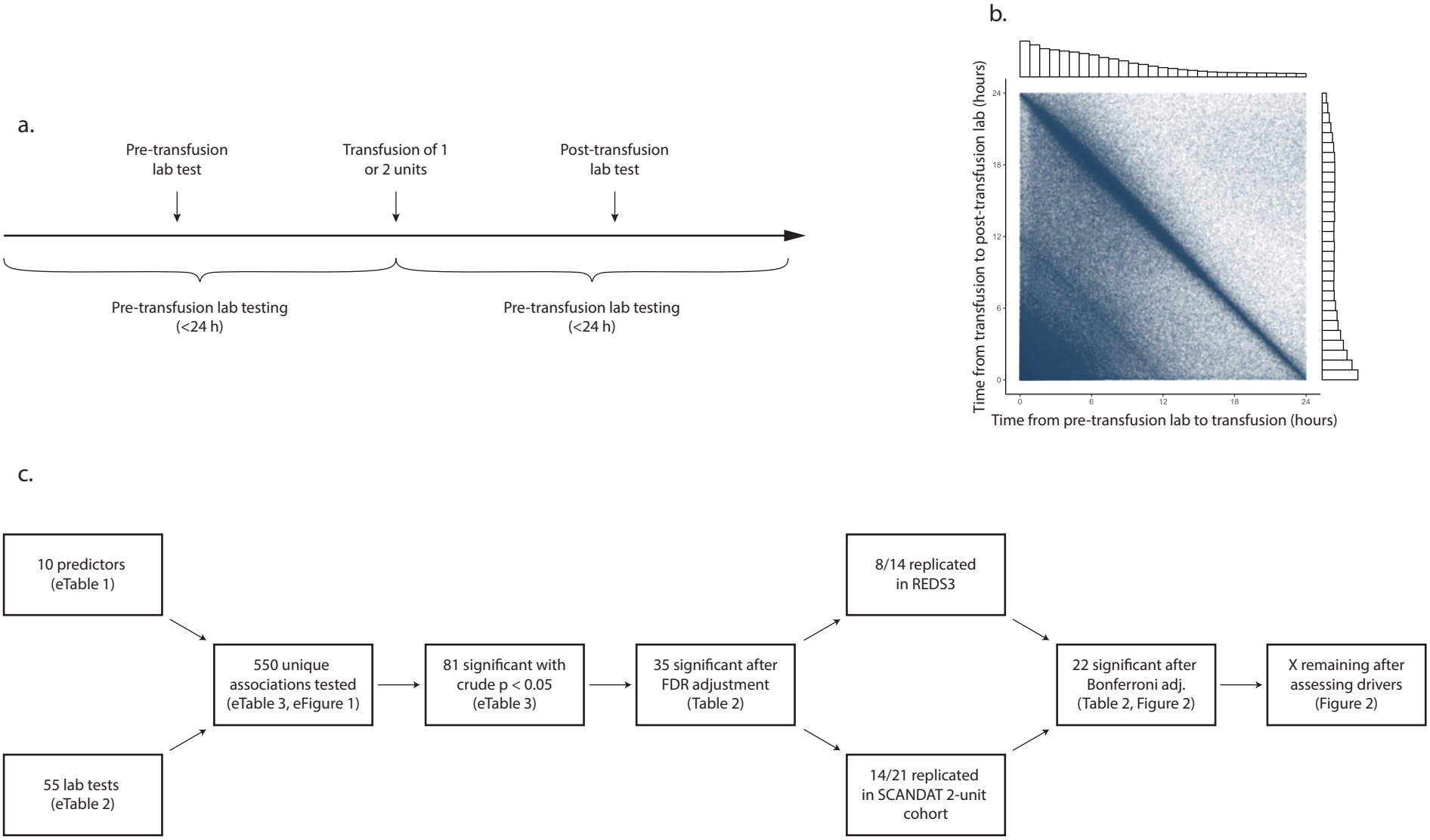Supplementary Figure X - Study concept schmatic