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# REFERENCE CHART FOR RELATIVE WEIGHT CHANGE TO DETECT HYPERNATRAEMIC DEHYDRATION

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Abstract

*Objective:* The validity of the rule of thumb that infants may have a weight loss of 10% in the first days after birth is unknown. We assessed the validity of this and other rules to detect breast-fed infants with hypernatraemic dehydration.
*Design*: A reference chart for relative weight change was constructed by the LMS method. The reference group was obtained by a retrospective cohort study.
*Participants*: 1,544 healthy, exclusively breast-fed infants with 3,075 weight measurements born in the Netherlands and 83 cases of breast-fed infants with hypernatraemic dehydration obtained from literature.
*Results*: The rule of thumb had a sensitivity of 90.4%, a specificity of 98.3%, and a positive predictive value of 3.7%. Referring infants if their weight change is below -2.5 SDS (0.6$^{th}$ centile) in the reference chart in the first week of life and the rule of thumb in the second week had a sensitivity of 85.5%, a specificity of 99.4% and a positive predictive value of 9.2%.
*Conclusions*: The rule of thumb is likely to have too many false positive results, assuming that for screening purposes the specificity needs to be high. A chart for relative weight change can be helpful to detect infants with hypernatraemic dehydration.

Introduction

Exclusive breast milk feeding up to the sixth month of life is important for optimum infant development and growth as it contains all the necessary nutrients in ideal proportions.[1] Breastfeeding protects against infections and allergies, and it plays a major role in mother-infant bonding.[2]

In the Netherlands, 78% of mothers initiated breastfeeding in the period 2001-2003. After one month 51% and after four months 25% of infants were fed primarily on human milk.[3] The WHO and UNICEF started the 'Baby Friendly Hospital Initiative' (BFHI) to promote breastfeeding.[4] In the Netherlands, this program is mainly focused on improvement of support and accompany of breastfeeding in general health care.

Almost all mothers are capable of breast feeding their infant successfully. However, in some cases initial milk supply is insufficient, because of poor start of milk production or transfer. If the infants' needs are not met for several days, dramatic weight loss and an increase in serum sodium concentration occurs and the infant develops hypernatraemic dehydration.[5][6][7] Hypernatraemic dehydration may cause serious complications, such as fits, disseminated intravascular coagulation, multiple cerebrovascular accidents and may even cause death.[8][9][10][11][12]

A retrospective, population-based study reported an incidence rate of 7.1 per 10,000 breast-fed infants.[4] This can be seen as a minimum incidence as cases probably have been missed because they occurred in infants before initial discharge from the hospital[13][14] or because appropriate investigations had not been performed. The clinical day of presentation of hypernatraemic dehydration is usually around 10 days of age.[6]

In clinical practice, weighing is an essential part of the assessment of an infants' growth and hydration status. However, no evidence-based consensus is present for a 'normal' and 'abnormal' early relative weight change (RWC). Several studies reported the normal ($50^{th}$ centile) or the extreme ($1^{st}$, $2.5^{th}$ or $5^{th}$) centile RWC for exclusively breast-fed infants.[6][15] However, these centiles are not precisely described with respect to day of measurement nor shown on standard growth charts. Several authors propose different rules of thumbs for 'abnormal' RWC.[16][17][18][19][20] It is suggested that many midwives use as a rule of thumb that infants may have a weight loss of 10% (=-10% RWC) and regain birth weight by 10-14 days.[5] To our knowledge, no evidence-based referral rule is available to detect infants with hypernatraemic dehydration.

This study defines a reference chart for breast-fed infants between postnatal day 2 and 11. This chart, together with cases of hypernatraemic dehydration obtained from literature, will be used to define an evidence-based referral rule. The centiles of the chart can be used as a test to detect infants with hypernatraemic dehydration. The test is considered positive if a breast-fed infants' relative weight decreases below a chosen centile, and negative if it stays above. Sensitivity, specificity and positive predictive value (PPV) will be used to optimize this rule. This test will be compared to the rule of thumb that infants may have a maximal weight loss of 10%.

