

UOG Journal Club: June 2015

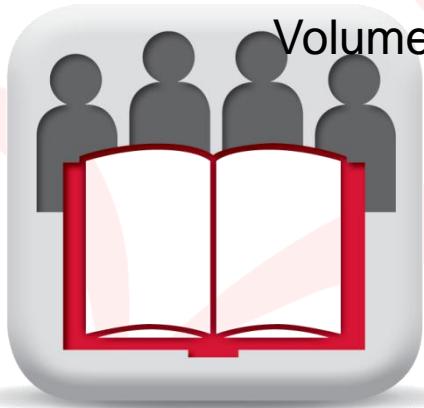
Prenatal diagnosis of critical congenital heart disease reduces risk of death from cardiovascular compromise prior to planned cardiac surgery: a meta-analysis

严重先天性心脏病的产前诊断可降低计划性心血管手术术前的死亡风险——Meta分析

BJ Holland, JA Myers and CR Woods Jr.

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Journal Club slides prepared by Dr Maddalena Morlando
(UOG Editor for Trainees)



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- Whether prenatal diagnosis improves the chance that a newborn with critical congenital heart disease will survive to undergo planned cardiac surgery is still debated
- 产前诊断是否能提高严重先天性心脏病的新生儿进行计划性心脏手术的存活率至今还存在争议
- Previous studies have focused on surgical and hospital outcomes and they have a number of limitations for assessing preoperative mortality:
- 先前的研究关注于手术和医疗结局，在评估术前死亡率存在许多局限

- Selection bias due to the exclusion of patients who died prior to surgery
- 排除了术前死亡的病人而存在的选择偏倚
- Small numbers of preoperative deaths
- 少量的术前死亡病例
- Heterogeneous patient populations with respect to anatomical diagnosis, the presence of known additional risk factors for mortality, and the family's desire to pursue cardiac surgery
- 基于解剖诊断、已知新增的死亡危险因素的存在和患者家属要求进行心脏手术而存在各种各样的患者人群

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Objective **研究目的**

The aim of this meta-analysis was to determine if prenatal diagnosis improves the chance that a newborn with critical congenital heart disease will survive to undergo planned cardiac surgery

Meta分析的目的在于研究产前诊断是否能够提高患有危重先天性心脏病新生儿进行计划性心脏手术的存活率

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Methods 方法

Eligibility criteria (PRISMA 2009 checklist - PICOS):

合格标准:

- **Participants:** newborns with critical congenital heart disease
- 参与者: 严重先天性心脏病新生儿
- **Interventions:** prenatal diagnosis of critical congenital heart disease
- 干预: 严重先天性心脏病的产前诊断
- **Comparisons:** detailed cardiac anatomy, presence of known additional risk factors for newborn mortality, parental desire to pursue cardiac surgery, detailed cause of death
- 对照: 详细的心脏解剖结构, 存在已知新增的新生儿死亡危险因素, 父母要求进行心脏手术, 详细的死亡原因
- **Outcomes:** preoperative mortality
- 结果: 术前死亡率
- **Study design:** meta-analysis
- 研究设计: 荟萃分析

