A CPG Is Born: A case study of Clinical Practice Guideline Development at a community hospital

By

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Abstract

This case study follows the development and codification of a Clinical Practice Guideline (CPG) by the OB/GYN department of a community hospital. The study discusses the history and purpose of CPGs as well as the standards for CPGs in different environments. In this case, the CPG was designed to provide evidence-based rules for the assessment of a number of "soft" risk factors in deciding whether and when to induce labor during the period of 35-38 weeks gestation. The process used to create the CPG diverged from the "gold standard" process in several ways, including the use of a narrative review of the literature, rather than a systematic review. The case study examines whether a systematic review of published research would have led to a different CPG. We found that a systematic review did not produce different guidelines from those resulting from the narrative review.

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Introduction

Many of the problems in modern medicine can be characterized as problems of scale. The complexity and scale at which medicine is practiced are greater now than at any time in history: hospitals are larger, the range of diseases that can be treated is wider, the number of drugs and tests available is higher, and the mountains of research papers are heavier. The variable in this equation that is least able to scale is, unfortunately, one that can have a disproportionate influence on medical outcomes – the individual physician.

The human brain and the human lifespan place inviolable natural limits on all physicians. There are limits to how much preparatory education a physician can undertake, how many cases a physician can see in a career, and how many courses of treatment a physician can memorize. The ongoing division of medical practice into smaller and smaller specialties is one attempt to confront the non-scalability of the physician, but even this has its limits: by 1996, a general medicine physician would have needed to read 7000 journal articles a year merely to remain current on primary research in his or her field (and according to self-reported weekly time constraints, the physician in question would have needed to budget a mere 30 seconds to reading each article)[1].

For the last century, the natural limitations on physicians' time, as well as their analytic and mnemonic capacity, have increasingly been seen by public health organizations (including governments, hospitals, and trade groups) as obstacles to the optimization of the quality of medical practice[2]. However, although the problem has long been acknowledged, no consensus solution has ever emerged. The solution that has come closest to consensus thus far emerged from a movement known as evidencebased medicine (EBM), which originated in the 1990s. This title is to some degree a misnomer – medicine has always aspired to be evidence-based, even in antiquity. The struggle, rather, has been over the definition of "evidence." If one thinks of evidence in the sense of "crime scene evidence," the modern medical patient is a limitless fountain of evidence. Detailed medical histories can be taken, hundreds of tests can yield thousands of numerical results, and entire genomes can even be sequenced. Physicians are awash in such "evidence" generated at each encounter. However, advocates of EBM see this as more of a handicap than an advantage: despite years of training and experience, physicians still have difficulty reliably distinguishing evidence that is *relevant* to care-related decisions from evidence that is irrelevant or misleading. For them, it is as if a detective investigating a homicide were unsure whether the channel playing on the victim's television meant that the murderer used a gun or a knife.

In fact, the E in EBM is more properly understood as *effectiveness*. To establish the efficacy of any given treatment, it is necessary first to scientifically establish that the treatment is correlated with a desirable outcome, and then to eliminate any spurious or confounding correlations, i.e. any other common element that might have a causal connection to the desired outcome. If the treatment continues to be associated with the desired outcome when deployed in real-world circumstances, this demonstrates its effectiveness. Advocates of EBM sought to identify which treatments were most likely to result in good outcomes, how often, and under what conditions. To achieve this goal, they closely analyzed the conditions under which research was being conducted and issued guidance to "teach doctors to examine the medical literature critically" [2] – in other words, to help medical professionals understand how much confidence one should have that the results of a given study could be generalized. Unfortunately, advocates of EBM found that, as Weisz et al. put it, "most doctors would not or could not directly evaluate the literature themselves[2]." To resolve this problem, advocates of EBM – which by the late 1990s had redefined itself as the more pragmatic "evidence-based

practice" (EBP) – co-opted an existing concept, the *medical guideline*, retitling it the Clinical Practice Guideline (CPG).

A medical guideline is a document that attempts to distill a large corpus of expertise, experience, and/or evidence down to essential rules. It directs physicians to provide certain treatments and interventions under certain conditions; its most basic formulation is "if X, then Y." The concept of a medical guideline had been in use since the early 20th century, when the growth of hospitals and third-party payers such as governments led to the first published guidelines for care. For example, the standards published in 1916 by the Associated Out-Patient Clinics of the City of New York set guidelines in subjects as varied as "space requirements, personnel, the kind of patients to be treated, record keeping and history taking"[3]. In the UK, the government-backed Radium Commission forced hospitals purchasing radium to adopt "specific standards of therapeutic practice"[2] as early as 1929. In 1955, the National Tuberculosis Association and the American Academy of Pediatrics both issued guidelines specifically addressing diagnosis and treatment. By this time, the demand for medical guidelines was well established: a search of national library catalogs in the US, UK, and France by Weisz et al. found over fifty medical guidelines published in the thirty years following World War II alone[2].

Guidelines were seen as documents reflecting "consensus," i.e. the majority opinion of expert practitioners in that field – said experts being selected, again, by consensus. The late 1970s saw the rise of guidelines produced in "consensus conferences," in which "the authority of experts in different fields was supplemented by both consumer representatives and strict procedural protocols[2]." Such guidelines ensured that an institution that followed them would be practicing medicine of the same quality as other institutions, but *not* that the institution would be practicing medicine that

achieved optimal outcomes. No systems were in place to ensure that the experts in these conferences were basing their opinions on anything stronger than anecdote.

The term *clinical practice guideline* begins to appear in the literature around 1991, reflecting the rise of EBM/EBP. Advocates of EBP sought to define a clinical practice guideline as a medical guideline based less on existing consensus and more on systematic reviews of research literature that give greater weight to results obtained under optimal evidentiary conditions, such as double-blinded randomized clinical trials. A side effect of this has been to advance the proliferation of guidelines – an institution wishing to produce or update a clinical practice guideline no longer needs to host a conference of eminent practitioners; one might facetiously claim that it simply needs to lock a team of information scientists in a room with a rubric and a connection to PubMed. The elevation of published evidence as a source of authority has also empowered groups other than physicians to produce clinical practice guidelines, including hospital administrators, nurses, dieticians, and even patient advocacy groups.

One interest group of particular importance in the formulation of clinical practice guidelines is the clinics themselves. Clinics, as well as individual departments within a hospital, have come to view clinical practice guidelines as documents that can be created essentially *ad hoc*, with rapid turnaround and limited resources, for use strictly within the institution that created them, rather than for promulgation to a wider audience. Given the limited goals of this type of clinical practice guideline, it is common practice to abridge the accepted standards for development of "official" clinical practice guidelines, such as might be produced by a national physicians' professional association. For example, the clinic may decide to conduct a narrative (i.e. expert-focused) review of the literature rather than the more exhaustive systematic review.

