Supplemental Appendix

Approach to Identifying the Final Patient Population:

Because patients suffering from AHA frequently experience misdiagnosis and delayed diagnosis, it is entirely possible that a patient with many CHA claims and only a few AHA claims is in fact a true AHA patient who was diagnosed late[[13](#_ENREF_13), [14](#_ENREF_14)]. Therefore, to capture an accurate patient sample of those with AHA and to avoid the arbitrary exclusion of patients who may have experienced misdiagnosis, records of patients with four or more CHA claims were individually reviewed by a hematologist. Figure 5 displays the methodology used when determining if a patient most likely had AHA vs CHA, described in detail below:

1. Firstly, the sequence of each patient’s diagnosis claims for both AHA and CHA were examined to determine if the diagnostic pattern indicated the patient has AHA. A patient may have multiple initial diagnoses of CHA, but later come to be diagnosed correctly with AHA. For example, if the sequence of diagnosis claims was CHA, AHA, AHA, CHA, AHA, AHA, AHA, AHA, AHA, AHA, AHA, AHA, AHA, the patient was retained as an AHA patient who received a late diagnosis. On the other hand, a patient with a sequence of diagnosis claims like CHA, AHA, AHA, CHA, CHA, CHA, CHA, CHA, CHA would be excluded from the patient population. **If it was immediately clear that a patient has either AHA or CHA, they were either included or excluded, respectively, from the study after this step**. If the patient’s true diagnostic status remained unclear after examining the sequence of diagnoses, the expert reviewer moved to the next step.
2. Each patient’s comorbidities were then holistically assessed to provide clarity on their true diagnostic status. A significant proportion of AHA have underlying autoimmune conditions, cancer, or lymphoproliferative malignancies, as described in the background, and thus patients with these types of conditions were identified as probable AHA patients (dependent on other patient characteristics and diagnosis frequency). Diagnoses for other common manifestations of AHA, such as subcutaneous bleeding (ecchymoses), hematoma (muscle bleeding), gastrointestinal bleeding (melena), and genitourinary bleeding (hematuria) were also used as an indicator that a patient has AHA[[15](#_ENREF_15)]. **If, after performing a holistic review of all of a patient’s comorbidities, it was clear that they had either AHA or CHA, they were either included or excluded, respectively, from the study after this step.** If a patient’s true diagnostic status remained unclear after examining the sequence of diagnoses and their entire comorbidity burden, the expert reviewer moved to the last step.
3. Where there may not be total confirmation of true diagnostic status from sequencing, comorbidities, and accompanying diagnoses, a patient’s sex and age was considered. As CHA mostly affects males, a female patient presenting with both AHA and CHA diagnosis claims and an autoimmune disease or cancer was identified as an AHA patient[[16](#_ENREF_16)]. Age was considered a much lesser consideration than the former criteria since the use of the Medicare LDS database presents an artificially elderly patient population. However, AHA largely affects the elderly[[17](#_ENREF_17)]. At this point in the decision tree process, each patient was categorized as AHA or CHA. **If there was any doubt that a patient had AHA, they were excluded from the patient sample.**