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Influence of temperature and rainfall on the evolution of cholera epidemics in Lusaka, Zambia, 2003–2006: analysis of a time series

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Summary In this study, we aimed to describe the evolution of three cholera epidemics that occurred in Lusaka, Zambia, between 2003 and 2006 and to analyse the association between the increase in number of cases and climatic factors. A Poisson autoregressive model controlling for seasonality and trend was built to estimate the association between the increase in the weekly number of cases and weekly means of daily maximum temperature and rainfall. All epidemics showed a seasonal trend coinciding with the rainy season (November to March). A 1 °C rise in temperature 6 weeks before the onset of the outbreak explained 5.2% [relative risk (RR) 1.05, 95% CI 1.04–1.06] of the increase in the number of cholera cases (2003–2006). In addition, a 50 mm increase in rainfall 3 weeks before explained an increase of 2.5% (RR 1.02, 95% CI 1.01–1.04). The attributable risks were 4.9% for temperature and 2.4% for rainfall. If 6 weeks prior to the beginning of the rainy season an increase in temperature is observed followed by an increase in rainfall 3 weeks later, both exceeding expected levels, an increase in the number of cases of cholera within the following 3 weeks could be expected. Our explicative model could contribute to developing a warning signal to reduce the impact of a presumed cholera epidemic.

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1. Introduction

The turn of the century has been marked by a worrisome emergence and re-emergence of infectious diseases worldwide. In fact, the number of cholera cases reported to the WHO between 2003 and 2006 has dramatically increased, reaching its highest values in more than a decade. In 2006, a total rise of 79% was observed compared with the previous year; 87% of cholera cases occurred in Africa.[1]

It is well established that environmental factors, through seasonal variations or as a consequence of global climate change, play an important role in the resurgence and dynamics of infectious diseases.[2–6] On the other hand, in addition to being linked to climate[7], cholera is closely related to poor environmental status and lack of basic infrastructure in developing countries. In this manner, high population densities as well as poor access to safe water and proper sanitation along with other environmental conditions contribute to the spread of cholera in Africa.[8,9]

Vibrio cholerae requires optimal temperature and physicochemical conditions (salinity, pH, humidity etc.) to survive. Nevertheless, it has also been shown to resist suboptimal conditions through specific associations of the bacterium with aquatic plants[10] or animals such as oysters, crabs and copepods.[11–14] As a result, the pathogen can persist for longer periods in aquatic habitats. Weather conditions such as an increase in environmental or sea surface temperatures favour plankton bloom. This link with temperature could explain the surge of cholera in endemic zones in cycles of 3–6 years, its expansion and its re-emergence after an absence of several years. In line with this observation, theoretical models were developed that included environmental variables as causal factors for cholera re-emergence in an attempt to describe its dynamics.[15] In real-life conditions, positive correlations were shown to exist between an upsurge in the number of cholera cases during an outbreak and the increase in sea surface temperature 8 weeks earlier.[16,17] Hence, upon describing epidemiological variables of outbreaks and analysing related climate variables, mathematical models can be built providing necessary information to predict the evolution of cholera epidemics.[18]

In Zambia, cholera is endemic and cases appear all year round. Certain regions of the country are more prone to epidemics, among which is Lusaka, the capital of Zambia. For 2003 it was estimated that 36% of the total country population lived in urban areas and only 55% had access to drinking water.[19] The last outbreak recorded occurred in 1999 and affected 7569 individuals. From 2003, epidemics re-emerged repeatedly, occurring during 3 consecutive years.[1]

The objectives of this study were to describe the evolution of the three cholera epidemics that took place in Lusaka during the period 2003–2006 and to explain the association between the increase in the number of cholera cases on the one hand and daily maximum temperature and rainfall recorded during the period under consideration on the other.

2. Methods

2.1. Study design

A descriptive and ecological study was carried out. The evolution and the impact of the three epidemics that occurred in Lusaka between 2003 and 2006 are described. Through an explicative model using time series analysis, an analytical component examined the influence of environmental factors, namely rainfall and temperature, on the appearance and increase in the number of cases of cholera.

