中国女性乳腺癌筛查与早诊早治指南(2021,北京)

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摘　要:乳腺癌是中国女性最常见的恶性肿瘤,发病率位居中国女性恶性肿瘤首位。国家癌症中心受国家卫生健康委员会疾病预防控制局委托,根据《世界卫生组织指南制定手册》制定本部女性乳腺癌筛查与早诊早治指南。制作系统评价流程参考 Cochrane 协作网的方法,证据质量与推荐强度的分级采用推荐意见分级的评估、制定及评价方法,并根据国际实践指南报告规范条目进行报告。在系统评价结果的基础上,结合中国国情,综合考虑了证据的利弊、证据的质量、筛查经济成本、多学科临床调查对象的反馈和面对面的专家共识意见,针对乳腺癌筛查与早诊早治中适宜人群、技术流程等进行循证推荐,旨在规范女性乳腺癌筛查与早诊早治实践,提升中国女性乳腺癌防控效果。

关键词:乳腺癌;女性;筛查;早诊早治;指南;中国
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China Guideline for the Screening and Early Detection of Female Breast Cancer(2021,Beijing)

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Abstract: Breast cancer ranks first in the incidence of female cancer in China. The guideline is commissioned and directed by the Bureau of Disease Control and Prevention of National Health Commission. Under the initiation of the National Cancer Center of China, a multidisciplinary guideline development group was established. The development of the guideline followed the principles and methods recommended by the World Health Organization. Among them, the method of Cochrane Collaboration is used to develop the systematic evaluation, GRADE method is adopted for the classification of evidence quality and recommendation strength, and the report is made according to the Reporting Items for Practice Guidelines in Healthcare item. Based on the most up-to-date evidence in breast cancer screening worldwide, as well as China's national conditions and practical experience in breast cancer screening, the guideline would include the screening population and technology, in order to enhance the effectiveness of female breast cancer screening prevention and control in China.

Key words: breast cancer; female; screening; early diagnosis and treatment; guideline; China

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一、引　言

乳腺癌是女性常见的恶性肿瘤，其发病率和死亡率分别位列我国女性恶性肿瘤的第 1 位和第 4 位。2015 年我国女性乳腺癌新发病例约 30.4 万例，占女性全部恶性肿瘤发病的 17.1%；死亡病例约 7.0 万例，占女性全部恶性肿瘤死亡的 8.2%[1-2]。近年来，随着我国人口老龄化的加速，工业化、城市化以及生活方式的改变，女性乳腺癌疾病负担日益加重[3-4]。提高早期乳腺癌的检出率并进行及时有效的治疗是降低乳腺癌死亡率的有效措施。多个国家（例如美国、德国、日本、澳大利亚等）已陆续开展人群乳腺癌筛查。我国现已开展包括乳腺癌筛查在内的多个国家重大公共卫生服务项目，如城市癌症早诊早治项目、全国农村妇女“两癌筛查”项目等，均取得了较好的社会效益[5-6]。

美国医师协会（American College of Physicians，ACP）、美国预防服务工作组（U.S. Preventive Services Task Force，USPSTF）、美国国家综合癌症网络（National Comprehensive Cancer Network，NCCN）、加拿大预防保健工作组（Canadian Task Force on Preventive Health Care，CTFPHC）等多个在世界上有影响力的学术组织和机构分别制定了各自的乳腺癌筛查指南[7-10]，中国抗癌协会也在 2019 年发布了《中国女性乳腺癌筛查指南》和《乳腺癌诊治指南与规范（2019 年版）》[11-12]。作为当前医疗实践中最常用的指导性文件，指南的发布与更新对提高应用决策的科学性和规范性发挥着重要的推动作用。高质量的指南是降低医疗成本和经济负担、改善医疗资源分布不均的有效工具，是规范医疗行为和提高医疗服务整体水平的重要手段[13-15]。为实现对潜在乳腺癌患者的早发现、早诊断、早治疗，提高筛查的科学性、可行性和适用性，制定符合我国国情的乳腺癌筛查与早诊早治指南是十分重要和必要的。

鉴于此，受国家卫生健康委员会疾病预防控制局的委托和指导，国家癌症中心按照循证实践指南制定的方法和步骤[16]，基于最新的研究证据，结合我国乳腺癌筛查实际情况，制定了《中国女性乳腺癌筛查与早诊早治指南（2021，北京）》（以下简称本指南）。

二、指南形成流程

本指南的设计与制定步骤参照世界卫生组织（World Health Organization，WHO）2014 年发布的《世界卫生组织指南制定手册》，并根据国际实践指南报告规范（Reporting Items for Practice Guidelines in Healthcare，RIGHT）和开发指南研究与评价工具（Appraisal of Guidelines REsearch and Evaluation Ⅱ，AGREE Ⅱ）进行报告[17-18]。

1. 指南发起机构与专家组成员：本指南由国家癌症中心发起。指南制定启动时间为 2020 年 4 月 1 日，定稿时间为 2020 年 12 月 23 日。

2. 指南工作组：本指南成立多学科工作组，主要涵盖肿瘤学、流行病学、超声学、乳腺内科、乳腺外科、放射治疗学、病理学、循证医学、卫生经济学、健康管理和政策研究等相关学科。证据的检索和评价由兰州大学和国家癌症中心合作完成。所有工作组成员均填写了利益声明表，与本指南不存在利益冲突。

3. 指南使用者与目标人群：本指南适用于各级医疗机构开展乳腺癌筛查工作。指南的使用者为各级医疗机构的医务工作者，包括影像科、乳腺外科等筛查相关学科医师及工作人员。指南推荐意见的应用目标人群为中国 40 岁及以上女性。

4. 临床问题的遴选和确定：本指南工作组通过系统查阅国内外乳腺癌筛查领域已发表的系统评价和指南，以及对全国 28 个省、自治区、直辖市各专业的 95 位临床医师开展第 1 轮问卷调研，初步拟定了 30 个临床问题。第 2 轮问卷调查邀请全国 50 位具备高级职称的临床医师对拟定临床问题进行重要性评价，并通过指南指导委员会会议，最终遴选出本指南拟解决的 16 个问题。

5. 证据的检索：指南制定工作组成立了证据检索与评价小组，针对最终纳入的关键临床问题，按照人群、干预、对照和结局（population，intervention，comparison and outcome，PICO）原则对其进行中英文数据库检索。具体检索数据库包括 PubMed、EMBASE、Cochrane Library、Web of Science、UpToDate、DynaMed、英国国家卫生与临床优化研究所（National Institute for Health and Care Excellence，NICE）、苏格兰校际指南网络（Scottish Intercollegiate Guide-

lines Network,SIGN)、中国知网、万方数据库、维普资讯网、中国生物医学文献数据库和 WHO 临床试验注册平台(International Clinical Trials Registry Platform,ICTRP),同时利用数据库的相似文献功能、追踪乳腺癌筛查相关综述和系统评价/Meta 分析的参考文献,继续补充检索。数据检索截止日期为 2020 年 6 月 26 日,检索策略见附件 A。

6. 证据的评价与分级:证据检索与评价小组运用系统评价偏倚风险评价工具对纳入的系统评价、Meta 分析进行偏倚风险评价[19-20]。使用 Cochrane Reviewer's Handbook 5.0.1 偏倚风险评价工具、诊断准确性研究的质量评价工具(Quality Assessment of Diagnostic Accuracy Studies,QUADAS-2) 和纽卡斯尔—渥太华量表(Newcastle-Ottawa Scale,NOS)等对相应类型的原始研究进行偏倚风险评价[21-23]。使用推荐意见分级的评估、制定及评价方法 (grading of recommendations assessment,development and evaluation,GRADE)对证据体进行分级[24-25],证据质量分级方法见表 1。评价过程由两人独立完成,若存在分歧,则共同讨论或咨询第三方解决。

7. 推荐意见的形成:专家组针对基于证据检索与评价小组提供的临床问题进行系统评价, 并基于证据给出推荐意见, 同时考虑我国患者的偏好与价值观、干预措施的成本和利弊后,提出了符合我国筛查实践的推荐意见, 分别于 2020 年 9 月 10 日和 2020 年 10 月 10 日进行 2 轮德尔菲法推荐意见调查,共收集到 166 条反馈建议,于 2020 年 11 月 13 日进行面对面商议并于 2020 年 12 月进一步修改,形成了本指南文本的推荐意见。本指南中的推荐强度指在一定程度上能够相对明确推荐意见的利弊,其中强(1):当前证据能够相对明确提示干预措施利大于弊或弊大于利;弱(2):当前证据尚不足以明确筛查的利弊,或提示利弊相当[26](表 1)。

8. 指南文稿的形成与外审: 本指南工作组参考 RIGHT 报告规范草拟指南文稿,内部审议后形成征求意见稿。通过在国家癌症中心组织的会议等方式公开征求意见,并送期刊外审的形式收集修改意见,根据反馈结果完善形成最终稿。

9. 指南的传播、实施与更新:指南发布后,本指南工作组将主要通过以下方式对指南进行传播和推广:①在相关学术会议中对指南进行解读;②有计划地在中国部分省份组织指南推广专场会议, 确保基层的癌症筛查工作人员充分了解并正确应用本指南;③在学术期刊和书籍出版社公开发表本指南;④通过媒体等进行推广。指南工作组将综合临床实践需求与证据现状,并参考更新版指南报告清单,对本指南进行更新。计划每 3 年对本指南的推荐意见进行更新。

三、关键问题及推荐意见

(一)流行病学特征

问题 1:我国女性乳腺癌发病率、死亡率和生存率情况

- ◆ 我国女性乳腺癌负担重, 是女性恶性肿瘤死亡的主要原因之一
- ◆ 我国女性乳腺癌发病率呈上升趋势, 并呈现出地区、年龄差异
- ◆ 我国女性乳腺癌死亡率呈上升趋势, 并呈现出地区、年龄差异
- ◆ 我国女性乳腺癌 5 年相对生存率近年来有所升高