As yet, scholars have published little research looking at whether these shortcuts materially affect the quality of intra-hospital clinical practice guidelines. If the conclusions of a clinical practice guideline based on a narrative review would be different from those based on a systematic review, the hospital may find itself with guidelines that conflict with later clinical practice guidelines developed under stricter standards, not to mention potentially harm patient outcomes. In this case study, we will examine one instance of a clinical practice guideline developed by the author at a community hospital using abridged standards, with particular attention to the abridged review process. By completing a counterfactual systematic review, we can isolate the influence of this single abridgement on the final clinical practice guideline and produce limited guidance for future clinical practice guidelines developed using this method.

We should note that this case study does not address the ongoing problem of physician adherence to clinical practice guidelines and other attempts to standardize care decisions. The primary obstacle has been that all proposed solutions infringe to some degree on physician autonomy – the right of a physician to use his or her own standards and intuition to decide how to treat individual patients.[4] Since the subject of this case study is a clinical practice guideline developed and applied within a single institution, adherence was not a major challenge in the development process: all physicians covered by the clinical practice guideline are employed by the hospital, so the hospital can use its leverage as employer to ensure adequate compliance.

Background: Clinical Practice Guidelines (CPGs)

Developing a clinical practice guideline is a path many have trod before. The Agency for Healthcare Research and Quality hosts the US Guideline Clearinghouse, which lists summaries of 2,451 published clinical practice guidelines, along with 289

listed as "in progress."[5] The UK's National Institute for Health and Care Excellence, which is funded out of the budget for the National Health Service to provide guidance on quality and value for money in health care, hosts a compendium of rigorously-developed guidelines.[6] The Guidelines International Network, headquartered in Berlin, also lists over 6,700 clinical practice guidelines.[7]

Who Publishes CPGs

• International NGOs, such as the World Health Organization, for example.

 National institutions, such as the National Institute for Healch and Clinical Excellence (NICE) in the United Kingdom, the United States' Veterans Administration and National Institutes of Health, and Germany's Ärztliches Zentrum für Qualität in der Medizin, among many others.

• Physician's and surgeons' professional associations, for example the American College of Surgeons, the American Congress of Obstetrics and Gynecology, the American Thoracic Society, the American College of Rheumatology, the American Academy of Pediatrics, the American Academy of Family Medicine, and many others, including nursing and other provider associations such as the American and Royal Colleges of Nursing.

• Academic institutions, especially academic medical centers.

Insurance companies ranging from the many Blue Cross/Blue
 Shield organizations to vertically integrated staff-model HMOs such as Kaiser
 Permanente, Group Health Cooperative of Puget Sound, Henry Ford Health
 System, and many others.

• Broad stakeholder groups such as the National Quality Forum, whose guidelines member groups agree to adopt.

Hospitals, especially quaternary academic medical centers or such systems as the Cleveland or Mayo Clinics.

This long list does not include clinical practice guidelines developed for in-house purposes at hundreds of health care institutions nationwide; these are usually described as "institution-specific" guidelines. Groups at these institutions responsible for clinical practice guideline creation include administrators and physician specialty departments.

Institution-specific CPG Development

Institution-specific clinical practice guidelines are usually tailored specifically to the needs of the institution that develops them, because developing a clinical practice guideline is not without costs. The institution must convene a development committee (consisting of those who sign up out of interest as well as those who sign up out of obligation), it must compensate committee members for their time in addition to losing their productivity elsewhere, and it must overcome any resistance to producing the clinical practice guideline among those responsible for enforcing it. Accordingly, institutions consider multiple incentives when deciding which subjects merit the effort to develop a clinical practice guideline:[8]

Is a condition or disease highly prevalent in the population served?

- Is a procedure overused or underused at the institution?
- Is the cost of treating the condition or using the procedure high?
- Is effective care available to treat the condition?
- Are the procedure's effects on mortality and morbidity unclear?

• Do providers at the institution adhere to a standard of care for the condition or a standard of execution for the procedure?

 Is the standard in place at the institution at variance with a nationally promulgated standard?

• Is there external pressure to reduce mortality and morbidity in a given area, e.g. from third-party payers, professional associations, or patient advocates?

• Do existing guidelines recommend the use of a drug or medical device that the institution does not or cannot currently provide?

Major centers of academic medicine, including those operated by the state, often produce in-house guidelines using the same rigorous development process as those designed for publication. At the other end of the spectrum, resource-limited institutions such as private clinics and small community hospitals may produce in-house clinical practice guidelines that incorporate very little original work. In most cases, these documents are alloys of published guidelines and other advisory material, such as "practice bulletins" published in professional research journals. Smaller hospitals that can still take advantage of residency and/or fellowship resources may compromise by conducting a limited or narrative review of the literature to answer questions about practice for which the hospital lacks a consensus opinion.

Gold Standard for CPG Development

The first standard definition of a clinical practice guideline was published in 1990 by Field and Lohr, who defined it as "a systematically developed statement to assist practitioner and patient decisions about appropriate health care for specific circumstances." [9] This definition was formalized by the Institutes of Medicine (IOM) in 1992: "clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options."[10]

No extant studies or procedures dictate a gold standard for how an institution decides to *begin* the process to develop and/or implement a clinical practice guideline. As noted above, there can be many influences at work, so the decision remains strictly a judgment call by the developing institution. However, once that decision has been made, strict guidelines have been published governing the remainder of the process. The IOM has set eight standards to be followed by institutions developing clinical practice guidelines to ensure trustworthiness: [11]

- Establish transparency in their methods
- Manage any conflicts of interest prior to selection of group

members

• Be multidisciplinary, including all stakeholders as well as members of the public

Include well-designed systematic reviews that meet established
standards

• Use evidence-based rating systems to establish the strength of the evidence

• Use clear and articulate language when publishing the

recommendation

Incorporate external reviewers whose comments may remain
anonymous

• Have a planned updating system to keep current with the relevant literature

Some authors argue that these standards are sufficiently resource-intensive that only nationally funded institutions with a mandate to produce guidelines, such as NICE in the UK, are capable of producing high-quality guidelines in volume sufficient to support modern medical needs[12]. Smaller institutions experience significant difficulty balancing scientific rigor with real-world pragmatism[13].

Development Committee

The institution should convene a committee of 8-10 people representing multiple disciplines [14], including:

• Providers (doctors and nurses) with daily experience in treatment of the subject

- Departmental chairs and other policy makers
- Risk management representatives
- Patient advocates

At least half of the people on the committee should have prior clinical practice guideline development experience, public health credentials such as an MPH degree, or experience with critical literature evaluation from an EBP perspective. Information scientists may be present to perform the literature search.

Once the committee is convened, it should review the issue(s) that triggered the formation of the committee and create a series of questions, arrived at by consensus, which the clinical practice guideline should answer. It should then nominate a subcommittee of 1-2 information scientists to conduct a systematic review of the literature in order to provide an evidentiary basis for answering these questions [15, 16].

