Trypanosoma brucei rhodesiense causes rhodesian sleeping sickness in humans. The disease is transmitted by tsetse flies and the distribution of the disease is highly localised to traditional foci. In Kenya, despite widespread distribution of Glossina pallidipes, rhodesian-sleeping sickness is only restricted to western parts of the country. Factors restricting disease distribution to traditional foci are not well understood. A comparative assessment of transmission dynamics and epidemiology of the disease was carried out in two G. pallidipes subpopulations of Kenya in an attempt to understand causes of the focalized distribution. Entomological, socio-economic, cultural and epidemiological risk indicators were studied. Results showed that tsetse flies from the Busia subpopulation had higher survival, longevity, susceptibility and transmission success than those from Nguruman subpopulation. Vector-host contact in both areas did not depend on prevailing weather conditions and, the influence of host movement on vector activity only became important at high host densities. Bovidae and suids were the most preferred hosts of G. pallidipes at Busia and Nguruman respectively. Livestock keeping was a higher risk activity than crop farming in both areas and, while women were more exposed by cultural activities at Busia, men were the most exposed by the same at Nguruman. Land use patterns showed that tsetse habitats have been significantly reduced by economic activities at Busia than Nguruman. Transmission risk at Nguruman was high during the dry season while that at Busia was high during the wet season. Although survival rates of the two subpopulations were similar, vector-host contact, teneral density and overall transmission risk were higher among the Busia subpopulation than the Nguruman subpopulation. Transmission risk projections showed that with increased contact, Nguruman subpopulation would pose significantly higher transmission risk than Busia subpopulation. The risk would however be reduced slightly by suppressed fly density but significantly by low teneral density. Results of this study therefore indicated significant differences in human-fly contact and in vectorial capacity of the two subpopulations. The differences sufficiently explain current epidemiological variations in disease occurrence in the two areas. Management of transmission risk would therefore require sustained suppression of vector population and avoidance of vector-host contact through strategic livestock grazing patterns that is out-of-phase with peak vector activity periods within respective seasons.