Introduction:
Sepsis is common, deadly, and heterogeneous. Prior work proposed clinical phenotypes of sepsis at presentation. However, little is known about how those phenotypes change over time. We explored trajectories of clinical sepsis phenotypes for 24hrs after presentation and contribution of phenotype cohesiveness to subsequent transitions.

Methods:
We analyzed a retrospective cohort of adult patients meeting Sepsis-3 criteria within 6hrs of presentation using electronic health data from 12 hospitals in a large health system in Pennsylvania. We predicted clinical phenotypes at 6-hr intervals over 24hrs using Euclidean distance anchored to previously published cluster centroids ($\alpha$, $\beta$, $\gamma$, $\delta$). We determined phenotype cohesiveness using probability of assignment at presentation, defining core members as $\geq$90% and marginal as $<90$% probability. We determined how members transitioned to other phenotypes over 24hrs using t-distributed stochastic neighbor embedding (tSNE) plots and determined the odds (95%CI) of transition.

Results:
We studied 37,198 adult sepsis encounters (median age 69, [IQR 57-81]; 51% male, median SOFA at arrival 3, [IQR 2-4]) hospitalized for at least 24hrs. At presentation, encounters were 28% $\alpha$-type, 30% $\beta$-type, 28% $\gamma$-type, and 14% $\delta$-type. Phenotype was unchanged over 24hrs among 68% of encounters. Transitions were most common for $\delta$-type (20% core, 57% marginal) and least common for $\alpha$-type (11% core, 39% marginal, Figure 1A). Core members were less likely to transition than marginal members for all phenotypes (p<0.01, Figure 1B,1C) The odds of ever transitioning from presenting phenotype increased significantly for marginal members vs. core for all phenotypes ($\alpha$: OR 5.3, 95%CI 4.7-6.0; $\beta$: OR 2.9, 95%CI 2.6-3.2; $\gamma$: OR 3.6 95%CI 3.2-3.9, $\delta$: OR 5.2, 95%CI 4.6-5.9, p<0.01 for all).

Conclusion:
More than half of patients had stable clinical sepsis phenotypes for 24hrs after presentation. Transitions to other phenotypes were significantly more common among marginal members and those in the $\delta$-type.
Figure 1. (A) Heap Map showing phenotype assignments at 6-hr intervals for first 24hrs after presentation. (B) Bar graph showing proportion of encounters transitioning from phenotype at presentation within 24hrs, by arrival phenotype assignment and probability of membership. (C) tSNE plots for α-type, β-type, γ-type, and δ-type, with core (dark), marginal (light), and non-members (grey) in plots on the left and core, marginal, non members, and transitioning members (black) on the right.