2.2. Data source and collection

Epidemiological data were collected by the non-governmental organisation Médecins Sans Frontières, which intervened in all three outbreaks in Lusaka. The main data source was medical registries at cholera isolation centres that the organisation put in place in collaboration with the Zambian Ministry of Health. Environmental data were taken at the meteorological station of the international airport of Lusaka (FLLS-676650), whose geographical coordinates are −15.31° latitude, 28.45° longitude and 1152 m altitude. Data were available through the website TuTiempo.net (http://www.tutiempo.net), which compiles and stores data from meteorological stations around the world.

Sociodemographic data regarding the inhabitants of Lusaka (capital of Zambia) were obtained from the UNFPA.[19]

2.3. Variables considered

The WHO case definition for cholera was used.[20] Cases were aggregated by epidemiological week. Deaths attributable to cholera and recorded at the isolation centres were also grouped by epidemiological week. Weekly arithmetic means of maximum temperature were calculated for the epidemiological weeks based on daily maximum temperature (maximum value in 24 h) and were expressed in °C. Rainfall (in mm) was the total daily precipitation recorded, summed up weekly in the same manner as for temperature. The period considered for analysis extended from the eighth epidemiological week of 2003 until the eighth week of 2006.

2.4. Statistical analysis

A descriptive analysis of the variables under study was performed using time plots. The outbreaks were described presenting epidemic curves, the total weekly number of cases, weekly incidence rate, attack rate, case fatality rate (CFR), duration of outbreak and strains isolated along with their serotype. A spectral analysis was then performed with a Fast Fourier transform procedure for detecting significant trend and periodicity in the univariate analysis of the weekly number of cholera cases. Then, to examine the association between the increase in the weekly number of cholera cases (the dependent variable) and climate factors (independent variables), a Poisson autoregressive model was used through a generalised linear model with family Poisson and link log controlling for seasonality. Akaike's information cri-

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terion (AIC) was used to find the best model. The variables were entered and omitted manually from the model in a stepwise manner, with the criterion for elimination being a *P*-value >0.05. In the case of overdispersion of the data, adjusted standard errors of coefficients were presented. Sin and cos functions were used in the model for building the independent variables that explain the seasonal component of the series. An autoregressive term at order 1 was incorporated into the model to control for the autocorrelation of cases of cholera of a current week with a previous week.[21] Based on our review of the literature, lags of up to 8 weeks for temperature were introduced to analyse the association between the occurrence and increase in the number of cholera cases and the mean maximum temperature 6 weeks before the onset of the outbreak.

Goodness of fit was assessed through the standard Poisson regression models by looking for the model that minimised the residual autocorrelation, graphically through examining the simple autocorrelation function (ACF) plot and the partial autocorrelation function (PACF) plot. In addition, the plot of standardised deviance residuals against the observed cases of cholera from the final model and the simulation approach for evaluating the goodness of fit of sparse data by Boyle et al.[22] was used.

Relative risks (RR) were derived from the determination coefficients and were presented with their 95% CI. Assuming that the whole population was exposed to the environmental factors, the attributable risk (AR) was calculated using the formula AR = RR−1/RR, applicable when RR is derived from Poisson regression models.[23] Analysis was performed using Stata v.10 (StataCorp., College Station, TX, USA).

3. Results

Outbreaks were confirmed and *V. cholerae* was isolated in all three situations; the strain identified was O1 El Tor Ogawa.

Epidemiological descriptions of the three outbreaks revealed many similarities. All three took place during the rainy season coinciding with epidemiological Weeks 47−15 and were of similar duration. Table 1 gives the attack rates and other characteristics. The epidemic curves show a high CFR at the beginning of the outbreak of 2003, which then drops and remains stable for 21 weeks. No mortality data were available for 2004. During the outbreak of 2005, the CFR was smaller in magnitude and duration. The number of cases was significantly lower in the second epidemic (Figures 1−3).

