

East-Western Dynamic and Driving Factors of Cholera Epidemics in the Democratic Republic of the Congo

Harry César Kayembe Ntumba¹, Doudou Batumbo¹, Jean-Marie Kayembe Ntumba², Julien Ntaongo¹, Lucien Bisimwa¹, Tonton Paul Vita¹ and Didier Bompangue Nkoko^{1,3,4}

¹Training and Research Unit on Ecology and Control of Infectious Diseases, Department of Microbiology and Medical Biology, University of Kinshasa, Democratic Republic of the Congo

²Department of Internal Medicine, University of Kinshasa, Democratic Republic of the Congo

³Chrono-Environnement Laboratory, CNRS, UMR 6249, Bourgogne Franche-Comté University, France

⁴Ministry of Health, Democratic Republic of the Congo

Article Information

Received date: May 31, 2018

Accepted date: Jun 11, 2018

Published date: Jun 13, 2018

*Corresponding author

Harry César Kayembe Ntumba, Unité de Recherche et de Formation en Ecologie et Contrôle des Maladies Infectieuses, Centre de Recherche et d'Etudes sur les Maladies Emergentes et Ré émergentes, Service de Microbiologie, Département de Biologie Médicale, Faculté de Médecine, Université de Kinshasa, Kinshasa, Democratic Republic of the Congo, B.P: 834, Kinshasa XI, Tel: (+243) 81-674-32-42; Email: dr15harrykayembe@gmail.com

Distributed under Creative Commons CC-BY 4.0

Keywords Spread; Cholera Epidemic; Driving Factors; El Niño; Armed Conflicts; IDPs

Abstract

The El Niño's impact on the incidence and endemicity of cholera is highlighted in coastal regions of South-Eastern Asia and inland regions of sub-Saharan Africa, namely in the eastern Democratic Republic of the Congo. This region is also a site of recurrent armed conflicts with subsequent internally displaced persons. However, the western DRC is sporadically affected consecutively to cholera spreading from the eastern endemic foci. We hypothesized that El Niño and both eastern armed conflicts and IDPs may play a central role in the spread of cholera epidemics in the DRC. Using Binomial Regression Models, our study showed that El Niño events were the main predictors of cholera epidemics spreading out of eastern endemic provinces. It implies that we may be able to provide an epidemiological tool to forecast the risk of cholera in the DRC.

Introduction

The understanding of the diffusion dynamic of emerging or re-emerging infectious diseases remains a challenge in controlling their epidemics. Many factors are incriminated influencing the spread of infectious diseases such as the transmissibility of the pathogen agent, the spatial structure and the heterogeneity of the population, the human mobility and the human interaction intensity [1-4]. The roles of demographic growth, antibiotic resistance, globalization and climatic conditions were also established [5].

Concerning climatic factors, their impact on the dynamics of infectious diseases' outbreaks such as cholera has been largely demonstrated [6-16]. In particular, the link between the El Niño Southern Oscillation (ENSO) and the seasonality of cholera has been also indicated [17-21]. ENSO is an inter-annual climate variability pattern associated with fluctuations in sea surface temperatures and wind strengths in the equatorial East Pacific Ocean [22]. El Niño warm events occur, on average, every 2-7 years and impact on large scale climate patterns: droughts in South-East Asia, parts of Australia and Southern Africa, and heavy rainfall and flooding in East Africa and South America.

Most of studies focused on ENSO's influence on the seasonality of cholera epidemics were performed in coastal regions of the Bay of Bengal [17-20]. In sub-Saharan context, especially in inland regions, some evidences about the ENSO-related impact on the increased incidence of cholera in the Great Lakes Region (GLR) [23] and East African regions [24] have also been highlighted.

The eastern Democratic Republic of the Congo (DRC), located to GLR, reports cholera outbreaks annually. This endemicity is maintained by the presence of lacustrine areas in which cholera cases persist during lull periods and outbreaks start and then spread to areas not yet affected [23,25,26]. Furthermore, this part of the DRC is considered as one of the most active foci of armed conflicts in the world. During the last 20 years, these conflicts have confronted the regular army, foreign forces, unidentified armed groups and local militias. The armed conflicts may lead consecutively to Complex Humanitarian Emergencies (CEs), namely massive population displacements and exposure to infectious diseases [27]. However, the western part of the DRC is sporadically affected. A little is known about driving factors involved in that dynamic even if some authors suggest that western cholera epidemics would be consecutive to cholera cases spreading along the Congo River from the eastern endemic lacustrine areas [28]. Also, western outbreaks occurred during or after years of El Niño warm events (1994-1995, 1997-1998, 2009-2010 and 2015-2016).