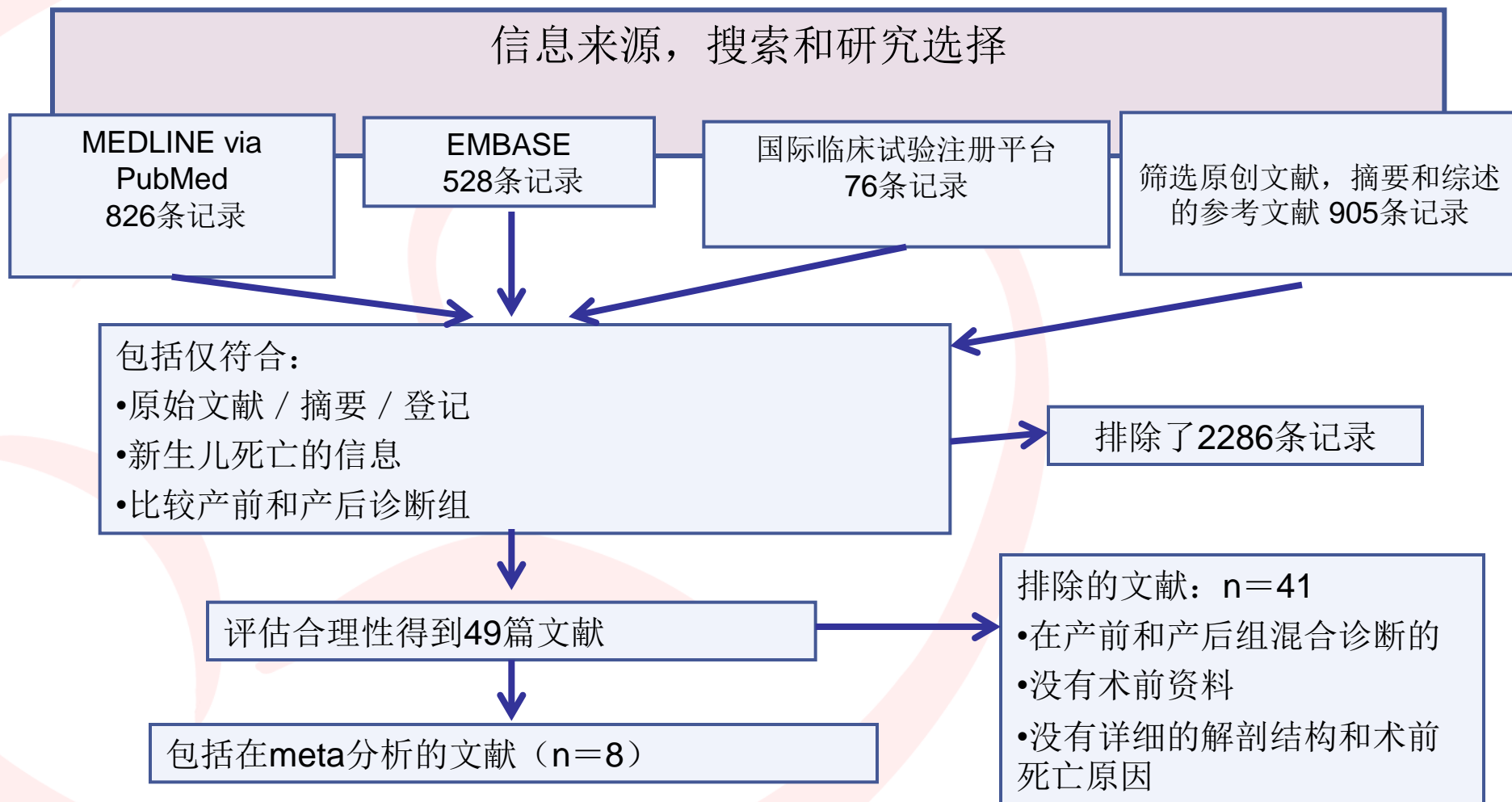
- **Search strategy:**
- MEDLINE, PubMed, EMBASE, The Cochrane Library, International Clinical Trials Registry Platform and the reference sections from identified original articles, abstracts and reviews.

搜索策略:

- MEDLINE, PubMed, EMBASE, The Cochrane Library, 国际临床试验注册平台, 来自确定的原始文献, 摘要和综述的参考文献。

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方法

Data items analyzed:

分析数据项目:

- 产前诊断的先天性心脏病
- 产后诊断的先天性心脏病
- 心脏解剖诊断
- 计划性心脏手术术前死亡的
- 心脏手术后存活
- 父母决定不做心脏手术
- 存在与死亡率升高相关的已知危险因素
- 死亡原因

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方法

统计分析

- 主要结果为术前死亡率
- 如果存在研究不均一性就采用随机效应模型
- $P < 0.1$ 或者 I^2 值 $> 50\%$ 为不均一性
- 结果以整体合并汇总统计95%CI的形式给出
- 采用Egger's测试评估合并死亡率，Harbord测试用于评价发表偏差
- 采用Newcastl-Ottawa 量表评估偏差危险