2020 年中国女性乳腺癌发病率为 59.0/10 万,居全国女性恶性肿瘤发病谱首位[27]。国家癌症中心公布的数据显示,2015 年中国女性乳腺癌新发病例为 30.4 万例, 占女性恶性肿瘤新发病例数的 17.1%。不同地域女性乳腺癌发病率存在差异,总体

表 1 GRADE 证据质量与推荐强度分级

项目	内容
证据质量:指在多大程度上能够确信预测值的正确性	
高(A)	非常有把握:观察值接近真实值
中(B)	有中等把握:观察值有可能接近真实值,但亦有可能差别很大
低(C)	把握有限:观察值可能与真实值有较大差别
极低(D)	几乎没有把握:观察值可能与真实值有极大差别
推荐强度:指在一定程度上能够相对明确推荐意见的利弊	
强(1)	当前证据能够相对明确提示干预措施利大于弊或弊大于利
弱(2)	当前证据尚不足以明确筛查的利弊,或提示利弊相当

为城市乳腺癌发病率(54.3/10万)高于农村(33.6/10万),女性乳腺癌发病率在城市和农村分别位列女性恶性肿瘤发病率首位和第2位[2]。不同地区之间女性乳腺癌发病率也存在差异（东部>中部>西部),2015年中国东部地区女性新发乳腺癌14.6万例,发病率为57.4/10万；中部地区新发病例9.5万例,发病率为42.4/10万；西部地区新发病例6.3万例,发病率为32.7/10万,女性乳腺癌发病率分别位列东、中和西部地区女性恶性肿瘤发病的第1位、第1位和第2位[28]。我国女性乳腺癌发病率呈上升趋势[4,29],2000—2014年各年份肿瘤登记地区的女性乳腺癌年龄别发病率分析结果显示，各年龄组女性乳腺癌发病率均有所上升，乳腺癌发病高峰年龄主要集中在50~59岁之间[30]。

2020年中国女性乳腺癌死亡率为16.6/10万,居全国女性恶性肿瘤死亡谱第4位[27]。根据国家癌症中心公布的数据显示,2015年中国女性乳腺癌死亡病例7.0万例。不同地域女性乳腺癌死亡率存在差异,总体为城市女性乳腺癌死亡率(12.2/10万)高于农村(8.4/10万),女性乳腺癌死亡率在城市和农村分别位列女性恶性肿瘤死亡第3位和第6位[2]。不同地区之间女性乳腺癌死亡率也存在差异,2015年中国东部地区女性乳腺癌死亡病例3.1万例,死亡率为12.0/10万；中部地区死亡病例2.4万例,死亡率为10.8/10万;西部地区死亡病例1.6万例,死亡率为8.2/10万,女性乳腺癌死亡率在东、中和西部地区分别位列女性恶性肿瘤死亡的第4位、第4位和第5位[28]。我国女性乳腺癌死亡率呈上升趋势[4,31-32]。乳腺癌年龄别死亡率随年龄的增长而上升,在85岁及以上年龄组达到最高[29],国家癌症中心数据显示,2014年85岁及以上年龄组女性乳腺癌死亡率高达52.8/10万[33]。

2003—2015年全国17个肿瘤登记地区数据显示,女性乳腺癌5年合计相对生存率从73.1%(95%CI:71.2%~75.0%)增长至82.0%(95%CI:81.0%~83.0%);城市地区和农村地区2012—2015年女性乳腺癌5年相对生存率分别为84.9%和72.9%[34]。

问题2:乳腺癌相关危险因素和保护因素

危险因素

- ◆ 部分良性乳腺疾病患者的乳腺癌发病风险高
- ◆ 子宫内膜异位症增加乳腺癌的发病风险
- ◆ 高内源性雌激素水平会增加乳腺癌的发病风险
- ◆ 特定的月经生育因素与乳腺癌发病相关
- ◆ 乳腺癌家族史是乳腺癌的危险因素
- ◆ 乳腺癌易感基因 *BRCA1/2* 突变与乳腺癌发病相关
- ◆ 肥胖是乳腺癌的危险因素
- ◆ 大量饮酒是乳腺癌的危险因素
- ◆ 吸烟是乳腺癌的危险因素
- ◆ 暴露于治疗性电离辐射的女性乳腺癌发病风险增高

保护因素

- ◆ 母乳喂养可以降低乳腺癌的发病风险
- ◆ 适宜的体育锻炼可以降低乳腺癌的发病风险

1. 目前研究已明确的危险因素如下:

(1)良性乳腺疾病:部分良性乳腺疾病(例如乳腺囊肿和乳腺上皮不典型增生等）患者的乳腺癌发病风险增高[35-37]。李红等[35]对2002—2012年发表的良性乳腺疾病与乳腺癌关系的7项研究进行Meta分析,结果显示,患有良性乳腺疾病者患乳腺癌的风险是无良性乳腺疾病者的2.24倍（OR=2.24,95%CI:1.23~4.09)。戴琼等[36]对1997—2007年发表的良性乳腺疾病与乳腺癌关系的31项研究(16 611例)进行Meta分析,结果显示,患良性乳腺疾病者患乳腺癌的风险是无良性乳腺疾病者的1.95倍（OR=1.95,95%CI:1.59~2.38)。裴广军等[37]对1996—2006年发表的良性乳腺疾病与乳腺癌关系的12项病例对照研究进行Meta分析,结果显示,患良性乳腺疾病者患乳腺癌风险是无良性乳腺疾病者的2.62倍(OR=2.62,95%CI:2.03~3.38)。

(2)子宫内膜异位症:子宫内膜异位症是乳腺癌的危险因素。Kvaskoff等[38]对1993—2019年子宫内膜异位症和乳腺癌关系的20项研究进行Meta分析,结果显示,患子宫内膜异位症者患乳腺癌的风险是无子宫内膜异位症者的1.04倍（RR=1.04,95%CI:1.00~1.09)。

(3)高内源性雌激素水平:无论是绝经前还是绝经后女性，高内源性雌激素水平均会增加乳腺癌发病风险。Key等[39]对18项前瞻性研究进行的Meta分析,以及Farhat等[40]的研究表明,对于绝经后女

性，激素水平上升与乳腺癌发病风险呈正相关。Key等[41]汇总分析了7项前瞻性研究，共纳入767例绝经前乳腺癌和1699名女性匹配对照者，结果显示，乳腺癌发病风险与雌二醇（OR=1.19，95%CI：1.06~1.35）、游离雌二醇（OR=1.17，95%CI：1.03~1.33）、雌激素酮（OR=1.27，95%CI：1.05~1.54）、雄烯二酮（OR=1.30，95%CI：1.10~1.55）、硫酸脱氢表雄酮（OR=1.17，95%CI：1.04~1.32）和睾酮（OR=1.18，95%CI：1.03~1.35）浓度呈正相关。

（4）月经生育因素：①初潮较早或绝经较晚：初潮年龄较早与乳腺癌发病风险较高有关。15岁或之后初潮的女性患雌激素受体/孕激素受体阳性乳腺癌的风险低于13岁之前初潮的女性（HR=0.76，95%CI：0.68~0.85）[42]。Cui等[43]进行的一项基于美国人群的病例对照研究显示，初潮年龄≥14岁患乳腺癌的风险降低（OR=0.70，95%CI：0.55~0.88）。一项纳入117项研究的个体病例数据Meta分析结果显示，初潮每推迟1年，乳腺癌发病风险下降5%[44]。此外，一项纳入了51篇文献的研究结果显示，在从未接受过激素治疗的人群中，绝经年龄每推迟1年，患乳腺癌的相对危险度增加3%（RR=1.03，95%CI：1.02~1.03）[45]。②未经产与初次妊娠的年龄较高：未经产和初次妊娠较晚的女性患乳腺癌的风险增加。一项研究显示，未经产女性患乳腺癌的风险是经产妇的1.32倍（OR=1.32，95%CI：1.06~1.63）[43]。在绝经期或接近绝经期的女性中，与未经产女性相比，首次生产年龄为20岁、25岁和35岁的女性乳腺癌的累积发病率（直到70岁）分别降低20%、10%和升高5%[44]。③流产：一篇针对有人工流产史中国女性的Meta分析共纳入36篇文献，结果显示，与没有人工流产史的女性相比，人工流产使其患乳腺癌的风险增加44%（OR=1.44，95%CI：1.29~1.59），对于人工流产达到两次或两次以上的女性，患乳腺癌风险分别增加76%和89%[46]。

（5）乳腺癌家族史：Nindrea等[47]对纳入的10项研究进行Meta分析，结果显示，乳腺癌家族史人群患乳腺癌风险为正常人群的3.34倍（OR=3.34，95%CI：2.68~4.15）；Vishwakarma等[48]对纳入的21 511例乳腺癌患者进行分析，结果显示，有乳腺癌家族史的人群乳腺癌发病风险为健康人群的5.33倍（OR=5.33，95%CI：2.89~9.82）。

（6）基因突变：乳腺癌易感基因（breast cancer susceptibility genes，*BRCA*）增加乳腺癌发病风险。具有*BRCA*1/2致病性突变的患者发生乳腺癌、卵巢癌及其他癌症的风险增加。对于*BRCA1*突变携带者，≤70岁时乳腺癌累积风险为55%~70%，*BRCA2*突变携带者的相应累积风险为45%~70%。此外发现，*BRCA1*突变携带者从成年早期到30~40岁时的乳腺癌发生率升高，*BRCA2*突变携带者从成年早期到40~50岁时的乳腺癌发生率升高，此后至80岁为平台期，发生率为20~30/1000人年[49-52]。与*BRCA*2突变携带者或*BRCA*1/2突变阴性者相比，*BRCA1*突变携带者更可能发生三阴性乳腺癌[53-54]。Guo等[55]在一项Meta分析中指出，*BRCA1*启动子高甲基化人群患乳腺癌的风险是一般人群的1.76倍（HR=1.76，95%CI：1.15~2.68）。

