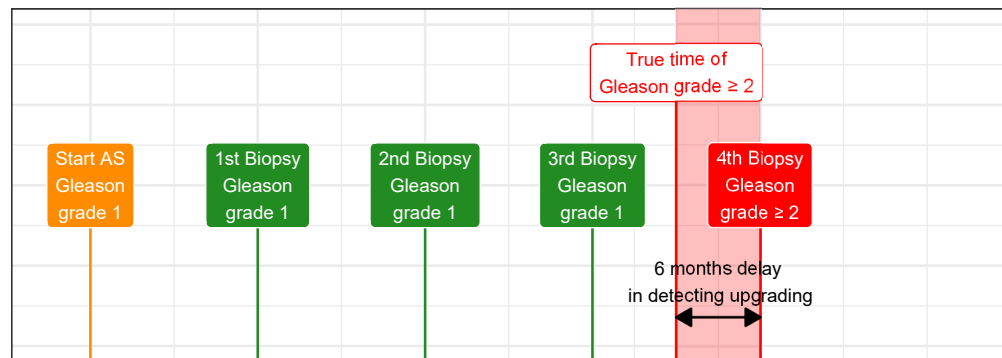


A Biopsy every year



B Biopsy every 2 years

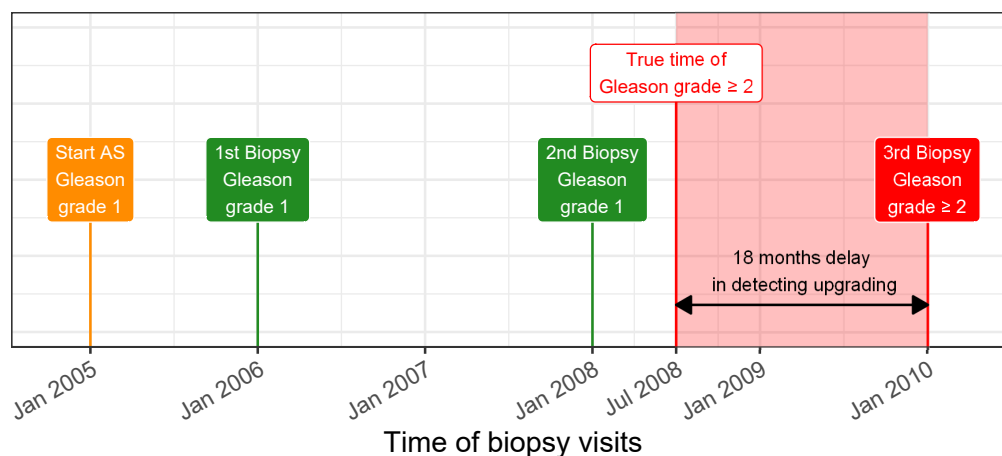


Figure 1: **Trade-off between the timing and number of biopsies (burden) and time delay in detecting Gleason upgrading (shorter is better):** The true time of Gleason upgrading (increase in Gleason grade group from group 1 to 2 or higher) for the patient in this figure is July 2008. When biopsies are scheduled annually (**Panel A**), upgrading is detected in January 2009 with a time delay of six months, and a total of four biopsies are scheduled. When biopsies are scheduled biennially (**Panel B**), upgrading is detected in January 2010 with a time delay of 18 months, and a total of three biopsies are scheduled. Since biopsies are conducted periodically, the time of upgrading is observed as an interval. For example, between Jan 2008–Jan 2009 in **Panel A** and between Jan 2008–Jan 2010 in **Panel B**. The phrase ‘Gleason grade group’ is shortened to ‘Gleason grade’ for brevity.