NICE, a new cause of death classification for stillbirths and neonatal deaths

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Background
Stillbirths and neonatal deaths are often the result of a complicated chain of events. For epidemiological purposes a classification into single cause of death groups is essential. For large-scale studies, a method is needed which enables such grouping based on available register data.

Methods
A cause of death classification system called NICE is presented. It is hierarchical and is aetiology orientated. A computerized method is adapted which makes use of data in four central Swedish registries. A validation of the computer method has been made from the medical records on a 10% sample of all stillbirths and neonatally dead infants in Sweden from 1983 to 1990.

Results
The specificity of the computer method is high, sensitivity is less satisfactory for some subgroups. A time trend analysis illustrates the usefulness of the classification system and shows a decline with time for two groups: placental abruption and obstetric complications.

Conclusions
The NICE classification system fulfills the criteria of an aetiology orientated classification system which can be used in a computerized environment.

Keywords
Cause of death, perinatal, neonatal, classification

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Stillbirths and neonatal deaths are often the result of a complex chain of events, sometimes difficult to elucidate. Nevertheless, for epidemiological purposes it is useful and at times necessary to classify deaths into single-cause categories which should be based on the primary or underlying cause of death. Over the years many different classification models have been proposed. The best known cause of death classification among obstetricians is the Aberdeen-classification, first described in 1954, by Sir Dugald Baird et al. The aim of this classification, is 'to classify each death in accordance with the factor which probably initiated the train of events ending in death'.

Another well-known classification is the one first suggested by the pathologist Wigglesworth in 1980. The aim of his classification was 'to subdivide cases into groups with clear implications for clinical management'. Both classifications are based on a combination of clinical data and pathological findings. Such information is usually obtained by 'perinatal audits', where the relevant medical documents are scrutinized for all perinatal deaths during a certain time period in a defined geographical area or in a hospital. This method of collecting information is both time-consuming and expensive and therefore not particularly suitable for continuous surveillance of perinatal or neonatal mortality on a national basis.

In a previous paper, we presented a computer-based method for a cause of death classification of stillbirths and neonatal deaths in Sweden, based on information obtained from four central registers. This method can be applied to large populations since it is not based on individual audits. In the report we used a modified Wigglesworth classification, but the construction of the computer programs makes it possible to use various classification models.

The aims of the present study are:
To present a new cause of death classification for stillbirths and neonatal deaths suitable for a computer-based method. The new classification is hierarchical and is aetiology orientated, aiming at identifying the underlying biological factor ultimately resulting in death. The classification is named Neonatal and Intrauterine Death Classification according to Etiology (NICE).
To compare the results of the NICE and the Wigglesworth classifications.

Material
The original study was restricted to the years 1983–1990, and comprised 6044 stillbirths or neonatal deaths occurring up to the age of 28 days, out of a total of 836,881 births in Sweden. The Swedish stillbirth definition (28 completed gestational
main factors that might be responsible for the train of events

gestational length. For the purpose of the actual classification
The analysis performed by the new classification program
characteristics, important for the decision on the cause of death.

Table 1

The NICE cause of death classification

| 1. Congenital anomalies. Includes stillborn and liveborn infants with lethal malformations or potentially lethal malformations that markedly increase mortality risk. Severe metabolic disorders such as amino acid disturbance are also included. |
| 2. Multiple births other than duplex, or duplex in combination with immaturity (<33 weeks) or intrauterine death. Twin-to-twin transfusion syndrome. |
| 3. Maternal disease. Includes maternal diabetes mellitus if the infant is stillborn or is large for date (>2.5 SD). Maternal pre-eclampsia, renal disease, hepatosis, epilepsy, systemic lupus erythematosus (SLE) included when combined with an infant either small-for-dates (<2.5SD), or immature (<33 weeks), or dead before labour. For maternal SLE also in combination with severe cardiac disease in the infant. |
| 4. Specific fetal conditions. Includes iso-immunization, unexplained hydrops fetalis, tumours, specific fetal infections. Accidents included when combined with stillbirth. |
| 5. Unexplained small-for-dates Infants (<-2.5 SD) without any evidence of maternal disorder. |
| 6. Placental abruption if combined with asphyxia, immaturity (<33 weeks) or intrauterine death. |
| 7. Obstetric complications. Includes uterine rupture, disproportion, malpresentation, cord prolapse, cord compression, placenta previa, fetal blood loss or precipitate labour. |
| 8. Unexplained antepartum stillbirths <37 gestational weeks. |
| 9. Unexplained antepartum stillbirths >37 gestational weeks. |
| 10. Specific infant conditions. Includes infants >32 weeks with septicemia, meningitis or pneumonia. Includes term infants with respiratory distress syndrome (RDS) or sudden infant death syndrome (SIDS). Accidents included when causing neonatal death. |
| 11. Unexplained asphyxia. Infants classified as asphyxia according to Wigglesworth, where the asphyxia is not explained and the case does not belong to groups 1 to 10 above. Immature infants <27 gestational weeks or <800 g are excluded. |
| 12. Unexplained immaturity. Infants classified as immature according to Wigglesworth (<33 gestational weeks and <2500 g or <1800 g if gestational age is unknown) where the immaturity is not explained and the case does not belong to groups 1 to 11 above. |
| 13. Unclassifiable cases. Cases not in groups 1 to 12. |
Results

Validation of the NICE classification program

The results of the validation are presented in Table 3 and sensitivity and specificity figures are given in Table 4. Specificity is generally high: 95–100%.

