

Control of konzo in the Democratic Republic of Congo

J.P.Banea,¹ G Nahimana,¹ C. Mandombi,² J Howard Bradbury,^{3*} Ian C. Denton³ and N. Kuwa.¹

¹ Programme National de Nutrition (PRONANUT), Kinshasa, DRC.

² Hopital General de Reference, Zone de Sante de Popokabaka, DRC.

³ EEG, Research School of Biology, Australian National University, Canberra, ACT 0200, Australia.

* Corresponding author. Tel.: +61 2 61250775; fax: +61 2 61255573. Email address: howard.bradbury@anu.edu.au

Konzo is an upper motor neuron disease that causes irreversible paralysis of the legs mainly in children and young women,^{1,2} due to consumption of large amounts of cyanogens from poorly processed cassava, the staple food of tropical Africa.³ Konzo occurs in the Democratic Republic of Congo (DRC), Mozambique, Tanzania, Cameroon, Central African Republic and Angola. In March 2010 the wetting method, which removes cyanogens from cassava flour,^{4,5,6} was taught to and used by the mothers of Kay Kalenge village. This reduced the total cyanide content of cassava flour to the FAO/WHO limit of 10 ppm.⁷ Cyanogen intake of school children, monitored by urinary thiocyanate analyses, decreased from mean values of 332 to 130 $\mu\text{mole/L}$. The percentage of urine samples that exceeded the danger level of about 350 $\mu\text{mole/L}$ decreased from 26 in March 2010 to zero by May 2011. In 2009 there were many new cases of konzo, but none in 2010-2011. Konzo was first identified in 1938 in Popokabaka area⁸ and it has now been prevented for the first time in the same area. This methodology is being used in three villages in Boko area and we believe it is the way to control konzo in tropical Africa.

Konzo epidemics occur as a result of (1) war⁹, such as the recent civil war in DRC, where people were forced from their homes and had to eat bitter cassava from the bush (2) drought^{9,10} which stresses the cassava plant and causes it to produce more of the cyanogenic glucosides (linamarin and a small amount of lotaustralin) than normal¹¹ and (3) short cut processing of cassava roots to make flour.¹² Persistent konzo also occurs in very deprived areas in Mozambique,

DRC and Tanzania.^{13,14,15} Konzo is present in four of the eleven provinces in DRC, viz. Bandundu, Kasai Oriental, Kasai Occidental and Kivu South.¹⁶ Protein malnutrition, particularly a shortfall of S-containing amino acids that are required to detoxify cyanide to thiocyanate in the body, may increase the blood cyanide concentration and trigger the onset of konzo,^{1,17,18} This explains the occurrence of konzo in areas where people did not have access to animal or fish protein, whereas people of the same ethnic group living only 5 km away did not get konzo, because they lived in a forest area¹⁹ or near Lake Victoria²⁰ or near the sea.²¹

In 2005 a simple wetting method was developed which reduced 3-6 fold the total cyanide content of cassava flour.^{4,5} Cassava flour was mixed with water and spread in a thin layer to allow hydrogen cyanide gas to escape, in the shade for five hours or in the sun for two hours.⁶ This method was found acceptable to rural women in field trials in Mozambique in 2005 and requires no extra work or equipment.³ Subsequently the wetting method was taught to 216 rural women in konzo-prone villages in Tanzania using illustrated, laminated posters in Kiswahili that explain the wetting method^{10,22}

In the largest village Kay Kalenge (location shown in Figure 1) and three nearby villages Indaba, Bilungu and Munkoki, the total number of konzo cases was 50 in a total population of 2206 with an overall prevalence rate of 2.3%. Konzo occurred abruptly in less than one day in 90% of cases and over 2-7 days with the remainder. There were no cases of partial improvement after attack and

