**>1:50**	**124.0**	**>1:50**	**Celiac disease after CLUE 2**
4	C	M	60	**102.9**	**>1:50**	**119.8**	**>1:50**	Osteoporosis/ Osteoarthritis
5	C	F	50	**67.3**	**>1:50**	**41.2**	**>1:50**	
6	C	M	25	**171.5**	**>1:50**	0.6	Neg	**Celiac disease after CLUE 1**
7	C	F	34	**6.4**	**>1:20**	**6.9**	**>1:20**	Osteoporosis/ Osteoarthritis/SLE
8	C	M	26	**9.5**	Neg	**17.1**	**>1:50**	
9	C	F	24	0.8	Neg	**17.4**	**>1:50**	SLE
10	C	F	53	1.4	Neg	**11.4**	**>1:10**	Diabetes /Osteoporosis/ Osteoarthritis
11	C	F	14	3.5	Neg	**8.1**	**>1:10**	Osteoporosis
12	C	F	54	3.3	Neg	**7.2**	**>1:20**	Osteoarthritis
13	C	F	37	0.2	Neg	**8.4**	**>1:20**	Arthritis
14	C	F	28	0.2	Neg	**68.4**	**>1:50**	Osteoporosis/ Osteoarthritis
15	C	M	27	0.1	Neg	**8.0**	**>1:50**	Diabetes / Arthritis
16	C	F	29	0.7	Neg	**7.1**	**>1:10**	Osteoporosis/ Osteoarthritis
17	C	F	41	**171.1**	**>1:50**	-	-	
18	C	F	52	**57.8**	**>1:20**	-	-	**Jejunal Cancer**

Anti-tTG antibodies in the Odyssey subjects with CD

(anti-tTg-IgA and EMA positive)

