

Number of preventable vitamin K deficiency bleeding cases

No. 2017/04Ae, The Hague, April 11, 2017

Background document to:

Vitamin K for infants

No. 2017/04e, The Hague, April 11, 2017

Health Council of the Netherlands



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Introduction

This background document provides an estimate of the number of late vitamin K deficiency bleeding cases that may be prevented if breastfed infants are switched from the current vitamin K regimen (one milligram orally as a starting dose at birth followed by 150 micrograms per day) to the recommended vitamin K regimen (one milligram intramuscularly at birth). These estimates are based on efficacy data from the vitamin K regimen in other countries, applied to the number of births in the Netherlands. Subsequently, these figures can be compared to the number of late vitamin K deficiency bleeding cases under the current Dutch regimen.

Two types of data are available for these estimates: i) the percentage of late vitamin K deficiency bleeding in infants with biliary atresia (a high-risk group) and ii) the incidence of late vitamin K deficiency bleeding in the general infant population based on surveillance data. Outcomes based on infants with biliary atresia likely indicate higher estimates of potentially preventable cases, while the outcomes based on incidence in the general population are likely a conservative estimate. The actual number of cases that may be prevented likely lies somewhere in between the two estimates.

Estimate based on data for infants with biliary atresia

First, an estimate of the number of late vitamin K deficiency bleeding cases in the Netherlands under the current regimen was made based on

the percentage of late vitamin K deficiency bleeding cases and cerebral bleeds due to vitamin K deficiency in infants with biliary atresia.¹ Next, the number of late vitamin K deficiency bleeding cases that would occur in the Netherlands if a switch was made to intramuscular administration of one mg of vitamin K was estimated. This was based on Danish data in the same high-risk group.¹ Dutch data on the number of births (see Table 1)², the type of nutrition³, the incidence of cholestatic liver disease⁴ and the incidence of biliary atresia were also used.¹

In order to estimate the number of preventable vitamin K deficiency bleeding cases, a number of assumptions were made: i) intramuscular administration of one milligram of vitamin K is as effective in the Netherlands as it is in Denmark, ii) the type of nutrition at birth is independent of whether or not cholestatic liver disease is present, iii) the type of nutrition does not change during the period in which vitamin K deficiency bleeding can occur, i.e. breastfed children continue to be breastfed; formula-fed children continue to be formula-fed, iv) no formula-fed child, breastfed child without cholestatic liver disease or child with a cholestatic liver disease other than biliary atresia develops late vitamin K deficiency bleeding, v) premature infants and infants who have been admitted to hospital since birth have the same risk of late vitamin K deficiency bleeding as term infants and infants not admitted to hospital since birth. The available data did not allow for an estimation of the consequences of these assumptions.



Table 1. Figures underlying the estimates for infants in the high-risk population

Information	Figure	
Number of births in the Netherlands in 2015 ²	170,510	
Nutrition type immediately after birth in the Netherlands in 2015: % breastfeeding ³	80%	
Nutrition type immediately after birth in the Netherlands in 2015: % formula ³	20%	
Incidence of cholestatic liver disease ⁴	1 : 5,000	
Incidence of biliary atresia in the Netherlands in 2011-2015 ¹	1 : 19,215	Incidence among all live births, both term and premature
Percentage of late vitamin K deficiency bleeding under current Dutch vitamin K regimen among breastfed infants with biliary atresia ¹	82%	Percentage calculated based on term infants (≥37 weeks, birth weight ≥2,000 grams)
Percentage of late vitamin K deficiency bleeding in the brain under current Dutch vitamin K regimen in breastfed infants with biliary atresia ¹	27%	Percentage calculated based on term infants (≥37 weeks, birth weight ≥2,000 grams)
Percentage of late vitamin K deficiency bleeding under current Danish vitamin K regimen among breastfed infants with biliary atresia ¹	4%	Percentage calculated based on term infants (≥37 weeks, birth weight ≥2,000 grams)
Percentage of late vitamin K deficiency bleeding in the brain under current Danish vitamin K regimen among breastfed infants with biliary atresia ¹	0%	Percentage calculated based on term infants (≥37 weeks, birth weight ≥2,000 grams)
Percentage of late vitamin K deficiency bleeding - combined data from Denmark and the Netherlands - in formula-fed infants with biliary atresia ⁵	1.1%	

Based on the percentage of late vitamin K deficiency bleeding in the high-risk population under the current Dutch regimen and the Danish regimen, and above-mentioned assumptions and data, the Committee calculated the following outcomes (Figure 1):

- Under the current Dutch regimen, there are an estimated 5.8 late vitamin K deficiency bleeding cases, including 1.8 cerebral bleeds,

annually.

