

# Screening for congenital heart malformation in child health centres

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**Background** Although screening for congenital heart malformations is part of the child health care programme in several countries, there are very few published evaluations of these activities. This report is concerned with the evaluation of this screening at the Dutch Child Health Centres (CHC).

**Methods** All consecutive patients, aged between 32 days and 4 years, presented at the Sophia Children's Hospital Rotterdam throughout a period of 2 years, with a congenital heart malformation were included in this study. Paediatric cardiologists established whether or not these patients were diagnosed after haemodynamic complications had already developed (diagnosed 'too late'). Parents and CHC-physicians were interviewed in order to establish the screening and detection history. Test properties were established for all patients with a congenital heart malformation ( $n = 290$ ), intended effects of screening were established in patients with clinically significant malformations ( $n = 82$ ).

**Results** The sensitivity of the actual screening programme was 0.57 (95% CI: 0.51-0.62), the specificity 0.985 (95% CI: 0.981-0.990) and the predictive value of a positive test result 0.13 (95% CI: 0.10-0.19). Sensitivity in a subpopulation of patients adequately screened was 0.89 (95% CI: 0.74-0.96). Adequately screened patients were less likely to be diagnosed 'too late' than inadequately screened patients (odds ratio [OR] = 0.20, 95% CI: 0.04-1.05). The actual risk of being diagnosed 'too late' in the study-population (48%) was only slightly less than the estimated risk for patients not exposed to CHC-screening (58%, 95% CI: 43%-72%). Adequately screened patients however were at considerably less risk (17%, 95% CI: 4%-48%).

**Conclusion** Screening for congenital heart malformations in CHC contributes to the timely detection of these disorders. The actual yield, however, is far from optimal, and the screening programme should be improved.

**Keywords** Screening, child health care, congenital heart malformation

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In several countries, periodic health examinations are part of the preventive child health care programme.<sup>1-5</sup> In the Netherlands, this programme is executed at the Child Health Centres (CHC). These examinations generally include routine medical check-ups of heart and circulation, and are aimed at the early detection of congenital heart malformations. However, there are no published examples of these screening activities.<sup>2,6</sup>

Screening evaluation aims at establishing both favourable and unfavourable effects of screening. Unfavourable effects are mainly due to false-negative and false-positive test results,

the numbers of which are determined by the test properties. Favourable effects are defined as the reduction of adverse outcomes of diseases as a result of early detection and subsequent intervention.<sup>7</sup>

Approximately half of all cases of congenital heart disease are detected soon after birth by neonatal examinations or due to the onset of symptoms. The remaining patients initially go unrecognized.<sup>8</sup> Child Health Centre screening is merely aimed at the latter; the first examination is scheduled at the age of one month.

Since many of these disorders spontaneously resolve and have no haemodynamic impact in the short or long run,<sup>9</sup> the intended effects of screening will only occur in clinically significant congenital heart malformations, which give rise to progressive disease.

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The adverse outcomes to be prevented are haemodynamic complications, notably heart failure and hypoxaemia. Disorders should be detected 'in time', i.e. before these complications occur. Children who have already developed haemodynamic complications at the first cardiological consultation, have been diagnosed 'too late', even if these complications are still reversible by therapy. Since haemodynamic complications can be prevented with the help of modern interventional paediatric cardiology<sup>10,11</sup> and cardiac surgery,<sup>12-16</sup> in most patients who are diagnosed 'in time', reducing the number of patients diagnosed 'too late' may be considered the target of the screening programme.

Compared to patients with moderate disorders, patients with severe disorders may be more at risk for developing complications. These patients are also less likely to have undergone screening prior to the development of complications due to rapid deterioration. In an observational evaluation of screening this may give rise to length bias, leading to an overestimation of the favourable effects of screening. This requires adjustment for confounding.<sup>17</sup>

Official guidelines for screening at the Dutch CHC regarding procedures and ages of investigation are defined by the Dutch National Association for Home Care.<sup>18</sup> There is, however, a substantial variation in the actual performance.<sup>19</sup>

The purpose of this paper is: (1) To estimate the test properties of the CHC screening programme for congenital heart malformations, as actually performed in the south-west of the Netherlands, and the maximum attainable sensitivity were all patients to be adequately screened according to the guidelines.

