Challenges in the diagnosis of asthma in children

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Conflicts

• None relating to this presentation
Topics covered

• Background:
  • Misdiagnosis – how common is it and who is most affected
  • Problem arising from mis- or non-diagnosis
  • How should asthma in children be diagnosed

• What are the challenges with the diagnosis
  • Not covered – preschool wheeze
Misdiagnosis in Europe

Over-diagnosis: 20%
Under-diagnosis: 33%

Under-diagnosis: 37-50%

Over-diagnosis: 50%
Under-diagnosis: 62%

Under-diagnosis: 32%
Reasons for misdiagnosis and variation in misdiagnosis rates

• Inconsistent European and international diagnostic approach

• Symptoms leading to asthma diagnosis in the Netherlands is often diagnosed and treated as bronchitis in Germany

• Variable use of objective tests in children
Consequences of misdiagnosis

- Prescription of inappropriate treatments
- Unnecessary medicinal side effects
- Increased healthcare costs
- Missing the real diagnosis with persistent on-going morbidity
- Poor quality of life and greater absence from school
- Potential for severe asthma attacks
Reluctance to code as asthma

- Major problem across Europe
- Undermines patient and family confidence and drives non-adherence
- Often leads to a lack of proper follow-up
- Drives SABA overuse
- Contributes to high rates of severe asthma attacks
Leicester UK experience with non-coded asthma

- Leicestershire (CHAMPIONS Study) - 10 GP/613 children
  - 30 to 70% of children on regular asthma inhalers in previous 12m not on the asthma register
- Not being on the register in UK means
  - No mandated annual asthma review
- These children had similar numbers of asthma attacks to children on the register

Lo D 2020, Thorax
Children from poorer backgrounds less likely to be coded as asthma

Spirometry and FeNO testing for asthma in children in UK primary care: a prospective observational cohort study of feasibility and acceptability – CHAMPIONS Study

Table 1. Characteristics of participating practices, N = 10

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>I</th>
<th>J</th>
<th>Study mean</th>
<th>England mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registered patients, n</td>
<td>10288</td>
<td>48196</td>
<td>10273</td>
<td>3519</td>
<td>8043</td>
<td>6956</td>
<td>10522</td>
<td>5229</td>
<td>4083</td>
<td>12861</td>
<td>11997</td>
<td>8035</td>
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<tr>
<td>Aged &lt;18 years, %</td>
<td>20.1</td>
<td>21.8</td>
<td>22.7</td>
<td>18.2</td>
<td>17.7</td>
<td>17.6</td>
<td>29.0</td>
<td>32.4</td>
<td>28.0</td>
<td>26.2</td>
<td>23.4</td>
<td>20.5</td>
</tr>
<tr>
<td>On asthma register, all ages, %</td>
<td>6.2</td>
<td>5.4</td>
<td>8.3</td>
<td>3.5</td>
<td>6.1</td>
<td>6.4</td>
<td>6.8</td>
<td>3.6</td>
<td>6.1</td>
<td>6.0</td>
<td>5.8</td>
<td>5.9</td>
</tr>
<tr>
<td>Deprivation index(^b)</td>
<td>10</td>
<td>4</td>
<td>6</td>
<td>4</td>
<td>7</td>
<td>10</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4 (median)</td>
<td>5 (median)</td>
</tr>
<tr>
<td>Non-white ethnicity, %</td>
<td>2.6</td>
<td>3.8</td>
<td>6.9</td>
<td>40.8</td>
<td>18.5</td>
<td>3.9</td>
<td>16.7</td>
<td>19.3</td>
<td>65.5</td>
<td>62.3</td>
<td>24.0</td>
<td>14.0</td>
</tr>
</tbody>
</table>

\(^a\)Unless otherwise stated. \(^b\)Weighted score for practice. Based on the Index of Multiple Deprivation (IMD) 2017. 1 = most deprived; 10 = least deprived.
How should we diagnose asthma in children?