Methods

## Population

We selected a representative reference group of healthy, exclusively breast-fed infants, and a group of breast-fed infants diagnosed with hypernatraemic dehydration. The reference group was obtained by a retrospective cohort study initiated in three primary care midwife practices across the Netherlands (metropolitan Amsterdam South-East, rural Heerhugowaard and the country town of Veenendaal). In the Netherlands, a midwife either assists the delivery at home or in an outpatient clinic, or is involved in the follow-up after hospital delivery by a gynecologist. We selected 1,544 infants born in 2002 with a weight measurement (in grams) at birth and at least one weight measurement between postnatal day 2 and 11. The infants were weighed at home by a midwife with a calibrated electronic scale. In this study, the midwife was constructed to weigh the infant routinely.

Cases hospitalized with hypernatraemic dehydration were obtained by a literature search. Articles written in Dutch, English, French or German published between 1970 and 2005 that describe infants with hypernatraemic dehydration were obtained by the search program PubMed with the Mesh terms “dehydration” and “breastfeeding”. References in these articles were used to increase the number of articles describing infants with hypernatraemic dehydration. We assumed that an infant had hypernatraemic dehydration, when the author(s) of the article diagnosed the infant as such. In 47 articles we obtained 129 cases of breast-fed infants with hypernatraemic dehydration with a weight measurement at birth and day of presentation or a calculated RWC at day of presentation. 83 Literature cases had a day of presentation between 2 and 11 days; these were used in this study.[6] [9] [11][14] [19][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42] Serum sodium concentration was known for 80 literature cases. All cases were born at term.

## Statistical Analysis

RWC was calculated as the difference in weight at day of presentation ($w(t)$) and birth weight ($w(t_0)$) divided by birth weight in percentage, or in formula: $100\% * (w(t) - w(t_0)) / w(t_0)$. Day of birth was represented by day 0. A reference chart for relative weight was obtained by the LMS method.[41] The LMS method summarises the distribution of relative weight as it changes according to age by three curves representing the Box-Cox power (L-curve), the median (M-curve) and the coefficient of variation (S-curve). The L-, M-, and S-curves were used to convert data into standard normally distributed data. Such a data point is called a Z-score or standard deviation score (SDS). Normality of SDS was tested by so called ‘worm plots’ for different age-groups.[42] A log power-transformation was applied to age in the LMS method. Since the LMS method works only with positive values, an amount of 25% was added to relative weight and afterwards subtracted from the centiles. Each infant had multiple weight measurements. All weights were included in the analysis and were treated as independent as we did not find an association between the number of measurements and birth weight (t-test, t=1.14, p=0.26).

The centiles of the curve and the 10% weight loss were used as a test. Specificity of the 10% rule was calculated as the mean of the percentiles of the reference chart that have 10% weight loss for each day. To calculate PPV, we assumed that the incidence of hypernatraemic dehydration is 7.1 per 10,000 breast-fed infants.[6]

Calculations for the LMS-method were performed with LMS light version 1.16 compiled 15 April 2002. All other analyses were performed with S-plus version 6.2.

## Results

Characteristics of the reference infants are given in Table 1. The number of reference infants and cases are shown in Table 2.

Table 1 Characteristics of healthy, breast-fed infants

| Characteristics | | healthy, breast-fed infants (N=1,544) |
|---|---|---|
| Maternal age in years | | 30 (4.7) |
| Girls (%) | | 49 |
| Gestation in wks # | | 39.5 (1.4) |
| Preterm <37 wks (%) | | 2.0 |
| Parity (%) | First | 45 |
| | Second | 36 |
| | Third or more | 19 |
| Delivery (%) | Spontaneous | 80 |
| | Caesarean section | 10 |
| | By vacuum extraction or forceps | 10 |
| Birth weight in kg | | 3.44 (0.46) |