86% said that their condition deteriorated over time. 12% were unable to walk, 32% used one stick and 56% were visibly spastic but used no stick. These values agree reasonably well with those of previous konzo studies in Popokabaka²³ and Kahemba zones.¹⁴ 14% had difficulty in speaking and 22% had eye trouble. Knee jerk bilateral reflexes occurred in 98% of patients and ankle reflexes were exaggerated bilaterally in 96% of patients. Children over 4 years old and women were most affected; 72% were female, 28% male. A similar result (77% females) was found in another study²³ but the female to male ratio is very variable between different studies,¹⁰ due to local unknown factors.¹⁵ The age of onset of the disease for children was typically 4-15 years. With women, 33% were nursing a baby at the time of the konzo attack, similar to that found in a study in Kahemba.¹⁴ The distribution of these konzo cases over the years is shown in Figure 2 with no konzo cases between 1997 and 2004, but konzo recurring from 2005 onwards and peaking at 17 cases in 2009. In other konzo studies in DRC^{14, 16, 23} there are small numbers of konzo cases in most years, which shows that persistent konzo is occurring in Bandundu and Kivu South provinces. Konzo can occur in any month of the year, but there is a marked peak in konzo incidence in the dry season between May and August when cassava consumption peaks.

A survey of food consumption and processing methods made in September 2009 showed that one third of households consumed only one meal per day, that cassava is the dominant food source, with very high consumption of *fufu* made from cassava flour and of pounded, boiled cassava leaves (*saka saka*).

The high protein, vitamin and mineral content of cassava leaves gives a good nutritional balance with the very starchy cassava root consumed as *fufu*,^{24,25} but the protein is deficient in the S-containing amino acids methionine and cysteine,²⁶ that are needed to detoxify cyanide to thiocyanate. This combination of high cyanogen intake from cassava and a shortfall of S-containing amino acids is thought to increase the blood cyanide level and trigger konzo.^{1,17} The method of processing cassava tubers was to immerse them in a pond of water for 1-2 days but actually 3-5 days was needed to remove cyanogens.¹²

In 2009 there were many new cases of konzo (Figure 2) but throughout the extended trial in Kay Kalenge village (March 2010 to September 2011), which included two dry seasons when konzo peaks, there were no new cases of konzo. Over the trial 12 women gave birth, and none of them contracted konzo after childbirth, whereas before the intervention there would have been at least one case of konzo after childbirth. Training of mothers to use the wetting method occurred mainly in March 2010, with two additional training sessions in August and December 2010, so that women in all 320 households learned the wetting method. Visits of the full team every four months and intervening monthly visits by the Caritas team ensured continued use of the wetting method. Illustrated, laminated posters in their own language (Kiyaka), supplied from Australia were also useful.²² <http://online.anu.edu.au/BoZo/CCDN/>. To ensure success of the wetting method in controlling konzo it is important that (1) the women understand that konzo comes from cyanogens (poisons) present in

cassava flour, (2) they are trained to use the wetting method to remove cyanogens and (3) they are committed to using it on a regular basis.

In August 2010 the mean total cyanide content of 9 cassava flour samples from households that were not using the wetting method was 22(12) ppm and 15 samples from households after using the wetting method was 10(9) ppm, (standard deviations in brackets), a significant ($P = 0.035$) reduction brought about by using the wetting method. Similar reductions were also observed in Tanzania.¹⁰ Cyanide analyses of 15-30 cassava flour samples after the wetting treatment in December 2010, May 2011 and September 2011 gave mean total cyanide contents of 4, 8 and 7 ppm respectively, all lower than the FAO/WHO safe limit of 10 ppm.⁷ The *fufu* made from flour treated by the wetting method had a much better flavour than *fufu* made from untreated flour, which had a bitter taste due to residual bitter linamarin²⁷ in the *fufu*. In December 2010, 303 women were surveyed on the characteristics of *fufu* made from treated and untreated flour and they concluded that the former tastes good, is not “heavy” or “elastic”, is similar to chikwangue, a high quality product made by soaking cassava roots for 3-5 days, squeezing, pounding, removing fibres, wrapping in leaves and steaming.¹² Also treated flour may be stored for up to 3 days, hence the wetting method does not need to be used every day.

Thiocyanate results on urine samples from 100 Kay Kalenge school children, showed that there were no significant differences in mean thiocyanate levels between (1) children from families with a case of konzo as compared with

children from families with no case of konzo, (2) boys and girls and (3) lower age (3-9 y) and older age (10-14 y) children. Mean urinary thiocyanate results (Table 1) from 100 school children showed that in March 2010 (before the intervention) the value of 332 $\mu\text{mole/L}$ urine was typical of that found previously in a konzo outbreak in Mozambique.¹³ A reduction occurred during the intervention to 100 $\mu\text{mole/L}$ in December 2010 (because many children were not eating much cassava during the rainy season²³), followed by an increase to 130 $\mu\text{mole/L}$ in May and September 2011. The results in Table 2 show a reduction of the numbers of school children with dangerously high thiocyanate levels of $>350 \mu\text{mole/L}$ from 24 in March 2010 to 0 in May and September 2011.