Conducting a Systematic Review

Systematic reviews are designed to reduce bias and random error and are meant to assure that the resulting collation of data is scientifically valid. They summarize large bodies of evidence by synthesizing the findings of similar but separate studies.[17] The studies to be synthesized are often primary investigations, but can include prior systematic reviews. Usually the most robust studies for determining the effectiveness of a treatment are randomized controlled trials. A systematic review may include a metaanalysis if one has been published that meets strong evidentiary criteria. Strategies for performing a systematic review were recently codified by the Institute of Medicine in *Finding What Works in Health Care: Standards for Systematic Reviews*.[16]

In general, well-conducted systematic reviews begin by defining the means by which studies will be identified, included or excluded, evaluated, and aggregated. This requires the review subcommittee to develop a search strategy on the basis of the review questions created by the guideline committee. The subcommittee collects information from several core electronic databases, including

- Cochrane Database of Systematic Reviews
- MEDLINE (created and supported by the American National Library of Medicine)

• EMBASE (a broad database including Medline and non-Medline sources, especially international and those with pharmaceutical foci);

CINAHL (the Cumulative Index of Nursing and Allied Health Literature);

• PsycINFO, the comprehensive electronic archive of psychological literature, in the case of behavioral, substance abuse, or psychiatric topics.

The goal is to develop a search strategy that is sensitive enough to capture all relevant articles, but precise enough not to produce overwhelming results. Standard filters (e.g. language or species-specific exclusion criteria) may be used to narrow the field, although such filters may produce bias that the subcommittee should account for. The search results are then sieved in stages to exclude studies that the subcommittee identifies as outside the topic of interest or lacking sufficient evidentiary confidence. Typical sieve stages include a removal of articles with obviously inappropriate *titles*, or *abstracts* that show the article is inappropriate, before movement to *assessment of full articles* for all remaining results. The subcommittee then reports out the remaining cohort of articles as the body of evidence to be evaluated by the committee.[15]

Grading Review Results

The next step is for the committee to designate a subcommittee of 1-2 people to assess the quality of the studies; this can be the same group that conducted the systematic review or a different group with greater experience in evidence assessment. Grading the data allows the guideline committee to flag poorly conducted studies for exclusion. Standardized grading tools also give the reader a transparent and easily accessible method for evaluating the strength of the evidence supporting the guidelines developed from the review. Several tools have been developed to assist the assessment, including

The Institute of Medicine's *Clinical Practice Guidelines We Can Trust*

• The U.S. Preventive Services Task Force's recommendations for grading evidence in a tiered system (see Appendix 4)

- The AGREE tool [18]
- AGREE II [19]

The grading subcommittee then reports out grades/rankings of confidence for each study result in the cohort.

Drafting the CPG Itself

Once the systematic review of the literature has yielded graded results, the guideline development committee should examine the literature and write the first draft of the recommendation, choosing wording that expresses the strength of the recommendation. The committee should make revisions through consensus using either informal or formal procedures, depending on the size of the committee and the tone of the proceedings. The committee may identify the need for more research before voting on the final document and then optionally enter a validation phase, in which it invites external peer review and stakeholders to comment on the guidelines. Any corrections are made before final publication.[15]

CPG Structure

A clinical practice guideline should begin with a preamble that includes the following components:

• **Scope**: To whom does the clinical practice guideline apply (for example, patients at this institution, patients in a given department, or patients nationwide)?

• **Target**: Who is the audience for the clinical practice guideline (for example, practitioners, administration, or risk management)?

- Background: What makes this topic of interest?
- Introduction: Instructions on implementing the guidelines that
 follow

The main section should consist of a sequence of concrete recommendations, with each recommendation structured as follows:

1. Title/topic

2. Definition of terms (e.g. if the guideline concerns stillbirth, define stillbirth)

3. Framing/exposition (Why is this issue important? What is the incidence/prevalence?)

4. Level of confidence (see Appendix 3)

5. One or more conditional statements (under these circumstances, take this action)

6. Commentary, such as risks, benefits, harms, or alternatives to the recommended action

Incentives to Use CPGs

As the cost of health care to society rises, the incentive to ensure that these costs are paying for effective care increases. The US, for example, spent over \$2.5 trillion annually as of 2010 on health care and related expenses, and the figure rises each year.[20] Health care providers who have access to clear and specific guidelines are more likely to provide care that is appropriate, timely, and correct. [21] At the hospital level, producing and implementing clinical practice guidelines reduces the hospital's risk of lost revenue via contested payment (such as Medicare rules that refuse payment when patients are readmitted) or malpractice penalties.

Obstacles to CPG Acceptance

Clinical practice guidelines seek to change professional behavior and institutional culture, a task as difficult to do as it sounds. The body of literature regarding implementation of guidelines is vast, and beyond the scope of this paper; however,

Pilling includes an excellent review.[17] Published research on guideline implementation demonstrates that change is possible, but the majority of interventions to support implementation have, at best, moderate effects.[22] Disseminating the guidelines is the first step; when a national body develops guidelines, it will usually disseminate them by publishing the results in the journal of the professional association as well as on an affiliated website. Motivating the changes to percolate through the profession is a harder task. Reminders to clinicians work best, followed by educational outreach, physician audit and immediate feedback mechanisms, which have more limited effects. The use of opinion leaders trails all other interventions. [22, 23] Complicating guideline implementation, of course, are the intricate organizations within which health care providers practice, and the inherent difficulty of changing a large system. Recently, electronic medical records have been developed to assist in clinical decision support, and these can be configured to remind physicians of institution-specific guidelines when appropriate.

An important criticism of clinical practice guidelines is that the bodies that produce them fail to update them. A survival analysis conducted in 2001 found that 10% of guidelines were substantially incorrect within 3.6 years and 50% were out of date within 5.8 years [21, 24]. The primary obstacle to keeping clinical practice guidelines up to date is that the gold standard requires a systematic review of the literature to be performed for each update cycle; the results of this review must then be graded and analyzed. Since institutions may have difficulty mustering the effort and manpower required to fulfill these criteria every few years, many forgo the update process entirely.[25] Nevertheless, many handbooks and "guidelines for guidelines" continue to recommend that clinical practice guidelines be updated every 3 years.[26]

Case Study

Lehigh Valley Health Network (LVHN) is a community hospital system located in Pennsylvania's Lehigh Valley. LVHN partners with medical schools at the University of South Florida and Penn State University to provide clinical training opportunities for medical students. The system comprises three hospital campuses with 988 licensed acute beds, the 500-member Lehigh Valley Physician Group, and nine community health centers. The medical staff has more than 1,100 physicians representing 95 specialties, and LVHN is the area's largest employer with more than 9,600 employees. In FY 2011, LVHN recorded over 65,400 admissions, 1.7 million outpatient visits, and 3,800 deliveries. LVHN trains 278 residents in 17 residency and fellowship programs. The nursing staff comprises 2,334 registered nurses and has a 5 percent nursing vacancy rate. Individual departments at LVHN have developed 50 institution-specific clinical practice guidelines since efforts began in 2008.[27] Examples include Emergency Department algorithms for managing chest pain, burn triage, and guidelines for declaring brain death.

