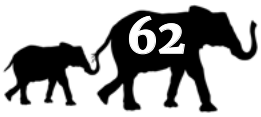

062: Delineating the incidence, accrual, and pathways to development of cardiovascular disease for 22q11.2 microdeletion using population-based and clinical data *

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Background: Most children with 22q11.2 microdeletion (22q) survive to adulthood, but adult health data remain limited. We investigated the incidence and accrual of cardiovascular outcomes in people with molecularly confirmed 22q compared with general population-comparators and further explored pathways to heart failure within the 22q cohort. **Methods:** Using a retrospective cohort study design, we linked 365 adult 22q-cases (median age 32 y; 51% female) to health administrative data for ~15 million individuals with universal healthcare, identifying 3,650 matched population-comparators. We used Poisson regression to estimate incidence rate ratios (IRRs) and 95% CI for five cardiovascular/risk conditions, and recurrent event modelling to assess their relative rate (RR) of accrual over a median 28 years of health data. We explored the progression from diabetes to heart failure and death among the clinical 22q cohort (n=405) using multi-state modelling and time-to-event analysis. **Results:** Accrual of cardiovascular conditions occurred at a significantly greater relative rate (RR) in 22q-cases than population-comparators (RR 3.8, 95% CI 2.9–4.8), even when restricting to 22q-cases with neither major congenital heart disease (CHD) nor schizophrenia (RR 3.6, 95% CI 2.4–5.4). Incidence was significantly greater in 22q-cases for hypertension and diabetes by age 18–24 (IRR 2.98, 95% CI 1.45–6.14; IRR 3.21, 95% CI 1.42–7.24, respectively), and by age 35–44 for heart failure. Among the clinical 22q cohort, heart failure was only observed among those with CHD, with no preceding diabetes. In a cause-specific model, the hazard of heart failure was lower for females (HR 0.13, 95% CI 0.04-0.47). **Conclusions:** A population-based approach provided new evidence for accumulating illnesses over young adulthood in 22q. Events observed during clinical follow-up did not show evidence of traditional cardiovascular disease development pathways in 22q, but longer follow-up is needed to further investigate established aging pathways.