The use of the wetting method on cassava flour by the mothers of Kay Kalenge village over 1.5 years including two dry seasons has reduced the cyanide content of cassava flour to safe levels, produced better and more tasty *fufu*, reduced the thiocyanate content of urine from school children to safe levels and prevented new cases of konzo. We believe that this is the first time that konzo has been prevented. The methodology described here is now being used successfully in three other villages in Boko health zone, supported financially by AusAID, and we believe it is the way to control konzo in tropical Africa.

Acknowledgments

We thank the mothers of Kay Kalenge village for wholeheartedly accepting and using the wetting method to remove cyanide from cassava flour which has prevented the occurrence of new konzo cases. We thank also the health care staff of Popokabaka health zone and Masina health center for their collaboration and encouragement of the Kay Kalenge mothers.

METHODS

Survey of four villages.

In September 2009, after discussion with the Popokabaka Health Zone team in Bandundu Province and permission of the village chiefs, a survey was conducted in four adjacent villages in Popokabaka Health Zone, the largest Kay Kalenge (see Figure 1) and Indamba, Bilungu and Munkoki with a total population of 2206. Suspect cases of konzo were examined for konzo using the WHO protocol.²⁸ Focus groups carried out a survey of foods consumed over a period of one week, and also obtained information on processing of cassava and its consumption.

Extended trial in Kay Kalenge.

The extended trial was carried out in the largest village, Kay Kalenge, which has 34 konzo cases in a population of 1250 giving a prevalence rate of 2.7%. In March 2010 the combined team from PRONANUT in Kinshasa and from

Caritas Popokabaka made their second visit to Kay Kalenge and subsequent visits by the combined team were made in August and December 2010 and in May and September 2011. Between visits of the combined team, monthly visits were made by the Caritas team from Popokabaka, to support the mothers of Kay Kalenge.

The wetting method^{4,5} for the removal of cyanogens from cassava flour involved adding cassava flour to a bowl and marking the level on the inside of the bowl. Water was added with mixing until the level of the wet flour reached the mark on the bowl. The wet flour was spread in a layer not greater than 1 cm thick on a basket to allow hydrogen cyanide gas to escape to the air, and left in the sun for about 2 hours⁶ or in the shade for 5 hours. In the traditional way the damp flour was mixed with boiling water to produce a thick porridge (*fufu*) which was eaten with something to give flavor, such as pounded, boiled cassava leaves (*saka saka*). Twelve women leaders of the village were trained to use the wetting method and they each trained 15-20 mothers of the village. Each group identified a mother who was responsible for collecting the flour after treatment and in the evening all 12 groups prepared *fufu* from their treated flour. Illustrated, laminated posters in Kiyaka that describe the wetting method were distributed.²² The women accepted the method spontaneously. Additional water (a precious commodity) was required if the wet flour was exposed in the sun for 2 hours, but not much water evaporated if the wet flour was left in the shade for 5 hours. During the August 2010 visit 10 new women leaders were trained in the wetting method and they trained other mothers. A further training

session was carried out in December 2010 and in this way the mothers of all 320 households in the village learned to use the wetting method. Seventeen focus groups and individual interviews were made involving 303 women to ascertain their opinions on the properties of *fufu* prepared from treated and untreated flour, and 270 small basins were distributed to households in Kay Kalenge.

Urinary thiocyanate analysis.

One hundred samples of urine were collected randomly from school age children and a record made of their age, sex and whether they were living in a family with a case of konzo or not. These samples were analysed in Kay Kalenge using the simple picrate kit D1,²⁹ subsequently field tested in Mozambique.¹³ A color chart was used with 10 shades of color from yellow to brown, corresponding to 0-100 mg thiocyanate/L urine = ppm. Results in ppm were multiplied by 17.2 to convert them to μ mole thiocyanate/L urine.²⁹
<http://online.anu.edu.au/BoZo/CCDN/>.

