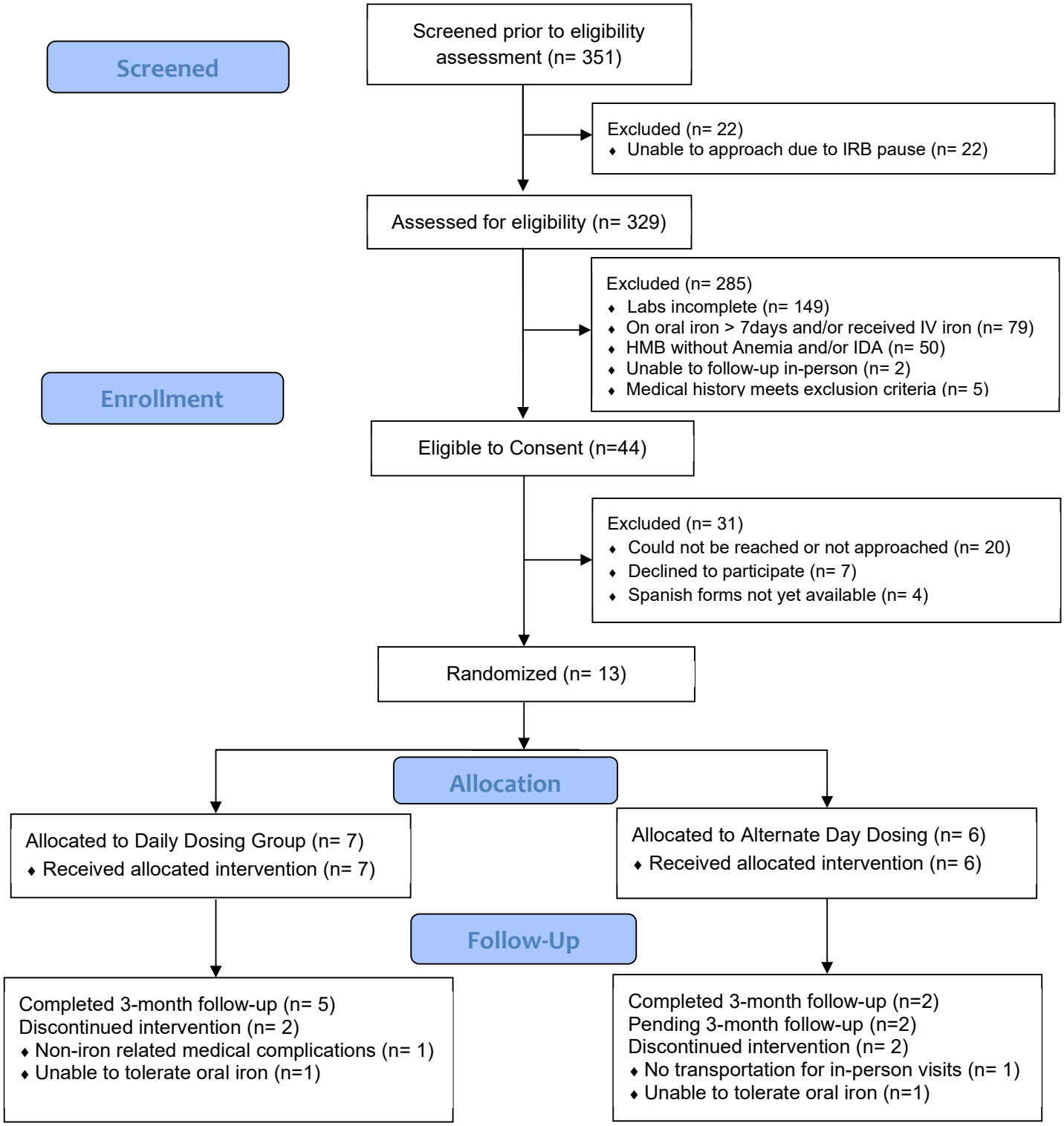Figure 1. Study flow diagram