Data are means (SD) or percentages.
# N=1,543

Table 2 Number of measurements between 2-11 days of life in healthy, breast-fed infants and infants with hypernatraemic dehydration

| Characteristics | | healthy, breast-fed infants | infants with hypernatraemic dehydration |
|---|---|---|---|
| Number of infants | | 1,544 | 83 |
| Number of measurements on | day 2 | 9 | 0 |
| | day 3 | 505 | 9 |
| | day 4 | 263 | 9 |
| | day 5 | 618 | 4 |
| | day 6 | 128 | 15 |
| | day 7 | 287 | 10 |
| | day 8 | 272 | 11 |
| | day 9 | 864 | 6 |
| | day 10 | 93 | 16 |
| | day 11 | 36 | 3 |

RWC was not normally distributed (Shapiro-wilk Normality test: $W = 0.975$, $p < 0.01$). To obtain normally distributed SDS for RWC, we used the LMS method with a Box-Cox power transformation of approximately 0.5. Normality of SDS was tested by worm plots of different age-groups. The shape of the worm plots was reasonable flat, indicating that the data follow the assumed distribution in this age-period.

<<FIGURE 1 ABOUT HERE>>
<<FIGURE 2 ABOUT HERE>>

Figure 1 shows a reference chart with standard deviation lines of RWC of healthy, breast-fed infants as well as RWC in 83 cases of hypernatraemic dehydration at their day of presentation. The rule of thumb of 10% weight loss is also included in this chart. The standard deviation lines or percentiles on this chart represent what percentages of infants have the same RWC. For example, if a five day old infant weighs 3315 grams and has a birth weight of 3750 grams, then the calculated RWC is 100%*(3315-3750)/3750= -11.6%. Notice that -11.6% RWC at day 5 on the chart corresponds to -2.6 SDS or 0.5th percentile. This means that only 0.5% of five day old infants have a RWC less than this infant. To avoid the user to calculate weight to a percentage, we converted the -2.5 SDS RWC centile to weights by age for a given birth weight. This converted -2.5 SDS centile is shown on Figure 2 for different weights of birth. The infant, in previous example, has a birth weight of 3750 grams. The -2.5 SDS centile for this infant is shown by the fourth line from above, starting at 3750 at day 0. Follow this line, until you reach day 5. Notice that 3315 grams at day 5 is just below the line.

Maximal negative RWC for healthy, breast-fed infants is at three days after birth, with a mean RWC of -6.0% (95% CI: -5.7% to -6.2%). The mean increases by approximately 1% per day from -6% at day 3 to 0% at day 8. However, even after 11 days about a third of these infants have not yet regained birth weight. In contrast with healthy, breast-fed infants the mean of the patients is consistently declining. The mean RWC for the cases with hypernatraemic dehydration is -18.5% (95% CI: -17.0% to -19.9%). The mean decreases by approximately 2% per day from -10% at day 3 to -25% at day 10.
Notice that there were no cases of hypernatraemic dehydration before day 3, probably due to the fact that it takes some time before insufficient breastfeeding will lead to weight loss. We therefore applied the rules from 3 days up until 11 days after birth.

Table 3 Sensitivity, specificity and positive predictive value (PPV) for several referral rules in the period from 3 days up until 11 days after birth.

| Test | Sensitivity (%) | Specificity (%) | PPV (%) |
|---|---|---|---|
| 10% | 90.4 | 98.3 | 3.7 |
| -2.5 SDS | 85.5 | 99.4 | 9.2 |
| -2 SDS | 90.4 | 97.7 | 2.7 |
| -2.5 SDS 3-6 days and 10% 7-11 days | 85.5 | 99.4 | 9.2 |

Table 3 shows sensitivity, specificity and PPV for several referral rules: the rule of thumb (10% test), the SDS rules and a combination of the -2.5 SDS test in the first week (3-6 days after birth) and the 10% test after the first week. All sensitivities for these tests were above 85% at the account of less than 3% false positives. Sensitivity of the 10% test was similar to the -2 SDS rule and specificity was slightly higher in the first week, however not significantly higher ($p>0.05$). Combining the -2.5 SDS test in the first week with the 10% rule after the first week results in a sensitivity of 85.5% and a specificity of 99.4%, this is similar to the -2.5 SDS test for the first two weeks. This specificity is significantly higher ($p<0.05$) than for the -2 SDS rule.