（7）肥胖：一项纳入了12项观察性研究的系统评价和Meta分析结果显示，在队列研究中脂肪含量最高的人群患乳腺癌风险是脂肪含量最低的人群的1.44倍（RR=1.44，95%CI：1.33~1.56）[56]。世界癌症研究基金会（World Cancer Research Fund，WCRF）和美洲癌症研究所（American Institute for Cancer Research，AICR）在2018年发布的癌症预防报告（第3版）[57]中汇总了肥胖与绝经前或绝经后女性乳腺癌发病风险的相关证据，大量流行病学证据和剂量—反应关系分析支持同样的结论，即肥胖会增加绝经后乳腺癌发病风险。

（8）生活方式因素：①饮酒：饮酒人群的乳腺癌发病风险增高[57-63]。WCRF/ AICR[57]共纳入10项研究对绝经前乳腺癌发病风险进行剂量—反应Meta分析，结果显示，每天摄入10g酒精可使乳腺癌发病风险增加5%（RR=1.05，95%CI：1.02~1.08）；对绝经后乳腺癌发病风险的剂量—反应Meta分析纳入22项研究，结果显示，每天摄入10g酒精可使乳腺癌发病风险增加9%（RR=1.09，95%CI：1.07~1.12）。陶苹等[63]对纳入的27项研究进行Meta分析，结果显示，有饮酒史人群患乳腺癌风险是无饮酒史人群的1.16倍（OR=1.16，95%CI：1.01~1.32）。Bagnardi等[58]对纳入的118项研究进行Meta分析发现，重度饮酒人群患乳腺癌风险是不饮酒和偶尔饮酒人群的1.61倍（RR=1.61，95%CI：1.33~1.94）。②吸烟：吸烟人群乳腺癌的发病风险增高[62-66]。美国卫生与公众服务部

于2014年系统汇总了吸烟与乳腺癌发病风险的相关证据[64]，纳入22项队列研究和27项病例对照研究，结果显示，曾经吸烟使乳腺癌发病风险升高10%。吸烟时间长(20年或以上)，每天吸烟量多(20支或以上)，则使乳腺癌发病风险显着增加13%~16%。陶苹等[63]对纳入的27项研究进行Meta分析，结果显示，有吸烟史人群患乳腺癌风险是无吸烟史人群的1.50倍(OR=1.50，95%CI：1.03~2.20)。Gaudet等[65]在美国癌症协会癌症预防研究的一项队列研究中发现，正在吸烟人群乳腺癌发病率是非吸烟人群的1.24倍(HR=1.24，95%CI：1.07~1.42)；有吸烟史人群是非吸烟人群的1.13倍(HR=1.13，95%CI：1.06~1.21)。

(9)暴露于治疗性电离辐射：暴露于治疗性电离辐射的女性患乳腺癌的风险增高[67-69]。Ron等[67]的研究显示，行多次胸部透视检查的女性肺结核患者患乳腺癌的风险增加。年轻时胸部暴露于电离辐射如接受过放射治疗的霍奇金淋巴瘤的女性，其患乳腺癌的风险增加，且女童肿瘤患者接受高剂量放疗后乳腺癌标化发病率比（standardized incidence ratio，SIR)为24.20(95%CI：20.70~28.30)[68]。另有一项研究显示，乳腺癌的发病风险随胸部放射剂量呈线性增加，与乳腺癌发病风险相关的电离辐射因素包括照射时的年龄、照射持续时间和辐射剂量等[69]。

2. 目前研究已明确的保护因素如下：

(1)母乳喂养：现有研究表明母乳喂养可以降低乳腺癌的发病风险[70-73]。一项评估母乳喂养对孕产妇健康结果影响的系统评价提示[70]，12个月母乳喂养可使乳腺癌的发病风险降低26%(OR=0.74，95%CI：0.69~0.79)，说明母乳喂养是乳腺癌的保护因素。与从不母乳喂养者相比，曾经进行母乳喂养者乳腺癌发病风险下降22%(OR=0.78，95%CI：0.74~0.82)，母乳喂养少于6个月和母乳喂养6~12个月者乳腺癌发病风险分别降低7%(OR=0.93，95%CI：0.88~0.99)和9%(OR=0.91，95%CI：0.87~0.96)。Victora等[71]的研究显示，母乳喂养可以预防乳腺癌，将母乳喂养普及化后，每年可减少20 000名因乳腺癌死亡患者。Shamshirian等[72]的Meta分析结果显示，13~24个月的母乳喂养是乳腺癌的保护因素（OR=0.68，95%CI：0.46~0.90)。一项纳入24篇研究的Meta分析结果提示，累计母乳喂养较长时间，与乳腺癌的发病风险呈负相关(RR=0.47，95%CI：0.37~0.60)[73]。

(2)体育锻炼：流行病学研究证据显示，适宜的体育锻炼可以降低女性乳腺癌的发病风险[57，74-75]。WCRF/AICR在2018年发布的癌症预防报告（第3版)[57] 共纳入4项研究对体育锻炼和绝经前乳腺癌发病风险进行Meta分析，结果无统计学差异(RR=0.93，95%CI：0.79~1.08)，体育锻炼对降低绝经前乳腺癌发病风险证据有限；在体育锻炼对绝经后乳腺癌发病风险影响的Meta分析中，共纳入8项研究，结果显示，高水平体育锻炼可使绝经后乳腺癌发病风险影响降低13%(RR=0.87，95%CI：0.79~0.96)。McTiernan等[74]的研究显示，与缺乏体育锻炼的女性相比，定期进行体育锻炼的女性乳腺癌的发病风险降低14%(RR=0.86，95%CI：0.78~0.95)。2016年的一篇针对38项前瞻性研究的Meta分析提示，与缺乏体育锻炼的女性相比，积极进行体育锻炼的女性乳腺癌发病风险下降12%(RR=0.88，95%CI：0.85~0.90)[75]。

(二)结局和定义

问题3：筛查相关乳腺癌病理分型和TNM解剖学分期

- 乳腺癌的组织学分型包括：①非浸润性癌：导管原位癌、小叶原位癌；②浸润性癌：浸润性癌非特殊型（no special type，NST)、浸润性小叶癌、小管癌、黏液癌等
- 根据美国癌症联合会TNM分期系统(第8版)，乳腺癌分为0期、Ⅰ期、Ⅱ期、Ⅲ期和Ⅳ期

乳腺癌的组织学分型推荐采用WHO乳腺肿瘤分类标准(2019年版)[76]。

乳腺癌解剖学分期系统推荐应用美国癌症联合会(American Joint Committee on Cancer，AJCC)第8版[77]，见表2。细化定义如下：

(1)原发性肿瘤(T)：T_X：原发性肿瘤无法评估；T_0：无原发性肿瘤证据；T_{is}：原位癌；T_1：肿瘤最大径≤20 mm；T_2：肿瘤最大径>20 mm但≤50 mm；T_3：肿瘤最大径>50 mm；T_4：肿瘤直接侵袭胸壁和(或)皮肤(溃疡或肉眼可见的皮肤结节)，不论大小。

(2)区域淋巴结(N)：pN_X：区域淋巴结无法评估(先前已切除，或未切除进行病理学检查)；pN_0：无区域淋巴结转移证据；pN_{1mi}：微转移(单枚淋巴结单张肿瘤切片中肿瘤，最大径>0.2mm和(或)多于200个

表 2　美国癌症联合会 TNM 解剖学分期对应表

TNM 分期	T	N	M
0	T_{is}	N_0	M_0
ⅠA	T_1	N_0	M_0
ⅠB	T_0	N_{1mi}	M_0
	T_1	N_{1mi}	M_0
ⅡA	T_0	N_1	M_0
	T_1	N_1	M_0
	T_2	N_0	M_0
ⅡB	T_2	N_1	M_0
	T_3	N_0	M_0
ⅢA	T_0	N_2	M_0
	T_1	N_2	M_0
	T_2	N_2	M_0
	T_3	N_1	M_0
	T_3	N_2	M_0
ⅢB	T_4	N_0	M_0
	T_4	N_1	M_0
	T_4	N_2	M_0
ⅢC	任何 T	N_3	M_0
Ⅳ	任何 T	任何 N	M_1

细胞，但≤2.0mm）；pN_{1a}：1~3 枚腋窝淋巴结转移，至少 1 枚转移灶>2.0 mm；pN_{1b}：在没有腋窝淋巴结转移的情况下，同侧内乳前哨淋巴结转移，且转移灶>0.2mm，孤立的肿瘤细胞群除外；pN_{1c}：同时出现 pN_{1a} 和 pN_{1b}；pN_2：4~9 枚腋窝淋巴结转移，或影像学检查显示同侧内乳淋巴结转移而无腋窝淋巴结转移；pN_3：10 枚或更多腋窝淋巴结转移（至少 1 枚转移灶>2.0mm）；或锁骨下淋巴结（属第Ⅲ水平腋窝淋巴结）转移（pN_{3a}）；或影像学检查显示同侧内乳淋巴结转移，伴 1 枚或多枚Ⅰ、Ⅱ级腋窝淋巴结转移；或 3 枚以上腋窝淋巴结转移，以及前哨淋巴结活检证实但临床未发现的内乳淋巴结微转移灶或宏转移灶（pN_{3b}）；或同侧锁骨上淋巴结转移（pN_{3c}）。

