Background: Type 2 diabetes (T2D) entails a worldwide epidemic. Obesity and dyslipidemia are included among T2D main known risk factors. However, the specific lipid molecular changes that may lead to insulin resistance and T2D remain unknown. Our aim was to identify lipidome patterns longitudinally associated with T2D, including analyses of their 1-year changes and the subsequent T2D risk in the context of a Mediterranean diet intervention trial.

Materials and methods: In this case-cohort study, 889 participants were included, 639 were in the subcohort (including 53 overlapping incident cases) and 197 were incident T2D cases (total incident cases = 53 + 197). Participants were followed-up during 3-8 years (median). We repeatedly measured 302 plasma known lipid metabolites at baseline and after 1-year of intervention. Principal component analysis was used to identify lipidome factors. Six factors were significantly associated with T2D. Considering common patterns among factors, lipid molecular species were grouped (summed) into scores depending on lipid classes.

Results: We found that baseline lysophosphatidylcholines and lysophosphatidylethanolamines (grouped as LP), phosphatidylcholine-plasmalogens (PC-PL), sphingomyelins (SM) and cholesterol esters (CE) were inversely associated with the risk of T2D ($P$ for linear trend = $<0.001$, $<0.001$, $<0.001$ and $<0.001$ respectively; adjusted for sex, age and intervention group). On the contrary, baseline triacylglycerols (TAG), diacylglycerols (DAG) and phosphatidylethanolamines (PE) were associated with a higher risk of T2D ($P$ for linear trend = 0.009, $<0.001$, $<0.001$, respectively). Although the results were not statistically significant, the associations between one year changes and the subsequent risk of T2D also pointed in the same directions.

Conclusions: Two plasma lipid patterns, comprising different lipid classes, were associated with the risk of T2D: one pattern including LP, PC-PL, SM, CE and CE-A was linked to a reduced risk of T2D while another pattern composed of TAG, TAG-A, DAG and PE was associated with a higher T2D risk.