(2) To estimate the effect of the present screening programme on the proportion of patients with clinically significant

malformations arriving 'too late' in a paediatric cardiology department, and the potential effect were all patients to be adequately screened, according to the guidelines.

(3) To inventory the actual deviations from the guidelines in the present screening programme.

## Methods

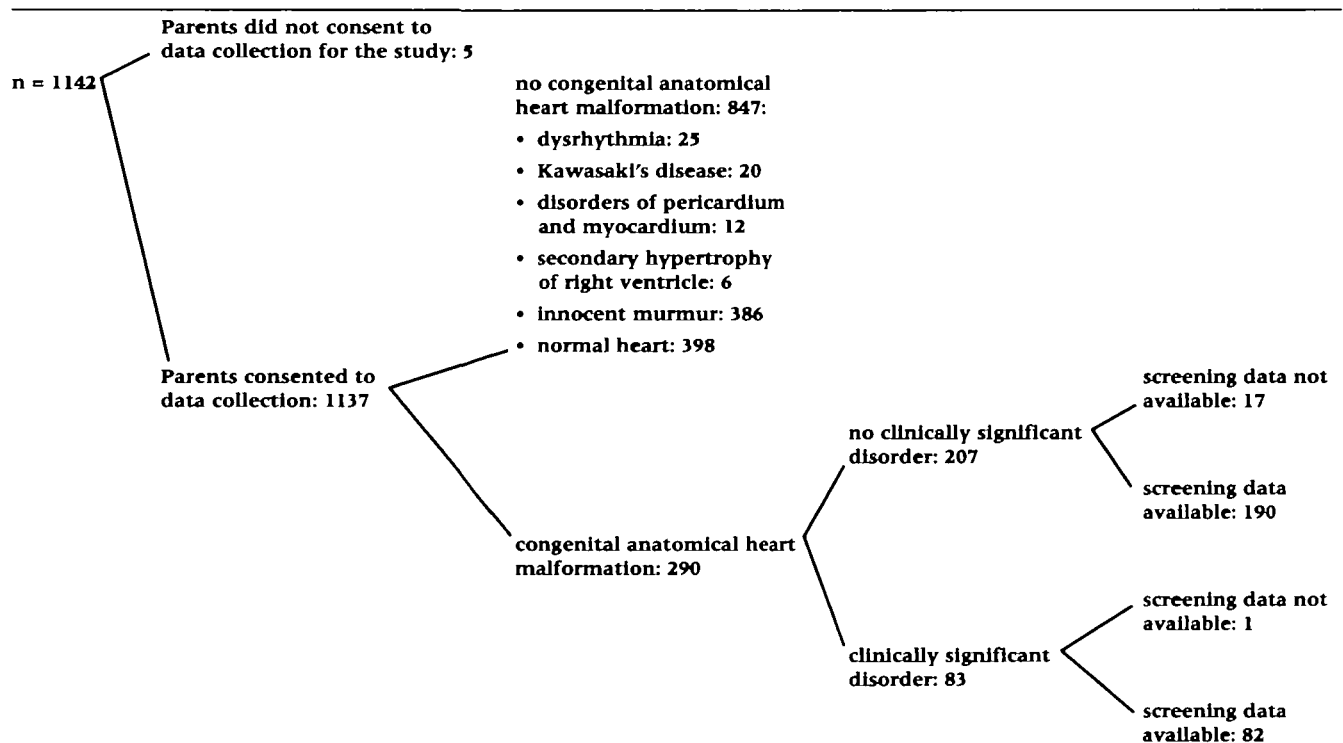
### Study group

All patients who fulfilled the following conditions were included in this study: First cardiological consultation at the Sophia Children's Hospital took place between 11 April 1994 and 11 April 1996; children were aged between 32 days and 4 years; children presented for the first time with a congenital anatomical heart malformation; children were resident in the south-west of the Netherlands, more specifically the area from which, by national agreement between paediatric centres, all children with cardiovascular disorders are referred to the Sophia Children's Hospital.

