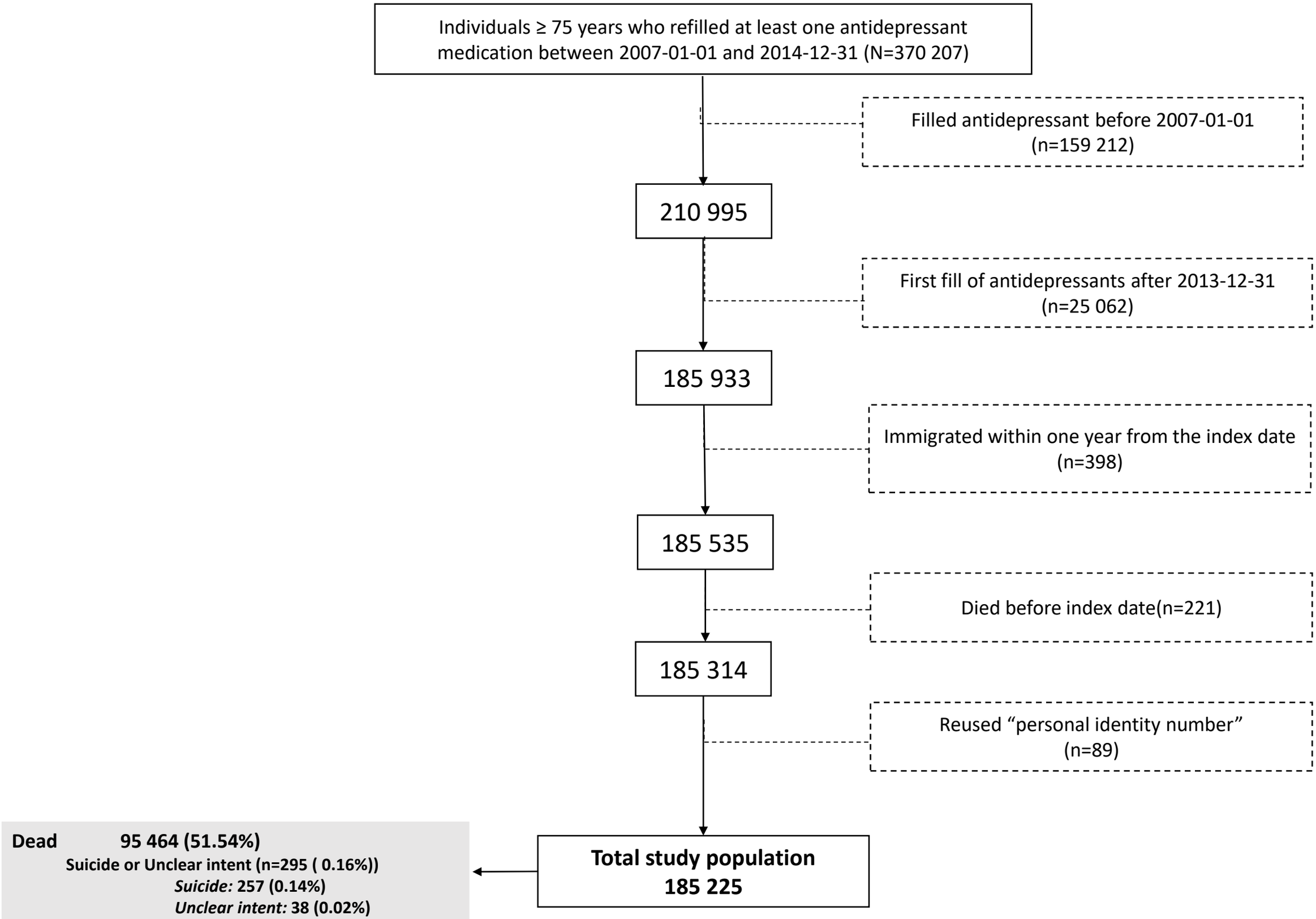


**Online Resource 1. Study flow diagram**