treatments and other reproductive factors, and RA risk with conflicting results [2, 3].

Objectives: To assess the relationships between endogenous and exogenous female hormonal exposures and the risk of RA in women involved in the E3N cohort.

Methods: E3N is an ongoing French prospective cohort that included 98,995 women aged 40-65 years in 1990. Women completed mailed questionnaires every 2-3 years on lifestyle, reproductive factors, and health-related information. Female endogenous hormonal exposures were assessed using age at menarche, age at menopause, and the duration of reproductive life. Exogenous hormonal exposures included oral contraception and menopausal hormonal treatment (MHT). Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of incident RA were estimated using Cox proportional hazards regression models with age as the time scale, first applied to the overall population, then stratified for smoking exposure.

Results: A total of 698 incident RA cases were validated among and 78,452 women over 1,865,213 women-years. Multivariate models for age at menopause and cumulative duration of MHT appear in Table. After stratification for smoking exposure, early age at menopause was associated with a somewhat stronger RA risk in women exposed to smoking (HR=1.6, 95% CI: 1.1-2.4; $p_{\text{linear trend}}=0.0270$) than in those with no smoking exposure (HR=1.3, 95% CI: 0.8-2.2; $p_{\text{linear trend}}=0.1811$). However when adjusting for cumulative duration of MHT, early age at menopause was no longer associated with incident RA, even in women exposed to smoking (HR=1.3, 95% CI: 0.8-2.2; $p_{\text{linear trend}}=0.7973$), while a cumulative duration of MHT > 4 years was borderline associated with RA in women exposed to smoking [HR=1.3, 95%CI: 1.0-1.7; $p_{\text{linear trend}}=0.09$] in comparison with women who did not received MHT. Age at menopause and duration of THM were strongly correlated: in women with early menopause duration of MHT was significantly longer: 7.01 (7.3) years versus 4.8 (5.0) years ($p<0.001$). There was no evidence of an association between oral contraception use, age at menarche and duration of reproductive life with the risk of RA.

	RA	HR (95% CI) for RA	P for trend
Age at menopause (N=78,452)			
≤45 years	68	1.50 (1.1-2.1)	
45-53 years	482	1.22 (0.9-1.5)	
≥53 years	148	1	0.0096
Cumulative duration of MHT in menopausal women (N=71,436)			
0	178	1	0.2417
30-41 years	102	1.15 (0.9-1.4)	
>4 years	208	1.14 (0.9-1.4)	

Multivariate models adjusted for age, smoking status, passive smoking during childhood, educational level, BMI, type of menopause (surgical or natural).

Conclusion: Early age at menopause and/or duration of MHT > 4 years use may increase the risk of RA. Further studies are requested to disentangle the effect of early menopause to that of long-term MHT.

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THE RISK OF SCHIZOPHRENIA AND EPILEPSY AMONG FAMILIAL MEDITERRANEAN FEVER PATIENTS: A BIG DATABASE ANALYSIS

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Background: Several autoimmune diseases have been associated with schizophrenia and epilepsy, however little is known about putative links with the auto-inflammatory conditions.

Objectives: We investigated the association between familial Mediterranean fever (FMF), a paradigmatic auto-inflammatory disease, schizophrenia and epilepsy, and assessed the impact of the latter disorders on the survival of FMF patients utilizing a large sample database.

Methods: A case-control study was performed by utilizing the database of Clalit Health Services. FMF patients were compared to age- and sex-matched counterparts in terms of prevalence of schizophrenia and epilepsy. The chi-squared test was used to assess the distribution of categorical variables, while the t-test were applied for continuous variables. Analysis regarding survival were performed using Kaplan-Meier curves, log rank test and multivariate Cox proportional-hazards method.

Results: The study included 7,747 FMF patients, and 10,080 age- and sex-matched controls. At the univariate analysis, schizophrenia and epilepsy as co-morbidities, 50 FMF patients (0.6%) and 89 controls (0.9%) had schizophrenia, respectively. On multiple logistic regression model, FMF was inversely associated with schizophrenia (OR 0.64 [95%CI 0.43-0.90], $p=0.0173$), while there was no association between FMF and epilepsy. Subjects having either FMF (HR 1.43 [95%CI 1.23-1.66]), schizophrenia (HR 3.97 [95%CI 1.47- 10.70]) or epilepsy (HR 2.54 [95%CI 1.72-3.75]) were independently associated with all-cause mortality. However, schizophrenia as co-morbidity in FMF subjects did not worsen their prognosis (HR 2.17 [95%CI 0.60-7.86]).

Conclusion: FMF patients have a significantly lower proportion of schizophrenia than controls. Patients with either FMF, schizophrenia or epilepsy are at higher risk of all-cause mortality, a finding that calls for assessment of better medical management on mortality outcome.

Table 1. Overall population basic characteristics.

Characteristic	All population (n=17,827)	Controls without FMF (n=10,080)	FMF patients (n=7,747)	Statistical significance (p-value)
Age (mean±SD)	38.43±19.62	37.69±19.55	39.38±19.68	NS
Age at diagnosis (mean±SD)	26.41±18.41	25.67±18.35	27.37±18.45	NS
Gender (female; %)	9,000 (50.5%)	5,121 (50.8%)	3,879 (50.1%)	NS
BMI (mean±SD)	24.81±63.91	24.42±50.61	25.30±77.41	NS
SES (n;%) ^a				$p=0.0054$ ($p=0.0200$ for trend)
Low	8,370 (50.6%)	4,729 (50.3%)	3,641 (51.1%)	
Medium	5,609 (33.9%)	3,153 (33.5%)	2,455 (34.5%)	
High	2,548 (15.4%)	1,524 (16.2%)	1,024 (14.4%)	
Smoking (n;%)	5,000 (28.0%)	2,588 (25.7%)	2,412 (31.1%)	<0.001
Schizophrenia (n;%)	139 (0.8%)	89 (0.9%)	50 (0.6%)	NS
Epilepsy (n;%)	267 (1.5%)	146 (1.4%)	121 (1.6%)	NS
All-cause mortality (n;%)	707 (4.0%)	341 (3.4%)	366 (4.7%)	<0.001

Table 2. Multivariate logistic regression assessing covariates associated with schizophrenia and epilepsy.