In 2012, the OB/GYN department convened a CPG committee to establish clinical practice guidelines under the direction of a Maternal-Fetal Medicine (MFM) specialist on staff. The OB/GYN department at LVHN employs 45 physicians as well as an ever-growing number of physician extenders and mid-level providers. It also employs 12 MFM specialists; these are board-certified OB/GYNs who have completed three additional years of fellowship training in managing high-risk pregnancies. An MFM specialist is present in the hospital at all times to provide patient care and train residents.

LVHN's Development Committee

The OB/GYN departmental CPG committee is a standing committee that meets monthly and is tasked with identifying areas in which clinical practice guidelines are

needed as well as all guideline production within the department. The committee roster consists of 20 members: 10 attending physicians (2-3 from each private practice), 2 resident physicians (one of whom is the author of this paper), 5 in-patient nurses, 2 risk management representatives, and the department chair. Although this total is over twice the number recommended by Shekelle et al. for optimal consensus formation, members are not expected to attend all committee meetings, so the number present at any given meeting is likely to approximate the ideal number.[14] Ideally, patient and public involvement should be included as practice guidelines that affect them are adopted, but this committee does not include those representatives.

The *de facto* leaders of the committee are the medical director of the department and the MFM specialist who suggested and convened the committee. They expect that the committee's methodology for development and implementation will become more robust as experience develops, but the committee has no mechanism in place to assure that it does.

The CPG committee has initiated, developed, reviewed, adopted, and disseminated three guidelines to clinical stakeholders; seven additional topics are under development. The guidelines that have been adopted have several goals in mind, including enablins providers at all levels of training to understand expected standards of care, providing emergency reference material, and providing critical data about specific OB/GYN topics in the most useful and accessible form.

CPG Development Process

1. LVHN has dictated that the committee must produce one clinical practice guideline each year in the subdisciplines of obstetrics, gynecology, and gynecological oncology.

 The committee selects an area in which a new clinical practice guideline is needed by considering the standard factors (see "Institution-specific CPG Development" above)

 An informal consensus is achieved; unanimous agreement is desired but not mandatory

4. Members of the committee with expertise in the chosen area develop a list of specific questions that the new guideline must address

5. A committee member is assigned to author the guideline

6. The guideline author may choose the literature to include in their narrative review themselves or the literature may be suggested by the leaders of the committee

7. The guideline author conducts a narrative review, collates the information, and drafts the guideline

8. The two committee members with the most expertise relevant to the topic review the draft and suggest revisions or additional research to include

9. The guideline author revises as needed and returns the second draft to the committee at large

10. The committee discusses the draft guideline and suggests further revisions

11. The guideline author revises the guideline as needed and produces a final draft

12. The committee conducts a formal vote to adopt the guideline

13. The guideline is published to an internal LVHN website and emailed to all members of the department

14. All clinicians in the department sign an agreement that they have read and understood the new guideline

15. The guideline author is responsible for continual review of the literature pertinent to their guideline, usually within 2 years

16. The committee schedules review of each clinical practice guideline after 3 years

Case Study CPG: Late Preterm and Early Term Indications for Delivery Guideline

Background

Preterm birth rates continue to rise in industrialized countries, despite preterm birth causing significantly increased risks of neurodevelopmental disabilities and infant morbidity and mortality. One reason for this rise is that many preterm births are iatrogenic, i.e. induced or initiated by a health care provider. Because we know so much now about pregnancy complications and their high risks, this is intentional: the provider is making a judgment call that the harm caused by the preterm birth is preferable to the risk of some greater harm that may be caused by allowing pregnancy to continue[28].

Substantial literature supports the increase in iatrogenic infant morbidity associated with early birth, with some studies showing late preterm births now reaching as much as 32% of all births, but Joseph and D'Alton argue that there is a "sound theoretical and empirical basis for medically indicated preterm delivery"[29]. They emphasize that there are several situations when early delivery is clearly preferable to continuing the pregnancy, even if the infant's first weeks of life are spent in the neonatal intensive care unit (NICU). These so-called "hard" indications for iatrogenic birth include:

Severe preeclampsia

Intrauterine growth restriction, with abnormal fetal testing
demonstrating decreasing physiological reserves

Acute placental abruption

Usually delivery is recommended as soon as the condition is diagnosed. Similarly, delivery at 32-34 weeks for monoamniotic/monochorionic twins is recommended, as the risk of intrauterine fetal demise increases substantially after this gestational age [30, 31]. However, experts disagree, and data can be scarce or conflicting, regarding what the potential harms are and how to calculate risks when iatrogenic preterm birth is being considered in the absence of these indications [32, 33].

Choosing a Subject

Although LVHN had not developed a formal clinical practice guideline governing "hard" indications for preterm delivery, the committee felt that a satisfactory standard of care was being followed by providers and that widespread agreement already existed among providers as to the proper diagnoses and responses governing these indications. Consequently, the committee opted to focus instead on so-called "soft" indications.

At the beginning of guideline development, MFM specialists developed a list of indications, based on their extensive clinical experience, to include in the guidelines. Soft calls are harder for providers to make; the committee needed to collect outcome data from good literature to be able to recommend appropriate action, knowing the risks of early delivery. The following nine indications were chosen by consensus for inclusion in the clinical practice guideline:

- 1. Hypertension-related indications:
 - a. Gestational hypertension

- b. Mild preeclampsia
- c. Preeclampsia superimposed on chronic hypertension
- 2. Fetal anomalies
- 3. Placenta accreta
- 4. Diabetes
- 5. Previous classical incision or myomectomy
- 6. Oligohydramnios
- 7. Placenta previa
- 8. Previous stillbirth
- 9. Uncomplicated multiple gestation

Assigning a Guideline Author

The author of this paper volunteered to undertake all tasks required to draft the guideline as part of this larger case study.

Narrative Review

A narrative review of scientific literature is distinguished from a systematic review in that, while both reviews strive to include all relevant literature for a given topic, a systematic review is required to state and follow stringent rules regarding the search for evidence; it must also reveal how the decisions were made about relevance of studies and the validity of the included studies. By contrast, a narrative review is not required to state or follow rules regarding the sieving or classification of evidence. This type of review includes reviews of a subset of literature that is determined arbitrarily, e.g. by only looking in certain journals or by accepting a predetermined list compiled by a third party. I performed a narrative review of the literature, looking for delivery recommendations for the nine indications listed above. The committee chairperson recommended fifteen articles to me.[29, 31-44] I identified further articles from the references and reviewed practice bulletins published in the journal of the American Congress of Obstetricians and Gynecologists (ACOG)[45-48]. ACOG practice bulletins are developed by expert committees to guide and standardize clinical practice among OB/GYNs, but are not intended to meet the standards of evidence required of a clinical practice guideline.