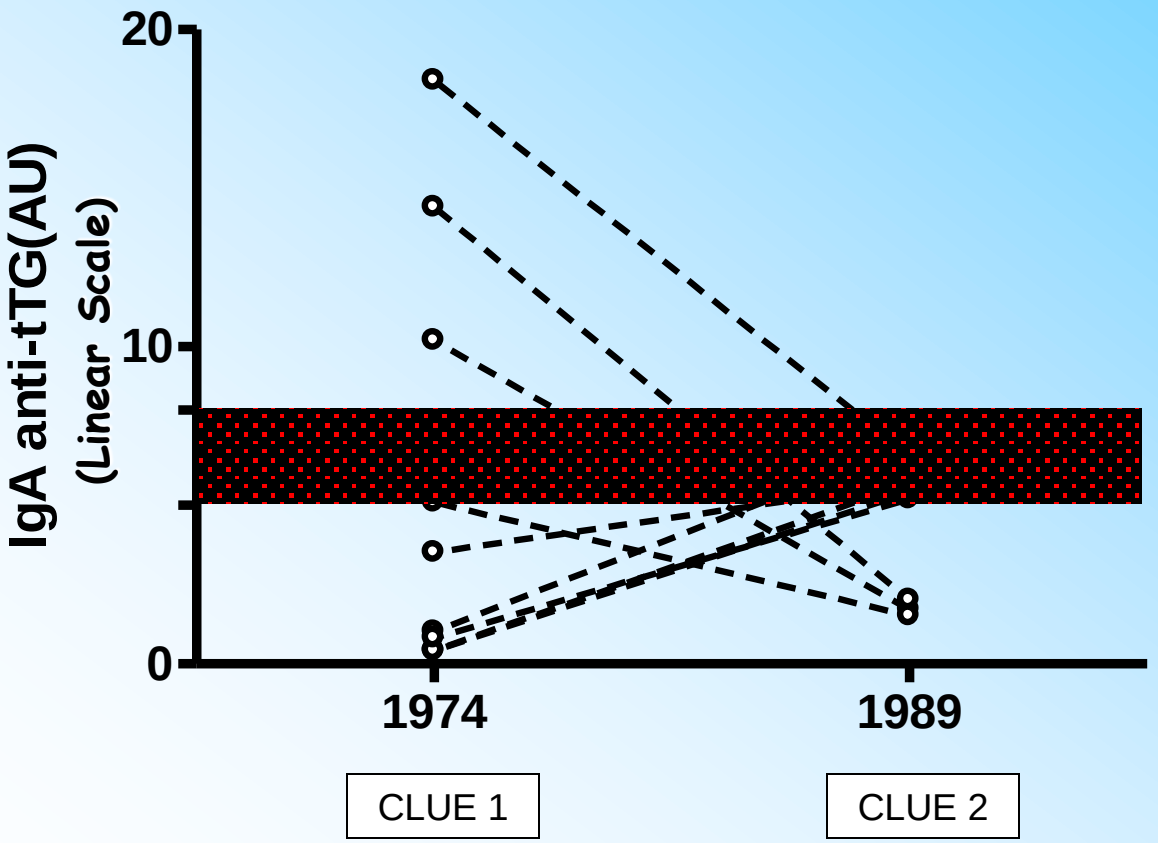
Fig. 1a



Antibody levels in subjects with isolated IgA anti-tTG positivity

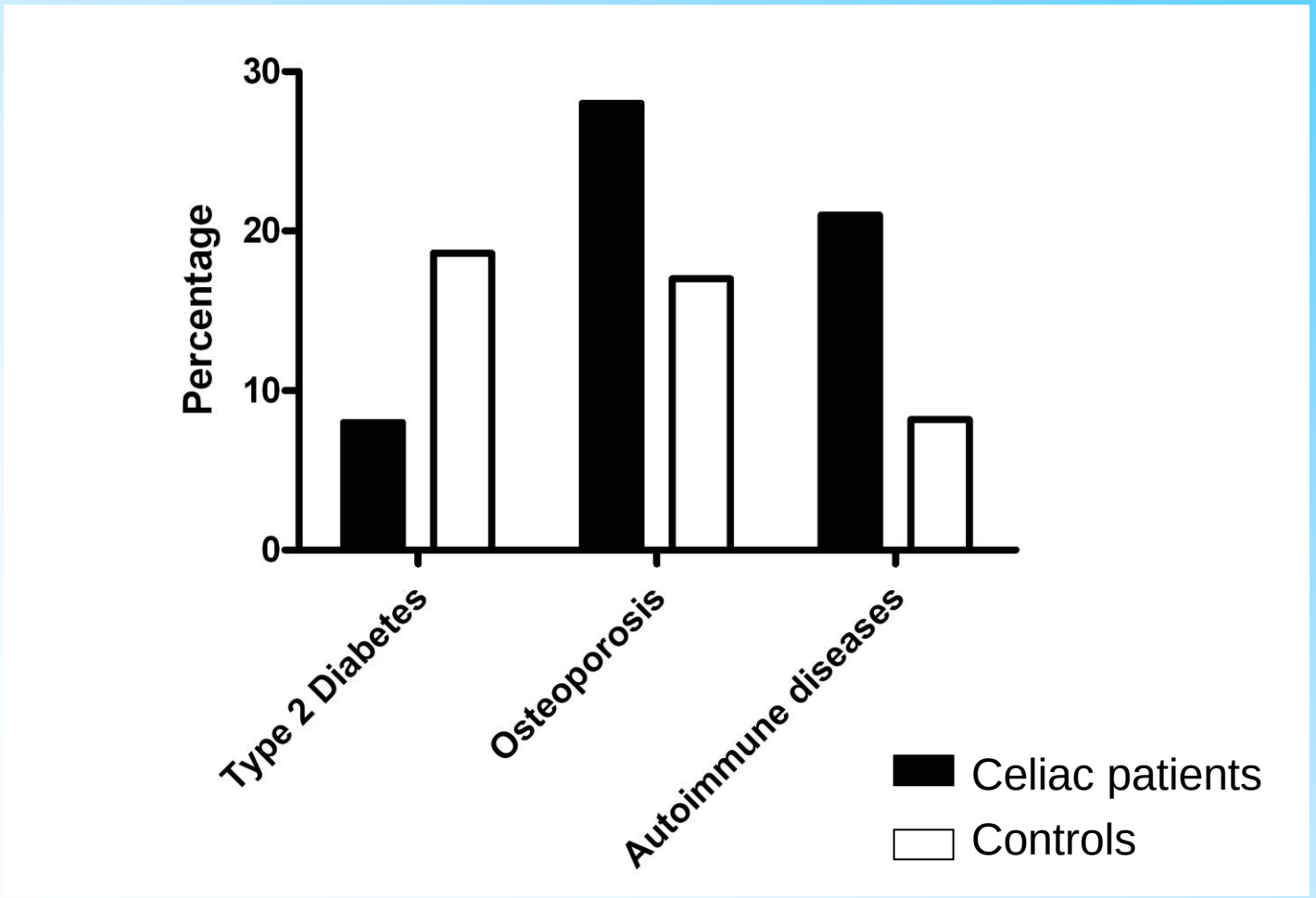
(EMA negative)