The present study aimed to describe cholera outbreaks from reported cases at the Health District (HD) level over the period 2000 to 2016 and to test the role that El Niño warm events and eastern

armed conflicts and related-Internally Displaced Persons (IDPs) may play in the spread of cholera epidemics in the DRC.

Material and Methods

From each HD, cholera notification data of the Ministry of Public Health were collected at a weekly time scale from 2000 through 2016. Based on the World Health Organization (WHO) standard case definition, cholera cases were diagnosed as acute watery diarrhea in a patient 5 year of age or older with or without vomiting, with an age limit lowered to 2 years for cases associated with confirmed cholera outbreaks [29]. Each new outbreak was confirmed through isolation of *Vibrio cholerae* O1 from stool samples in culture [29].

The data on weekly number of conflicts and IDPs were extracted from databases of the Armed Conflict Location & Event Data Project (<http://www.acledata.com/data/>) and the Office for the Coordination of Humanitarian Affairs (<http://www.ehtools.org/data/>), respectively. The formers were collected from 2000 through 2016 and the last ones, from 2009 through 2016. Also, during our study period, the years of occurrence and no occurrence of El Niño warm events were considered. For El Niño years, the event was suggested to run from July through June of the following year [24]. In this case, the years of 2002- 2016 were considered as El Niño years.

The data obtained from the 515 HDs allowed to establish a geographic information system for showing the annual geographic distribution of cholera cases, number of conflicts and number of IDPs across the all country. ESRI shape files were used to produce all maps. We also tested correlation between western cholera case count and eastern armed conflicts and between IDPs and armed conflicts.

Using Generalized Linear Models (GLM) of the binomial family, we statistically analyzed the epidemiological association between the spread of cholera epidemics out of eastern provinces in which endemic lake side HDs are located and El Niño years, both eastern armed conflicts & IDPs. Two types of model were tested: without interaction between variables and with interaction between them. The best model was finally selected by using the Akaike index criterion. Computations and analyses were conducted with R version 3.3.3.

Results

Overall, from January 2000 to December 2016, a total of 368,375 cholera cases including 9,870 deaths were recorded in the DRC, resulting in a Case Fatality Rate (CFR) of 2.7%. The spatial analysis of cholera per year showed heterogeneities in the outbreaks' reports characterized by an east-central-west geographic cleavage of cholera cases (Figure 1). In the years 2001, 2007, 2009-2010 and 2014, cholera outbreaks were confined to the eastern part of the DRC. During years 2002-2006, 2008 and 2015, cholera outbreaks were notified both in central and eastern DRC. In 2000, 2011-2013 and 2016 cholera outbreaks were also reported in the west.

More than 80% of armed conflicts were reported from the eastern provinces with cholera endemic foci: Ituri, North Kivu, South Kivu, Tanganyika, Haut Lomami and Haut Katanga (Figure 2). Years with exacerbation of conflicts armed in North and South Kivu were superposable with years of cholera's occurrence in the western DRC. Western cholera cases were slightly correlated with eastern armed conflicts (Pearson $r = 0.23$, $p < 0.001$).