Cases with a positive -2 or -2.5 SDS test had a significant higher mean serum sodium concentration (163 mM) compared to cases with a negative -2 SDS test (149 mM) ($t=2.6$, $df=78$, $p=0.01$) and with a negative -2.5 SDS test (151 mM) ($t=3.0$, $df=78$, $p=0.004$). Of the cases with a positive -2.5 SDS test, 89% had a concentration >149 mM, so the test detects the more severe cases of dehydration. Of the cases with a concentration >149 mM, 91% had a positive -2.5 SDS test and 97% a positive -2 SDS test, and of the cases with a concentration >159 mM, all cases had a positive -2.5 SDS test (and therefore a positive -2 SDS test).

Eight cases of hypernatraemic dehydration had a very small RWC. Three cases had a RWC between -2 SDS and -1 SDS and five cases had a weight change above -1 SDS.[19] [35][36][42] Clinical information is given in some studies: only mild and transient symptoms in these infants were reported. Serum sodium concentration was reported for six cases: four cases had a concentration below 149 mM and two cases above 149 mM (both 157 mM).

## Discussion

We defined a reference chart for breast-fed infants between postnatal day 2 and 11. This chart, together with cases of hypernatraemic dehydration obtained from literature, was used to define an evidence-based referral rule. As far as we know, this is the first reference chart for RWC and evidence-based investigation on referral rules. Our results show that a reference chart for RWC can be helpful to detect infants with hypernatraemic dehydration.

The RWC chart shows that the mean maximal weight loss occurs 3 days after birth and is 6% for a healthy, breast-fed infant. This is in agreement with several other studies which reported that breast-fed infants may lose up to 6% [45][46][47] or 7% [15][19][48][49] of their birth weight during the first week of life. The American Academy of Pediatrics and others also reported that normal weight loss reaches its peak at 3 to 5 days after birth.[50] Livingstone and the American Academy of Pediatrics Work Group on Breastfeeding suggested that a weight loss of greater than 7% from birth weight indicates possible breastfeeding problems.[19][50] Others suggested that a weight loss of 8% or more warrants further investigation.[16][17][18]

Most authors reported that many midwives use as a rule of thumb that infants may lose up to 10% of birth weight. Our results show that most cases of hypernatraemic dehydration have a weight loss of 10%. However, referral to a hospital of all infants with a weight loss more than 10% would probably lead to many false positive results in the first week of life, assuming that for screening purposes the specificity needs to be sufficiently high. Therefore, we suggest to apply the $0.6^{th}$ centile (-2.5 SDS) as a criterion for referral to a hospital in the first week of life or a weight loss more than 10% after the first week of life. At the hospital, further diagnostic biochemical testing should be carried out. It should be realized that it takes some time before insufficient breastfeeding will lead to weight loss. Therefore, in the first two days after birth, clinical differentiation between normal infants and cases is hardly possible. Infants with a weight loss >10% (or < -2 SDS) in the first week, but after day 2, should be monitored more closely and require more intensive evaluation of breastfeeding and possible intervention to correct problems with breast feeding. Furthermore, it should be realized that referral may also be warranted in infants with other clinical symptoms of dehydration even if weight loss is not extremely high. Clinicians should combine RWC with examination of the infant, knowledge of feeding patterns, and number of wet diapers, frequency and quality of stools. We suggest using the flowchart in figure 3.