The Poisson distribution of the number of cholera cases as the dependent variable was verified. The weekly numbers of cases for the period 2003−2006 varied between a minimum of 2 and a maximum of 911 cases, with a median of 89 and an interquartile range of 304 weekly cases. The weekly daily maximum temperature per epidemiological week had a minimum of 21.9 °C and a maximum of 36 °C. Rainfall had a minimum of 0 mm and a maximum of 307.1 mm. In the time plots, an increase in temperature and rainfall was observed in the weeks prior to the appearance of the epidemics (Figures 4 and 5). Univariate analysis of cholera cases for the 3 years showed a seasonal pattern that corresponded to the months from December through April, confirmed using spectral analysis and periodograms (Supplementary Figure 1), but no trend. Analysis of the association between the weekly number of cases and climate factors using a Poisson autoregressive model controlling for seasonality showed a statistically significant association between the increase in the number of cases and the increase in temperature 6 weeks earlier and the increase in rainfall 3 weeks earlier.

The final model was overdispersed. To compensate for overdispersion, standard errors were scaled using the square root of the Pearson χ^2 dispersion. The final model was adjusted for sin and cos variables to control for seasonality (sin 365°, 120°, 60° and cos 365°, 180°), and autoregressive term at order 1 of cholera cases for controlling autocorrelation. Among all models examined, the following model showed the lowest AIC value:

Weekly number of cholera cases$=\beta_0 + \beta_1$ seasonality $+ \beta_2$ autoregressive component order at $1+\beta_3^{\circ}$Temp 6 weeks earlier $+ \beta_4$ rainfall 3 weeks earlier

Table 1 Characterisation of three cholera outbreaks in Lusaka, Zambia, 2003−2006 (Médecins Sans Frontières, unpublished data)

	2003−2004	2004−2005	2005−2006
Population	1 234 600	1 283 984	1 335 343
Isolated strain	Ogawa	Ogawa	Ogawa
Year of last epidemic	1999	2003	2004
Years without epidemics	4	0	0
Epidemiological weeks affected	47−15	43−14	46−14
Duration in weeks	23	24	21
Total no. of cases	6471	888	5710
Maximum no. of cases per week	911	92	581
Absolute no. of deaths	205	ND	87
Case fatality rate (%)	3.2	ND	1.5
Attack rate (epidemic) (%)	0.5	0.1	0.4
Duration (weeks) of the peak	3	6	2
Epidemiological week of 1st peak	14	10	11

ND: no data available.

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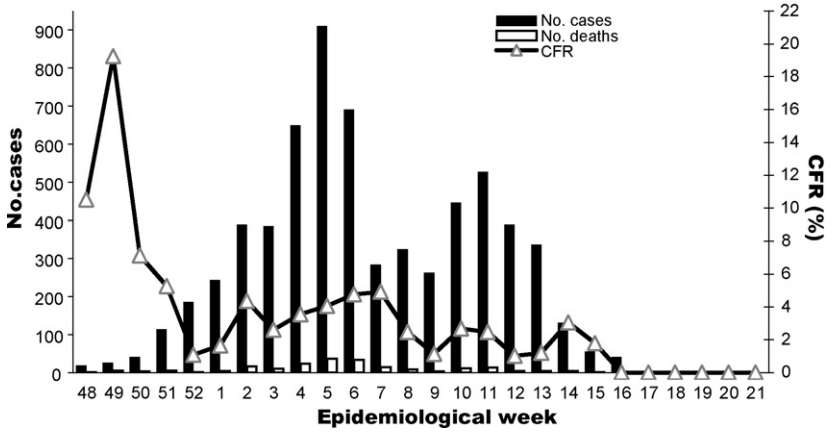

Figure 1 Distribution of cholera cases, deaths and case fatality rate (CFR) per epidemiological week ($n = 6471$ cases and 205 deaths) in the 2003—2004 outbreak in Lusaka, Zambia (Médecins Sans Frontières, unpublished data).