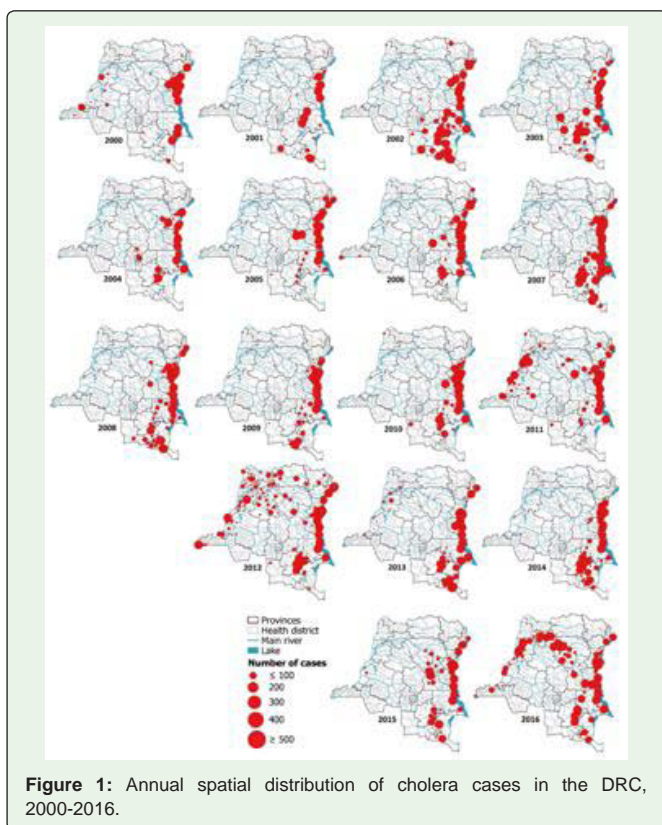


Figure 1: Annual spatial distribution of cholera cases in the DRC, 2000-2016.

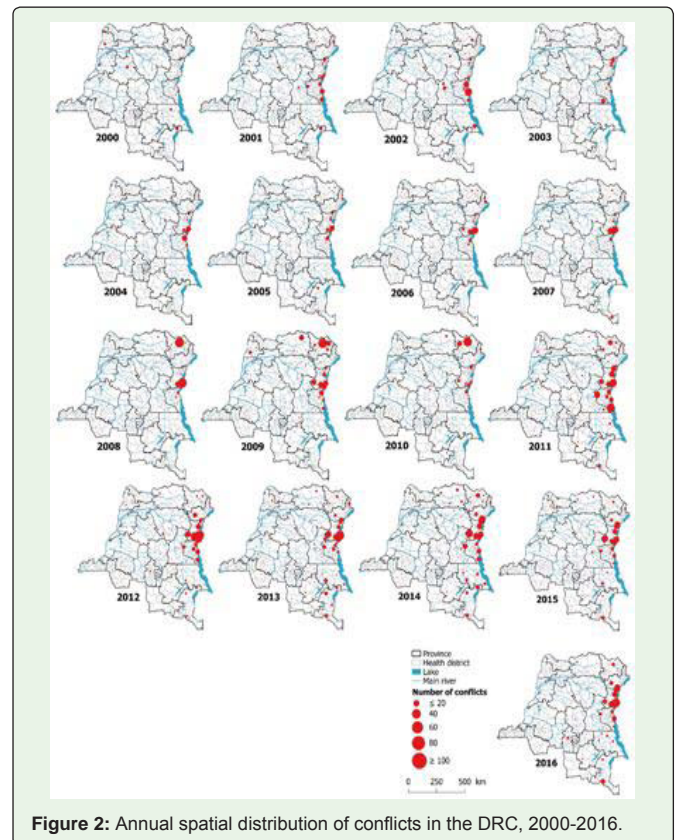


Figure 2: Annual spatial distribution of conflicts in the DRC, 2000-2016.

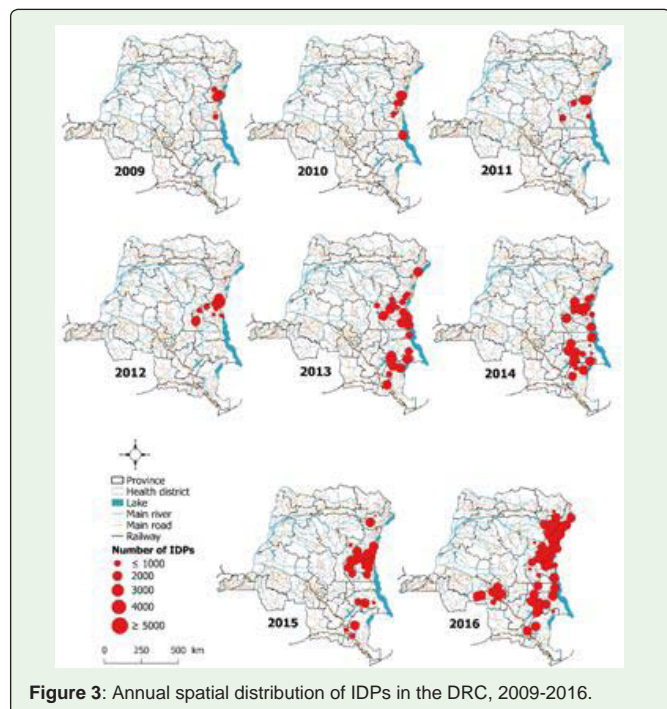


Figure 3: Annual spatial distribution of IDPs in the DRC, 2009-2016.