（3）远处转移（M）：M_0：没有远处转移的临床或放射影像学证据；M_1：临床和放射影像学方法确定和（或）组织学证实存在>0.2mm 的远处转移灶。

问题 4：乳腺早期癌和癌前病变定义

- 乳腺早期癌指肿瘤直径<2cm，同侧腋窝淋巴结未见转移，且无远处转移
- 乳腺癌前病变包括小叶肿瘤（不典型小叶增生）、柱状细胞病变（扁平上皮不典型增生）和导管上皮不典型增生

早期乳腺癌和癌前病变定义主要参考来源包括 WHO 乳腺肿瘤分类（2019 年版）、中国女性乳腺癌筛查指南和中国抗癌协会乳腺癌诊治指南与规范（2019 年版）等多部国内外指南和专家共识[11-12,76]。

问题 5：筛查危害

- 筛查的危害是指与未筛查相比，个人或群体在参与筛查过程中产生的任何负面效应
- 过度诊断是指发现一种病变，即便它没有被诊断，也不会导致疾病发病率或死亡率的增加。假阳性是指根据筛查结果而推荐进行后续其他诊断性检查（包括进一步的影像学检查或组织取样检查），但在其后 1 年内未查出乳腺癌的情况；以及部分被诊断的恶性肿瘤，即使未接受临床治疗，终生也不会死于该恶性肿瘤的情况。
- 假阳性结果导致的压力：筛查个体得到假阳性结果后由于压力导致产生的焦虑、抑郁、沮丧等负面情绪
- 其他：乳腺 X 线检查所带来的躯体不适或疼痛导致人群筛查依从性降低
- 假阴性漏诊导致的负面效应

乳腺癌筛查危害主要参考 UpToDate 数据库《乳腺癌筛查的策略与推荐》[78]、《乳腺癌筛查：效果和危害的证据》[79] 以及 NCCN 和 USPSTF 发布的乳腺癌筛查指南[7,10]。具体包括：

（1）筛查的危害：乳腺癌筛查的危害包括过度诊断、假阳性结果、患者焦虑和不必要的治疗及其风险。乳腺癌筛查最严重的危害是过度诊断、假阳性结果。

（2）过度诊断：筛查的过度诊断是指通过筛查手段发现的早期癌症患者，其中部分癌症并不会继续生长、转移并导致患者死亡。这些患者如果不通过筛查发现，就不会在临床上出现有重要意义的疾病的诊断。过度诊断会导致不必要的检查和治疗，以及癌症诊断和治疗的心理负担及其他后果。在所有诊断为乳腺癌的女性中，过度诊断率从≤10%到>50%不等[80-81]。这些差异可能来源于研究设计不同，比如各研究纳入的研究对象不同（如是否纳入乳腺导管内原位癌、纳入研究的年龄段），使用的测量和估算的方法不同等。过度诊断使某些患者接受了针对恶性

肿瘤的治疗，但恶性肿瘤未被发现也不会造成伤害，从而使得筛查既带来不利影响（躯体和心理）也未降低死亡率。

（3）假阳性结果：增加假阳性风险的因素包括：年轻、乳腺密度高、乳腺癌家族史或个人史、既往乳腺活检、正在使用雌激素、较短的筛查间隔、未与之前检查结果对比以及放射科医师个人的过度解读倾向[82-83]。假阳性结果在较年轻女性中更常见，因为这类人群中乳腺X线检查的特异性较低[84]。此外，因为乳腺癌常规筛查推荐每年或隔年进行复查，所以假阳性风险会随着复查频率而升高，并且相较于每2年1次的筛查，每年1次的筛查会使这一风险升高更快[85]。

（4）假阳性结果相关性焦虑：一项Meta分析显示，乳腺X线检查结果为假阳性后的焦虑是针对乳腺癌和乳腺X线检查，不会导致广泛性焦虑障碍[83]。有关假阳性乳腺筛查结果对以后筛查行为的影响，报道结果各异，如美国女性在出现一次假阳性筛查结果后进行常规筛查的可能性更高，但假阳性筛查结果对欧洲女性没有影响[83]。虽然乳腺X线检查出现假阳性结果可能导致对卫生保健资源的浪费[86]，但有关假阳性结果对医疗的信任度和卫生保健服务利用情况的影响还需进一步研究。

（5）辐射：如果每年乳腺筛查中接受一次乳腺X线检查，据估计，一生中辐射诱导恶性肿瘤导致的女性死亡率为16/10万[87]。乳房较大的女性发生辐射诱导乳腺癌的风险可能更高。

（6）不适：由于需要挤压乳房以获取满意的图像，乳腺X线检查筛查可引起不适或疼痛。目前有关减轻不适方法的高质量研究很少[88]。一项随机试验纳入了操作很可能引发其疼痛的女性，结果显示，在乳房和胸壁局部涂敷4%利多卡因凝胶可减少不适，但对乙酰氨基酚或布洛芬前期用药则没有这种效果[89]。减轻不适感可增加患者返回进行下一次筛查的意愿。

（7）假阴性结果导致的负面效应：由于筛查的手段对于乳腺癌检出概率并不能达到百分之百[90]。

（三）筛查人群风险分类

问题6：一般风险人群定义

◆ 推荐意见：一般风险人群：乳腺癌一般风险女性即除了乳腺癌高风险人群（见问题7）以外的所有适龄女性

问题7：高风险人群定义

◆ 推荐意见：高风险人群：符合下列（A）、（B）和（C）任意条件的女性为乳腺癌高风险人群

A 有遗传家族史，即具备以下任意一项者：
（1）一级亲属有乳腺癌或卵巢癌史；
（2）二级亲属50岁前，患乳腺癌2人及以上；
（3）二级亲属50岁前，患卵巢癌2人及以上；
（4）至少1位一级亲属携带已知*BRCA*1/2基因致病性遗传突变；或自身携带*BRCA*1/2基因致病性遗传突变。

B 具备以下任意一项者：
（1）月经初潮年龄≤12岁；
（2）绝经年龄≥55岁；
（3）有乳腺活检史或乳腺良性疾病手术史，或病理证实的乳腺（小叶或导管）不典型增生病史；
（4）使用“雌孕激素联合”的激素替代治疗不少于半年；
（5）45岁后乳腺X线检查提示乳腺实质（或乳房密度）类型为不均匀致密型或致密型。

C 具备以下任意两项者：
（1）无哺乳史或哺乳时间<4个月；
（2）无活产史（含从未生育、流产、死胎）或初次活产年龄≥30岁；
（3）仅使用“雌激素”的激素替代治疗不少于半年；
（4）流产（含自然流产和人工流产）≥2次。

注：一级亲属指母亲、女儿以及姐妹；二级亲属指姑、姨、祖母和外祖母。

一般风险人群（average-risk population）指患癌风险处于平均或较低水平的人群。目前关于一般风险人群的定义在全球各国家所指定的乳腺癌筛查指南或共识中的标准有一定的差异，详见表3。大多数指南将乳腺癌终生风险作为判定风险程度的一个重要指标。例如，国际癌症研究机构（International Agency for Research on Cancer，IARC）[91]、NICE [92]、美国放射学会（American College of Radiology，ACR）[93]和乳腺家族史外科协会指南小组（Association of Breast Surgery Family History Guidelines Panel，ABSFHGP）[94]均将乳腺癌终生风险作为判定风险程度的一个重要指标，对于有乳腺癌、卵巢癌、输卵管癌

或腹膜癌家族史的女性，USPSTF 推荐了 5 种简明筛查工具，用于确定哪些女性需要接受遗传咨询、致病型 *BRCA1* 和 *BRCA2* 基因突变检测以及考虑化学预防、预防性手术和筛查推荐[95-96]。推荐的模型包括：安大略家族史风险评估量表[97]、曼彻斯特评分系统[98]、转诊筛查量表[99]、系谱评估量表[100]和 7 条目家族史筛查量表[101]。

全球各国家的乳腺癌筛查指南中对于高风险人群（high-risk population）的定义或标准有一定差异，见表 4。除奥克兰放射协会（Auckland Radiology Group，ARG）[104]外，其他指南都将发生乳腺癌的终生风险作为衡量高危风险人群的一个标准，但仍有不同。IARC 的指南[91]中指出欧洲和美国的标准分别是 30%和 20%，加拿大安大略癌症治疗中心（Cancer Care Ontario，CCO）[105]与 ABSFHGP[94]将该标准权重同定为 25%。乳腺癌家族史、胸部放射治疗史、携带 *BRCA* 基因的人群及其一级亲属被 ACR[93]、CCO[105]和 ARG[104]定义为高风险人群。

（四）乳腺癌筛查起始年龄及筛查频次

问题 8：乳腺癌筛查起始年龄

◆ 推荐意见：对于一般风险人群，推荐从 45 岁开始进行乳腺癌筛查（强推荐，GRADE 证据分级：中）

表 3　国外指南中对乳腺癌一般风险人群定义汇总

提出组织/机构	时间	适用人群	一般风险人群定义
国际癌症研究机构[91]	2015	通用	乳腺癌终生风险<15%
英国国家卫生与临床优化研究所[92]	2017	通用	乳腺癌终生风险<17%
美国放射协会[93]	2017	美国	乳腺癌终生风险<15%
乳腺家族史外科协会指南小组[94]	2004	英国	乳腺癌终生风险<1:6
美国癌症协会[102]	2015	美国	无以下危险因素的人群： · 乳腺癌个人史 · 确认或疑似增加患乳腺癌风险的女性（例如 *BRCA*1/2）基因突变 · 曾对胸部进行过放射治疗的病史
美国医师学会[103]	2019	美国	· 无乳腺癌个人史 · 无高危乳腺病变的诊断 · 儿童时期未接受过胸部放射治疗