<<FIGURE 3 ABOUT HERE>>

Besides the 10% weight loss, another rule of thumb among midwives is that infants regain birth weight by 10-14 days. The chart in this study shows that 50% of infants regain birth weight 8 days after birth, which is also consistent with other studies.[6][15] This study also shows that even after 11 days, about a third of infants have not yet regained birth weight. We also expect that at day 14 a high percentage of infants will not have regained birth weight. Therefore, we assume that this rule will lead to many false positive results. Macdonald et al.[15] suggested a revised intervention criterion: offering additional breast feeding support to those losing 10% but still considering this as normal and only considering weight loss above 12.5% or failure to regain birth weight by 21 days as being out-with normal requiring medical assessment. We applied the 12.5% weight loss rule to our data with infants from birth to 11 days old and found a sensitivity of 83.1% and a specificity of 99.9%. This rule has a better specificity (+0.5%) at the cost of a lower sensitivity (-2.4%) compared to the -2.5 SDS rule. With the 12.5 weight loss rule, 2.4% of the cases are missed. We think that a decrease in sensitivity of 2.4% is high and we therefore recommend using the proposed flow chart. However, one could consider using the 12.5% weight loss rule at day 3 as the -2.5 SDS line reaches almost 12.5% at day 3.

In our study we used cases with hypernatraemic dehydration reported in the literature. We expected that these cases will be biased towards the more severe cases of hypernatraemic dehydration, since severe cases are more likely to be reported than mild cases. Recently Moritz et al.[51] found that only 17% of cases of hypernatraemic dehydration had nonmetabolic complications. Therefore, sensitivity and PPV in this study is likely to be lower for all cases with hypernatraemic dehydration. On the other hand, PPV may also be an underestimate as this value was based on a minimum incidence rate of hypernatraemic dehydration. It can be very interesting in the future to test and possibly optimize our proposed referral rules to new cases with dehydration.

There is evidence that the degree of weight loss in babies born in a particular environment may be associated with the way that environment is managed.[52][53] In populations with a "baby friendly" care the prevalence of hypernatraemic dehydration may be lower than in populations with a care that is less baby friendly. We assumed that the prevalence will be 7.1 per 10,000 breast-fed infants. Based on this prevalence we calculated the PPV of several referral criteria. Since PPV is dependent on prevalence, it should be realised that in population with a lower prevalence (perhaps due to baby friendly care) PPV may be lower. Whereas in populations with a higher prevalence, PPV of the same referral criteria will be higher.

We assumed that RWC expressed as a percentage is uncorrelated with birth weight. This means that a heavy child and a light child have the same distribution of RWC. However, this may not be true in detail, as the degree, timing and variability of RWC may be quite different in small infants compared to large infants. We therefore tested the relation between birth weight and RWC corrected for age by a linear mixed-effects model (residual variance=1.53, AIC=15864). We found that an infant with a birth weight of 2.5 kg has on average a 1% larger RWC than an infant with a birth weight of 4.5 kg. As this is a relatively small difference for a large difference in birth weight, we decided to use the methodology unconditional on birth weight. The latter approach is also more convenient in practice than, for instance, various RWC curves for different categories of birth weight.

In this study, the weights of the infants were obtained in a research setting. The midwife was constructed to weigh the infant routinely. This means that the number of measurements should not depend on the status of the infants. To study if this is indeed the case, we tested the dependence of the number of measurements and the status of the infants by testing the difference in RWC at each day between the infants who were having their first weight (besides birth weight) and those who were being reweighed by standard two-sample t-tests. We refitted the LMS method without the cases that were possible reweighed because of strong RWC and found that the difference between the median RWC in the newly constructed growth chart and the reference chart based on all infants was negligible small (<=-0.2%).

We conclude that the rule of thumb that infants may have a relative weight loss of 10% is an excellent rule after the first week of life. However, in the first week of life this rule will lead to too many false positive results. A chart for RWC can be helpful to detect infants with hypernatraemic dehydration.

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What is already known on this topic?

Several authors proposed different rules of thumbs for 'abnormal' RWC. It is suggested that many midwives use as a rule of thumb that infants may have a weight loss of 10% (=-10% RWC) and regain birth weight by 10-14 days.