Process Results

I reviewed the articles and composed a draft clinical practice guideline based on the evidence obtained from the articles. For ease of practitioner use – since ease of use was one of the major criteria for a clinical practice guideline to be approved by the committee – I also created a Working Summary of the Clinical Practice Guideline (for these two documents, see Appendix 1 and 1a).

Following the workflow outlined above, MFM specialists reviewed my draft guideline and I revised it according to their suggestions. Upon submission of the second draft to the committee at large, the committee voted to adopt the guideline as written.

Divergence from Gold Standard

Although LVHN's OB/GYN department has greater resources to devote to development of clinical practice guidelines than a private clinic, it is nevertheless constrained by a number of circumstances:

No LVHN employees are compensated for time spent working for
a committee

 Certain job categories at LVHN require participation in a committee

 No potential committee members are formally trained in information science

• All potential committee members have full-time jobs, mostly

providing patient care

These resource constraints led to a number of practices that were at variance with the gold standards enumerated earlier:

• Some committee members were on the committee simply to fulfill

institutional requirements and did not have a direct stake in the outcome

- The committee did not include:
 - Reviewers from outside the department
 - Patient advocates
 - Information scientists
- The guideline author was directed to gather evidence via narrative

review instead of systematic review

• The guideline author was directed not to formally grade the quality

of studies identified in the review

• Periodic updating of the guideline is nominally planned, but no

process is in place to trigger, produce, or review any updates

Implementation and Aftermath

Indicated Late Preterm and Early Term Birth was adopted by the CPG Committee in December 2012 and implemented in January 2013 by widespread consensus. Practicing clinicians were required to read and understand the new recommendations. Assessing whether or not clinicians follow the guidelines is an obvious next step in guideline evaluation. Some estimate that clinicians practice firmly within evidence-based clinical decision-making only 55% of the time.[22, 49, 50]

At LVHN, this problem is partially overcome by corporate decree. LVHN is a public hospital; all employees must follow the hospital's rules or risk their livelihood. The hospital has given departments power to regulate their own clinicians, and the OB/GYN department has decided that the CPG committee's recommendations are to be followed. Therefore, individual clinicians, who have already bought into the system by virtue of their employment, are professionally bound to follow the guidelines. The risk management department ensures adherence through QA sessions in the case of poor outcomes.

A more subtle reason that clinical practice guideline implementation may be easier at LVHN than elsewhere is that the MFM team has been given a special hierarchical status in the department's internal culture. Even with their own private patients, clinicians will defer to an MFM's judgment. The CPG committee is endorsed and managed by the MFM specialists, and therefore most clinicians buy into the recommendations that emerge from the group.

The CPG committee also contains other stakeholders, which is a key part of creating guidelines that are acceptable to those meant to be following them. An important barrier to guideline implementation is the problem of handing guidelines down from on high and expecting practitioners in a fiercely autonomous profession to adopt them. Arguably, by including stakeholders from multiple strata of practice, good CPGs have a smaller hurdle to overcome to achieve wide implementation. [20]

Counterfactual Systematic Review

Introduction

The purpose of this part of the case study is to shed light on the effect that the variance from gold standard practices had on the final clinical practice guideline. The best way to analyze these effects is to isolate them by replicating the development process using gold standard practices and then to compare the results. Since it would be infeasible to assemble an entire counterfactual committee, I have focused instead on the latter half of the variant practices:

- Narrative review instead of systematic review
- No formal grading of the literature identified

By completing a counterfactual systematic review, using the literature available at the time, and by formally grading the literature according to gold standard grading systems, I was able to make the closest comparison of the actual guideline to a hypothetical ideal guideline that was possible under the circumstances.

Methods

The question that this systematic review intended to answer is

"When is the optimal time for delivery in pregnancies complicated by: prior stillbirth, placenta accreta, stable placenta previa, vasa previa, gestational hypertension, preeclampsia (mild and severe), multiple gestation, prior classical Cesarean, prior myomectomy, fetal anomalies, oligohydramnios, and diabetes (gestational, pregestational)?" Because a randomized controlled trial would be unethical and unacceptable when fetal death is a likely outcome, retrospective reviews have been used to determine the best possible gestational age at which to plan delivery in high-risk pregnancies. I included other clinical practice guidelines in my search as well. Appendix 2 includes the full search parameters.

The initial search was performed on March 5, 2013 and resulted in 786 articles. The following standard filters culled the data to 513 articles:

- Abstract and full-text available
- Humans
- English

This cohort was further refined on title alone to include 55 articles. Criteria resulting in exclusion included:

- Case reports
- Editorials and letters
- Research performed outside of Western Europe, Australia, and

North America

To be included, titles needed to indicate that the article addressed timing of delivery, outcomes, complications or delivery within the gestational age the CPG includes. Titles were also rejected if the article mainly addressed spontaneous preterm labor. Culling abstracts of articles further reduced the articles to a final number of 30. These 30 papers I reviewed in full to discover if they made recommendations about optimal time of delivery; if not, I noted why they did not.

				Quality of	Guideline Evidence	Article
Identifiers	Condition	Recommendation?	Agree?	Evidence	Level	Туре
21962629	Gest HTN	> 37 wks	Yes			Analysis (sec) of RCT
PCOG						
(NoPMID)	Previa	38wks	Yes	1	Level A	Guideline
[RCOG (NoPMID)]*	Acreta	36-37wks	Yes	1	Level A	[Guideline]
22220321	HTN	≥ 38 wks	Yes	1	Level A	Guideline
21962624	Prior ut incs	≥ 39 wks	Yes	II-A	Level B	Guideline
19300347	Prior stillbirth	≥ 39 wks	Yes		Level C	Guideline
15738045	Pregest DM	By due date	Yes	1	Level A	Guideline
22855972	Mult gest	38 wks	Yes	1	Level A	Guideline
21962631	Prior stillbirth	≥ 39 wks	Yes	II-A		Lit review/ex pert consensus
[21962627]*	Mult gest	38 wks	Yes			[Lit review/ex pert consensus]
21962628	Oligobydrampios	> 24 whs	Vec			Lit review/ex pert
21902028	Ongoriyuraninios	2 34 WAS	165			Lit review/ex pert
21962625	IUGR	37-38 wks singl	Yes	II-B		consensus
21962625	IUGR	34-36 wks TIUP				Lit review/ex pert consensus
21962626	Fetal anomalies	Case-dependant	Yes			Lit review/ex pert consensus
						Lit review/ex pert
21962623	Accreta	34-35 wks	Yes	II-A	Level B	consensus
16401210	Mult gestation	32-34 wks	Yes	II-A		Literature review

Table 1. Summary of Articles by Recommendation and Type

					Literature
					review,
					expert
21962630	DM	Case-dependant	Yes	I	consensus
					Retrospec
					tive
10879335	Mult gest	≥ 38 wks	Yes	II-B	cohort
					Retrospec
					tive
22302586	Mult gest	≥ 36 wks	No	II-B	cohort
					Retrospec
					tive
16801956	HTN	39wks	Yes	II-B	cohort
					Retrospec
					tive
16801956	DM	40-41 wks		II-B	cohort
					Retrospec
					tive
21585638	Multiple gest	🗲 32 wks	Yes	II-B	cohort
					Retrospec
11228502	Mult gest	37-38 wks	Yes	II-A	tive pop

SOURCE: literature search by author conducted on 3/5/13-3/8/13. See appendix for full details of search strategy and full search results.