- If the vitamin K regimen of one milligram intramuscularly were introduced in the Netherlands, an estimated 0.3 late vitamin K deficiency bleeding cases and no cerebral bleeds related to vitamin K deficiency would occur annually.

The difference between these figures indicates that 5.5 late vitamin K deficiency bleeding cases could be prevented annually if a change were made to a regimen of one milligram intramuscularly, including 1.8 cerebral bleeds.

Estimate based on surveillance data in the general infant population

First, international incidence data⁶⁻¹¹ were combined to calculate a weighted average incidence figure per vitamin K regimen; i.e. one milligram intramuscularly or three doses of two milligrams orally (Table 2). These figures apply to the general infant population. These weighted incidence figures were then applied to the number of births in the Netherlands in order to estimate the number of late vitamin K deficiency bleeding cases and cerebral bleeds in the Netherlands, if the vitamin K regimens in question were applied. Subsequently, surveillance data from the Netherlands [personal communication by Dr. P.M. van Hasselt based on recent unpublished data from the Netherlands Paediatric Surveillance Unit (NSCK)] was used to estimate the number of late vitamin K deficiency bleeding cases and cerebral bleeds due to vitamin K deficiency occurring



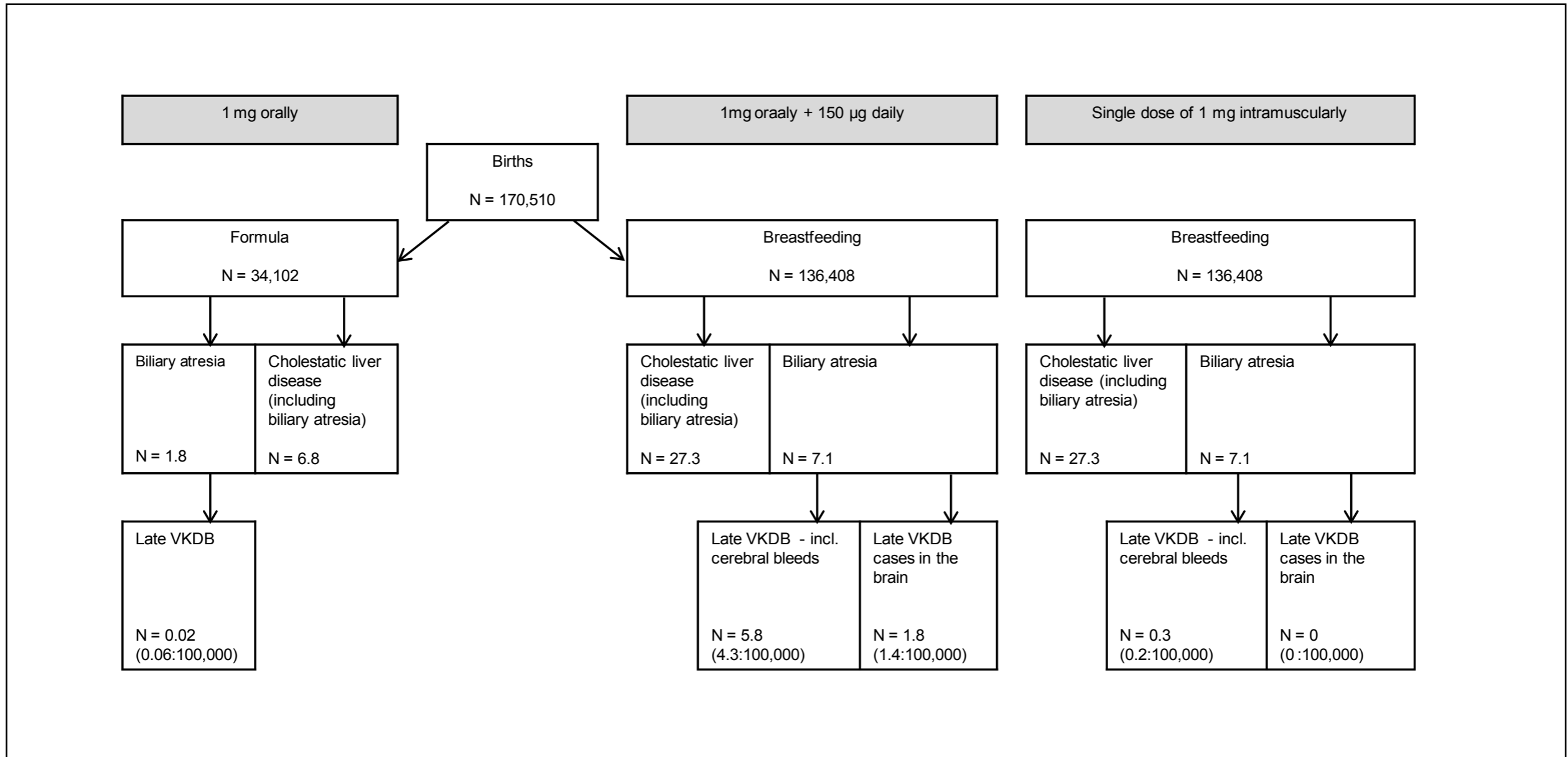


Figure 1. Estimated number of late vitamin k deficiency bleeding (VKDB) cases per year in the Netherlands based on data of infants with biliary artresia



per year in the general infant population in the Netherlands under the current Dutch regimen (Table 3).

When outcomes are compared, the switch to an intramuscular regimen with an oral alternative has the potential to prevent two late bleeding cases (range 0.67-2.65) including about one cerebral bleed.

Table 2. Figures underlying the estimates for the general infant population

	Number of late VKDB cases - including cerebral bleeds	Number of late VKDB cases in the brain	Number of births	Incidence of late VKDB cases per 100,000 - including cerebral bleeds	Incidence of late VKDB cases in the brain per 100,000