注：*BRCA*：乳腺癌易感基因

表 4　国外指南中对乳腺癌高风险人群定义汇总

提出组织/机构	时间	适用人群	高危风险人群定义
国际癌症研究机构[91]	2015	通用	美国定义为发生乳腺癌的终生风险>20%，欧洲定义为发生乳腺癌的终生风险>30%
英国国家卫生与临床优化研究所[92]	2017	通用	发生乳腺癌的终生风险>30%
美国放射协会[93]	2017	美国	· 具备遗传因素导致患乳腺癌风险增加的女性 · 有胸部放疗史（30 岁之前累积放疗剂量≥10Gy） · 40 岁以前被诊断为乳腺癌、导管上皮不典型增生或小叶肿瘤者 · 个人发生乳腺癌的终生风险>20%
乳腺家族史外科协会指南小组[94]	2004	英国	乳腺癌终生风险>1:4
奥克兰放射协会[104]	2007	奥克兰	· 家族中有直系亲属曾患乳腺癌 · 有胸部放射治疗史 · 乳腺导管上皮不典型增生 · 活检时发现小叶原位癌 · 有乳腺癌疾病史
加拿大安大略癌症治疗中心[105]	2019	加拿大	· 携带 *BRCA* 等基因 · 一级亲属携带有已知 *BRCA* 基因致病性遗传突变 · 有乳腺癌病史或既往活检中发现高危标志物 · 有胸部放射治疗史 · 有乳腺癌家族史且个人发生乳腺癌的终生风险>25%

注：*BRCA*：乳腺癌易感基因

◆ 推荐意见：对于高风险人群，推荐从 40 岁开始进行乳腺癌筛查（强推荐，GRADE 证据分级：中）

推荐说明：根据我国国家癌症中心肿瘤登记数据，2015 年，我国女性 45 岁起乳腺癌发病率呈上升趋势且维持在较高水平（图 1），比西方女性乳腺癌高发年龄提前。出现 45~55 岁这个特定发病高峰的原因，有学者认为是出生队列效应影响。中国和日本等多数国家出生队列研究中普遍存在着月经和生育模式变化，加之其他生活方式和环境因素影响，这一效应使得乳腺癌发病风险因素在年龄较轻的女性中凸显[106-107]。

本指南证据检索与评价小组于 2020 年开展系统评价，对参与乳腺癌筛查人群的乳腺癌死亡率和乳腺癌发病率效果进行评价，共纳入 8 个试验[108-115]，结果显示：①乳腺癌死亡率（n=671 346，8 个试验）：40~49 岁年龄段筛查是否获益不确定（RR=0.89，95CI%：0.79~1.00），50~69 岁年龄段获益（50~59 岁：RR=0.84，95%CI：0.73~0.96；60~69 岁：RR=0.71，95%CI：0.59~0.85），70~74 岁年龄段筛查是否获益不确定（RR=0.80，95%CI：0.52~1.22）。②晚期乳腺癌发病率（n=444 744，4 个试验）：40~49 岁年龄段晚期乳腺癌发病率无差异（RR=0.98，95%CI：0.74~1.28），对 50 岁以上人群筛查可降低晚期乳腺癌发病率（RR=0.62，95%CI：0.47~0.80）。证据级别均评为中等质量。鉴于所纳入随机对照试验均源于欧美国家，结果外推需谨慎，而我国暂缺乏乳腺癌筛查大型人群随机对照试验结果。该指南制定过程中专家共识会议中综合考虑我国女性乳腺癌发病年龄流行病学特征、相关危险因素和卫生经济学现况，推荐一般风险人群从 45 岁开始进行乳腺癌常规筛查，高风险人群筛查起始年龄提前至 40 岁。

问题 9：乳腺癌筛查频次

◆ 推荐意见：对于一般风险人群，推荐每 1~2 年进行 1 次乳腺癌筛查（强推荐，GRADE 证据分级：中）

◆ 推荐意见：对于高风险人群，推荐每年进行 1 次乳腺癌筛查（强推荐，GRADE 证据分级：中）

推荐说明：本指南证据检索与评价小组于 2020 年开展了系统评价，对乳腺癌筛查频次对人群乳腺癌死亡率、乳腺癌发病率、累积假阳性召回率和累积假阳性有创召回率的影响进行评价，共纳入 13 个研究[116-128]。结果显示：①在乳腺癌死亡率比较中（n=934 113，4 个研究[117,120,125-126]），筛查频次为 2 年 1 次或 3 年 1 次与 1 年 1 次结果差异无统计学意义（RR=1.04，95%CI：0.93~1.16）；对于 75 岁以上人群，与 2 年筛查 1 次相比，筛查间隔>2 年组死亡风险增加（RR=1.87，95%CI：1.34~2.61）。②在乳腺癌发病率比较中（n=1 278 256，7 个研究），筛查频次为 2 年 1 次时，乳腺癌发病率相比 1 年 1 次时增高（RR=1.07，95%CI：1.04~1.10）。③在累积假阳性召回率和累积假阳性有创召回率的比较中（n=1 508 136，6 个

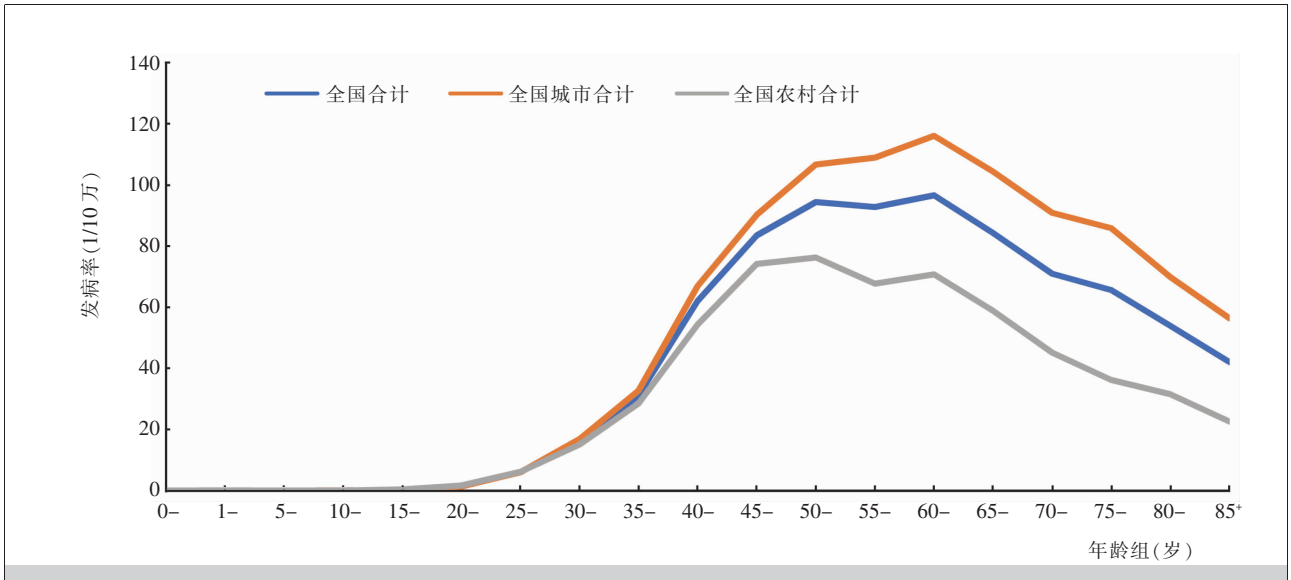

图 1　2015 年所有登记区域内女性乳腺癌年龄别发病率（数据来源国家癌症中心）

研究),2 年1 次筛查频次的 10 年累积假阳性召回率为 32.07%(95%CI:20.69%~43.45%),累积假阳性有创召回率为 4.79%(95%CI:3.81%~5.78%);1 年 1 次筛查频次的 10 年累积假阳性召回率为 49.96%(95%CI:36.09%~63.84%),累积假阳性有创召回率为 8.73%(95%CI:7.31%~10.15%)。2 年 1 次筛查频次较 1 年 1 次筛查频次其乳腺癌死亡率、乳腺癌发病率略有增加,但假阳性召回率等相关风险降低。证据级别均为中等质量。

(五)筛查措施

问题 10:单独使用乳腺 X 线检查筛查效果

- ◆ 推荐意见:对于一般风险人群,可考虑使用乳腺 X 线检查进行筛查 (强推荐,GRADE 证据分级:中)
- ◆ 推荐意见:对于高风险人群,不推荐单独使用乳腺 X 线检查进行筛查(强推荐,GRADE 证据分级:低)

推荐说明:本指南证据检索与评价小组于 2020 年开展了系统评价,对乳腺 X 线检查筛查乳腺癌对比诊断结果和随访结果的诊断准确性进行评价,共纳入 87 个研究。在所有人群中单独使用乳腺 X 线检查进行筛查(n=1 191 809, 87 个研究)[129-215]:56个研究合并的灵敏度为 80.00%(95% CI:75.00%~84.00%;31 个无法合并研究的灵敏度介于 33.60%~100.00%),56 个研究合并的特异度为 96.00%(95%CI:94.00%~97.00%;24 个无法合并研究的特异度介于 67.90%~99.10%),LR+为 17.30(95%CI:12.50~24.00),LR-为 0.21 (95%CI:0.17~0.27),DOR 为 82.00(95%CI:51.00~130.00),SROC AUC 为 0.95(95%CI:0.93~0.97)。一项纳入 6 个前瞻性筛查试验的个体病例数据(individual patient data,IPD)Meta 分析[216],对乳腺 X 线检查在具有乳腺癌家族史的高危人群中的筛查诊断准确性进行了评价。结果显示,在高危人群中,乳腺 X 线检查筛查的灵敏度为 55.00%(95%CI:48.00%~62.00%),特异度为 94.00%(95%CI:92.70%~95.30%)。