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8项研究一共包含了1373位病人：

- 297 (22%) 有产前诊断
- 1076 (78%) 有产后诊断

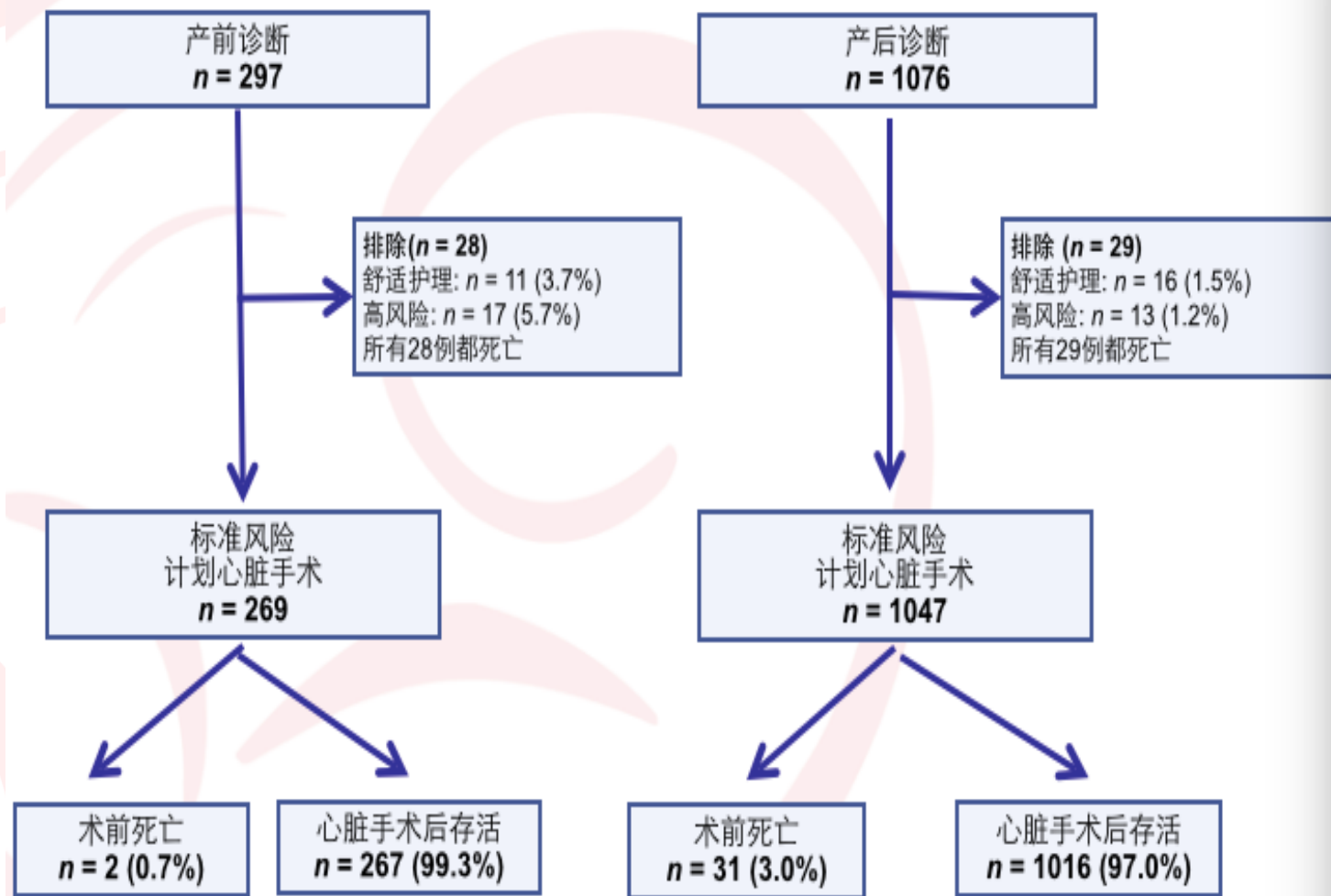
Study	Cardiac diagnosis	Number of patients (n)
Kumar (1999)	左心发育不良综合征	217
Kumar (1999)	D-大动脉转位	422
Eapen (1998)	严重左心梗阻	63
Kipps (2011)	左心发育不良综合征	87
Bonnet (1999)	D-大动脉转位	261
Franklin (2002)	主动脉缩窄	32
Tzifa (2007)	肺动脉闭锁	58
Swanson (2009)	永存动脉干	112
Raboison (2009)	D-大动脉转位	121
Total		1373