Parents were informed and consented to their children's participation in the study and so the study group thus comprised 290 patients (Table 1).

The intended effects of screening can only be established in patients with clinically significant congenital heart malformations. A malformation was defined as clinically significant when it was decided to perform a therapeutic intervention within 9 months after the first cardiological consultation. Eighty-three patients satisfied this condition, of whom 82 were included in the analysis (Table 1).

**Table 1** Patients aged between 32 days and 4 years, who were first seen at the Sophia Children's Hospital, Department of Paediatric Cardiology between 10 April 1994 and 10 April 1996



### Data collection and definition of variables

To establish whether patients were diagnosed 'too late' or 'in time' a questionnaire was filled in by the paediatric cardiologist in charge at the first cardiological consultation. The following aspects were examined: extent of heart failure, resulting from pressure- or volume-load (none, moderate, serious, very serious); degree of hypoxaemia (none, moderate, serious, very serious); risk of deterioration; estimated duration of symptoms. Another paediatric cardiologist was asked to give a second opinion by filling in an identical questionnaire independently. In the event of differences between the answers of the two physicians, a third colleague was asked to make the final judgement.

Diagnosis was considered to have been established too late if: heart failure or hypoxaemia was classified as serious or very serious; heart failure or hypoxaemia was classified as moderate, the risk for deterioration was considered realistic and the symptoms were estimated to have existed for over one month. All other disorders were considered to have been diagnosed in time.

To make it possible to adjust for length bias paediatric cardiologists were also asked to appraise the severity of the disorder by opting for one of four qualifications: trivial, moderate, severe, and very severe.

In order to establish whether or not their child's disorder was detected as a result of the CHC screening programme, parents were interviewed by a nurse at the first cardiological consultation. If necessary, additional information was collected from CHC physicians, general practitioners and clinical specialists. Disorders were assumed to have been detected by the physician who was the first to initiate a referral for a cardiovascular disorder. Patients were classified as having been detected by a CHC physician or not.

In order to establish the screening history, the CHC physicians of all patients were approached for an interview. The first author, who was not informed about the nature and severity of the disorder, performed all interviews. Questions were asked about the doctor's normal screening routine and about the actual procedure in this particular case.

A screening history was classified as 'adequate' if: until the first cardiological consultation the CHC was visited at least according to the standard visit schedule, which entails: one visit before the age of 35 days, one in the age interval between 35 and 95 days (first DTPP-Hib-vaccination), one in the age interval between 3 and 14 months (MMR-vaccination) and subsequently one visit every year until the age of 4, and during all these visits the CHC physician performed at least auscultation of the thorax, judged skin colour, size of the liver and weight gain and asked questions aimed at assessing the child's exercise tolerance, and the child was referred as soon as one of the following symptoms was found: heart murmur classified by the CHC physician as suspect; central cyanosis; enlarged liver; combination of heart murmur classified by the CHC physician as non-suspect and weight gain classified by the CHC-physician as insufficient; combination of heart murmur classified by the CHC physician as non-suspect and anamnestic clues for exercise intolerance; combination of weight gain classified by the CHC physician as insufficient and anamnestic clues for exercise intolerance.

Screening history was either classified as adequate or as inadequate. For 'inadequate' screened patients the reasons for this classification were specified.

To determine screening test properties additional data were collected: all referrals for congenital heart malformation by Rotterdam CHC physicians were registered during the second half of 1996; figures on births in Rotterdam and the south-west of the Netherlands including Rotterdam were acquired from Statistics Netherlands.