As shown in Figure 3, IDPs were quasi annually unregistered where armed conflicts were signaled, especially in the eastern part of the DRC, even if they were weakly correlated (Pearson $r = 0.19$, $p < 0.001$). The situation of IDPs observed in the Kasai space has occurred in the second half of 2016. It was consecutive to the Kamwina Nsapu rebellion instigated by the Kamwina Nsapu militia against state security forces that led to more than a million IDPs ten months later.

The HDs of non-endemic provinces located to central and western parts of the country were affected during or following years of El Niño warm events, namely in 2002-2006, 2008, 2011-2013, 2015 and 2016 corresponding to El Niño years of 2002-2007, 2009-2010 and 2015-2016 (Figure 4).

Table 1 showed that in the model with interaction between El Niño and eastern cholera cases associated with eastern armed conflicts and IDPs, the risk of cholera spreading out of eastern endemic provinces was significantly higher with the occurrence of El Niño warm events (odds ratio [OR] 3.3, 95% Confidence Interval [CI] 1.86-5.93) and eastern armed conflicts (OR: 1.07, 95% CI: 1.05-1.09).

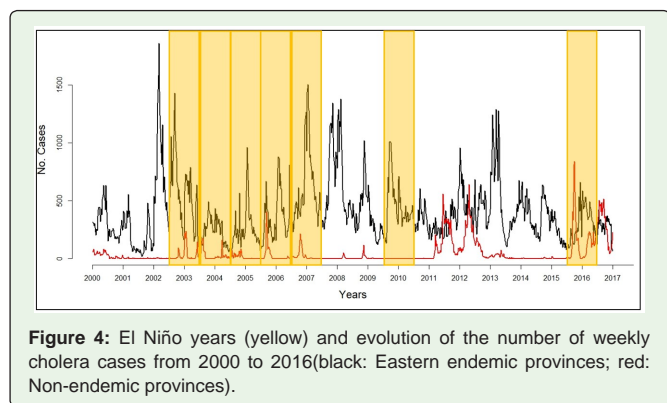


Figure 4: El Niño years (yellow) and evolution of the number of weekly cholera cases from 2000 to 2016(black: Eastern endemic provinces; red: Non-endemic provinces).

Table 1: Model parameters and Odds ratios of the binomial regression model.

| | Odds ratio | 95% CI ¹ | p value |
|----------------------------|------------|---------------------|---------|
| Intercept | 0.36 | 0.25-0.51 | |
| El Nino | 3.30 | 1.86-5.93 | < 0.05 |
| Cases ² | 1.00 | 1.00-1.00 | < 0.01 |
| Conflicts ³ | 1.07 | 1.05-1.09 | < 0.001 |
| IDPs ⁴ | 1.00 | 1.00-1.00 | < 0.001 |
| El Nino*Cases ² | 1.00 | 1.00-1.00 | < 0.05 |

¹CI, confidence interval; ²Cases, eastern cholera cases; ³Conflicts, eastern armed conflicts; ⁴IDPs, eastern IDPs; *, interaction between variables.

Discussion

The present study showed an east-central-west geographic cleavage at national level in cholera outbreaks reported over the period 2000 to 2016. This geographic cleavage was determined by the dynamic process of cholera epidemics spreading from Eastern endemic lacustrine foci. We hypothesized that El Niño warm events and eastern armed conflicts as well as related-IDPs may play the role of driving factors of observed spreading dynamics.