Variable	Coefficient	Std. Error	Wald	P	OR	95% CI
Schizophrenia						
Age	0.02	0.00	10.75	0.0010	1.02	1.01 to 1.03
Sex (female)	-0.28	0.19	2.16	0.1421	0.76	0.52 to 1.10
FMF	-0.45	0.19	5.67	0.0173	0.64	0.44 to 0.92
SES (medium)	0.26	0.20	1.66	0.1974	1.29	0.87 to 1.91

SES (high)	0.13	0.27	0.22	0.6374	1.13	0.67 to 1.91
Smoking	0.91	0.19	21.83	<0.0001	2.48	1.69 to 3.63
BMI (kg/m ²)	0.00	0.00	0.01	0.9136	1.00	1.00 to 1.00
Constant	-5.71	0.28	428.26	<0.0001		
Epilepsy						
Age	0.01	0.00	10.50	0.0012	1.01	1.01 to 1.02
Sex (female)	-0.16	0.14	1.43	0.2321	0.85	0.66 to 1.11
FMF	-0.09	0.14	0.41	0.5216	0.92	0.70 to 1.19
SES (medium)	-0.04	0.15	0.08	0.7769	0.96	0.72 to 1.28
SES (high)	-0.34	0.21	2.49	0.1148	0.72	0.47 to 1.09
Smoking	-0.03	0.15	0.03	0.8638	2.48	1.69 to 3.63
BMI (kg/m ²)	-0.01	0.01	0.24	0.6272	0.99	0.97 to 1.02
Constant	-4.28	0.26	267.26	<0.0001

Figure 1. a+b. Kaplan-Meier survival plot of study cohorts

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ASSESSMENT OF THE QRISK2, QRISK3, SLE CARDIOVASCULAR RISK EQUATION, FRAMINGHAM AND MODIFIED FRAMINGHAM RISK CALCULATORS AS PREDICTORS OF CARDIOVASCULAR DISEASE EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is recognized as an independent risk factor for cardiovascular disease (CVD), and patients

with SLE are at an elevated risk of CVD compared to the general population¹. The complex interplay between conventional CVD risk factors, the inflammation caused by SLE and the pharmacological treatment of SLE contributes toward CVD risk¹. Despite knowledge of this increased risk, there is no agreement on the use of risk assessment tools in the prediction of CVD in SLE. The Modified Framingham Risk Score (mFRS), QRISK3 and SLE Cardiovascular Risk Equation (SLECRE) have been introduced as promising CVD risk assessment tools considering SLE in prognosticating patients.

Objectives: To determine which cardiovascular risk assessment tool amongst the QRISK2, QRISK3, SLECRE, Framingham (FRS) and mFRS best predicts CVD events in SLE.

Methods: Single-centre analyses on prospectively collected data of 1887 SLE patients were performed to compute 10-year CVD risk scores for each tool. Tools' scores were evaluated against CVD events at or within ten years for cases (CVD events) and controls (no CVD events). For cases, the index date for risk score calculation was chosen 10 years, or as close to 10 years as possible prior to the CVD event. For controls, risk scores were calculated as close to 10 years as possible prior to the most recent clinic appointment. Proportions of patients classified as low (<10%), median (10-20%) and high risk (>20%) of developing CVD according to each tool were determined. Sensitivity, specificity, positive/negative predictive values and c-statistics of these tools were analysed.

Results: 232 total CVD events were identified in the cohort including myocardial infarction, stroke, transient ischemic attack, heart failure and CVD death. QRISK2 and FRS risk-stratification was similar, while QRISK3 and mFRS risk-stratification was similar (Figure 1). The SLECRE classified the highest number of patients as median-high risk (Figure 1). The sensitivities and specificities are as follows for each tool: QRISK2 (19%, 93%), FRS (22%, 93%), mFRS (46%, 83%), QRISK3 (47%, 78%), SLECRE (61%, 63%). The tools were similar in negative predictive value, ranging from 89% (QRISK2) to 92% (SLECRE). The FRS and mFRS had the greatest c-statistics, both equalling 0.73, demonstrating the greatest predictive accuracy amongst the tools, while the QRISK3 had the lowest (0.67).

Figure 1. Percentage of patients considered low (<10%), median (10-20%) and high risk (>20%) between cases (CVD, n=232) and controls (no-CVD, n=1655) according to the FRS, mFRS, QRISK2, QRISK3 and SLE CRE.

Conclusion: While the mFRS performance was superior to the FRS, the QRISK3 did not outperform the mFRS. Although the SLECRE had the highest sensitivity, it had the lowest specificity, demonstrated by grouping the most cases and controls in the median-high risk category. Several factors are important to consider when deciding which risk assessment tools to utilize: ease of use/computation, sensitivity/specificity, and laboratory data accessibility. Of the tools currently available, the mFRS is a practical tool with a simple, intuitive scoring system appropriate for the ambulatory clinic setting based on the initial weighting of the FRS while adjusting for SLE. However, much room for improvement exists in predicting CVD in SLE.

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