*One guideline and one literature review examined two conditions and made a recommendation for each. Their recommendations are presented on two separate rows for ease of review, but they are not separate articles.

I also graded the literature based on the USPSTF grading system and the ACOG method of grading recommendations. (See Appendix 3)

Results

Of the 30 full-text articles reviewed, 20 gave recommendations for optimal time of delivery. Of these 20, all agreed with our guideline's recommendations, for a total agreement of 100%. All 20 papers were also published before the original narrative review took place, thus avoiding any problems of anachronism when comparing the two reviews.

Discussion

As a first-year resident physician in the OBGYN department, I was eager to become involved in delivering patient care. I found – and this experience is common to newly-minted doctors – that although much of the standard patient care we were expected to provide had its roots in evidence-based medicine, the existing culture of LVHN exerted substantial influence on clinical decisions, particularly when there was perceived to be no single method that far outperformed the others. Many different providers translated into slightly divergent standards of care. "Going to the data" to clarify best practices was often a daunting task, due to the wealth of data available and the sometimes conflicting or unclear recommendations derived from that data. However, in medical school, we are taught to be life-long learners, and a clear assessment of the current data and standard best practices is exactly the kind of thing we have been trained to do.

Late preterm and early term birth increases the risk of perinatal morbidity and long-term disabilities. To deliver early, therefore, and risk the associated iatrogenic morbidity, a clinician must feel comfortable that she has strong reasons. Such certainty is hard to come by. The evidence-based literature provides us with information we can use to make educated guesses, taking account of the risks and benefits of our decisions.

As I began this case study, my training had biased me to assume that without a full and time-intensive systematic review of the literature, the clinical practice guidelines we developed would be at best incomplete and at worst harmful for having ignored or missed important evidence. My review of the policy literature and the results of the systematic review I completed have shown me that our process for guideline development was not unusual for smaller institutions. Nor were the results so horribly off-base. Although we did not account for bias, this is a fundamental flaw that can be addressed only through full review of the literature, both published and unpublished, in all languages and across all countries – a feat that is often impossible in practice for any institution.

Shekelle and colleagues assessed whether current clinical practice guidelines in practice are up-to-date, and found that a distressing proportion of national guidelines were not [51, 52].

Browman points out that Shekelle's method may have been the important conclusion to his article – specifically, that there are practical obstacles to achieving perfection (or close) in guideline development. A possible solution may be a process that starts with a methodologically strong literature review that would build a "foundation" guideline, one that met all possible criteria of trustworthiness. Then, future updates – Thompson's "aftercare" of the guidelines – could be more easily limited to a focused literature search and the guidance of experts. Shekelle suggests guidelines be revised every three years.

In effect, this is how *Indicated Late Preterm and Early Term Birth* was born. We started from several national medical guidelines (the ACOG Practice Bulletins). We then had expert guidance about which indications were important and an expert-focused narrative review of the literature regarding these indications. A counterfactual systematic review with language and geographic limitations has been shown to back up our conclusions. Given the significant

emphasis placed on systematic reviews as critical to the development of guidelines, it is interesting that we did not need to perform a more thorough review of the literature to reach the same conclusions for these clinical questions.

Perhaps the lack of discrepancy between narrative and systematic review is specific to the particular questions. A clinical problem with a more robust body of ongoing literature (e.g. asthma) and higher population prevalence might benefit from frequent and detailed review of new literature. Perhaps these particular clinical questions don't have enough current research to change the management; the studies that are available are purely retrospective. Published research about high-risk pregnancies tends to take a very conservative approach because the results of a less-conservative management plan can be so disastrous; if a baby is delivered early and there are complications of prematurity, providers may console the patient and themselves that at least the baby is not an intrauterine fetal demise. There are many retrospective and observational studies, but they all agree with each other and all qualified their recommendations with words like "presumably," "apparently," and "seems reasonable to." Thus, it is possible that the study of high-risk pregnancy is an outlier: studies tend to show similar results because study designs tend to be conservative and reflect only retrospective analyses of conventional care, rather than experimental care that intentionally breaks with convention and might produce innovative (but possibly deadly) results.

Despite initially finding frightening the idea that we did not need to perform a full systematic review to make an accurate recommendation, I am rethinking this assumption [13, 51, 53]. We know that making gold-standard guidelines is expensive in time, training, talent and institutional resources. It requires significant attention to minimizing biases. It requires attention to conflicts of interest and multidisciplinary committee membership. However, if we can come up with a viable method for practical guideline creation and show that the method is valid, perhaps
we needn't limit ourselves to poor guidelines or no guidelines in the real world. If, for instance, we take Shekelle's work as a good place to start, and develop guidelines based on a foundation of excellent evidence with frequent updates to save our guidelines from languishing, forgotten, as the literature marches on without them, we can make headway into guidelines for the rest of us.

Conclusion

Published literature regarding the development of EBP-oriented clinical practice guidelines has always stressed the need to begin with a systematic review. In some cases, the authors of these papers have argued that guidelines developed without systematic review are worse than no guidelines at all [1, 12, 20]. So health care providers seem to have two options: develop guidelines using the resource-intensive, slow, gold standard process or use no guidelines at all and rely on each provider to review the literature individually (during their free 30 seconds per article per day, naturally). However, this case study superficially appears to demonstrate that a guideline developed using a narrative review could be just as good as one developed using a systematic review. What explains the discrepancy?

One easily overlooked explanation is that the guideline developed in this case study was an *iterative* guideline, i.e. it relied strongly on practice bulletins that had previously been published by a national institution (ACOG) that itself used systematic review. This enabled the committee specialists to select only notable literature that they felt added to the perspective found in the practice bulletins. The fact that a counterfactual systematic review accorded with the narrative review in all significant aspects indicates what might be termed a potential third way: guidelines developed via narrative review that bootstrap from one or more existing systematic reviews.

In order for this third option to be viable, certain conditions need to be met:

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• The CPG must incorporate one or more "foundational" guidelines that were compiled using systematic reviews that were exhaustive and methodologically sound.

• The development committee must have at least one member who has working knowledge of significant published research in the years since publication of any foundational guidelines (those satisfying the above criterion).

