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# Factors that determine the effectiveness of screening for congenital heart malformations at child health centres

Rikard E Juttmann,[a] John Hess,[b] Caspar WN Looman[a] and Paul J van der Maas[a]

**Background** The actual yield from current screening for clinically significant congenital heart malformations in Dutch child health care is far from optimal. In this study factors that determine the effectiveness of this screening are identified and recommendations for the optimization of the screening programme are formulated.

**Methods** Eighty-two patients with a clinically significant congenital heart malformation were consecutively included in this study. Parents and child health centre physicians were interviewed in order to establish the screening, detection and referral history. Paediatric cardiologists established whether these patients were diagnosed 'in time' or 'too late'.

**Results** Incomplete performance of the screening examination has more influence on the occurrence of delayed diagnoses than failure by parents to adhere to the complete visit schedule. Adequate screening advances detection of congenital heart malformations. Severity, however, is the most predominant determinant of the age at referral and diagnosis, as well as of the risk of complications. In only 7 out of 39 patients diagnosed 'too late', could no avoidable cause for an adverse outcome be found. In 10 cases (25%) there was a prolonged interval between first referral and diagnosis.

**Conclusion** To optimize the yield of the screening programme, improvement in the performance of the child health centre physicians and the co-operation of other physicians involved in reducing the interval between referral and diagnosis are required. Thus a considerable improvement in the prevention of complications of congenital heart malformations can be obtained.

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

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Screening for congenital heart malformations is common practice in child health care in several countries.[1–3] Evaluations of this practice, however, are scarce. In a previous report we estimated the test properties of such a screening programme in the south-west of the Netherlands and we demonstrated that adequately screened patients have a better chance of being diagnosed 'in time', i.e. before haemodynamic complications arise, than inadequately screened patients. The actual yield from the present screening programme, however, turned out to be far from optimal.[4] In this paper several factors determining the effectiveness of this screening are identified and recommendations for the optimization of the screening policy are formulated. Three topics will be addressed:

### Contribution of screening attendance and performance

The adequacy of the screening is defined by both the attendance of the parents and the performance of the physicians. We will estimate the contribution of these two factors to the effectiveness of the screening programme separately. We will subsequently demonstrate how different elements of the screening contributed to the referral of the patients.

### Interaction between adequacy of screening and severity of the disorder

Adequate screening is supposed to lead to diagnosis before the occurrence of complications as a result of advancing the detection of the disorder.[5] However, for congenital heart malformations, severity of the disorder may also be a very important factor affecting both the risk of complications and the age at first

[a] Department of Public Health, Erasmus University, Rotterdam, The Netherlands.

[b] Department of Paediatric Cardiology, the Sophia Children's Hospital and Erasmus University, Rotterdam, The Netherlands.

Reprint requests to: RE Juttmann, Department of Public Health, Erasmus University Rotterdam, Room EE 2008, PO Box 1738, 3000 DR Rotterdam, The Netherlands. E-mail: juttmann@mgz.fgg.eur.nl

referral and diagnosis.[6] We will clarify the influence of adequacy of screening as well as severity of the disorder on the outcome of the screening process.

### General impact of screening as prevention programme

We will estimate to what extent this prevention programme contributes to diagnosis before the occurrence of complications (in time), and to what extent failure of the programme may cause diagnosis after the occurrence of complications (too late).

## Methods

### Subjects

This study comprised all patients participating in our original effect evaluation study[4] with a clinically significant congenital heart malformation: 82 of such patients, aged between 32 days and 4 years, consecutively presented at Sophia Children's Hospital Rotterdam during a period of 2 years.

### Data collection and definition of variables

In order to establish the screening history, the child health care physicians of all the patients were approached for a structured 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 subsequently about the actual procedure in this particular case. Screening history was classified as 'adequate' if, prior to the first cardiological consultation, the standard visit schedule had been attended in full, and during these visits the child health centre physician performed a complete examination. For a definition of the standard visit schedule and a complete examination we refer to our previous report.[4] Screening history was either classified as 'adequate' or as 'inadequate'.

In order to establish when their child's disorder was first detected, parents were interviewed by a nurse at the first cardiological consultation. If necessary, additional information was collected from child health centre physicians, general practitioners and specialists.

The first referral was considered to have taken place as soon as any physician started referral for congenital heart disease for the first time. The first cardiological consultation was taken as date of the diagnosis.

To establish whether diagnosis took place after or before haemodynamic complications had occurred ('too late' versus 'in time'), two paediatric cardiologists each independently filled in a questionnaire. In cases where the answers of these two doctors failed to agree a third colleague was asked to make the final judgement. As for the criteria for classifying the children in categories too late or in time we also refer to our previous paper.[4]

In the same questionnaire paediatric cardiologists were asked to rank the severity of the malformation as 'moderate', 'severe' or 'very severe'.