- GINA strategy document (updated yearly)
- UK National Institute for Health and Care Excellence (NICE) – 2017
- ERS clinical practice guidelines
European Respiratory Society clinical practice guidelines for the diagnosis of asthma in children aged 5-16 years


Eur Respir J. 2021
Robust evidence based clinical practice guidelines

- 9 systematic literature reviews on relevant PICO questions
- Quality Assessment of Diagnostic Accuracy Studies - 2 (QUADAS-2) tool to evaluate the risk of bias
  - For each paper included in the guidelines
- GRADE methodology
  - Grading of Recommendations, Assessment, Development and Evaluations is a transparent framework for developing and presenting summaries of evidence
- GRADE provides a systematic and high quality approach for making clinical practice recommendations and helps to
  - Assess certainty of the evidence
  - Confidence in the strength of recommendations in health care
Diagnostic algorithm

Child aged 5 to 16 years with symptoms of asthma (wheeze* +/- cough +/- breathing difficulty)

Perform Spirometry

- Spirometry abnormal
  - Perform reversibility testing
    - BDR positive ≥ 12% and/or 200ml: Asthma confirmed
    - BDR negative < 12% and/or 200ml: Perform FeNO measurement
      - FeNO ≥ 25ppb: Consider asthma treatment; review after 4-8 weeks
      - FeNO < 25ppb: Asthma unlikely. Refer for specialist opinion
        - Repeat spirometry
        - Spirometry improved: Asthma confirmed
        - Spirometry abnormal & Symptoms not improved: Refer for specialist opinion
  - Spirometry abnormal & Symptoms improved: Asthma confirmed

- Spirometry normal
  - Perform FeNO measurement
    - FeNO ≥ 25ppb: Consider PEF variability testing
      - Challenge test positive: Asthma confirmed
      - Challenge test negative: Asthma unlikely
    - FeNO < 25ppb: Perform challenge testing
      - PEFR variability ≥12%: Asthma confirmed
      - PEFR variability <12%: Asthma unlikely
      - If symptoms persist: Refer for specialist opinion

1. Spirometry normal
2. BDR positive ≥ 12% and/or 200ml
3. Perform reversibility testing
4. Perform FeNO measurement
5. Consider asthma treatment; review after 4-8 weeks
6. Consider differential diagnoses
7. PEF variability testing
8. Spirometry abnormal & Symptoms improved
Guidelines summary

- Spirometry, BDR and FeNO as 1st line tests
  - PEFR variability testing can be used if 1st line tests inconclusive
- Arrange direct or indirect bronchial challenge tests if diagnosis remains in doubt

- No evidence to support
  - Clinical diagnosis alone
  - Trial of preventer treatment based on symptom improvement alone
  - Allergy testing
Diagnostic challenges

• Spirometry and FeNO equipment unavailable in many healthcare settings
• Time constraints in many healthcare settings including UK primary care to perform 1st line tests
• Lack of funding
• Lack of training to perform and interpret tests
• Access to challenge tests even more difficult
Challenges relating to 1st line tests

- **Routine spirometry**
  - low sensitivity (0.12 to 0.52)
  - Moderate to good specificity (0.72 to 0.93)
- **Repeat testing may be required and particularly useful when the child is symptomatic**

- **FeNO**
  - Relatively costly (equipment and tests)
  - Difficult test in children < 8 years outside specialist settings
How useful are the 1st line tests

- In the CHAMPIONS Study 109 children were not on the asthma register but received asthma treatment

- 12% had abnormal spirometry and + BDR – diagnosed

- Further 6% had FeNO ≥ 35ppb and abnormal spirometry – should be offered treatment as likely asthma

Lo D 2020, Thorax
Diagnosis of asthma in children: findings from the Swiss Paediatric Airway Cohort

- Observational study of 514 children aged 5 to 17 years under investigation for asthma in high resource setting
- FeNO, spirometry, BDR and body plethysmography attempted in all children
- Only 91 (17.7%) children could be passed through the GINA algorithm to ‘treat for asthma’
- Only 38 (7.3%) children could be passed through the UK NICE algorithm. Children got stuck at the 2 week peak flow diary step, which was not performed
What do families and children want?