What this study adds

As far as we know, this is the first reference chart for RWC and evidence-based investigation on referral rules for infants with hypernatraemic dehydration.

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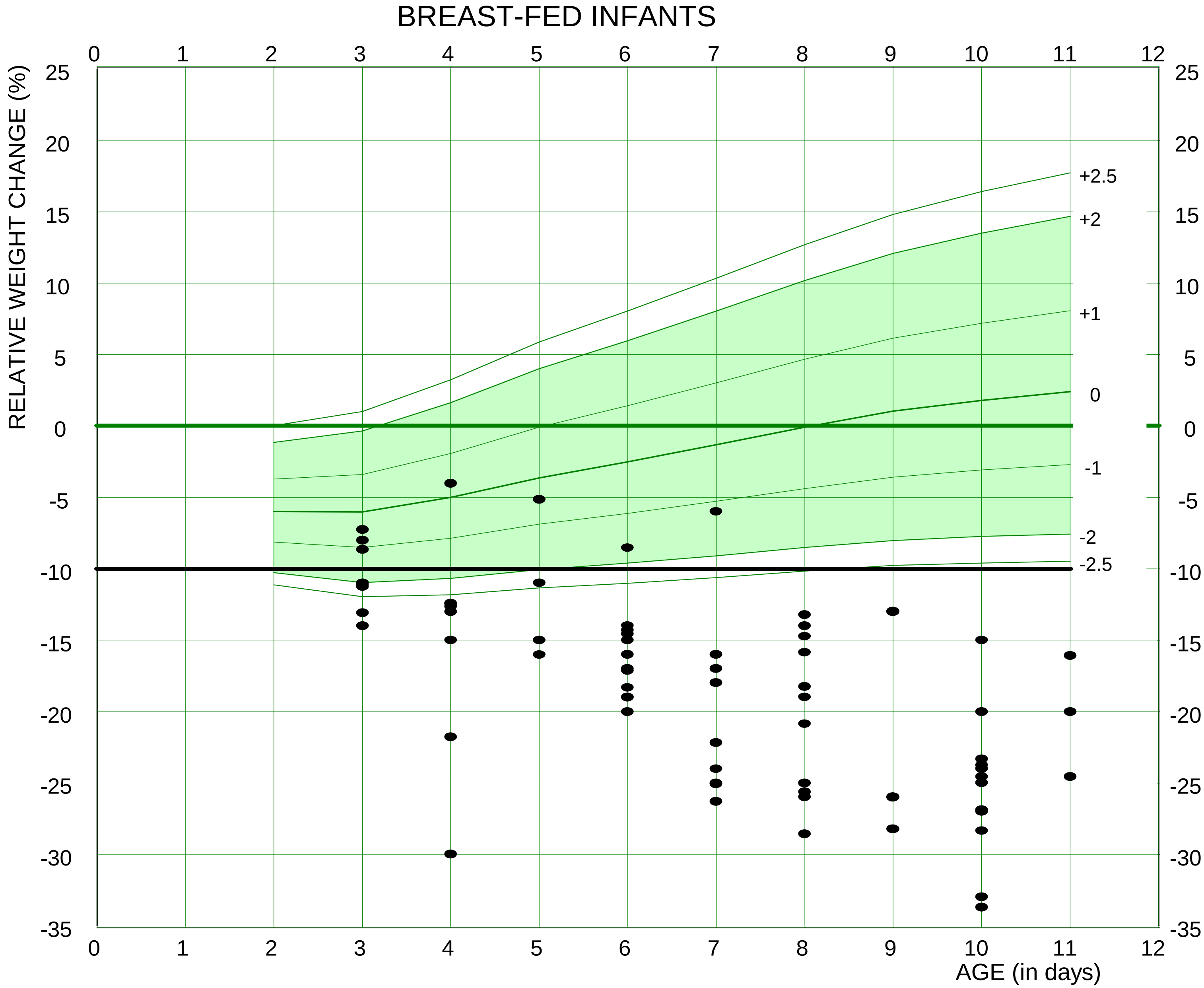
Figure legends

Figure 1
Reference chart with standard deviation lines of relative weight change (=100 %* (weight – birth weight) / birth weight) for healthy, breast-fed infants as well as relative weight change in 83 cases of hypernatraemic dehydration at their day of presentation (day of birth is day 0) and the rule of thumb of 10% weight loss.