<i>One milligram orally and 150 micrograms daily for breastfed infants</i>					
The Netherlands	6	3	333,333	1.8	0.90
<i>One milligram intramuscularly with oral alternative</i>					
England	4	4	1,700,000	0.24	0.24
Canada	5	5	1,360,000	0.37	0.37
Australia ^a	9	n.r.	1,500,000	0.60	n.r.
New Zealand ^a	9	4	642,857	1.40	0.62
Total late VKDB	27		5,202,857	0.52	
Total late VKDB in the brain ^b		13	3,702,857		0.35
<i>Three doses of two milligrams</i>					
Germany	29	20	3,138,695	0.92	0.64
Switzerland	4	1	458,184	0.87	0.22
Total VKDB and late VKDB in the brain	33	21	3,596,879	0.92	0.58

n.r.: not reported; VKDB: vitamin K deficiency bleeding.

^a Number of births not listed in article, estimated based on number of late bleeding cases and incidence rate.

^b Australia is not included in this total, as no separate data on cerebral bleeds were reported.

Table 3. Estimated number of late vitamin K deficiency bleeding cases per year in the Netherlands based on surveillance data from the Netherlands and abroad in the general infant population

	Incidence per 100,000 (range)	Number of births in the Netherlands in 2015	Total number of events per year (range)	Number of preventable events per year because of new regimen (range)
<i>Late vitamin K deficiency bleeding cases - including cerebral bleeds</i>				
Current regimen in the Netherlands	1.8	170,510	3.06	
One milligram intramuscularly with oral alternative	0.52 (0.24-1.40)	170,510	0.89 (0.41-2.39)	2.17 (0.67-2.65)
Three doses of two milligrams	0.92 (0.87-0.92)	170,510	1.57 (1.48-1.57)	1.49 (1.62-2.38)
<i>Late vitamin K deficiency bleeding cases in the brain</i>				
Current regimen in the Netherlands	0.90	170,510	1.53	
One milligram intramuscularly with oral alternative	0.35 (0.24-0.62)	170,510	0.60 (0.41-1.06)	0.93 (0.47-1.12)
Three doses of two milligrams	0.58 (0.22-0.64)	170,510	0.99 (0.37-1.09)	0.54(0.44-1.16)

Literature

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DR=G1&STB=T&VW=T. Consulted: 10/03/2017.

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