After testing the association between the interaction El Niño years-eastern cholera cases with armed conflicts and IDPs, we found that El Niño years enhanced the risk of cholera epidemics spreading out of eastern provinces with cholera endemic lakeside areas to central and western HDs (OR: 3.3, 95% CI: 1.86-5.93). This finding confirms our field observations reporting that western cholera outbreaks occurred during or following El Niño years. To our knowledge, this is the first study that suggested the influence of El Niño warm events on the spread of cholera epidemics in inland Africa. Recent researches have demonstrated that El Niño conditions were linked with increased number of cholera cases [23,24]. Moore et al. have specifically highlighted changes in the geographic distribution of cholera burden in continental East Africa with 50,000 additional cases during El Niño years [24]. Furthermore, these authors have shown a higher cholera incidence with substantial heavy rainfalls during El Niño years in East Africa. A previous study in Uganda also found a positive association between El Niño rains and increase in cholera case counts [30]. In our context, the westward spatio-temporal dynamics of cholera spreading from eastern endemic lakeside HDs [28] is consistent with our field observations. Indeed, flood events consecutive to heavy rainfall occurred mainly during El Niño years (1997-1998, 2009-2010 and 2015-2016). But, recently, no clear positive association between cholera incidence and rainfall was reported in areas of Central Africa with below-average rainfall during El Niño years [24]. Based on the hypothesis of the relationship between El Niño years, excess of rainfall during the corresponding years and cholera in the equatorial region of Africa [23], our field observations sustained by our findings require further studies to explore the potential role of El Niño warm events on local climatic factors in cholera epidemic spreading at a finest spatial scale.

Our results have also shown an association between eastern armed conflicts and the spread of cholera epidemics out of eastern endemic provinces (OR: 1.07, 95% CI: 1.05-1.09). Indeed, conflicts situations present several risk factors that enhance transmission of infectious diseases. In our case, the exacerbation of eastern armed

conflicts was slightly correlated with eastern IDPs and the occurrence of western cholera outbreaks. It would indicate that several conditions are necessary for an armed conflict situation to father the spread of a cholera epidemic including environmental conditions, inadequate surveillance and response systems, destruction of infrastructures, collapse of health systems and disruption of disease control programs and infection control practices [27]. Also, some of the IDPs escaping from the conflict area should be potentially infected or should move into areas already affected by cholera [26].

Conclusion

The results of this study have mainly shown the El Niño's impact on the spread of cholera epidemics out of eastern provinces with endemic lakeside areas. Even if there is a need for further researches to understand the epidemiological link between El Niño, local climatic factors and the spread of cholera epidemics at a finest scale, our findings imply that we may be able to provide early warning systems to forecast the risk of cholera in the DRC. For operational field, it could help to trigger public health preventive measures because El Niño events are predictable 6 to 12 months in advance.

Acknowledgements

We thank all the authors for their commitment in the achievement of the present work.

