Is there ANA risk?
A retrospective analysis assessing the long-term psychiatric outcomes in patients testing positive for antinuclear antibodies, in the absence of an autoimmune disease diagnosis.

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Introduction

Antinuclear antibody (ANA) is a sensitive but non-specific blood test frequently undertaken as part of the clinical assessment for a number of autoimmune diseases.

While ANA positivity is associated with a wide range of autoimmune diseases, such as systemic lupus erythematosus (SLE), approximately one fifth of the population will test positive without having or subsequently developing an autoimmune disease in their lifetime.

Evidence shows that patients with an autoimmune disease are more likely to develop psychiatric disorders such as schizophrenia, the risk of this in patients who test positive for ANA but who never develop an autoimmune disease has not been established.

This is of clinical importance, given that ANA is frequently included in the medical workup for patients presenting with first episode psychosis (FEP).

Aims

To compare the risk of **incident psychiatric diagnoses (HR) 3months- 10 years** after first ANA test in:

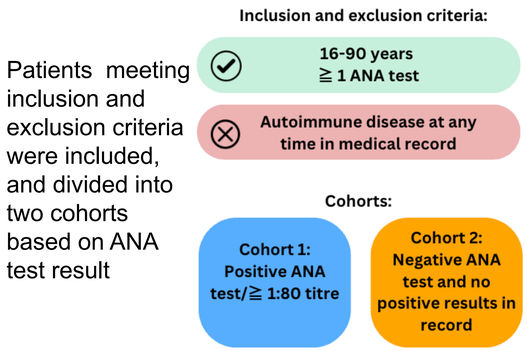
1º **ANA +ve vs ANA -ve patients aged 16-90 years**

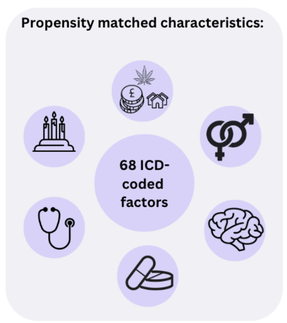
2º **ANA +ve vs ANA-ve patients of typical FEP age (16-30 yrs)**

ANA +ve patients years with low (1:40-1:160) vs high (≧1:320) titres

Methods

A retrospective cohort analysis was undertaken using TriNetX, a large real-world population database, consisting of anonymised health records of over 250 million patients across 19 countries.





Potential confounders such as pre-test age, sex, sociodemographics, medical and psychiatric co-morbidities; and psychotropic medication use were were accounted for through 1:1 propensity score matching

Incident psychiatric diagnosis was defined as recorded ICD-10 diagnosis in the patient's medical record 3 months- 10 years after the ANA test. Patients with this diagnosis prior to ANA test were not included in the analysis.

Results

After 1:1 matching, 558102 patients were included in the primary analysis, 279051 in each cohort.

Risk of psychotic disorders:

There was **no statistically significant difference** in the risk of diagnosis of

- overall F20-29 diagnoses (HR 0.96 p= 0.2)
- F20 Schizophrenia (HR 0.92 p=0.2)
- F23 Brief Psychotic Disorder (HR 0.89 p= 0.23)

This was consistent across secondary analyses (Fig.1 red and blue bars)

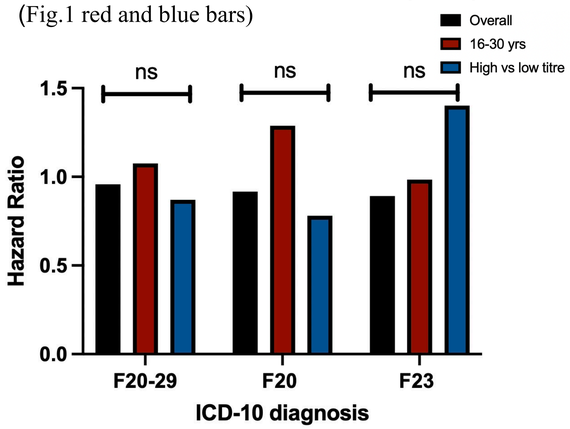


*Figure 1. Hazard ratios for psychotic ICD diagnoses in ANA +ve vs ANA –ve patients and age and titre related sub analyses. ns= p>0.05, *= p<0.05 ** = p<0.001*

Risk of affective and anxiety disorders:

Interestingly patients with an ANA positive result had a **statistically significantly lower risk** of incident diagnosis of:

- affective disorders (HR 0.921 p<0.001, Fig.2.)
- anxiety disorders (HR 0.931 p<0.001, Fig.2.)

Although the statistical significance of these findings was markedly reduced for affective disorders (p0.04), **and no longer statistically significant for all other outcomes when comparing low and high titre patients** (Fig.2. blue bars).

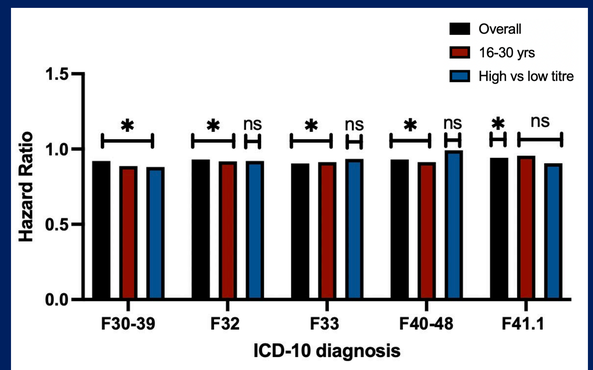


*Figure 2. Hazard ratios for affective and anxious ICD diagnoses in ANA +ve vs ANA –ve patients, and age and titre related sub analyses. ns= p>0.05, *= p<0.05 ** = p<0.001*

Further research is required to establish whether this effect is due to increased ANA testing in patients presenting with affective and anxious symptoms, rather than due to a protective role of antinuclear antibody.

Conclusions

- ANA positivity in the absence of an autoimmune disease was not associated with an increased long-term risk of psychotic disorders, including schizophrenia.
- This result was consistent across patients of typical FEP age, and in ANA positive patients with higher ANA titres.
- **These findings suggest routine clinical testing of ANA in patients presenting with psychiatric disorders without features suggestive of a systemic autoimmune disease may be unwarranted.**

Acknowledgements

TriNetX- for access to the network which enabled this analysis.