To estimate the general impact of the current screening activities, patients were classified into four categories.

#### *'Too late', not due to an incompletely attended or performed screening*

First referred before reaching first screening age or between screening ages after a completely performed screening with a negative test result. (This implies that for this analysis we consider a false negative test result after a completely performed screening examination, as a result of the test properties inherent to this kind of screening, and at present not amenable to further improvement.)

#### *'Too late', possibly due to an incompletely attended or performed screening*

First referred as a result of screening, which, however, was delayed due to incomplete attendance, or first referred after an incompletely performed screening with a negative test result.

#### *'In time', possibly due to screening*

First referred as a result of screening, timely followed by a visit to paediatric cardiologist. An interval between first referral and diagnosis of 4 weeks or less was considered acceptable. Longer intervals were classified as 'prolonged'.

#### *'In time', probably not due to screening*

First referred by others or as a result of screening followed by a visit to paediatric cardiologist after 4 weeks.

### Analysis

The influence of performance and attendance on the effect of screening are expressed in odds ratios (OR) established by logistic regression. Since severity of the disorder may induce length-bias, leading to overestimation of favourable effects of screening,[7] all effect outcomes will be corrected for severity.[4] Geometric means of ages at first referral and diagnosis are established in several sub-groups and *P*-values for differences between these sub-groups are calculated on the basis of rank numbers. To evaluate the extent of differences, rates of geometric means are calculated, including 95% CI. Both distributions of age at first referral and diagnosis are non-normal, which can only partly be adjusted by using a logarithmic scale. Therefore the 95% CI, as calculated for the rates of geometric means, will not concur completely with the *P*-values calculated on the basis of rank numbers. As far as age distributions are concerned the latter must be considered as the most reliable in assessing the significance of differences between two groups.[8]

## Results

### Contribution of screening attendance and performance

Table 1 shows that incomplete screening examination by the child health centre physicians will significantly reduce the chance of being diagnosed in time, if the parents visited the child health centre according to schedule (OR = 0.13, 95% CI : 0.02–0.69). Incomplete examination seems to reduce this chance regardless of whether the visits were made according to schedule (i.e. unchanged compared to the current practice), although in this case the OR just lacks statistical significance (OR = 0.32, 95% CI : 0.10–1.04).

Incomplete attendance by parents will not significantly reduce the chance of being diagnosed in time, either if the physician performed complete examinations, or regardless whether the physician did so. In the former case the OR is low but evidently lacks statistical significance (OR = 0.20, 95% CI : 0.02–1.82); in the latter case the OR even exceeds 1, but also lacks statistical significance (OR = 1.20, 95% CI : 0.48–3.00). After correction for severity the OR remain similar and the confidence intervals widen somewhat.

**Table 1** Influence of attendance by parents (a) and screening performance by child health centre (CHC) physicians (p) on whether or not patients with congenital heart malformations were diagnosed 'in time'

| | In time | Too late | Total | OR[a] (95% CI) for being in time[b] | Corrected for severity |
|---|---|---|---|---|---|
| **OR (95% CI)** | | | | | |
| 1. a+ p+ | 10 | 2 | 12 | 1.00 | |
| 2. a+ p– | 10 | 16 | 26 | 0.13 (0.02–0.69) | 0.14 (0.02–0.85) |
| 3. a– p+ | 3 | 3 | 6 | 0.20 (0.02–1.82) | 0.26 (0.02–2.74) |
| 4. a– p– | 20 | 18 | 38 | 0.22 (0.04–1.15) | 0.24 (0.04–1.30) |
| **OR corrected for attendance (95% CI)** | | | | | |
| 1. p+ | 13 | 5 | 18 | 1.00 | |
| 2. p– | 30 | 34 | 64 | 0.32 (0.10–1.04) | 0.32 (0.09–1.10) |
| **OR corrected for performance (95% CI)** | | | | | |
| 1. a+ | 20 | 18 | 38 | 1.00 | |
| 2. a– | 23 | 21 | 44 | 1.20 (0.48–3.00) | 1.19 (0.45–3.16) |

[a] Odds ratio.

[b] Category 1 is the reference value.

a+ = the standard CHC visit schedule was *attended* completely.

a– = the standard CHC visit schedule was *attended* incompletely.

p+ = performance by CHC-physicians of a complete investigation.

p– = performance by CHC-physicians of an incomplete investigation.