• CHAMPIONS Study
• Of 613 participants 97% stated they would recommend tests to friends and family

'I am very happy to have breathing tests for my daughter, that is great chance to check if she have asthma or not.'

'It only felt like playing a video game, didn’t see it being a test in any way!' (child)

'Has enhanced diagnosis, given confidence in diagnosis, made me aware of other causes i.e. rhinitis, insight and training can only improve care.'

'Able to explain better to parents and make better diagnosis.'
What do families and children want?

- Major shift in clinical practice in many UK and European healthcare settings

- All the patient representatives involved with the ERS guidelines recruited through the European Lung Foundation preferred objective tests to confirm the diagnosis
Key messages

• Diagnosing asthma in children correctly matters for children and families
• A diagnosis without objective tests is frequently wrong and often leads to poor treatment and control
• We need to work together to overcome challenges and get better access to spirometry and FeNO testing for children in Europe and Worldwide
• We need to continue to refine asthma diagnostic algorithms
• Challenge for the future is to find novel objective ways to increase asthma diagnostic yield
Thank you for listening
Challenges in diagnosis of asthma in children in low-resource settings

Rebecca Nantanda

PATS & ERS Paediatric Webinar

Tuesday 14th June 2022
Conflict of interest

I have no conflict of interest to declare
Outline of presentation

• Burden of childhood asthma in sub-Saharan Africa

• Overview of care practices for children with asthma

• Implications of the ERS guidelines on management of childhood asthma in low-resource settings (LRS)
## Burden of asthma

<table>
<thead>
<tr>
<th>Authors/year/country</th>
<th>Age group (years)</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asher, MI et al, 2021 (GAN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nigeria</td>
<td>13-14</td>
<td>10.6</td>
</tr>
<tr>
<td>Sudan</td>
<td>13-14</td>
<td>5.7</td>
</tr>
<tr>
<td>Kiboneka, et al, 2016, Botswana</td>
<td>13-14</td>
<td>16.8</td>
</tr>
<tr>
<td></td>
<td>6-7</td>
<td>15.9</td>
</tr>
<tr>
<td>Aniku, G et al, 2015, Uganda</td>
<td>9-12</td>
<td>Urban (21%), rural (13%)</td>
</tr>
</tbody>
</table>
Under-diagnosis of childhood asthma

• Only 33.5% had been diagnosed
• Of those with severe asthma, only 33.5% had been diagnosed

Of 561 with asthma, only 56% had ever been diagnosed

Baard CB, et.al ERJ Open Res 2021

Mpairwe H, et.al 2019
Under-diagnosis of asthma

Asthma and Pneumonia among Children Less Than Five Years with Acute Respiratory Symptoms in Mulago Hospital, Uganda: Evidence of Under-Diagnosis of Asthma

Rebecca Nantanda¹, James K. Tumwine², Grace Ndezi², Marianne S. Ostergaard²

1 CMM Health and Development Centre, Makerere University College of Health Sciences, Kampala, Uganda, 2 Department of Paediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda, 3 The Research Unit for General Practice and Section of General Practice, Department of Public Health, University of Copenhagen, Copenhagen, Denmark

41.2% (253/614) under-fives had asthma syndrome

Only 9.5% of them had a diagnosis of asthma

95.3% of them had been diagnosed as pneumonia and prescribed antibiotics
Common practices in diagnosis of asthma in children in LRS

• Many children with asthma symptoms only present for management of exacerbations

• Difficult to perform spirometry with severe exacerbations

• Most times the lung function lab is not in the same building/hospital

• High loss to follow up after management of exacerbations

• Many children are diagnosed based on presence of recurrent symptoms of cough, difficult breathing and wheezing but risk of misdiagnosis

• Use of trial of controllers as a diagnostic criteria is very common

• Loss to follow up after initiation of treatment is also very common

https://www.brit-thoracic.org.uk/qualityimprovement/guidelines/asthma/
Translation of the guidelines into clinical practice in LRS