Total cyanide analysis.

In August 2010 cassava flour samples were taken for analysis just before the use of the flour to prepare *fufu*, from households who used the wetting method and from those who did not. In subsequent visits flour samples were taken for analysis only after use of the wetting method. The analyses were done in Kay

Kalenge using a simple picrate kit B2 to determine the total cyanide content of cassava flour,^{30, 31} which was subsequently field tested in Mozambique,³² A protocol was followed that was supplied with the kit <http://online.anu.edu.au/BoZo/CCDN/>. A color chart was used with 10 shades from yellow to brown, that correspond to 0-800 mg HCN equivalents/kg cassava flour = ppm.³¹

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Captions for figures

Figure 1. Map showing health zones of Bandundu Province, DRC, modified from(http://reliefweb.int/sites/reliefweb.int/files/resources/3A4632031B94F342852572DC006BFC2E-ocha_REF_cod070508.pdf), which includes Popokabaka and Boko health zones and location of Kay Kalenge village.

Figure 2. Annual distribution from 1989-2009 of konzo cases in the four villages surveyed.

Table 1

Mean urinary thiocyanate content ($\mu\text{mole/L}$ urine) of urine samples from 100 school children at Kay Kalenge school

Time of visit	Mean urinary thiocyanate content ($\mu\text{mole/L}$ urine) ¹
March 2010	332 (280)
August 2010	213 (172)
December 2010	101 (139)
May 2011	132 (89)
September 2011	130 (84)

¹ Standard deviations shown in brackets

Table 2

Numbers of urinary thiocyanate samples in each level, obtained from Kay Kalenge school children¹

Urinary thiocyanate level (μ mole/L)	<u>Numbers of urine samples in each level in</u>				
	Mar 2010	Aug 2010	Dec. 2010	May 2011	Sep 2011
0	1	1	16 ²	6	3
17	4	3	26 ²	6	7
34	6	6	8	7	7
69	2	9	7	9	13
103	13	15	19	25	24
172	25	38	13	37	38
344	25	21	8	10	8
688	18	6	3	0	0
1030	6	1	0	0	0

¹ At each visit 100 urine samples were analysed from Kay Kalenge school children selected randomly.

² Low urinary thiocyanate results are because many children do not eat much cassava during the rainy season.²³