• The development committee must have at least one member who has training or experience in formal grading of evidence from an EBM perspective.

• Development committees may profit from assuring that representatives of cross-cutting or overlapping disciplines are participating in the development effort. In this case, the perspectives of a neonatologist may have been helpful.

• The institution must schedule and execute updated narrative reviews every three years under these same conditions.

 In addition to regular updates, the institution must assure that it has a mechanism in place to monitor and respond rapidly to new developments in the literature.

If these conditions are obtained, an institution could use a development process similar to the one described in the case study and possibly emerge with a clinical practice guideline that exhibited a high degree of correlation with a hypothetical gold standard guideline covering the same material. If this occurred, it would encourage more institutions to attempt development of more guidelines, contributing to an overall improvement in patient care. On the other hand, the specific circumstances of this case study, as discussed earlier, may render it an outlier, unable to offer predictive power about guideline development in other specialties.

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It should also be possible to extend this case study by evaluating the success of practice change after guideline implementation. Clinical practice guidelines have had moderate success in changing practice in some situations. Gibbins et al. recently reported success in implementing new OB guidelines[54]. They also measured, over several months, how practice management successfully changed in their institution after implementation. Perhaps LVHN can also change, despite the frequent literature findings that discourage such a possibility. The practice population in the Gibbins study is similar to that at LVHN, and the project is likely to be generalizable. Such a study is well within the scope of a resident research project.

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Appendices

- Appendix 1: LVHN Clinical Practice Guideline
- Appendix 1a: CPG Summary and Addenda
- Appendix 2: Systematic Review Search Terms
- Appendix 3: Grading the Literature
- Appendix 4: Systematic Review Search Results

Appendix 1

Lehigh Valley Health Network

PATIENT CARE SERVICES PATIENT CARE MANUAL CLINICAL PRACTICE GUIDELINE

Indicated Late Preterm and Early term Birth

I. KEY POINTS

- 1. A large proportion of neonatal morbidity and mortality is secondary to preterm delivery (prior to 37 weeks gestation).
- 2. The majority of neonatal complications are seen in neonates born before 34 weeks, however data has recently shown numerous respiratory and other complications in late preterm (34-37 weeks) and even in early term births (37-39 weeks).
- 3. True indications for late preterm or early term delivery include severe preeclampsia, intrauterine growth restriction (IUGR) with abnormal fetal testing, and acute placental abruption.
- 4. Conditions for which the optimal timing of delivery is debatable include prior fetal demise, stable placenta previa/accreta, mild preeclampsia or gestational hypertension, multiple gestations, prior classical hysterotomy or myomectomy, fetal anomalies, maternal medical conditions including diabetes and cholestasis, IUGR with reassuring fetal testing, and alloimmunization in pregnancy.

I. SCOPE:

This clinical practice guideline (CPG) applies to all pregnant women cared for at Lehigh Valley Health Network. It represents recommendations, not binding standards and reflects the most recent recommendations.

II. SKILL LEVEL:

Obstetricians, Certified Nurse Midwives under the direction of an Obstetrician, Obstetrical residents.

III. INTRODUCTION/PURPOSE:

Definitions:

<u>Preterm Birth</u>: Birth before 37 weeks gestation. <u>Late Preterm Birth</u>: Birth between 34 0/7 weeks and 36 6/7 weeks gestation.

Early Term Birth: Birth between 37 0/7 weeks and 38 6/7 weeks gestation.

Preterm birth occurs in approximately 12% of all pregnancies, however contributes to a large proportion of neonatal morbidity and mortality. Although recently there has been a slight decrease in overall rate of preterm birth, the rate of late preterm birth is steadily increasing. Late preterm birth has been associated with numerous neonatal complications, including respiratory distress syndrome, transient tachypnea of the newborn, pneumonia, respiratory failure, surfactant use, ventilator use, sepsis, hyperbilirubinemia, interventricular hemorrhage, and necrotizing enterocolitis. Long term data has shown that cerebral palsy, mental retardation, and developmental disabilities are significantly more common in infants born in the late preterm period when compared to term.

Similarly, early term birth has been associated with increased rates of these same complications, including neonatal death. These complications lead to more neonatal intensive care unit (NICU) admissions and longer hospital stays for the infant.

Some late preterm and early term births occur due to spontaneous preterm or term labor, and are therefore unavoidable. Many late preterm and early term births are considered to be "indicated". True indications would include severe preeclampsia, intrauterine growth restriction (IUGR) with abnormal fetal testing, and acute placental abruption. There are a number of other indications for which the optimal timing of delivery is debatable. These include prior fetal demise, stable placenta previa/accreta, mild preeclampsia or gestational hypertension, multiple gestations, prior classical hysterotomy or myomectomy, fetal anomalies, maternal medical conditions including diabetes and cholestasis, IUGR with reassuring fetal testing, and alloimmunization in pregnancy.

The purpose of this guideline is to determine the optimal timing of delivery for the above-mentioned debatable indications for late preterm/early term birth.

IV. GUIDELINES

A. Previous Stillbirth

- Definition: <u>Stillbirth</u>: Death of a fetus at 20 or more weeks gestation.
- Background

- Overall rate of stillbirth recurrence is between 0-8%.
- The highest risk is associated with an earlier gestational age of the stillbirth, more than one prior stillbirth, stillbirth associated with IUGR, and in non-Hispanic black women.
- \circ Lower risk if prior stillbirth was unexplained.
- Women with a prior stillbirth have increased risk of adverse pregnancy outcomes in subsequent pregnancies, including preeclampsia, placental abruption, IUGR, preterm birth, and cesarean delivery.
- Prospective fetal mortality rates do not significantly increase until after 40 weeks gestation.
- No clear evidence that iatrogenic late preterm or early term birth reduced the rate of recurrent stillbirth.
- Timing of Delivery Guidelines (Level III)
 - Elective delivery at 39 weeks gestation.
 - Elective delivery between 37-38 6/7 weeks if earlier delivery is strongly preferred by the patient AND fetal lung maturity is documented by amniocentesis.
- B. Known Placenta Accreta
 - Definitions:
 - <u>Placenta Accreta</u>: Abnormal placental attachment such that the chorionic villi attach to myometrium rather than being restricted to the deciduas basalis.
 - o Placenta Increta: Chorionic villi invade the myometrium
 - <u>Placenta Percreta</u>: Chorionic villi invade through the myometrium

In this guideline, the general term accreta will refer to all three grades of these abnormal placental attachments.