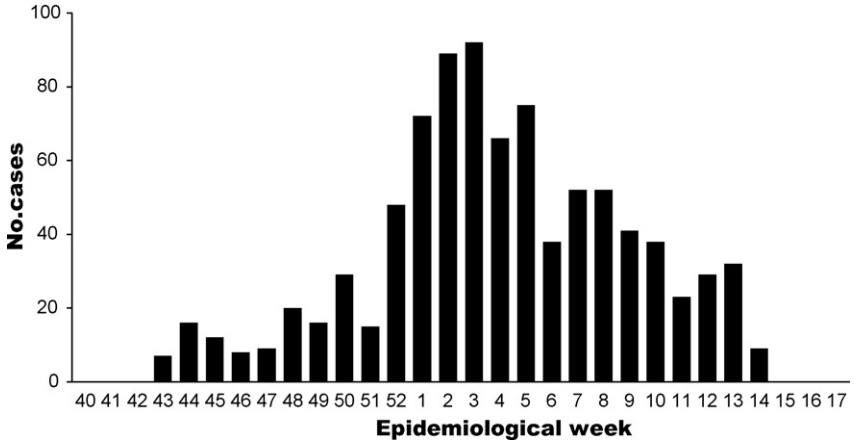

Figure 2 Distribution of cholera cases per epidemiological week ($n = 888$ cases) in the 2004—2005 outbreak in Lusaka, Zambia (Médecins Sans Frontières, unpublished data).

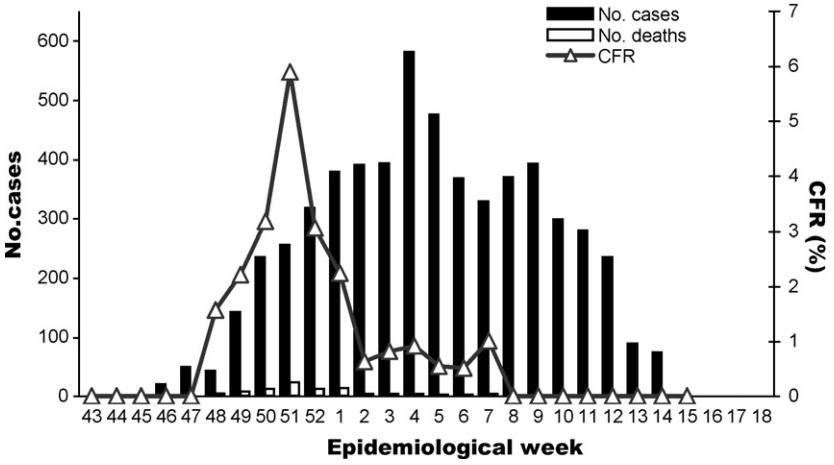

Figure 3 Distribution of cholera cases, deaths and case fatality rate (CFR) per epidemiological week ($n = 5710$ cases and 87 deaths) in the 2005—2006 outbreak in Lusaka, Zambia (Médecins Sans Frontières, unpublished data).

Examining the functions of PACF and ACF of residuals confirmed their random distribution, indicating proper adjustment of the model. The plot of standardised deviance residuals against expected cases of cholera from the model also showed a good fit of the data. The line plot of the predicted cases of cholera from the model and observed cases showed a good fit with a correlation coefficient of 0.9 ($P < 0.001$) (Supplementary Figure 2). As the overdispersion

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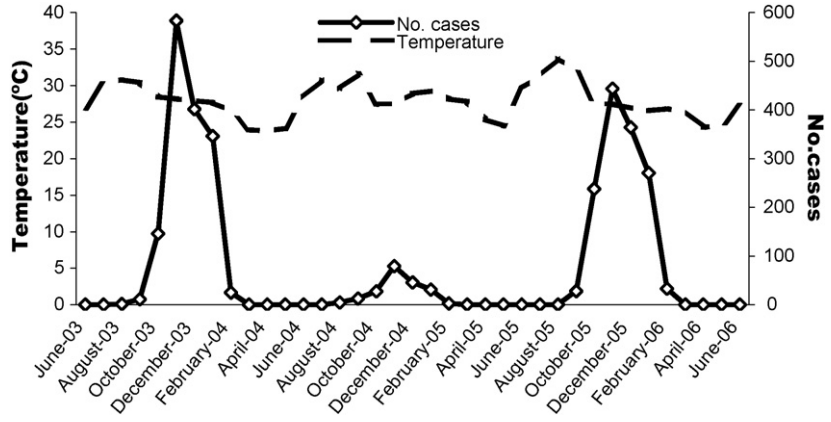

Figure 4 Time plots of number of cholera cases per month and monthly mean temperature (°C) in Lusaka, Zambia, 2003—2006 (Médecins Sans Frontières, unpublished data).