The sensitivity score for ‘maternal disease’ (group 3) was only 64%, probably due to lack of paternal diagnoses in the Medical Birth Registry. Four of the missing cases were placed in the ‘small-for-dates’ group (group 5), four in the ‘placental abruption’ group (group 6), and three in the ‘immaturity group’ (group 12). This is a logical allocation if information on maternal disease is missing in the register.

Sixteen cases were falsely diagnosed as ‘placental abruption’ by the computer program; all had ICD-codes for placental abruption but had marginal bleedings (not included in the clinical definition).

ICD-codes for obstetric complications were often missing, especially in stillbirths, and the sensitivity figures are consequently low, only 38%. Instead of an allocation to ‘obstetric complications’ (group 7), most of the deaths were placed in the two groups for ‘unexplained antepartum death’ (groups 8 and 9).

The sensitivity figure (73%) for the ‘unexplained immaturity’ group (group 12), is negatively influenced by the 10 cases with marginal bleedings, misplaced as ‘placental abruption’ higher up in the hierarchy.

The unclassified cases were few, only eight by record scrutiny and six by the computer program, i.e. about 1% of the random sample.

The computer program gives a total concordance of 77% (467/603). This figure is low compared with the concordance (88%) in the previous paper,7 and is a consequence of the further specification into 13 subgroups.

<table>
<thead>
<tr>
<th>NICE classification</th>
<th>Computer program</th>
<th>Record study</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Congenital anomalies</td>
<td>134</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 Total</td>
</tr>
<tr>
<td>2. Multiple births</td>
<td>0 30</td>
<td>0 0 0 0 2 0 0 0 0 0 0 34</td>
</tr>
<tr>
<td>3. Maternal disease</td>
<td>1 1 29</td>
<td>0 4 4 0 2 1 0 0 0 3 45</td>
</tr>
<tr>
<td>4. Specific fetal conditions</td>
<td>1 0 0 14</td>
<td>0 0 0 4 1 0 2 0 0 22</td>
</tr>
<tr>
<td>5. Unexplained small-for-dates infants</td>
<td>0 0 0 0 30</td>
<td>0 0 1 0 0 0 0 32</td>
</tr>
<tr>
<td>6. Placental abruption</td>
<td>0 0 0 0 1</td>
<td>40 1 0 1 0 0 0 44</td>
</tr>
<tr>
<td>7. Obstetric complications</td>
<td>0 0 0 0 0</td>
<td>0 12 6 12 0 1 1 0 32</td>
</tr>
<tr>
<td>8. Unexplained stillbirth &lt;37 weeks</td>
<td>0 1 2 1</td>
<td>0 39 6 0 2 0 6 51</td>
</tr>
<tr>
<td>9. Unexplained stillbirth &gt;37 weeks</td>
<td>0 1 1 0 1 1</td>
<td>2 2 58 0 0 0 66</td>
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<tr>
<td>10. Specific infant conditions</td>
<td>0 1 0 0 0</td>
<td>0 0 0 6 0 0 1 8</td>
</tr>
<tr>
<td>11. Unexplained asphyxia</td>
<td>3 0 0 0 0 1</td>
<td>3 1 4 0 22 2 0 36</td>
</tr>
<tr>
<td>12. Unexplained immaturity</td>
<td>0 2 1 0 0</td>
<td>10 4 0 0 4 49 0 70</td>
</tr>
<tr>
<td>13. Unclassifiable</td>
<td>3 0 0 0 0</td>
<td>0 0 0 0 1 1 3 8</td>
</tr>
<tr>
<td>Total</td>
<td>142</td>
<td>36 34 15 42 56 25 58 85 6 39 60 5 603</td>
</tr>
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</table>
obstetric complications is found in 323 cases (38%), 522 of the cases still remain unexplained. In the intrauterine death group the NICE model finds an explanation for 41% and in the immaturity group the NICE model finds an underlying biological explanation for 53% of the cases.

Comparison between the Wigglesworth cause of death classification and the NICE classification

For this comparison we used data for all stillbirths and neonatal deaths in Sweden between the years 1983 to 1992. The results are given in Table 5 as a cross tabulation of all 7703 deaths, distributed among the six groups of Wigglesworth and the 13 groups of NICE.

In this way, the NICE model could find a causal explanation for the three large Wigglesworth groups 'intrauterine death', 'asphyxia', and 'immaturity'. For the 845 asphyxia cases according to Wigglesworth an explanation like placental abruption or obstetric complications is found in 323 cases (38%), 522 of the deaths in Sweden between the years 1983 to 1992. The results are given in Table 5 as a cross tabulation of all 7703 deaths, distributed among the six groups of Wigglesworth and the 13 groups of NICE.