References

- Dushoff J, Levin S. The effects of population heterogeneity on disease invasion. *Math Biosci.* 1995; 128: 25-40.
- Grenfell BT, Bjørnstad ON, Kappey J. Travelling waves and spatial hierarchies in measles epidemics. *Nature.* 2001; 414: 716-723.
- Li R, Wang W, Di Z. Effects of human dynamics on epidemic spreading in Côte d'Ivoire. *Phys Stat Mech Its Appl.* 2017; 467: 30-40.
- Merler S, Ajelli M. The role of population heterogeneity and human mobility in the spread of pandemic influenza. *Proc R Soc B Biol Sci.* 2010; 277: 557-565.
- Knobler S, Mahmoud A, Lemon S, Pray L, éditeurs. Institute of Medicine (US) Forum on Microbial Threats. The Impact of Globalization on Infectious Disease Emergence and Control: Exploring the Consequences and Opportunities: Workshop Summary [Internet]. Washington (DC): National Academies Press (US); 2006.
- De Magny GC, Thiaw W, Kumar V, Manga NM, Diop BM, Gueye L, et al. Cholera outbreak in Senegal in 2005: was climate a factor? *PLoS One.* 2012; 7: e44577.
- Constantin de Magny G, Guégan J-F, Petit M, Cazelles B. Regional-scale climate-variability synchrony of cholera epidemics in West Africa. *BMC Infect Dis.* 2007; 7: 20.
- Constantin de Magny G, Colwell RR. Cholera and climate: a demonstrated relationship. *Trans Am Clin Climatol Assoc.* 2009; 120:119-128.
- Emch M, Feldacker C, Islam MS, Ali M. Seasonality of cholera from 1974 to 2005: a review of global patterns. *Int J Health Geogr.* 2008; 7: 31.
- Luque Fernández MA, Bauernfeind A, Jiménez JD, Gil CL, El Omeiri N, Guibert DH. Influence of temperature and rainfall on the evolution of cholera epidemics in Lusaka, Zambia, 2003-2006: analysis of a time series. *Trans R Soc Trop Med Hyg.* 2009; 103: 137-143.
- Hashizume M, Armstrong B, Hajat S, Wagatsuma Y, Faruque ASG, Hayashi T, et al. The effect of rainfall on the incidence of cholera in Bangladesh. *Epidemiol Camb Mass.* 2008; 19:103-110.
- Leckebusch GC, Abdussalam AF. Climate and socioeconomic influences on interannual variability of cholera in Nigeria. *Health Place.* 2015; 34:107-117.
- Koelle K, Rodó X, Pascual M, Yunus M, Mostafa G. Refractory periods and climate forcing in cholera dynamics. *Nature.* 2005; 436: 696-700.
- Mendelsohn J, Dawson T. Climate and cholera in KwaZulu-Natal, South Africa: the role of environmental factors and implications for epidemic preparedness. *Int J Hyg Environ Health.* 2008; 211: 156-162.
- Paz S. Impact of temperature variability on cholera incidence in southeastern Africa, 1971-2006. *EcoHealth.* 2009; 6: 340-345.
- Escobar LE, Ryan SJ, Stewart-Ibarra AM, Finkelstein JL, King CA, Qiao H, et al. A global map of suitability for coastal *Vibrio cholerae* under current and future climate conditions. *Acta Trop.* 2015; 149: 202-211.
- Colwell RR. Global climate and infectious disease: the cholera paradigm. *Science.* 1996; 274: 2025-2031.
- Pascual M, Rodó X, Ellner SP, Colwell R, Bouma MJ. Cholera dynamics and El Niño-Southern Oscillation. *Science.* 2000; 289:1766-1769.
- Rodo X, Pascual M, Fuchs G, Faruque ASG. ENSO and cholera: a nonstationary link related to climate change? *Proc Natl Acad Sci U S A.* 2002; 99:12901-12906.
- Cash BA, Rodó X, Kinter JL, Yunus M. Disentangling the Impact of ENSO and Indian Ocean Variability on the Regional Climate of Bangladesh: Implications for Cholera Risk. *J Clim.* 2009; 23: 2817-2831.
- Patz JA, Campbell-Lendrum D, Holloway T, Foley JA. Impact of regional climate change on human health. *Nature.* 2005; 438: 310-317.
- Rasmusson EM, Wallace JM. Meteorological aspects of the el nino/southern oscillation. *Science.* 1983; 222: 1195-1202.
- Bompangue Nkoko D, Giraudoux P, Plisnier P-D, Tinda AM, Piarroux M, Sudre B, et al. Dynamics of cholera outbreaks in great lakes region of Africa, 1978-2008. *Emerg Infect Dis.* 2011; 17: 2026-2034.
- Moore SM, Azman AS, Zaitchik BF, Mintz ED, Brunkard J, Legros D, et al. El Niño and the shifting geography of cholera in Africa. *Proc Natl Acad Sci U S A.* 2017; 114: 4436-4441.
- Bompangue D, Giraudoux P, Handschumacher P, Piarroux M, Sudre B, Ekwanzala M, et al. Lakes as Source of Cholera Outbreaks, Democratic Republic of Congo. *Emerg Infect Dis.* May 2008; 14: 798-800.
- Bompangue D, Giraudoux P, Piarroux M, Mutombo G, Shamavu R, Sudre B, et al. Cholera Epidemics, War and Disasters around Goma and Lake Kivu: An Eight-Year Survey. *PLoS Negl Trop Dis.* 2009; 3:436.
- Gayer M, Legros D, Formenty P, Connolly MA. Conflict and emerging infectious diseases. *Emerg Infect Dis.* 2007; 13: 1625-1631.
- Bompangue D, Vesenbeckh SM, Giraudoux P, Castro M, Muyembe J-J, Ilunga BK, et al. Cholera ante portas - The re-emergence of cholera in Kinshasa after a ten-year hiatus. *PLOS Curr Disasters.* 2012.
- World Health Organization. Guidelines for Cholera Control [Internet]. 1993.
- Alajo SO, Nakavuma J, Erume J. Cholera in endemic districts in Uganda during El Niño rains: 2002-2003. *Afr Health Sci.* 2006; 6: 93-97.