**Table 2** Ages at first referral and diagnosis

| | N | Geometric mean (months) | *P*-value difference 1 and 2 based on rank number | Rate of geometric mean (2/1) (95% CI) | Standardized geometric mean after correction for severity (months) | *P*-value difference 1 and 2 based on rank number corrected for severity | Rate of geometric mean (2/1) (95% CI corrected for severity) |
|---|---|---|---|---|---|---|---|
| **Age at first referral** | | | | | | | |
| 1. moderate | 29 | 6.4 | 0.0014 | 0.38 (0.22–0.63) | | | |
| 2. (very) severe | 53 | 2.3 | | | | | |
| 1. adequately screened (a+c) | 12 | 2.1 | 0.048 | 1.76 (0.82–3.75) | 1.9 | 0.017 | 1.93 (0.94–3.78) |
| 2. inadequately screened (b+d) | 70 | 3.7 | | | 3.7 | | |
| 1. 'in time' (c+d) | 43 | 4.1 | 0.32 | 0.68 (0.40–1.16) | 3.5 | 0.98 | 0.89 (0.51–1.52) |
| 2. 'too late' (a+b) | 39 | 2.8 | | | 3.1 | | |
| **Age at diagnosis** | | | | | | | |
| 1. moderate | 29 | 7.4 | 0.0076 | 0.45 (0.28–0.72) | | | |
| 2. (very) severe | 53 | 3.4 | | | | | |
| 1. adequately screened (a+c) | 12 | 3.0 | 0.17 | 1.59 (0.82–3.10) | 2.7 | 0.061 | 1.80 (0.96–3.40) |
| 2. inadequately screened (b+d) | 70 | 4.8 | | | 4.9 | | |
| 1. 'in time' (c+d) | 43 | 5.9 | 0.058 | 0.58 (0.63–0.92) | 5.2 | 0.33 | 0.72 (0.45–1.16) |
| 2. 'too late' (a+b) | 39 | 3.4 | | | 3.8 | | |

In total 41 patients were detected at the child health centre through a clearly positive test result. All these children presented with a cardiac murmur audible at auscultation of the thorax. Thirty-nine murmurs were indicated as 'suspect' of which 10 were combined with other positive test results such as central cyanosis (5), insufficient weight gain (6), clues for exercise intolerance (6), and an enlarged liver (1). Two murmurs were indicated as 'non-suspect', of which, however, one was combined with insufficient weight gain and one with clues for decreased exercise tolerance. Four patients were referred by child health centre physicians on rather uncertain grounds (only a murmur classified by the physician as 'non-suspect' or only anamnestic clues for decreased exercise tolerance).

## Interaction between adequacy of screening and severity of the disorder

In Table 2 the differences in age at first referral and diagnosis are indicated between patients with moderate and (very) severe disorders, between adequately and inadequately screened patients and between patients diagnosed in time and too late.

Severe and very severe congenital heart malformations were on average referred at a significantly earlier age than moderate ones (2.3 versus 6.4 months). A similar difference was found for the ages at diagnosis (3.4 versus 7.4 months).

Adequately screened patients were on average referred at a significantly earlier age than inadequate screened ones (2.1 versus 3.7 months). This difference increased after correction

**Table 3** General impact of screening

| | N | n: interval>28 days | Geometric mean age at detection | Geometric mean age at diagnosis |
|---|---|---|---|---|
| 1. 'too late' not due to incomplete attendance or performance of the screening programme | 11 | 4 | 2.0 | 2.9 |
| 2. 'too late' possibly due to incomplete attendance or performance of the screening programme | 28 | 6 | 3.1 | 3.6 |
| 3. 'in time' possibly due to screening | 12 | 0 | 1.8 | 2.4 |
| 4. 'in time' probably not due to screening | 31 | 27 | 5.6 | 8.3 |

for severity. They were also on average diagnosed at an earlier age (3.0 versus 4.8 months), although this difference was not statistically significant. After correction for severity however, the difference increases and only just lacks statistically significance.

Patients diagnosed too late were on average referred at an earlier age than patients diagnosed in time (2.8 versus 4.1 months). This difference is statistically not significant. After correction for severity, the difference decreased considerably. No reversal, however, was seen. As for the age at diagnosis the same trend is visible, although not so marked.

### General impact of screening as prevention programme

Table 3 shows, that for 11 out of 39 patients diagnosed too late, this adverse outcome could not be attributed to an incomplete attendance or incomplete examination by the child health centre physician. On average, these patients were detected at 2.0 months and diagnosed at 2.9 months. Four were subject to a prolonged referral interval. Conversely, in the other 28 patients diagnosed too late the adverse outcome could possibly be attributed to inadequate attendance or screening performance, although prolonged interval between referral and diagnosis also occurred in six cases. These 28 patients were on average detected and diagnosed later (respectively at 3.1 and 3.6 months) than the 12 patients diagnosed in time, in whom this favourable outcome might be attributed to the screening (respectively 1.8 and 2.4 months). Differences in ages at referral or diagnosis between these relatively small groups are not statistically significant. In 31 patients, screening had not evidently contributed to the timely detection. These patients were referred at the average age of 5.6 months and diagnosed at 8.3 months. The majority (n = 27) had a prolonged interval between first referral and diagnosis.