Bandundu Health Zones

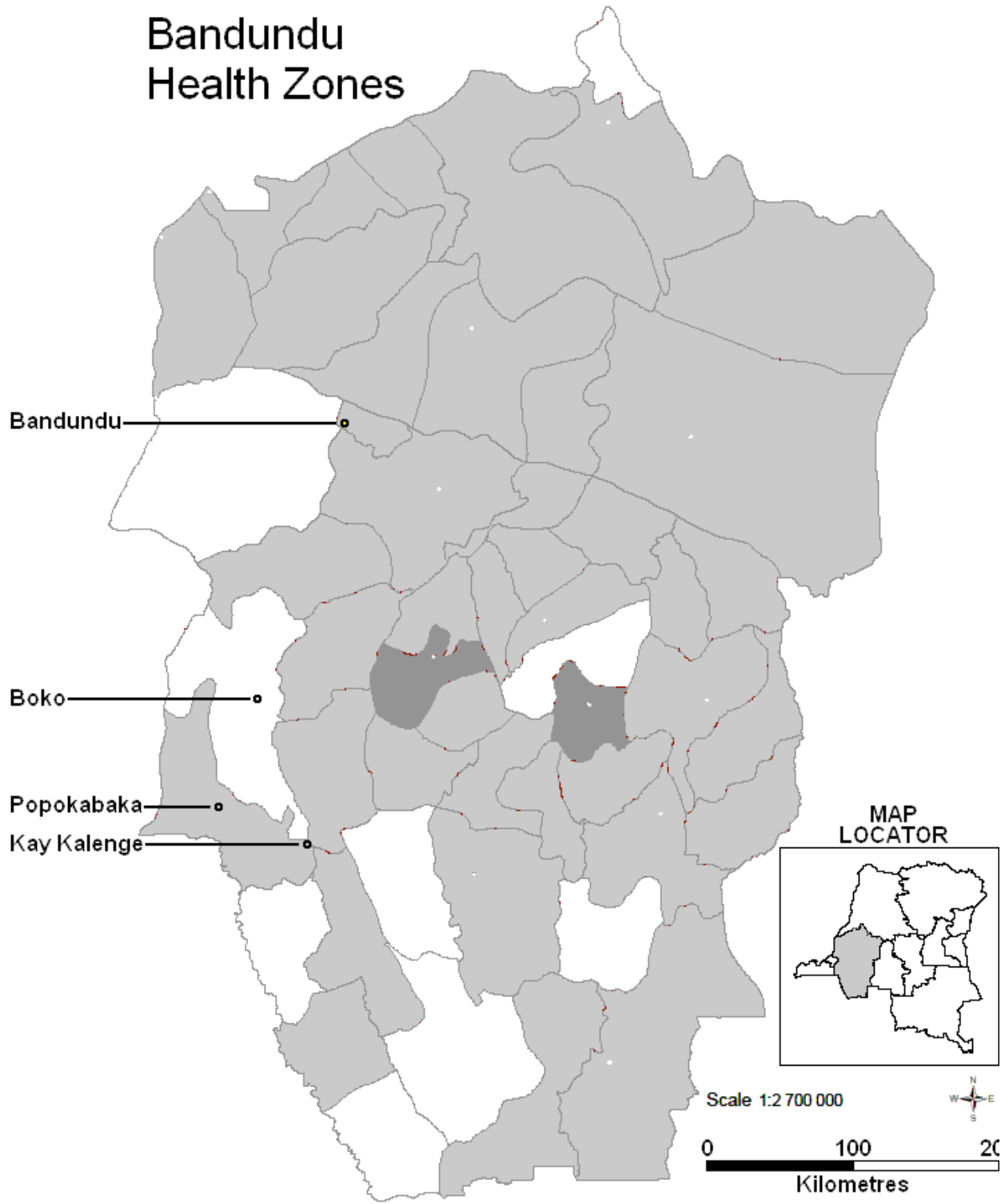
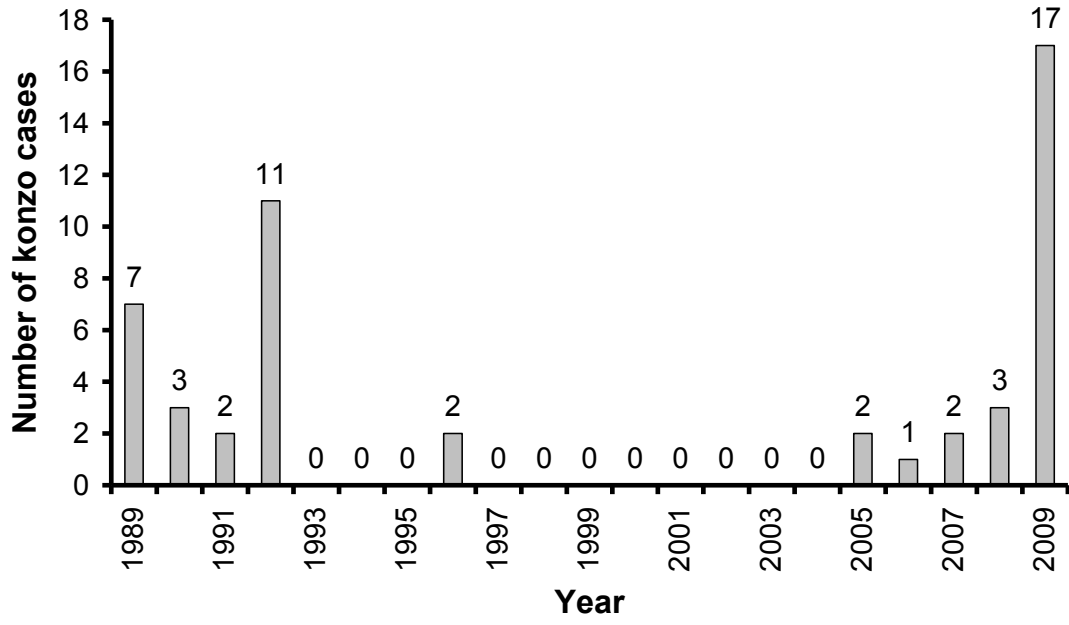