Fig. 1b



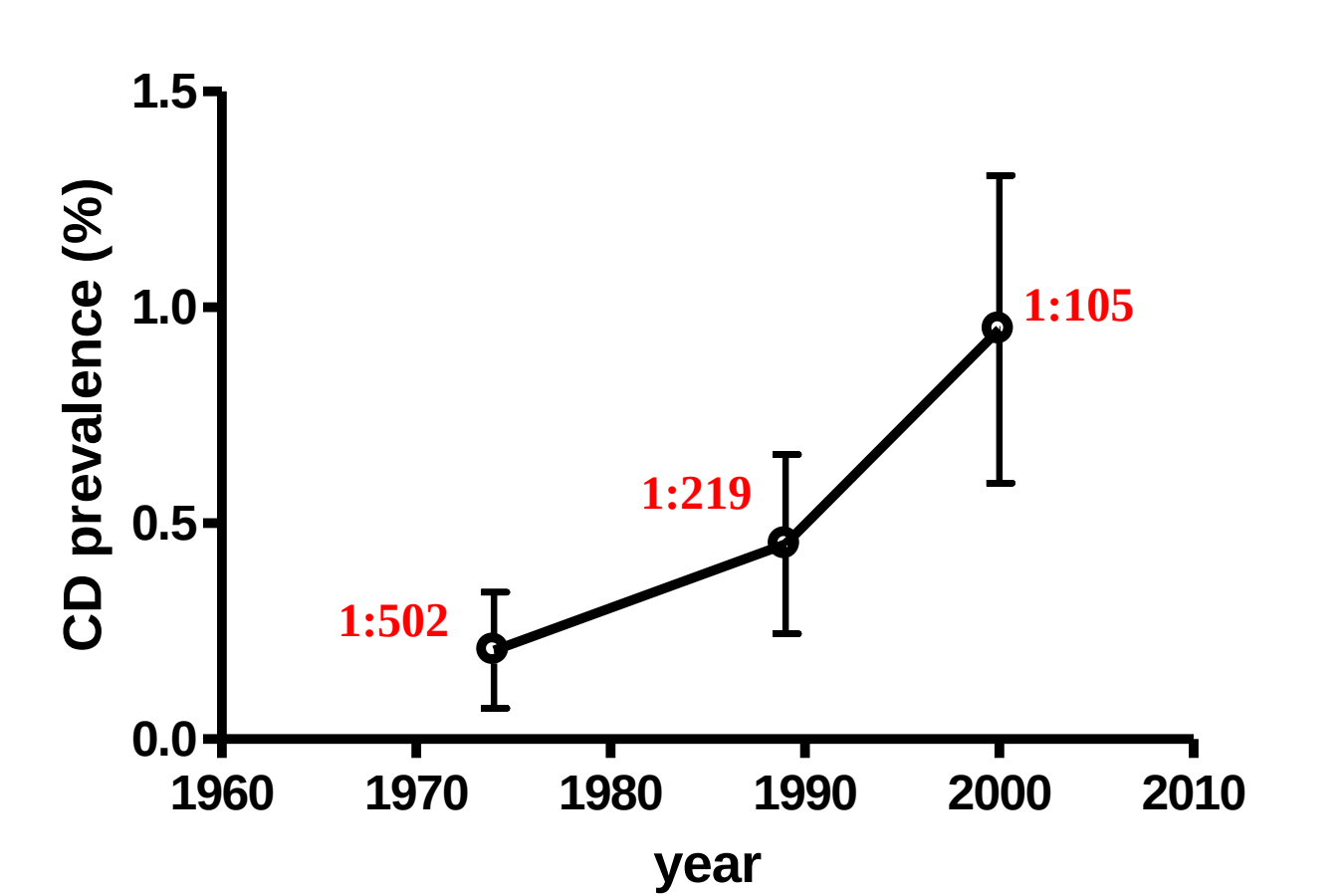
Results

Clinical Outcome year 2007



Results

Increasing prevalence of CD in the United States over time



Conclusions

- Gluten tolerance in individuals that are genetically predisposed to CD can be lost at any age, even in adulthood.
- CD patients reported more autoimmune connective tissue disorders and osteoporosis than age- and gender- matched controls
- Decreased T2D in CD patients
  - Possibly due to malabsorption
- There has been a 5 fold increase in the prevalence of CD in the US during the past 3 decades
- Our data suggest that the prevalence of CD is doubling every 15 years