Increased familial IBD risk over thirty years: Insights from two population-based IBD-cohorts in South-Eastern Norway

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Background

The highest risk factor of inflammatory bowel disease (IBD) is having a first-degree relative (FDR) with IBD. Although the prevalence of IBD in Norway is among the highest in the world, its incidence has remained steady throughout the 21st century.

Aims

The overall aim of this study was to explore the role of a positive family history of IBD in an era of stable incidence.

For familial IBD (at least one FDR with IBD), we wanted to explore (i) the age at diagnosis (AAD) and (ii) severity of disease among Crohn's disease (CD) and ulcerative colitis (UC) cases between familial and sporadic cases in the IBSEN III cohorts.

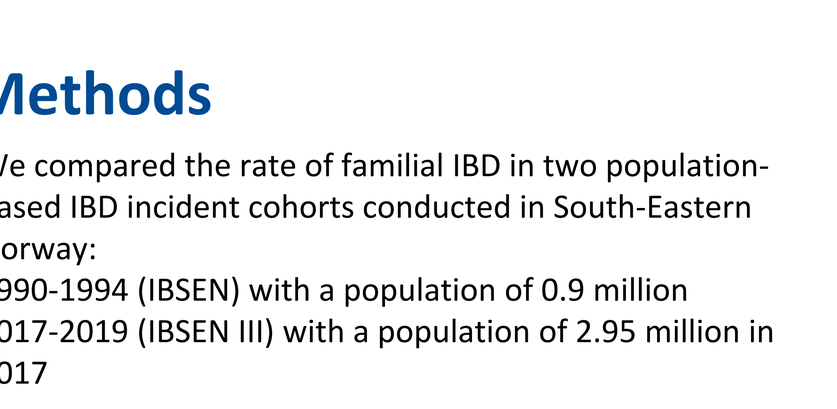
For multiplex family IBD (more than one FDR with IBD), we wanted to explore generational differences in (i) age at diagnosis and (ii) severity of disease among CD and UC.

Further, we examined (iii) the association between the length of shared household and the phenotype of IBD.

Methods

We compared the rate of familial IBD in two population-based IBD incident cohorts conducted in South-Eastern Norway:
1990-1994 (IBSEN) with a population of 0.9 million
2017-2019 (IBSEN III) with a population of 2.95 million in 2017

Those who reported more than one FDR with IBD in the IBSEN III cohort were invited to participate in a multiplex-family IBD study.(Fig1)
Severe disease was defined as extensive colitis in Ulcerative colitis (UC), and the presence of perianal, stricturing, or penetrating disease in Crohn`s disease (CD).



Results

A total of 785 and 1561 IBD patiens >18 years were recruited in the IBSEN and IBSEN III studies respectively. In the IBSEN and IBSEN III cohort 7.3 % (57) and 10.9% (170) reported a positive family history of IBD, respectively. The rate of familial IBD increased by 49.3% (p=0.008) over 30 years.

Familial IBD

Table 1 Familial IBD -IBSEN III

IBSEN III (n1561)						
	Familial IBD (n170)			SporadicIBD (1391)		
	IBD	CD(n55)	UC(n115)	IBD	CD(n451)	UC(n942)
AAD(SD)	38.7 (14.5)	39.4 (14.0)	38.4 (14.7)	39.1 (15.0)	40.4 (15.8)	39.2 (15.0)
Severe disease (%)	45 (26.5)	10 (18.2)	35 (30.4)	449 (32.3)	87 (29.3)	362 (38.5)

The only significant result was in the sporadic group of IBD with more frequent cases of severe disease among UC 362/ 940 (38.5%), compared to CD 87/451 (19.3%) (p< 0.001)

The length of shared households within multiplex families from the initial IBD diagnosis among FDRs to subsequent diagnoses of CD or UC in others, was 11.8 years and 17.1 years, respectively (p=0.026).

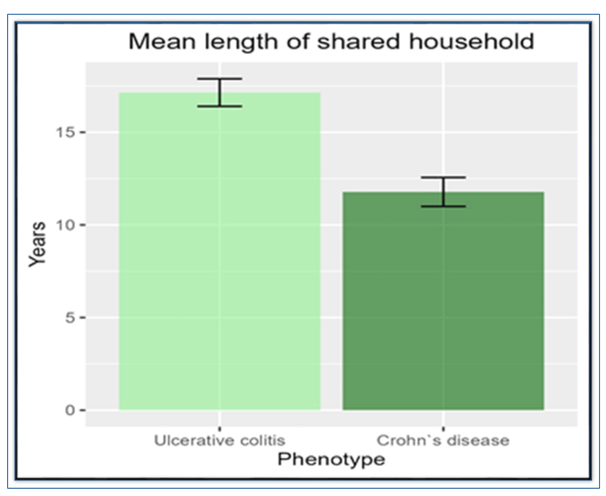
Multiplex familial IBD

Table 2 Multiplex familial IBD

Multiplex families (n14)		
	Parents(n18)	Children(n30)
AAD (SD)	33.3 (16.5)	25.1 (13.0)
Severe disease (%)	9 (56.3)	8 (30.8)
Length of shared household from initial IBD diagnosis (SD)	CD(n14)	UC(n18)
	11.78 (7.2)	17.14 (5.3)

The mean AAD was 25.1 years (13.0) among the children and 33.3 years (16.5) among the parents (p=0.063) (tab2).

Figure 2 Shared household from the initial IBD diagnosis



Conclusion

The rate of a positive family history of IBD has increased substantially over thirty years, underscoring the importance of shared environmental factors for the development of the IBD diagnosis. Shorter time of shared household was significantly associated with development of familial CD.

Disclosure: Vendel A. Kristensen has reported advisory boards from Takeda and Tillotts Pharma, consultant fees from Janssen Cilag, Takeda, and speaker fees from Thermo Fischer Scientific.Marte Lie Høivik has reported investigator-initiated research grants from Takeda, Pfizer, Tilllotts, Ferring and Janssen, speaker honoraria from Takeda, Tillotts, Ferring, AbbVie, Galapagos, MSD and Meda and Advisory board Takeda, Galapagos, MSD, Lilly, Janssen, Pfizer and AbbVie. The other authors of this abstract have no Conflict of Interest.

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IBSEN III