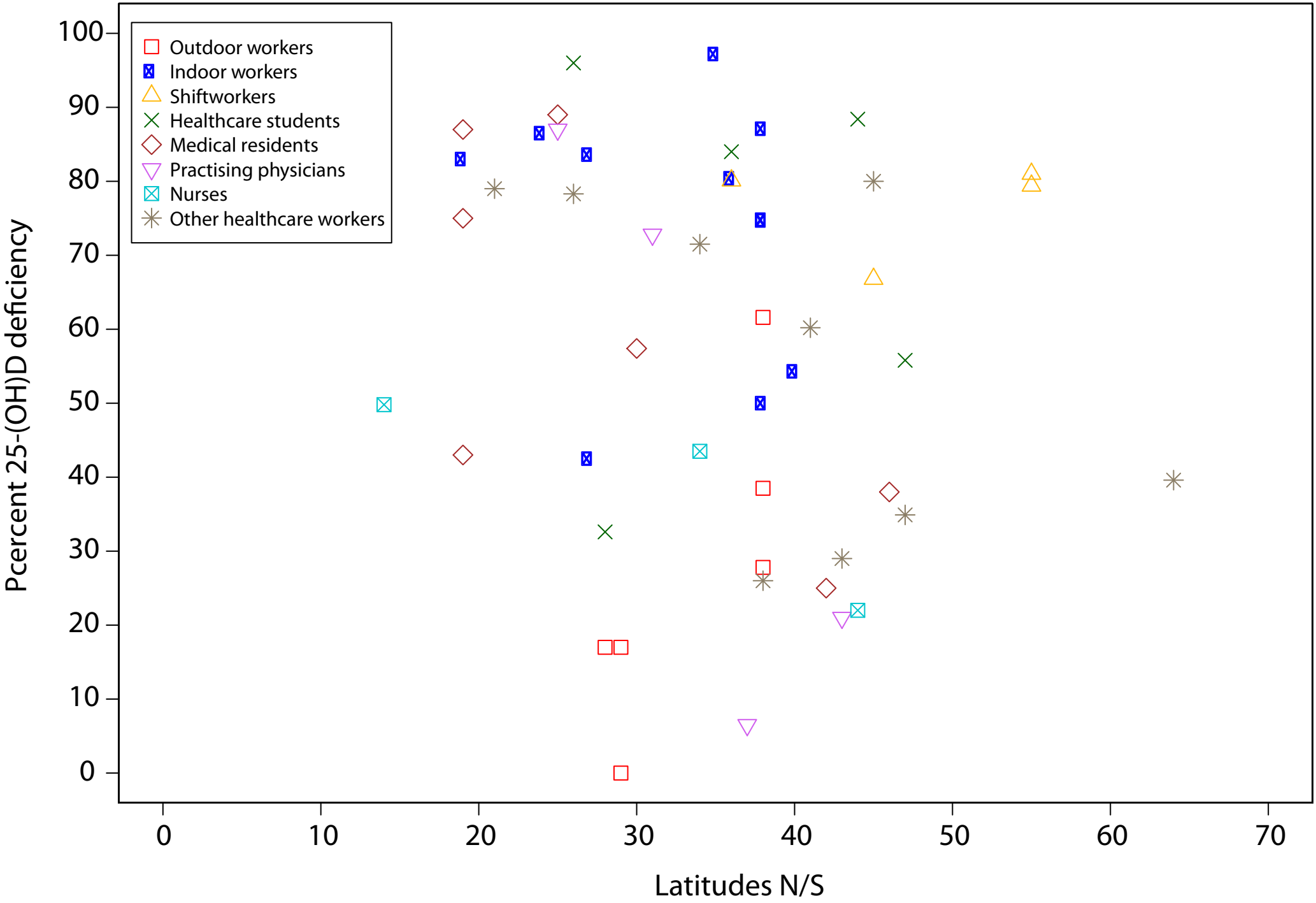Supplementary Fig. 5A