问题 11:单独使用乳腺超声筛查效果

- ◆ 推荐意见:对于一般风险人群,推荐单独使用乳腺超声进行筛查(强推荐,GRADE 证据分级:低)
- ◆ 推荐意见:对于高风险人群,不推荐单独使用乳腺超声进行筛查(强推荐,GRADE 证据分级:低)

推荐说明:本指南证据检索与评价小组于 2020 年开展了系统评价, 与诊断结果和随访结果相比,对单独使用超声进行乳腺癌筛查的诊断准确性进行评价,共纳入 28 个研究。结果显示:①在所有人群中单独使用超声进行筛查 (n=972 357, 28 个研究)[149,153,165,190,202-203,209,215,217-236],22 个研究合并的灵敏度为 68.80%(95%CI:66.10%~71.40%;6 个无法合并的研究灵敏度介于 29.40%与 100.00%之间),特异度为 98.90%(95%CI:98.80%~98.90%;2 个无法合并的研究特异度分别为 75.00%和 57.40%),LR+为 19.96(95%CI:8.08~49.31),LR-为 0.41(95%CI:0.30~0.56),DOR 为 53.32 (95%CI:20.82~136.50),SROC AUC 为 0.87(95%CI:0.67~1.00)。证据级别为低质量。②在无症状普通人群中单独使用超声进行筛查(n=935 041,12 个研究)[149,153,165,190,202-203,209,215,233-236]:9 个研究合并的灵敏度为 70.50%(95%CI:56.40%~81.60%;3 个无法合并的研究灵敏度介于 30.20%与 48.20%之间), 特异度为 99.00%(95%CI:97.90%~99.50%;2 个无法合并的研究特异度分别为 75.00%和 57.40%),LR+为 67.47(95%CI:29.14~156.24),LR-为 0.30(95%CI:0.19~0.46),DOR 为 226.50(95%CI:68.74~746.34),SROC AUC 为 0.97(95%CI:0.95~0.98)。证据级别为低质量。

问题 12:乳腺 X 线检查联合乳腺超声筛查效果

- ◆ 推荐意见:对于致密型乳腺的一般风险人群,推荐使用乳腺 X 线检查联合乳腺超声进行筛查(强推荐,GRADE 证据分级:中)
- ◆ 推荐意见:对于高风险人群,推荐使用乳腺 X 线检查联合乳腺超声进行筛查 (强推荐,GRADE 证据分级:中)

推荐说明:本指南证据检索与评价小组于 2020 年开展了系统评价,对与诊断结果和随访结果相比,使用超声联合乳腺 X 线检查进行乳腺癌筛查的诊断准确性进行评价,共纳入 26 个研究。结果显示:①在致密型乳腺人群中使用乳腺 X 线检查联合乳腺超声进行筛查 (n=142 796,17 个研究)[219,237-252]:15 个研究合并的灵敏度为 96.20%(95%CI:89.70%~98.60%;1 个无法合并的研究灵敏度为 90.60%),特

异度为 92.60%(95%CI:87.50%~95.80%;1 个无法合并的研究特异度为 96%),LR+为 13.05 (95%CI:7.58~22.45),LR-为 0.04 (95%CI:0.02~0.14),DOR 为 315.30 (95%CI:98.12~1013.19),SROC AUC 为 0.98(95%CI:0.97~0.99)。证据级别为中等质量。②在高风险人群中使用超声联合乳腺 X 线检查进行筛查 (n=161 057,26 个研究)[219,223-225,227,237-257]:22 个研究合并的灵敏度为 93.20%(95% CI:85.40%~97.00%;3 个无法合并研究的灵敏度介于 44%与 100%之间),特异度为 92.80%(95%CI:88.20%~95.70%;1 个无法合并的研究特异度为 96.00%),LR+为 13.01(95%CI:7.81~21.67),LR-为 0.07(95%CI:0.03~0.16),DOR 为 177.99(95%CI:64.49~491.23),SROC AUC 为 0.98(95%CI:0.96~0.99)。证据级别为中等质量。本次系统评价结果显示,超声联合乳腺 X 线检查无论在致密型乳腺人群还是高危人群中均有较好的诊断准确性,综合考虑卫生经济学和筛查实际情况,推荐高风险人群和致密型乳腺人群使用乳腺 X 线检查联合乳腺超声进行乳腺癌筛查,一般风险人群在经济能力较好地区可考虑使用乳腺 X 线检查联合乳腺超声进行乳腺癌筛查。

问题 13:单独使用乳腺核磁筛查效果

◆ 推荐意见:对于一般风险人群,不推荐使用乳腺核磁筛查为常规筛查(强推荐,GRADE 证据分级:中)

◆ 推荐意见:对于 *BRCA*1/2 基因突变携带者,可考虑使用乳腺核磁筛查,但不推荐作为筛查的首选方法(强推荐,GRADE 证据分级:中)

推荐说明:本指南证据检索与评价小组于 2020 年开展了系统评价,以活检或随访作为金标准,对核磁筛查乳腺癌的诊断准确性进行评价,共纳入 25 个研究。①在所有人群中单独使用乳腺核磁进行筛查[173,223-224,229-231,253,258-275](n=29 192, 25 个研究):13 个研究合并的灵敏度为 82.30%(95%CI:71.10%~89.80%;12 个无法合并研究的灵敏度介于 71%~100%),13 个研究合并的特异度为 92.20%(95%CI:87.70%~95.20%;5 个无法合并研究的特异度介于 81.00%~93.60%),LR+为 110.60(95%CI:6.63~16.96),LR-为 0.19(95%CI:0.11~0.32),DOR 为 52.21(95%CI:25.54~119.36),SROC AUC 为 0.94(95%CI:0.92~0.96),证据级别为中等质量。②在 *BRCA*1/2 基因突变携带者中单独使用乳腺核磁进行筛查 (n=10 955,11 个研究)[224,229,259-261,264-265,268,270-271,275]:7 个研究合并的灵敏度为 78.30%(95%CI:66.70%~86.70%;4 个无法合并研究的灵敏度介于 71.00%~93.80%);7 个研究合并的特异度为 93.80%(95%CI:91.10%~95.70%;2 个无法合并研究的特异度分别为 90.00%和93.60%),LR+为 12.65(95%CI:8.78~18.21),LR-为 0.23(95%CI:0.15~0.37),DOR 为 54.61 (95%CI:28.76~103.70),SROC AUC 为 0.94(95%CI:0.92~0.96),证据级别为中等质量。目前,乳腺核磁检查的灵敏度和特异度在所有单独筛查措施中较高,但综合考虑核磁检查费用、检查时长和设备普及率等原因,并不将乳腺核磁作为乳腺癌人群筛查的首要推荐。对于 *BRCA*1/2 基因突变携带者,可结合筛查地区经济能力考虑使用乳腺核磁进行筛查。

(六)筛查组织与管理随访

问题 14:乳腺癌筛查组织流程

建议乳腺癌筛查的流程参考图 2,主要包括签署知情同意书、问卷调查(附件 B)、风险评估、筛查技术选择和结果管理与随访

问题 15:知情同意书的签署

◆ 推荐意见:建议所有参加筛查者在自愿的原则下签署知情同意书

◆ 推荐意见:建议知情同意书的内容至少包括:筛查目的、意义、过程、参加筛查可能获得的益处和风险、筛查费用、保密原则和自愿原则、签字及日期

推荐说明:知情同意能确保筛查对象在筛查过程中获得合理及有效的医疗支持,能帮助筛查对象和医院及医师之间建立良好的信任[276]。我国在 2019 年发布的大型人群队列研究数据安全技术规范[277]中提到,数据采集人员应向研究对象提供其接受调查必需的所有信息,通过完整充分的说明和介绍,对筛查对象的有关询问进行全面必要的回答和解释,使筛查对象全面了解调查内容及隐私数据安全性保证。因此,本指南建议在乳腺癌筛查之前要签署知情同意书,明确乳腺癌筛查的目的、意义、过程、参加筛查可能获得的益处和风险、筛查费用,并解释说明筛