Comparison between the computer-based Wigglesworth cause of death classification and the NICE classification using data for all stillbirths and neonatal deaths in Sweden 1983-1992, a total of 7703 deaths. For the NICE cause of death groups both the total numbers and the percentage figures for each subgroup are given.

Table 4 Validation of the NICE classification. The Table gives the number of infants with presence (YES) or absence (NO) of each cause of death group according to the computer program and the record study. Sensitivity and specificity refer to the computer program

Table 5 A comparison between the computer-based Wigglesworth cause of death classification and the NICE classification using data for all stillbirths and neonatal deaths in Sweden 1983-1992, a total of 7703 deaths. For the NICE cause of death groups both the total numbers and the percentage figures for each subgroup are given.
One important observation is the absence of perturbation due to the change of the ICD codes from ICD-8 to ICD-9 in 1987. For most subgroups, no clear-cut time trend is seen even though yearly numbers are low for some, resulting in unstable rates (e.g. specific fetal [D] and specific infant conditions [J]). There is, however, a clear-cut decline with time in the two subgroups of placental abruption (F) and obstetric complications (G).

Discussion

In epidemiological studies, including surveillance of pregnancy outcome in a population, there is a need for methods of cause of death classification which makes it possible to study a large number of cases. The specific perinatal audit approach is usually impractical because it is both time-consuming and expensive, which results in small study groups. The use of underlying cause of death from the death certificates exclusively, has been criticised, but has recently been used in the so-called ICE classification.

We propose the use of information from a computer-based linkage of various national health registers, including the cause of death register (both underlying and contributing causes of death). This is available for all infants born in Sweden as from 1973 when the Medical Birth Registry started. In this way, a more specific cause of death diagnosis can be reached, even though comparison between the diagnoses reached by the computer analysis of the registers and those reached by a detailed scrutiny of the relevant medical records revealed some discrepancies and weaknesses of the method. They are, however, quantitatively less important and permit the use of the method for epidemiological purposes, including surveillance.

For each dead infant, a number of conditions are often found which may have contributed to the death. This necessitates some kind of hierarchic grouping. We have used two such models of grouping: the modified Wigglesworth classification and a new classification, the NICE model, which is conceptually similar to the Aberdeen model. The Wigglesworth classification has fewer groups than the NICE classification, which is directed more towards the underlying biological causes of death, whereas the Wigglesworth classification aims at identifying the areas of health care provision most in need of alteration. For example, with the NICE model a placental abruption is identified as a cause of death, not the intrauterine death, asphyxia, or immaturity which was the result of the abruption and finally lead to the death. Multiple birth as well as maternal disease as important causes of immaturity and intrauterine death can be
disentangled by NICE. Thus even when the aim of a classification of cause of death would be to improve maternal health care during pregnancy or obstetric care the NICE classification has advantages, since this classification highlights the association between some maternal conditions and obstetric complications with infant death, which might lead to additional preventive activity.

When all underlying conditions have been identified, there still remains a large group of infants with intrauterine death, asphyxia, or immaturity with no identified specific underlying causes—which may just mean that the available information is not detailed enough to identify them. Even so, it seems likely that the NICE model will result in a higher precision in an epidemiological investigation of causes of death than the Wigglesworth model would give, especially when the focus of interest is the etiology of causes of death—and of course still more so than if only crude death rates are used, or imprecise causes of death like any model exclusively based on the concept of the Underlying Cause of Death stated in death certificates.

At the validation of the NICE model we found a consistently high specificity but for some subgroups a less satisfactory sensitivity. Provided the low sensitivity and specificity is independent of the outcome variable a low sensitivity would very little affect the risk estimate in epidemiological analyses of risk factors e.g. case-control studies, whereas a low specificity to a slightly higher degree would result in more conservative risk estimates i.e. a loss of power. This loss of power is easily balanced by the enormous increase in power which can be achieved by using much larger numbers of cases in a computerized rather than a non-computerized 'perinatal audit'. In epidemiological surveys a low sensitivity or specificity would only affect the results if the sensitivity or specificity would differ over time or geographical area.

Even if the sensitivity for the subgroup placental abruption is only 86% (Table 4), the declining risk with year of birth seen in Figure 1 identifies a trend which may have a biological explanation. Maternal smoking is known to be a strong risk factor for placental abruption and during the time period studied, maternal smoking during pregnancy in Sweden has declined markedly.

The sensitivity for obstetric complications is still lower (38%) and yet a declining trend is seen for this subgroup which may indicate a change in obstetric practice—or could mirror a declining sensitivity with time due to a less and less complete registration of the obstetric complications, which seems unlikely.

In conclusion, our new computerized aetiology-oriented cause of death classification provides a new tool for large epidemiological case-control studies and surveys which may be important for future preventive strategies.

Acknowledgements

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References