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结果

- 产前诊断的患者术前死亡的发生率为30/297（10.1%），而在产后诊断是60/1076（5.6%）
- 产前诊断死亡的患者的可能是产后诊断的两倍（汇总OR=1.90; 95% CI, 1.20-3.01）
- 产前诊断的的患者更趋于：
 - 高风险（n=17, 5.7% vs n=13, 1.2%）
 - 选择舒适护理（n=11, 3.7% vs n=16, 1.5%）
- 高风险病人和选择舒适护理的病人在进一步的研究中被排除；所有的这些病例死于新生儿期



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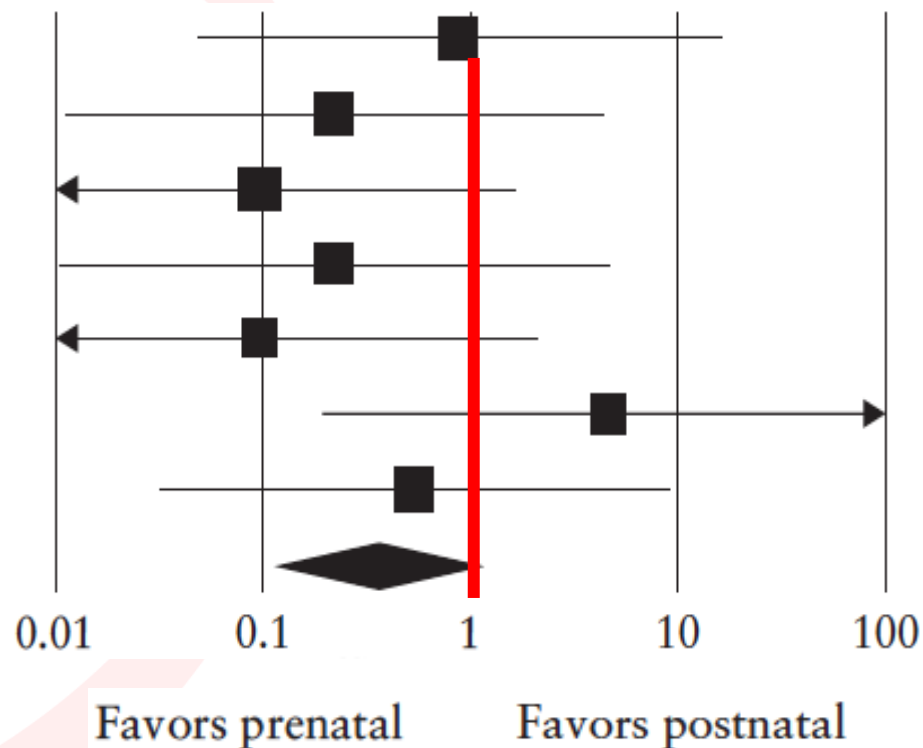
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结果

标准风险和计划心脏手术病人的分析

- 8项研究
- 产前诊断的术前死亡发生率为2/269 (0.7%)，产后诊断为31/1047 (3.0%)
- 产前诊断和产后诊断的病人的意向性治疗meta分析在术前死亡显示没有统计学显著性差异 (汇总OR=0.36; 95% CI, 0.12-1.12)

Odds ratio and 95% CI



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Results

并非所有产前诊断组的病人都得最理想的护理

- 一位产前诊断为D-TGA的病人未送达或接近能够进行球囊房间隔造口术的心脏中心。这位病人在出生3 h被转送到心脏中心加强护理单元。该婴儿在尝试心脏手术前死亡。
- **An ‘optimal care’ meta-analysis was performed on all patients with standard risk, planned cardiac surgery and optimal care**, being defined as delivery of newborns with a prenatal diagnosis of critical congenital heart disease at or near a hospital with specialized newborn cardiac care.
- “最佳护理” meta分析是具有标准风险、计划心脏手术和最佳护理的所有病人中进行，定义为分娩有产前诊断危重先天性心脏病新生儿的或靠近具有特殊的新生儿心脏护理的医院。
- The study with the single patient described above who did not receive optimal care was excluded from this analysis.
排除了没有接受最佳护理的单个患者。