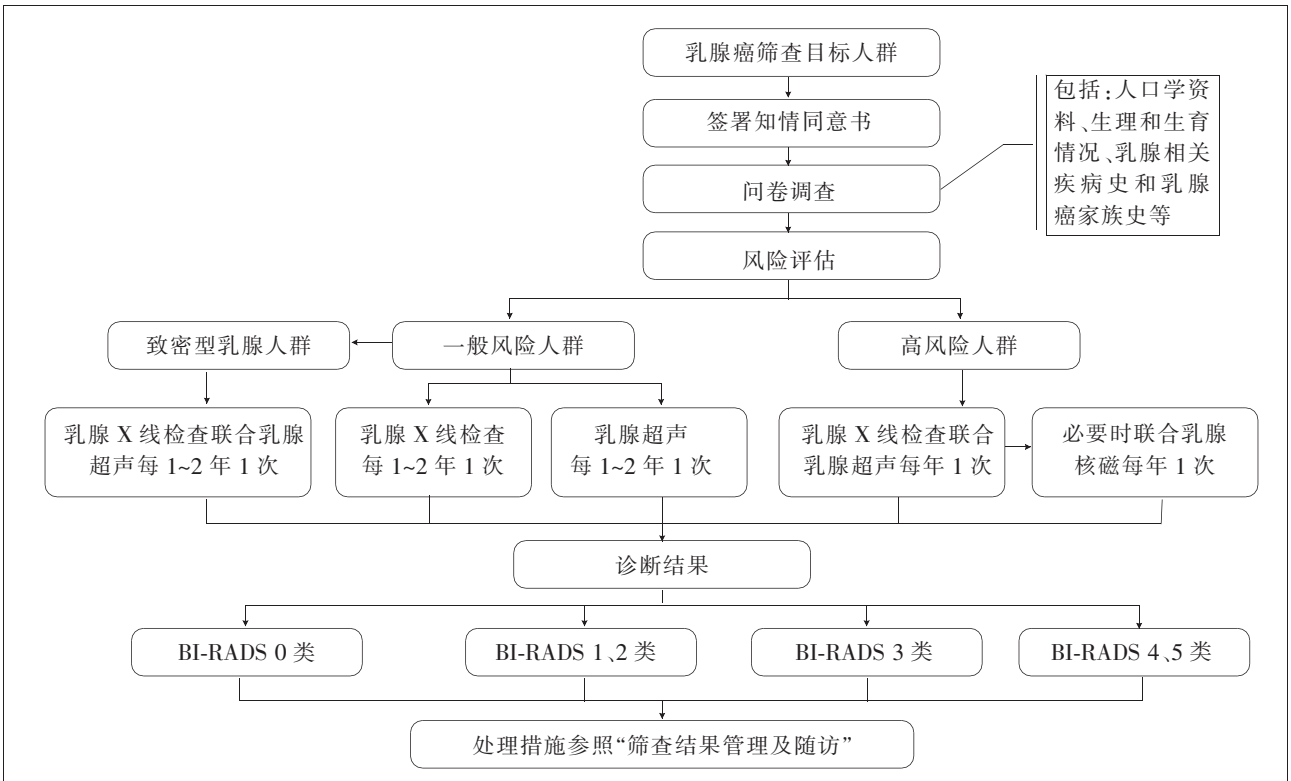

图2　乳腺癌筛查流程图

查的保密原则和自愿原则。

问题16:筛查结果管理与随访流程

◆ 推荐意见:可参考《中国抗癌协会乳腺癌诊治指南与规范(2019年版)》、国家癌症中心2018年发布的《中国乳腺癌筛查与早诊早治指南》以及ACR制定的被国际广泛采用的乳腺影像报告及数据系统(breast imaging reporting and data system,BI-RADS),对影像学诊断结果进行记录、分析[11-12,93]

推荐说明:①对于BI-RADS 1类和BI-RADS 2类:无需特殊处理。②对于BI-RADS 3类:乳腺X线检查评估为3类病灶,建议在此后6个月时对病灶侧乳腺进行乳腺X线检查复查,第12个月与24个月时对双侧乳腺进行乳腺X线检查复查。如果病灶保持稳定,则可继续随诊;2~3年随访无变化者可以降为BI-RADS 2类,如果随诊过程中病灶消失或缩小,可直接评估为BI-RADS 2类或BI-RADS 1类。若随诊过程中病灶有可疑发现,应考虑活检。超声评估为BI-RADS 3类病灶,建议3~6个月时行超声随访复查,2年随访无变化者可以降为BI-RADS 2类。③对于BI-RADS 4a类:可进一步影像学检查,必要时活检。④对于BI-RADS 4b类:可进一步影像学检查,可进行活检。⑤对于BI-RADS 4c类和BI-RADS 5类:可进行活检。⑥对于单项影像学检查(乳腺X线检查或超声)评估为BI-RADS 0类:建议加做其他影像学检查进行联合诊断。例如:致密型乳腺女性的乳腺X线检查检查结果,当发现不确定病灶时,归为BI-RADS 0类时,有必要补充乳腺超声检查。

四、总　结

本指南聚焦于我国40岁及以上女性乳腺癌筛查,是由多学科背景的专家团队,按照国内外公认的规范和方法制定,适用于各级医院开展癌症筛查的医务工作者。与其他已发表的相关指南对比,本指南工作组通过临床问题调研、证据收集与评价、专家共识等过程,最终形成了基于证据、平衡获益与风险、综合考虑筛查者意愿、卫生经济学与专家经验的临床问题推荐意见,是循证医学应用于临床实践的

代表性指南。本指南对于规范我国现阶段乳腺癌筛查具有切实的指导意义，预期可降低乳腺癌死亡率，提升群体筛查获益，并最终达到降低癌症治疗成本，提升社会与经济效益，提高癌症筛查服务的均质化和同质化目标。

但是，目前指南还存在以下三个方面的局限性。首先，我国暂缺关于乳腺癌筛查的高质量人群随机对照试验，本土高质量证据相对缺乏，基于国外证据得出推荐意见需考虑我国女性乳腺癌发病特征和我国国情；第二，原始研究对人群危险因素合并情况等信息描述不足，导致部分问题无法进一步细化推荐意见，或是依托专家意见形成推荐意见；第三，筛查的诸多问题暂缺卫生经济学证据，本指南未进一步细化对我国不同经济发展地区推荐意见。全国各医疗机构在使用本指南进行乳腺癌筛查的实践过程中仍然会存在差异，指南制定工作组也将关注后效评价，在指南更新时改进这些问题。

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英文缩略语中英文全称对照表

缩写	中文全称	英文全称
ABSFHGP	乳腺家族史外科协会指南小组	Association of Breast Surgery Family History Guidelines Panel
ACP	美国医师协会	American College of Physicians
ACR	美国放射协会	American College of Radiology
ACS	美国癌症协会	American Cancer Society
AGREE Ⅱ	开发指南研究与评价工具	Appraisal of Guidelines for REsearch and Evaluation Ⅱ
AMSTAR 2	系统评价偏倚风险评价工具	A Measurement Tool to Assess systematic Reviews
ARG	奥克兰放射协会	Auckland Radiology Group
AUC	曲线下面积	Area Under Curve
CCO	加拿大安大略癌症治疗中心	Cancer Care Ontario
CheckUp	更新版指南报告清单	Checklist for the Reporting of Updated Guidelines
CI	置信区间	Confidence Interval
CTFPHC	加拿大预防保健工作组	Canadian Task Force on Preventive Health Care
DOR	诊断比值比	Diagnostic Odds Ratio
ESMO	欧洲肿瘤学会	European Society for Medical Oncology
GRADE	推荐意见分级的评估、制定及评价	Grading of Recommendations Assessment,Development and Evaluation
IARC	国际癌症研究机构	International Agency for Research on Cancer
LR+	阳性似然比	Positive Likelihood Ratio
LR-	阴性似然比	Negative Likelihood Ratio
NCCN	美国国家综合癌症网络	National Comprehensive Cancer Network
NICE	英国国家卫生与临床优化研究所	National Institute for Health and Care Excellence
NOS	纽卡斯尔—渥太华量表	Newcastle-Ottawa Scale
QUADAS 2	诊断准确性研究的质量评价工具	Quality Assessment of Diagnostic Accuracy Studies
RIGHT	国际实践指南报告规范	Reporting Items for Practice Guidelines in Healthcare
RR	相对危险度	Risk Ratio
SROC	集成受试者工作特征曲线	Summary Receiver Operating Characteristics
USPSTF	美国预防服务工作组	U.S. Preventive Services Task Force

en with familial risk(FaMRIsc):a multicentre,randomised,controlled trial[J]. Lancet Oncol,2019,20(8):1136–1147.
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附件 A

#1 "乳腺肿瘤"[不加权:扩展] OR "单侧乳腺肿瘤"[不加权:扩展] OR "原位乳腺癌"[不加权:扩展] OR "癌, 导管, 乳腺"[不加权:扩展] OR "癌, 小叶状"[不加权:扩展] OR "乳腺肿瘤, 男性"[不加权:扩展] OR "炎性乳腺肿瘤"[不加权:扩展] OR "遗传性乳腺癌和卵巢癌综合征"[不加权:扩展] OR "三阴性乳腺癌"[不加权:扩展] OR "乳腺肿瘤"[常用字段:智能] OR "乳癌"[常用字段:智能] OR "乳房癌"[常用字段:智能] OR "乳房肿瘤"[常用字段:智能] OR "乳腺癌"[常用字段:智能] OR "乳腺瘤"[常用字段:智能] OR "乳腺导管癌"[常用字段:智能] OR "小叶状癌"[常用字段:智能] OR "浸润性导管癌"[常用字段:智能] OR "乳腺癌症"[常用字段:智能]
#2 "早期诊断"[不加权:扩展] OR "癌症早期检测"[不加权:扩展] OR "早期诊断"[全部字段:智能] OR "筛查"[全部字段:智能] OR "鉴别"[全部字段:智能] OR "早诊"[全部字段:智能] OR "早期检测"[全部字段:智能]
#3 "自我检查"[不加权:扩展] OR "触诊"[不加权:扩展] OR "乳腺自我检查"[不加权:扩展] OR "自我检查"[常用字段:智能] OR "触诊"[常用字段:智能] OR "按诊"[常用字段:智能] OR "乳腺自我检查"[常用字段:智能] OR "乳房自我检查"[常用字段:智能]
#4 "乳房 X 线摄影术"[不加权:扩展] OR "乳房干板摄影术"[不加权:扩展] OR "3D–乳房 X 线摄影术"[常用字段:智能] OR "数字乳腺断层摄影"[常用字段:智能] OR "数字乳腺 X 线摄影"[常用字段:智能] OR "X 线乳腺断层扫描层摄影"[常用字段:智能] OR "乳腺干板放射摄影术"[常用字段:智能] OR "乳房 X 线"[常用字段:智能] OR "钼靶"[常用字段:智能]
#5 "超声检查, 乳房"[不加权:扩展] OR "乳腺超声"[常用字段:智能] OR "乳房超声"[常用字段:智能] OR "超声"[常用字段:智能]
#6 "基因, BRCA1"[不加权:扩展] OR "基因, BRCA2"[不加权:扩展] OR "BRCA1"[常用字段:智能] OR "BRCA2"[常用字段:智能]
#7 "磁共振成像"[不加权:扩展] OR "回波平面成像"[不加权:扩展] OR "磁共振血管造影术"[不加权:扩展] OR "磁共振成像, 电影"[不加权:扩展] OR "弥散磁共振成像"[不加权:扩展] OR "胰胆管造影术, 磁共振"[不加权:扩展] OR "19F 核磁共振成像"[不加权:扩展] OR "磁共振成像"[常用字段:智能] OR "核磁共振"[常用字段:智能] OR "核磁共振成象"[常用字段:智能] OR "MRI"[常用字段:智能] OR "NMRI"[常用字段:智能] OR "MR 断层摄影术"[常用字段:智能] OR "NMR 断层照相术"[常用字段:智能] OR "磁共振"[常用字段:智能]
#8 #1 AND #2 AND #3(自我检查)
#9 #1 AND #2 AND #4(钼靶)
#10 #1 AND #2 AND #5(超声)
#11 #1 AND #2 AND #6(BRCA 基因)
#12 #1 AND #2 AND #7(核磁)