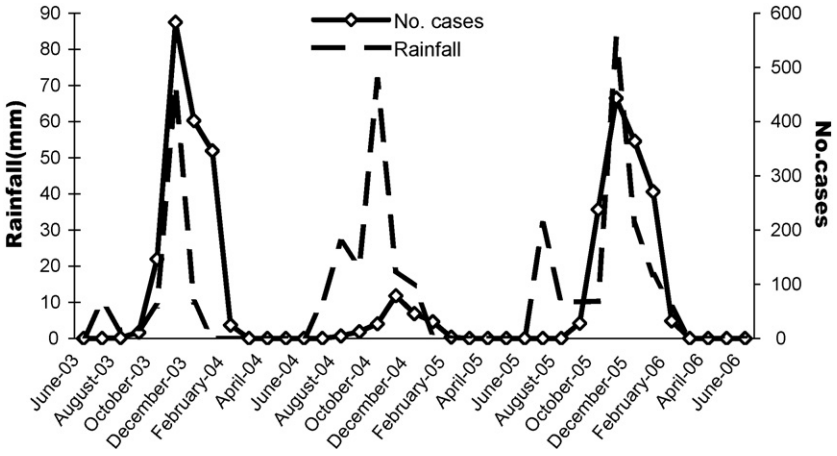

Figure 5 Time plots of number of cholera cases per month and monthly mean rainfall (mm) in Lusaka, Zambia, 2003—2006 (Médecins Sans Frontières, unpublished data).

of the data is due to the high number of null values, the interpretation of the deviance χ^2 is unreliable. Thus, using the simulation approach for evaluating the goodness of fit of sparse data by Boyle et al.[22], the deviance was 5.3 with 142 d.f., the test of goodness of fit of deviance >0.05 and AIC 3.4.

Hence, an ambient temperature increase of 1 °C 6 weeks before the beginning of the outbreaks explained 5.2% of the weekly augmentation of cholera cases observed, and an increase of 50 mm in rainfall 3 weeks earlier explained another 2.5% (Table 2).

4. Discussion

A recent review of WHO cholera incidence and mortality data (1960—2005) raised the question of Africa as a 'new homeland' for cholera.[24] Our results showed recurrent cholera outbreaks in Lusaka, Zambia, within a period of 3 years and characterised by high incidence and CFRs.

The seasonal trend for cholera incidence observed in our time series and coinciding with the rainy season is consistent with what is known for the region.[25,26]

Table 2 Association between the number of cholera cases and climate variables: final autoregressive Poisson model including lags of weekly mean temperature and rainfall (Médecins Sans Frontières, unpublished data)[a]

	Coefficient (SE)[b]	RR (95% CI)	% change[c]	AR (%)	*P*-value
Temperature (6 weeks earlier)	0.05 (0.006)	1.05 (1.04—1.06)	5.2	4.7	<0.001
Rainfall (3 weeks earlier)	0.02 (0.01)	1.02 (1.01—1.04)	2.5	1.9	0.011

RR: relative risk; AR: attributable risk.
[a] Adjusted for seasonality.
[b] Standard errors (SE) scaled using square root of Pearson χ^2 based dispersion.
[c] Percent change in expected count for 1 °C increase in temperature and 50 mm in rainfall.

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In recent years, numerous studies have demonstrated the association between the re-emergence and dynamics of infectious diseases and environmental factors.[7,27] We identified such an association between temperature and rainfall and the increase in the number of cholera cases in three outbreaks occurring in Lusaka (2003—2006), which is in concordance with suggested environmental theories for re-emergence of infectious diseases. It is worth noting that most studies relating climate to cholera describe coastal regions.