Child aged 5 to 16 years with symptoms of asthma (wheeze* +/- cough +/- breathing difficulty)

- Perform Spirometry
  - Spirometry abnormal
    - Perform reversibility testing
      - BDR positive ≥12% and/or ≥200ml
        - Asthma confirmed
          - Consider asthma treatment review after 4-8 weeks
            - Repeat spirometry
              - Spirometry improved Symptoms improved
                - Asthma confirmed
              - Spirometry abnormal & Symptoms not improved
                - Asthma confirmed
        - FeNO ≥25ppb
          - Consider asthma treatment review after 4-8 weeks
            - Repeat spirometry
              - Spirometry improved Symptoms improved
                - Asthma confirmed
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        - Perform FeNO measurement
          - FeNO ≥25ppb
            - PEF variability ≥12%
              - Challenge test positive
                - Asthma confirmed
                - Referral for specialist opinion
            - Challenge test negative
              - Asthma unlikely
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            - PEF variability <12%
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                - Asthma confirmed
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            - Challenge test negative
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  - Spirometry normal
    - Perform FeNO measurement
      - FeNO ≥25ppb
        - Consider differential diagnoses
        - If symptoms persist refer for specialist opinion
      - FeNO <25ppb
        - Consider differential diagnoses
        - If symptoms persist refer for specialist opinion

*Wheeze* refers to the sound produced by air being forced through narrowed airways during expiration.
Lung function tests in sSA

Gaps in access to LFTs

• Availability of equipment, supplies and technical support

• Limited training opportunities

• Lack of skilled lung function technicians
  ▪ 192 trained spirometry technicians in 7 countries
  ▪ How many are in active practice?
  ▪ How many have had refresher training?

• Equipment maintenance support
Lung function tests in sSA

• Limited training opportunities/training programmes

• Availability of testing guidelines

• Limited research in Spirometry

• Limited scope of tests- most labs offer spirometry but not FeNO or bronchoprovocation tests

• Cost of Spirometry is not affordable
In Uganda,

- Spirometry equipment was available in only 24.4% of the 45 facilities surveyed
- All were urban-based, 34.8% public and 13.6% private
- Peak flow meters were available in only 6.7%
- Cost of Spirometry was 36.1USD equivalent to 27.8 days’ wages

In a study on asthma control in children,

- Only 8.2 % of 561 participants had ever had LFT done
- Only 0.4% had ever use a Peak flow meter at home

Kibirige et.al 2017, Mpaire H, et.al 2019
Other challenges

- Despite the documented high and increasing burden of asthma in children, the health system in Africa is still designed for acute care
- Lack of clear pathways for asthma care
- Very few asthma care clinics, overwhelmed
- Severe lack of specialists and other staff
More than half (52%) of primary care health workers are not comfortable in assessing and managing patients with chronic respiratory diseases.
Other key issues in the ERS guidelines

- Require at least 2 abnormal tests (Spirometry, BDR, FeNO, PEFR)
- If test is normal despite presence of symptoms, repeat the test- a normal test does not exclude asthma
  - Loss to follow up
  - Cost to the patients
  - Workload
  - Perception of the caregivers/patients
Proposed solutions

1. Research

• Baseline survey on LFTs- functional laboratories, human resource, costs and cost-savings

• Under and over-diagnosis attributable to lack of diagnostic services

• Implementation Research- Operationalizing the guidelines in different settings
  ▪ Feasibility in different settings
  ▪ Acceptability
  ▪ Costs
  ▪ Impact on asthma outcomes
2. Awareness and advocacy for better services for children with asthma

- Health care workers
- Care givers and patients
- Health Care planners and policy makers at all levels
Key messages

• Diagnosis of asthma in children is a big challenge in LRS in Africa

• Root causes of the challenges are multi-factorial

• The ERS guidelines will help to reduce the problem of under-diagnosis and over-diagnosis of asthma in children

• Need to have a strategy to operationalize the guidelines in different settings in Africa
THANK YOU