图 A1　中国生物医学文献数据库中文检索策略

PubMed

#1 "Breast Neoplasms"[Mesh] OR "Breast Carcinoma In Situ"[Mesh] OR "Breast Neoplasms, Male"[Mesh] OR "Carcinoma, Ductal, Breast"[Mesh] OR "Carcinoma, Lobular"[Mesh] OR "Hereditary Breast and Ovarian Cancer Syndrome"[Mesh] OR "Inflammatory Breast Neoplasms"[Mesh] OR " Triple Negative Breast Neoplasms"[Mesh] OR "Unilateral Breast Neoplasms"[Mesh] OR phyllodes tumor [Title/Abstract] OR breast sarcoma[Title/Abstract] OR mamma cancer* [Title/Abstract] OR mammary cancer* [Title/Abstract] OR mammary gland cancer* [Title/Abstract] OR Mammary Ductal Carcinoma*[Title/Abstract] OR breast gland cancer*[Title/Abstract] OR breast gland neoplasm*[Title/Abstract] OR Breast Neoplasm*[Title/Abstract] OR Breast Tumor* [Title/Abstract] OR Breast Cancer* [Title/Abstract] OR Mammary Cancer* [Title/Abstract] OR Breast Malignant Neoplasm*[Title/Abstract] OR Breast Malignant Tumor*[Title/Abstract] OR Human Mammary Carcinoma*[Title/Abstract] OR Human Mammary Neoplasm*[Title/Abstract] OR Breast Carcinoma*[Title/Abstract] OR Lobular Carcinoma*[Title/Abstract]

#2 "Early Diagnosis"[Mesh] OR "Early Detection of Cancer"[Mesh] OR Early Detection [Title/Abstract] OR Early Diagnosis [Title/Abstract] OR Screening[Title/Abstract]

#3 "Breast Self-Examination"[Mesh] OR Breast Self Examination*[Title/Abstract]

#4 "Mammography"[Mesh] OR "Xeromammography"[Mesh] OR Mammograph*[Title/Abstract] OR Breast Tomosynthesis[Title/Abstract] OR Breast Tomosyntheses[Title/Abstract] OR Breast Xeroradiography[Title/Abstract] OR Xeromammograph*[Title/Abstract]OR mamilloscopy[Title/Abstract] OR mammilloscopy[Title/Abstract] OR mammography[Title/Abstract] OR mammogram[Title/Abstract] OR mastography[Title/Abstract] OR breast scintigraphy[Title/Abstract] OR breast scintiscanning[Title/Abstract] OR mammary gland scintigraphy[Title/Abstract] OR breast xerography[Title/Abstract]

#5 "Ultrasonography, Mammary"[Mesh] OR Ultrasonic Mammograph*[Title/Abstract] OR Ultrasound Mammograph*[Title/Abstract] OR Mammary Ultrasonograph* [Title/Abstract] OR Breast Ultrasonograph* [Title/Abstract] OR breast echograph* [Title/Abstract] OR breast ultrasound[Title/Abstract]

#6 "Genes, BRCA1"[Mesh] OR "Genes, BRCA2"[Mesh] OR BRCA2 Gene*[Title/Abstract] OR BRCA1 Gene*[Title/Abstract]

#7 "Magnetic Resonance Imaging" [Mesh] OR "Cholangiopancreatography, Magnetic Resonance" [Mesh] OR "Diffusion Magnetic Resonance Imaging"[Mesh] OR "Diffusion Tensor Imaging"[Mesh] OR "Echo-Planar Imaging"[Mesh] OR "Fluorine-19 Magnetic Resonance Imaging"[Mesh] OR "Magnetic Resonance Angiography" [Mesh] OR "Magnetic Resonance Imaging, Cine" [Mesh] OR "Multiparametric Magnetic Resonance Imaging"[Mesh] OR nuclear magnetic resonance imaging[Title/Abstract] OR NMRI[Title/Abstract] OR NMR imaging[Title/Abstract] OR magnetic resonance imaging[Title/Abstract] OR MR tomography[Title/Abstract] OR MRI[Title/Abstract]

#8 #1 AND #2 AND #3(自我检查)

#9 #1 AND #2 AND #4(钼靶)

#10 #1 AND #2 AND #5(超声)

#11 #1 AND #2 AND #6(BRCA 基因)

#12 #1 AND #2 AND #7(核磁)

图 A2　中国生物医学文献数据库英文检索策略

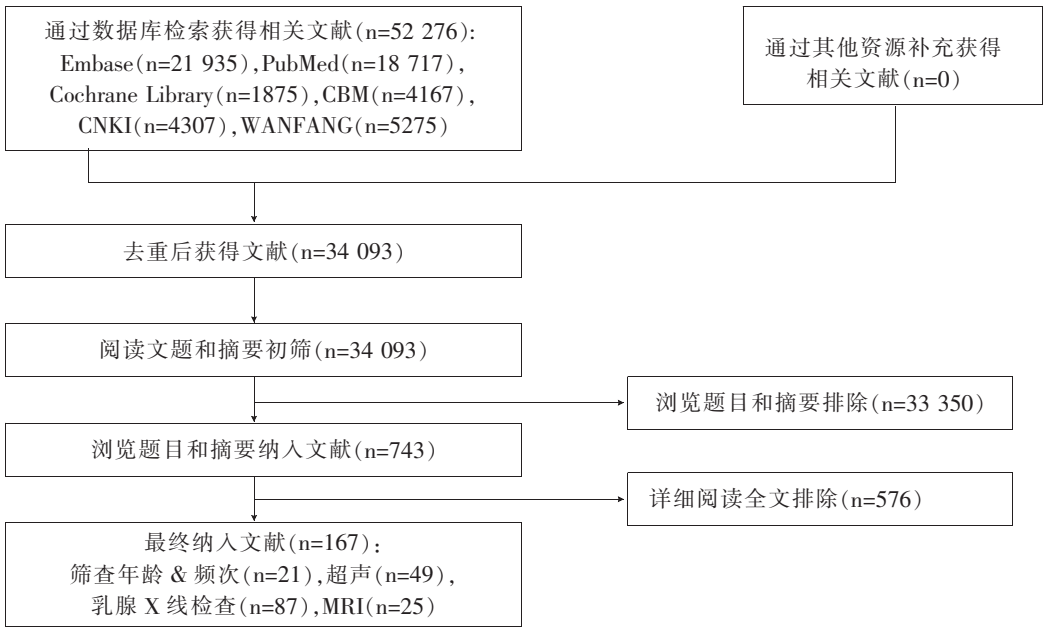

图 A3　文献筛选流程图

附件 B

乳腺癌风险评估问卷

以下为乳腺癌风险评估可参考内容。

姓名：_____

出生日期：_____年_____月_____日(请填写阳历生日)

籍贯：_____省_____市_____县(区)

民族：1. 汉族　2. 蒙古族　3. 回族　4. 满族　5. 壮族　6. 维吾尔族　7. 哈萨克族
8. 其他，请注明_____

身份证号：_____

本人联系电话：_____(手机)；_____(座机)

联系人 1 电话：_____(手机)　联系人 2 电话：_____(手机)

常住地址：_____　工作单位：_____

1. 生理和生育情况
1.1　您的首次月经年龄是(周岁)？
1.2　您是否已绝闭经？0.否　1.是 1.2.1 若是，停经年龄(周岁)
1.3　您是否使用激素替代治疗？　0. 否 1. 是，仅雌激素(如更宝芬、补佳乐、协坤、维尼安、更乐、倍美力、得美素、欧适可、松奇、康美华、尼尔雌醇等) 2. 是，雌孕激素联合(如诺康律、诺更宁、克龄蒙、倍美安、倍美盈等) 1.3.1 若是，使用月数
1.4　您是否有活产史？　0. 否(未生育、流产、死胎均包括)　1.是 1.4.1 若是，初次活产年龄(周岁)
1.5　您是否有哺乳史？0.否　1. 是 1.5.1 若是，累计哺乳月数(不足 1 个月按 1 个月计)
2. 乳腺相关疾病史
2.1　您是否曾有乳腺活检史或乳腺良性疾病手术史？0. 否　1.是 2.1.1 若是，请注明次数
2.2　您是否曾进行过 *BRCA* 基因检测，结果显示携带有 *BRCA*1/2 基因致病性遗传突变　0. 否　1.是
2.3　您是否曾进行过乳腺 X 线检查，显示为乳腺实质(或乳房密度)类型为不均匀致密型或致密型　0. 否　1.是
3. 乳腺癌家族史
3.1　您是否有一级亲属(母亲、姐妹及女儿)曾患乳腺癌？　0. 否　1.是
3.2　您是否有一级亲属(母亲、姐妹及女儿)曾患卵巢癌？　0. 否　1.是
3.3　您是否有二级亲属(祖母、外祖母及姑姨)50 岁前曾患乳腺癌？　0.否　1. 是 3.3.1 若是，请注明人数
3.4　您是否有二级亲属(祖母、外祖母及姑姨)50 岁前曾患卵巢癌？　0.否　1. 是 3.4.1 若是，请注明人数
填写人签字：_____ 填写日期：_____