### Analysis

It is our opinion that it is essential for patients, parents and their physicians to be informed of any congenital heart malformation present, even if the disorder should eventually prove to have no haemodynamic consequences. Therefore test properties were established for all 290 patients with a congenital heart malformation. To establish the intended effects of screening, however, the analysis was restricted to the 82 patients with clinically significant disorders.

With regard to the latter, logistic regression was used to derive odds ratios (OR), including 95% confidence intervals (CI), for being diagnosed too late depending on whether or not being screened adequately and on whether or not being detected by CHC screening. In both analyses, correction for severity was applied in order to adjust for length bias.

To appreciate the effects of screening the proportions of patients diagnosed too late and in time in an imaginary population not exposed to screening are estimated. We assume that these proportions will be appropriately estimated by the proportions 'too late' and 'in time' among patients with clinically significant disorders, who were not detected by a CHC physician, corrected for severity (in this imaginary population a distribution of severity similar to the complete study group may be expected). This estimate was compared to the proportions of diagnoses made too late and in time in the complete study population (i.e. exposed to screening as it was actually performed) and in the sub-population with an adequate screening history (proportions in this sub-population ( $n = 12$ ) could not be corrected for severity, since numbers of patients were too small).

## Results

### Patient inclusion

As shown in Table 1, of all 1142 patients aged between 32 days and 4 years, who were examined during the study by a paediatric cardiologist in the Sophia Children's Hospital for the first time, 290 appeared to have a congenital heart malformation. The screening history of 272 of these patients could be documented. Eighty-three patients were eventually diagnosed as having a clinically significant disorder, of whom in 82 the screening history could be collected. The findings of the two paediatric cardiologists were identical in 79 cases. A third opinion was necessary in three cases. Forty-nine patients (60%) suffered from large left-to-right shunts. Cyanotic heart disease was found in 15 patients (18%) and disorders resulting in increased pressure-load were seen in seven patients (9%). The remaining 11 patients (13%) had miscellaneous malformations.

### Test properties

Of 290 patients 164, had been detected by a CHC physician. In 36 (out of 272) patients all requirements for adequate screening had been met. Thirty-two of these were detected by a CHC physician. The number of referrals for congenital heart

**Table 2** Calculation of incidence of cases of congenital heart malformation (CHM) diagnosed between 32 days and 4 years, the test properties of the actual CHC screening activities during 2 years in the south-west of the Netherlands and the sensitivity of this screening in a subset of adequately screened patients. (Numbers in parentheses indicate adequately screened patients)

|                                     | CHM             |                            | Total  |
|-------------------------------------|-----------------|----------------------------|--------|
|                                     | +               | -                          |        |
| <b>Screening</b>                    |                 |                            |        |
| +                                   | 164 (32)        | 1083                       | 1247   |
| -                                   | 126 (4)         | 74 068                     | 74 194 |
| <b>Total</b>                        | 290 (36)        | 75 151                     | 75 441 |
| Incidence                           | 290/75 441 =    | 3.8 per 1000 children      |        |
| Sensitivity:                        | 164/290 =       | 0.57 (95% CI 0.51-0.62)    |        |
| Specificity:                        | 74 068/75 151 = | 0.985 (95% CI 0.981-0.990) |        |
| Predictive value positive test.     | 164/1247 =      | 0.13 (95% CI 0.10-0.19)    |        |
| Sensitivity if adequately screened: | 32/36 =         | 0.89 (95% CI 0.74-0.96)    |        |