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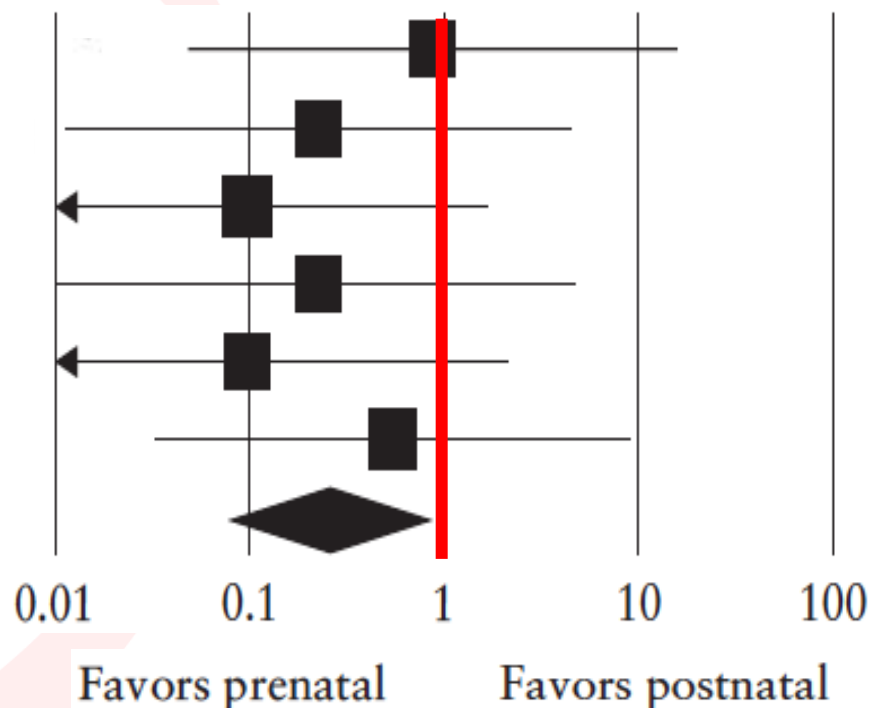
Holland et al., UOG 2015

结果

标准风险、计划心脏手术和最佳护理病人的分析

- 7项研究
- 产前诊断的术前死亡发生率为1/221 (0.5%)，产后诊断为31/974 (3.2%)
- 对于获得最佳护理、计划心脏手术和标准风险的病人，其产前诊断与少量术前死亡相关 (汇总OR=0.25; 95% CI, 0.08-0.84)

Odds ratio and 95% CI



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结果

Analysis of heterogeneity and publication bias

不均匀性和发表偏倚分析

- 在meta分析中没有观察到异质性 ($I^2 = 0.0\%$, $P = 0.859$)
- 包含的8项研究没有发表偏差的证据
- Egger's 和Harbord测试结果是非常重要的, 揭示了个体研究对汇总效果具有很大影响
- Newcastle-Ottawa评分表提示低偏差风险

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结论

危重先天性心脏病的产前诊断提升了新生儿的术前存活率

- 有标准风险和产前诊断的新生儿只要遵循了他们提供的最佳分娩时机进行计划心脏手术几乎都增加了存活机会
- 总体新生儿存活率的提高，鼓励加倍努力提高常规产检期间先天性心脏病的产前筛查。
- 研究中包括的少数死亡病例显示未来多中心合作能提供最有用的信息

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优势

- 此meta分析侧重于术前新生儿存活率
- 包含的研究是比较解剖诊断相同的病人
- 只合并了少量个体研究的病人
- 高风险和舒适护理的病人从meta分析中排除，以排除其他引起新生儿死亡的混淆作用
- 包含的研究没有观察到异质性
- 包含的研究不存在发表偏差

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不足

- 没有包含尸检诊断和远程转诊病人，这可能会低估了产前诊断的存活效益
- 意向治疗分析在新生儿死亡中没有显示显著降低，因其明显受到单个病人死亡的影响。单个病例的统计效果支持将来的研究要有更大的样本量
- 许多包含的研究在新生儿脉搏血氧筛查出现之前就已经完成。将来一些先天性心脏病的新生儿应该更早检测
- 只包含最危重先天性心脏病。已观察到的存活效益并不能应用于其他心脏缺陷。
- 8项研究都是回顾性研究，本质上具有不完整和不正确数据的可能性

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讨论要点

- 在常规产检期间，我们是否需要改善先天性心脏病的产前筛查？
- 我们是否应该考虑对超声医师培训做出改变？
- 我们是否需要更新超声检查的推荐？
- 我们应该改善胎儿超声心动图的准入？
- 在临床上做到这些改变需要多长时间和资源？