INTRODUCTION AND AIMS: The clinical interpretation of a raised level of high-sensitivity troponin T (hsTnT) or NT-pro-B-type natriuretic peptide (NT-pro-BNP) is uncertain in patients with chronic kidney disease (CKD) due to the relationship of these biomarkers to reduced kidney function. We sought to examine the distribution of hsTnT and NT-pro-BNP with decreasing eGFR in the setting of advanced CKD, and investigate the association between eGFR-specific distributions of both biomarkers and long-term cardiovascular (CV) events.

METHODS: This was a prospective analysis of 1977 participants from a pan-Canadian cohort of individuals with moderate to advanced CKD who were all under the care of a nephrologist. We describe age- and sex-adjusted predicted mean values of hsTnT and NT-pro-BNP (both log-transformed) per 1 mL/min/1.73m² decrease in eGFR. Within each tertile of eGFR (9–21, 22–30, 31–50 mL/min/1.73m²) we created tertiles of hsTnT and NT-pro-BNP. We used Cox Proportional Hazards regression to examine the association between eGFR-specific distributions of each biomarker and time to first CV event, a composite of ischaemic heart disease (fatal or non-fatal myocardial infarction or the need for coronary revascularization), congestive heart failure, stroke and sudden cardiac death. All outcomes were independently adjudicated by a panel of physicians using source documentation.

RESULTS: Mean age of the cohort was 68 years, 63.5% were male and 49% had a diagnosis of diabetes. The majority (76%) of patients had a value of hsTnT above the upper limit of the laboratory reference range (>14 ng/L). Predicted mean (95% confidence interval) values of hsTnT were 15.3 (14.2–16.4) and 37.1 (35.1–39.2) ng/L at an eGFR of 45 and 15 mL/min/1.73m², respectively. A total of 339 CV events were recorded during a median follow-up time of 4.3 years (6948 person years at risk). In the lowest eGFR tertile, after adjusting for demographics and CV risk factors, the association between hsTnT and CV events only became evident (hazard ratio 1.9 [95% confidence interval 1.3–3.5]) in the highest tertile of hsTnT (range 43–566 ng/L). In contrast, the relationship between NT-pro-BNP tertiles and CV events was strong and graded across the range of eGFR, was independent of CV risk factors, and did not vary by the presence or absence of baseline cardiac disease. Even in the lowest eGFR tertile, each unit increase in NT-pro-BNP was associated with steadily increased risk (HR 3.8 [1.7–8.1]) and 7.0 [3.2–15.2] for tertiles 2 and 3 respectively). Results were unchanged after censoring for the onset of renal replacement therapy.

CONCLUSIONS: Our findings have several important implications. From an epidemiological perspective, our data suggest that the utility of hsTnT for CV risk discrimination is lower in advanced CKD as compared to earlier stages. The robust risk estimates for NT-pro-BNP indicate that subclinical volume overload, rather than ischaemia, is the dominant pathophysiological mechanism contributing to CV risk in these patients. From a clinical perspective, the use of eGFR-specific reference ranges, built on the risk of CV endpoints, represents an alternative to laboratory reference ranges that could refine the interpretation of cardiac biomarkers in CKD. Finally, this approach may be useful for inclusion of CKD patients into CV event-driven clinical trials, by using eGFR-specific thresholds of hsTnT or NT-pro-BNP to stratify CV risk at the time of study enrolment.