Figure 2
The -2.5 SDS relative weight change centile converted to weights by age for a given birth weight.

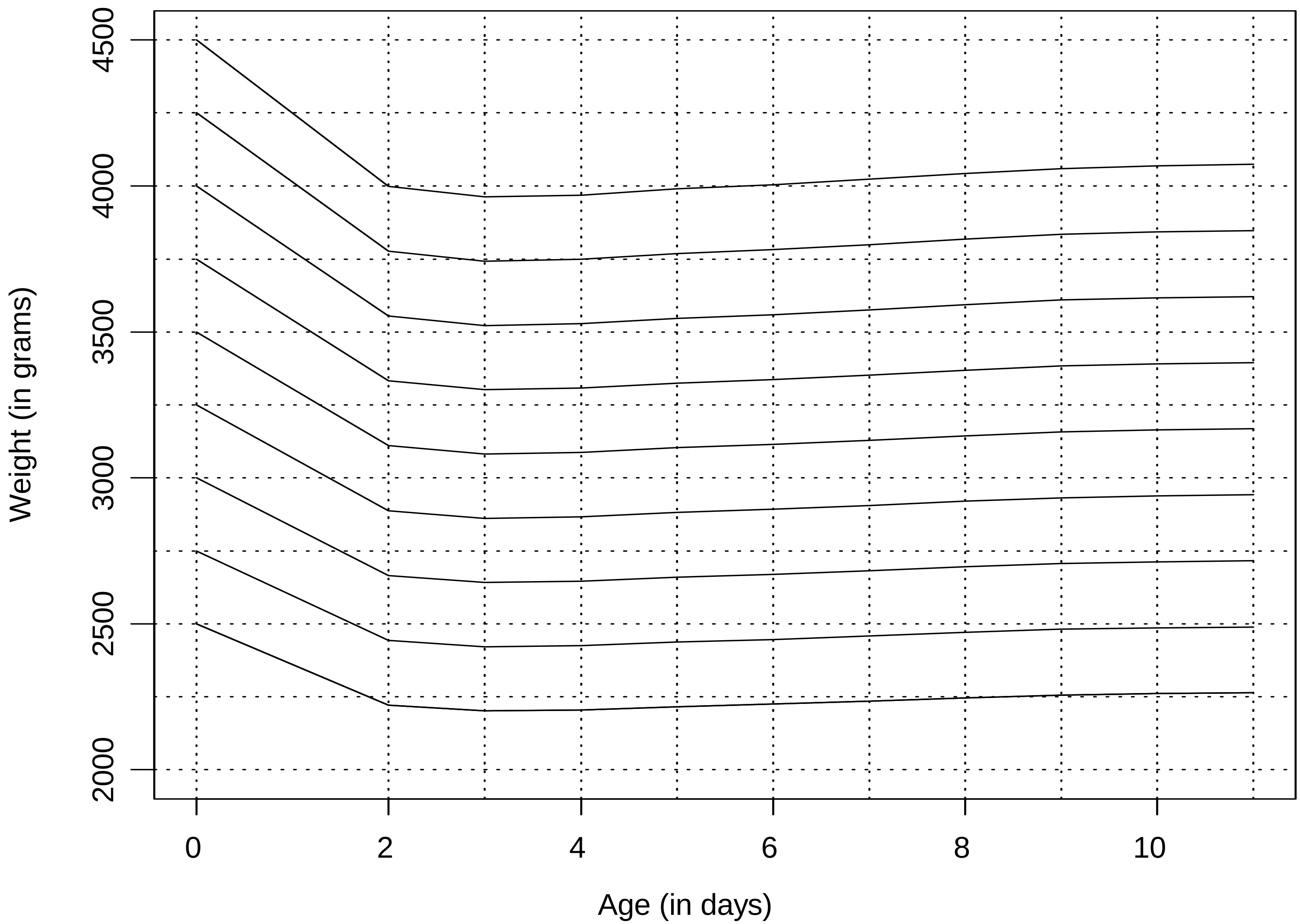
Figure 3
Flowchart to detect dehydrated infants or infants that are at risk of dehydration.