**Table 3** Classification of the 82 patients with clinically significant disorders diagnosed 'too late' and 'in time' in categories 'adequately screened' and 'inadequately screened', and 'detected by Child Health Centres [CHC]' and 'not detected by CHC'

|                       | Too late | In time  | Total     |
|-----------------------|----------|----------|-----------|
| Adequately screened   | 2 (17%)  | 10 (83%) | 12 (100%) |
| Inadequately screened | 37 (53%) | 33 (47%) | 70 (100%) |
| <b>Total</b>          | 39 (48%) | 43 (52%) | 82 (100%) |
| Detected by CHC       | 16 (36%) | 29 (64%) | 45 (100%) |
| Not detected by CHC   | 23 (62%) | 14 (38%) | 37 (100%) |
| <b>Total</b>          | 39 (48%) | 43 (52%) | 82 (100%) |

**Odds Ratios:** for being 'too late' depending on whether or not adequately screened.

= 0.18, 95% CI: 0.04-0.87

= 0.20, 95% CI: 0.04-1.05 corrected for severity.

for being 'too late' depending on whether or not detected by CHC screening

= 0.34, 95% CI: 0.14-0.83

= 0.39, 95% CI: 0.15-1.00 corrected for severity

malformation by Rotterdam CHC physicians in 6 months was 60. The numbers of births in the south-west of the Netherlands and Rotterdam during 1994-1995 were 75 441 and 14 524 respectively. Hence the number of CHC referrals throughout a period of 2 years in the area under discussion is estimated as  $75\,441/14\,524 \times 4 \times 60 = 1247$ . On the basis of these figures, test properties are calculated and subsequently presented in Table 2. The sensitivity of the actual screening programme was 0.57, the specificity 0.985 and the predictive value of a positive test result 0.13. Sensitivity in the adequately screened sub-population was 0.89.

These data also allow calculation of the incidence rate of congenital heart malformations in children aged from one month until 4 years: 0.38%.

### Effectiveness

For the 82 patients with a clinically significant disorder, distributions of screening and detection history in relation to the outcome measures (diagnosed 'too late'/'in time') are shown in

Table 3. Of these 82 patients, not surprisingly none was qualified as having a trivial disorder. Twenty-nine (35%) of these patients proved to have a moderate, 40 (49%) a severe and 13 (16%) a very severe disorder. Table 3 shows that adequately screened children were less likely to be diagnosed too late than inadequately screened ones. This was also the case for patients detected by CHC physicians compared to patients detected otherwise. After correction for severity, both OR hardly increased, although both CI now just include 1.00.

In an imaginary population not exposed to CHC screening, the estimated percentage of children diagnosed too late and in time, based on proportions among children not detected by CHC physicians after correction for severity, are 58% and 42% respectively.

As summarized in Table 4, the risk of being diagnosed too late in a population exposed to CHC screening as actually performed in the present study population, is not much lower than the estimated risk for patients in a population not exposed to CHC screening. In an adequately screened population, however, patients would probably be at considerably less risk of being diagnosed too late.

### Inventory of deviations from guidelines

Only 12 patients with clinically significant disorders (15%) qualified as having been screened adequately according to the guidelines (Table 5). Four children (5%) visited the CHC at recommended ages and were correctly screened by the CHC physician, but were not referred in spite of a positive test. The other children were either not screened at recommended ages (10; 12%), or not correctly screened by the CHC physician (22; 27%) or both (34; 41%); including the seven children who never have visited the CHC.

### Discussion

The incidence of congenital heart malformations in the Netherlands is estimated at 0.8%.<sup>9</sup> Half of these cases are likely to be diagnosed before the age of one month.<sup>8</sup> These data coincide with the incidence rate of 0.38% for congenital heart malformations in children aged from one month until 4 years found in this study.