In the model presented, a 1 °C rise in temperature 6 weeks before the beginning of the outbreaks explained 5.2% of the increase in cholera cases. It could be that in continental zones, the increase in environmental temperature affects water temperature and salinity and favours growth of copepods, zooplankton, phytoplankton[16,17,28] or algal blooms, to which *V. cholerae* attaches and gains survival advantages.[10] Thus, the disease cholera can no longer be considered a simple equation of bacteria and human host, but represents a complex network that includes global weather patterns, aquatic reservoirs, phages, zooplankton and collective behaviour of surface-attached cells.[29] A rise of 50 mm in rainfall 3 weeks earlier explained 2.5% of case augmentation. For proper comparison, we would ideally refer to studies from the same region with comparable parameters of population, environment etc., but such results are not available.

To our knowledge, this is the first study reporting an association between cholera and climate factors in sub-Saharan Africa. In Peru, an association was found between environmental temperature and an increase in diarrhoea cases. A 1 °C increase in temperature corresponded to an 8% increase in hospital admissions due to diarrhoea in Lima.[30]

In Bangladesh, positive correlations existed between the increase in cholera cases during an outbreak and rising sea surface temperature 8 weeks before. A recent study carried out in South Africa reports the association between cholera incidence and increased sea surface temperature and precipitation.[31]

One of the limitations of our study was the unavailability of data on cholera cases between epidemics, which did not allow for analysis using autoregressive integrated moving average (ARIMA) predictive models that would have represented a valuable tool for forecasting future cholera outbreaks in Lusaka.

Regarding the magnitude of cholera outbreaks, cases included in the study were patients in isolation centres thus probably presenting more severe symptoms, which suggests the overall number of affected individuals might have been underestimated. Nevertheless, this selection bias does not discredit our chronological analysis since all centres recruited and operated comparably throughout the three outbreaks.

Furthermore, ecological fallacy cannot be excluded when extrapolating results to individual risks through presenting attributable risks.

We recognise that in our analysis only temperature and precipitation as explicative variables intervened whilst other factors not targeted here play an important role in the rise in the incidence of cholera.

Examining the evolution of the outbreaks permitted a clear seasonal pattern associated with the beginning of the rainy season and specific prior increases in temperature and rainfall to be established. These observations could be useful for developing a warning signal aiming to facilitate public health authority interventions in the region with the arrival of the rainy season. In fact, the second outbreak had a lower burden and attack rate, possibly due to acquired immunity as is often observed following large outbreaks whereby the following ones are shorter and less severe.[18] Moreover, intervention teams were present long after the first outbreak and substantial efforts were put into implementing prevention and control measures. Therefore, public sensitisation to the problem, resource mobilisation and lessons learned from the previous outbreak could have played a role.

Our results suggest that towards the end of August and beginning of September, an increase in the average maximum temperature above expected (pre-established based on historical data) followed by an increase in rainfall 3 weeks later could be indicators of a potential increase in cholera cases during October to November.

As pointed out by Pascual et al.[18], climate factors are not enough to understand the size and timing of cholera outbreaks. To improve our insight into cholera epidemics, immunity levels of the population in the region should be taken into account.

According to experts, global warming is likely to increase the severity and frequency of extreme weather events in the future. Considering this threat and the cholera burden in sub-Saharan Africa, we recommend characterising cholera outbreaks further, linking their occurrence to factors other than rises in temperature or precipitation. To develop an early warning system for outbreaks, forecasting methods would be interesting, although a comprehensive understanding of the disease dynamics and all parameters involved is necessary. The model for environmental cholera transmission proposed in the literature[15] would be helpful.

In conclusion, our results show an association between an increase in the number of cholera cases and climate variables. If 6 weeks prior to the beginning of the rainy season an increase in temperature is observed followed by an increase in rainfall 3 weeks later, both exceeding expected levels, we may be confronted with an increase in the number of cases of cholera within the following 3 weeks. Our explicative model could contribute to developing a warning signal to reduce the impact of a presumed cholera epidemic.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.trstmh.2008.07.017.

Authors' contributions: MALF, AB, NEO and DHG developed the concept and design for the study; AB acquired the data; JDJ and CLG developed the model and supervised the analyses; MALF, JDJ and CLG analysed and interpreted the data; MALF drafted the manuscript. All authors revised the manuscript critically for intellectual content and read and approved the final version. MALF is guarantor of the paper.

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Conflicts of interest: None declared.

Ethical approval: Not required.

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