# Figure 1



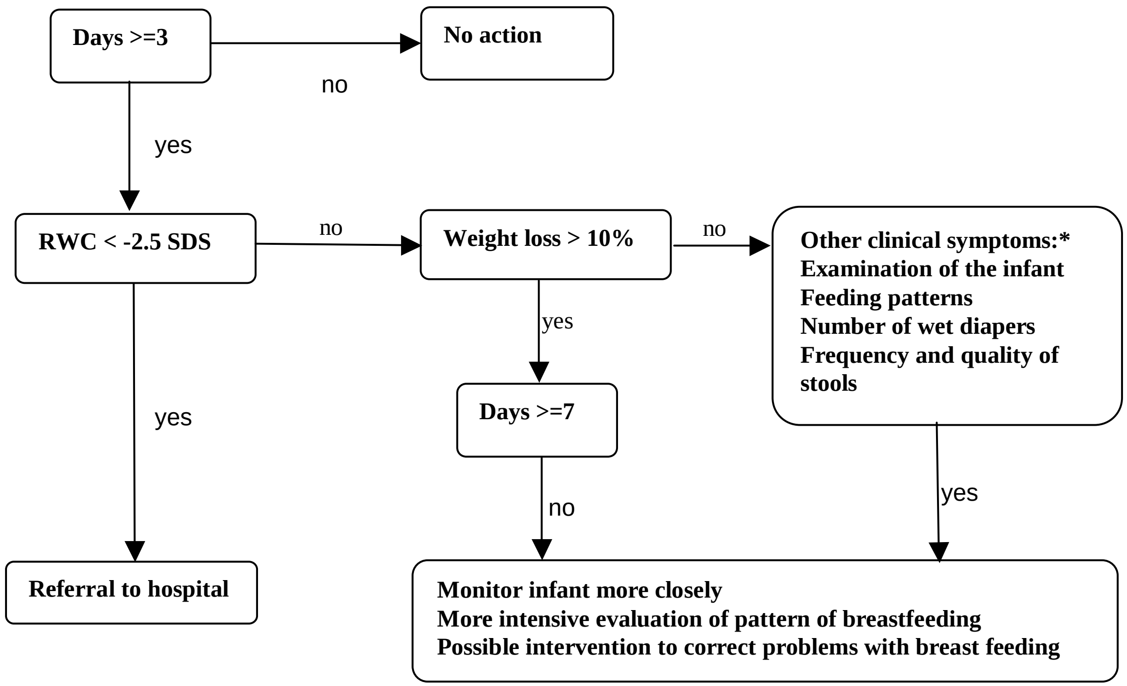
BREAST-FED INFANTS
RELATIVE WEIGHT CHANGE (%)
AGE (in days)
0
1
2
3
4
5
6
7
8
9
10
11
12
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
+2.5
+2
+1
0
-1
-2
-2.5

Figure 2



Weight (in grams)
4500
4000
3500
3000
2500
2000
0
2
4
6
8
10
Age (in days)

**Figure 3**


Days >=3
no
No action
yes
RWC < -2.5 SDS
no
Weight loss > 10%
no
Other clinical symptoms:*
Examination of the infant
Feeding patterns
Number of wet diapers
Frequency and quality of stools
yes
yes
Days >=7
no
yes
Referral to hospital
Monitor infant more closely
More intensive evaluation of pattern of breastfeeding
Possible intervention to correct problems with breast feeding