While the notion of “transnationalism” has been widely explored in immigration studies since the 1990s, its implications in health research, including HIV/AIDS research, in the context of immigration have been little considered. Most studies have examined HIV risk faced by immigrants in their host countries, ignoring the simultaneous impacts of the home country (not limited to its culture) on these immigrants’ risk awareness, risk behaviours, and help-seeking practices. Consisting of multi-disciplinary researchers from three countries (Canada, China and France), our research team aims to understand the vulnerability to HIV faced by the current generation of Chinese immigrants, one of the largest groups of newcomers to Canada, who are living in what are increasingly recognized as “transnational spaces”, spaces in which their lives are not limited by the territorial boundaries of Canada (as the host country) and China (as their home country). This paper discusses some of the theoretical contributions and practical challenges of conducting a CIHR-funded international project on transnationalism and HIV risk. Researching transnationalism makes it possible to understand HIV risk from a broader theoretical perspective that goes beyond the traditional state-centric approach to health research that has been increasingly challenged by the ongoing globalization processes. However, “doing” transnationalism turns out to be challenging for two major reasons: a) the technical difficulties in implementing the abstract idea of “transnationalism” in the various phases of research (eg, research design, data collection, and data analysis), and b) the practical complexities associated with the different social, cultural, political, and linguistic contexts in the two countries under study. The changing context and novel aspects of HIV research call for new theories and new methods. It is concluded that incorporating “transnationalism” into HIV/AIDS research opens up a promising new research field, yet its complexities at a practical level merit further reflection and discussion by researchers and policy makers.