Considering Table 2, we estimate that under the actual screening regime in the south-west of the Netherlands, over a period of 2 years, 126 patients with a congenital heart malformation will not be detected by CHC physicians but by others (false-negatives). Overall 1082 children will be referred for a congenital heart malformation by CHC physicians, although further clinical assessment will fail to reveal such disorders (false-positives). If all children were screened adequately, it is estimated that the number of false-negatives would be reduced to  $(4/36) \times 290 = 32$ . Whether such an improvement will change the false-positive rate is difficult to predict and no estimates can be based on the present data. Distress caused by false-positive test results is generally considered to be less severe than distress and adverse health effects caused by false-negative test results.<sup>7</sup> For this reason and in the light of the substantial reduction in numbers of false-negatives, a considerable increase in the number of false-positives would be required to neutralize the positive effects of such a change in policy. If for example the relation between the harm caused by false-negative and false-positive

**Table 4** Proportions of patients diagnosed 'too late' and 'in time' in populations subjected to different screening expositions

|                                                           | Too late             | In time              |
|-----------------------------------------------------------|----------------------|----------------------|
| Imaginary population not exposed to CHC screening         | 58% (95% CI : 43–72) | 42% (95% CI : 28–57) |
| Population exposed to CHC screening as actually performed | 48%                  | 52%                  |
| Population exposed to adequate screening                  | 17% (95% CI : 4–48)  | 83% (95% CI : 52–95) |

**Table 5** Causes of deviation from guidelines for screening procedures

| Screening history                                                                                             |                  |
|---------------------------------------------------------------------------------------------------------------|------------------|
| <b>Adequately screened</b>                                                                                    |                  |
| Screening at recommended ages, correctly performed and referred in case of a positive test result             | 12 (15%)         |
| <b>Inadequately screened</b>                                                                                  |                  |
| Screening at recommended ages, correctly performed but <i>not referred in spite of a positive test result</i> | 4 (5%)           |
| Screening <i>not at recommended ages</i> , though correctly performed                                         | 10 (12%)         |
| Screening at recommended ages, but <i>not correctly performed</i>                                             | 22 (27%)         |
| Screening both <i>not at recommended ages</i> and <i>not correctly performed</i>                              | 34 (41%)         |
| <b>Total</b>                                                                                                  | <b>82 (100%)</b> |

test results is expressed as a ratio of 10:1, the number of false-positives will almost have to be doubled to  $1082 + (126 - 32) \times 10 = 2022$  to neutralize the effect of the reduction of false-negatives.

From a methodological point of view the most appropriate design for evaluating potential benefits of screening is a randomized controlled trial (RCT). Should practical and ethical grounds render a RCT infeasible for evaluating a screening programme, which is already established and running, observational designs must be resorted to, meticulously considering possible sources of confounding.<sup>7</sup>

A patient follow-up design is used in our study, in which the determinants (screening and detection history) are established retrospectively and the outcome measure (in time/too late) prospectively. In order to use this design, it is essential that treatment for the disorder under discussion can be safely postponed until the disease has progressed up to a stage in which spontaneous resolution can no longer be expected. Consequently, overestimation of the positive effects of screening as result of overtreatment of regressive disorders can be avoided. The management approach in modern paediatric cardiology is cautiously expectant. The decision to treat is always postponed until haemodynamic complications are judged to be inevitable in the short or longer run. Given the nature of the disorders under discussion—relatively large anatomical defects—and the extensive research data on the natural history, paediatric cardiologists may be assumed to be reliable in their prognosis of the natural course.<sup>20–23</sup>

The differences between adequately and inadequately screened patients may partly be induced by selection bias. If we presume that after correction for severity this bias will be of little consequence, we may conclude that adequately screened children are better off than those inadequately screened and that increasing the proportion of adequately screened children will reduce the incidence of haemodynamic complications from congenital heart malformations. Inadequate screening is a result of both insufficient attendance by parents and incorrect

performance by CHC physicians. We are convinced that both aspects can be improved by health education and management provisions.

## Conclusion

The present study indicates that systematic screening for congenital heart malformation in CHC in the Netherlands contributes to the timely detection and treatment of these disorders. The actual yield of the programme, however, is far from optimal, and screening attendance and performance should be improved. Optimization of screening participation and performance may improve screening considerably, resulting in timely treatment of most patients.

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