## Discussion

From a methodological point of view the most appropriate design for evaluating the potential benefits of screening is a randomized controlled trial (RCT). Should practical and ethical grounds preclude an RCT of a screening programme already established and running, observational designs must be resorted to. In this project we used a partly retrospective, partly prospective patient follow-up study. The most important condition for using such a design is that treatment for the disorder under discussion can safely be postponed until the disease has progressed up to a stage in which spontaneous resolution can no longer be expected. Consequently, overestimation of screening effectiveness as a result of overtreatment of regressive disorders can be avoided. In our previous paper we discussed the applicability of this design for the evaluation of the screening programme presently under discussion.[4]

### Contribution of screening attendance and performance

The combination of a completely fulfilled screening protocol by child health centre physicians and attendance according to schedule by parents is the best guarantee for a timely diagnosis. A complete screening examination, however, is apparently the most significant determinant. Although correction for severity inevitably influences the already limited power unfavourably, since after correction the OR hardly change, actually length-bias is of little consequence in this part of the evaluation.

Detection by screening is predominantly a result of discovering heart murmurs by auscultation of the thorax. Most physicians, including those who do not perform all required tests, usually do perform auscultation. Probably physicians who are aware of what a complete screening examination entails and who are used to acting accordingly, are also more aware of all the possible implications of congenital heart disease and therefore more competent in discovering and interpreting murmurs at auscultation than less skilled and meticulous colleagues.

Optimal training of child health centre physicians is probably the most important condition for improvement of the yield of the screening programme for congenital heart malformations. In the Netherlands, child health centre physicians, unlike school health care physicians, are not fully trained in social paediatrics.[9] In the 10-day course which trainee doctors are obliged to follow in order to be appointed as a child health care physician, only one lecture is dedicated to paediatric cardiology.[10] Apparently this is insufficient.

Health education aimed at optimizing attendance by parents may also help to improve the yield. Parents should be encouraged to visit the consulting room in time. Such measures, however, should not be expected to boost the yield of the programme to any major extent.

### Interaction between adequacy of screening and severity of the disorder

An effective screening programme is expected to advance the age of referral and diagnosis, to enable the necessary intervention procedure to be carried out before complications occur. Patients with severe disorders are more likely to be detected at an early age as well as more likely to develop early complications than patients with less severe disorders. In our study severity is obviously the most predominant determinant of the

age at referral and diagnosis, as well as of the risk of complications. Paradoxically patients diagnosed too late are on average referred and diagnosed at an earlier age than patients detected in time, undoubtedly because of overrepresentation of rapidly deteriorating disorders among patients who were diagnosed too late. As these differences are decreased after correction for severity, the operational definition for severity provides a useful, but not absolute, indicator for speed of progression. After total correction for speed of progression, an inversion of the observed correlation would be expected.

Thus, although severity has little influence on the OR for being diagnosed before the occurrence of complications, as far as the actual advancement of detection and diagnosis is concerned, evaluation of screening for congenital heart malformation by observational studies produces a distinct example of length bias.

### General impact of screening as prevention programme

Since patients diagnosed too late, not due to inadequate screening, are detected and diagnosed at a rather early age, accelerated deterioration is probably the predominant cause for the occurrence of complications in these cases. In four of these cases, however, a prolonged referral interval may also have played a role. This may also be the case in six patients in whom the delayed diagnosis could possibly be attributed to inadequate screening. Patients diagnosed too late, possibly because of inadequate screening, seem to be referred and diagnosed at an older age than those patients whose timely diagnosis may have been due to the screening programme. The patients in whom screening did not contribute to avoiding complications probably had slowly progressive disorders. Apparently in most of these cases neither delayed detection and diagnosis nor prolonged interval between the two had an unfavourable effect on the outcome.

These findings suggest that screening for congenital heart malformations, although not effective in swiftly deteriorating diseases or in slowly progressive ones, is quite successful in the relatively large middle group of patients with disorders progressing at a medium rate.

In only 7 out of 39 patients diagnosed too late, was no avoidable cause for an adverse outcome indicated.

## Conclusion

The results of this study suggest that the prevention of complications of congenital heart malformations can be considerably improved. This requires improving the screening performance, following strict criteria, of child health care physicians and more alert referral practices by the physicians who play a part in this prevention programme.

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