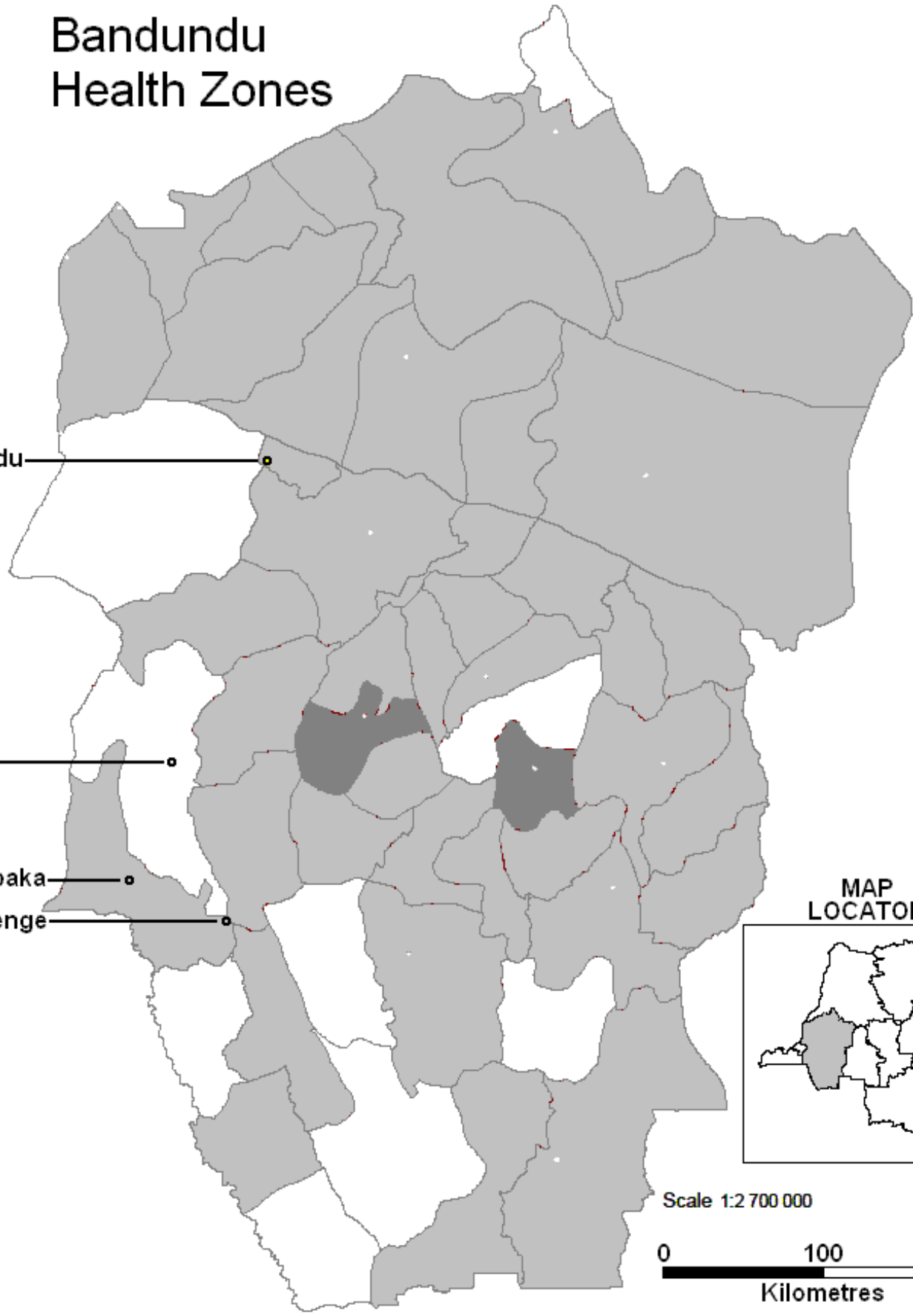
Figure 1

Figure 2



Bandundu Health Zones

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Bandundu

Boko

Popokabaka

Kay Kalenge

MAP LOCATOR

Scale 1:2 700 000

0 100 200
Kilometres



Figure 2