- Background
 - Greatest risk is maternal hemorrhage accreta is associated with large volume postpartum transfusions, as well as significantly increased risk of peripartum hysterectomy.
 - Strongly associated with placenta previa and prior uterine surgeries. Increasing incidence parallels increasing cesarean section rate.
 - Maternal mortality reported as high as 5.6% in some studies
 - Diagnosed by U/S and/or MRI, though only 2/3 cases known prior to delivery
 - Less dangerous to fetus than to mother- in absence of maternal bleeding, data does not support increased fetal mortality or IUGR
 - Incidence of maternal bleeding beyond 39 weeks is 93%

- 44% rate of emergency delivery <36 weeks for maternal hemorrhage in recent study
- Timing of Delivery Guidelines (Level III)
 - Planned delivery via cesarean section at 34-35 weeks, with or without FLM testing
 - Goal is to avoid emergency cesarean hysterectomy
- C. Stable Placenta Previa
 - Definition: <u>Placenta Previa</u>: Placenta that overlies or is proximal to the internal cervical os
 - Background
 - Greatest risk is maternal hemorrhage and associated consequences: transfusion, peripartum hysterectomy, DIC, ICU admission and death.
 - The presence of a previa at the time of delivery is an indication for cesarean section to avoid maternal hemorrhage.
 - It is often a cause of iatrogenic preterm delivery secondary to bleeding or preterm labor.
 - Approximately 17% of women with placenta previa deliver <34 weeks, a rate that increases to 45% if midtrimester cervical length <3cm. (Includes both iatrogenic and spontaneous delivery)
 - The advantage of earlier delivery is a decreased probability that a patient will present with acute hemorrhage and require an emergent cesarean delivery. This may reduce the risk of surgical complications.
 - Major clinical decision requires weighing the benefits of avoiding emergent delivery against neonatal risks of prematurity.
 - Timing of Delivery Guidelines (Level III)
 - In a stable patient- Planned delivery between 36-37 weeks with documented fetal lung maturity by amniocentesis or at 38 weeks without an amniocentesis.
 - In a patient with comorbidities (Obesity, multiple prior cesarean sections) or who has had multiple antepartum episodes of vaginal bleeding- Scheduled delivery between 36-37 weeks without amniocentesis.
- D. Vasa Previa

- Definition: Vasa previa: Obstetric condition characterized by fetal vessels that traverse the membranes located over the internal cervical os and thus in advance of the fetal presenting part.
- Background:
 - Main risk in vasa previa is rupture of the fetal vessels, which can occur with or without membrane rupture. This can result in fetal exsanguinations in a very short period of time.
 - In monochorionic twin gestations, the perintal mortality is high for both twins, even if the vasa previa is associated with only one twin, due to the presence of placental vascular anastomoses.
 - The fetal vessels are also at risk of compression from the fetal presenting part since they are not protected by the umbilical cord.
- Timing of Delivery Guidelines (Level III)
 - Cervical length ultrasound should be performed between 33-34 weeks
 - If cervical length >2.5cm, planned delivery at 36 weeks without amniocentesis
 - If cervical length <2.5cm, planned delivery at 34-35 weeks without amniocentesis.
- E. Mild preeclampsia/Gestational HTN
 - Definitions:
 - Mild Gestational Hypertension: Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in a previously normotensive pregnant woman who is ≥20 weeks of gestation and has no proteinuria
 - <u>Severe Gestational Hypertension</u>: Sustained elevations in systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg with no proteinuria.
 - Mild Preeclampsia: New onset of hypertension (≥140/90 mmHg) and proteinuria after 20 weeks of gestation in a previously normotensive woman.
 - Severe Preeclampsia: Sustained elevations in systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg with severe proteinuria (>5g), or other signs/symptoms of end-organ injury present
 - Background
 - Infants born to hypertensive women have increased risks of admission to the neonatal intensive care unit, longer hospital

stays, and higher rates of respiratory distress syndrome (may be related to higher rates of IUGR).

- Risks of expectant management between 34-37 weeks gestation include progression to severe hypertension, eclampsia, HELLP syndrome, placental abruption, pulmonary edema, fetal growth restriction, and fetal death.
- There is no data to support that expectant management between 34-37 weeks improves perinatal outcomes or increase maternal/fetal risks.
- HIPITAT trial (Induction of labor versus expectant monitoring for gestational hypertension or mild preeclampsia after 36 weeks gestation)
 - Multicenter randomized controlled trial
 - Induction at <u>></u>36 weeks was associated with reduction in composite outcome of HELLP syndrome, pulmonary edema, placental abruption, eclampsia, maternal ICU admission, and cesarean delivery
 - No difference in neonatal outcomes between two groups (perinatal death, 5-minute Aprag <7, Cord Ph <7.05, NICU admission, and respiratory distress syndrome).
- Timing of Delivery Guidelines (Level I)
 - Severe gestational hypertension and severe preeclampsia-<u>></u>34 weeks (for diagnoses made at or after 34 weeks).
 - Mild gestational hypertension and mild preeclampsia- <u>></u>37 weeks
- F. Multiple Gestation
 - Definition: <u>Multicystic encephalomalacia</u>: Cystic lesions in the cerebral white matter of areas supplied by the anterior and middle cerebral arteries, associated with profound neurologic abnormalities.
 - Background
 - Multifetal gestations carry a number of perinatal risks, including low birth weight, preterm delivery, cerebral palsy, neonatal and infant death, respiratory distress syndrome and longer hospital stay. These risks vary based on type of multiple gestation.
 - Dichorionic twins
 - Risk of stillbirth at 39 weeks exceeds that of a post term singleton pregnancy.

- Twins at 37-38 weeks have stillbirth rates similar to post term singleton pregnancies.
- Monochorionic-diamniotic twins
 - Risk of stillbirth and other perinatal complications is higher compared to dichorionic pregnancies.
- Monochorionic-monoamniotic twins
 - Risk of stillbirth of both fetuses is 10-20%. This is most often due to consequences of cord entanglement, which occurs in most cases.
 - Management prior to delivery can include close outpatient surveillance (NST's 2-3 times a week) or inpatient surveillance (NST's multiple times a day or continuous monitoring). There are insufficient data to determine which strategy is better, though recent observational data suggests that some amount of inpatient monitoring may decrease fetal mortality.
- Single-Twin Intrauterine fetal demise (IUFD)
 - Occurs in 0.5-6% of twin pregnancies and can have significant sequelae on the surviving fetus.
 - Sequelae include:
 - Multicystic encephalomalacia and/or multiorgan damage in 20-30% of monochorionic pregnancies
 - Preterm labor and delivery in all twin pregnancies (no increased risk of infection but higher rates of cesarean delivery due to nonreassuring fetal status of surviving twin).
 - Maternal consumptive coagulopathy (very uncommon if baseline maternal hematologic studies are normal).
- Timing of Delivery Guidelines (Level III)
 - Dichorionic twins
 - Elective delivery at 38 weeks gestation in well-dated and uncomplicated dichorionic pregnancies
 - If the patient desires prolongation of pregnancy past 38 weeks, there must be evidence of normal fetal growth, amniotic fluid, umbilical artery Doppler studies, and twice weekly antenatal testing (at least one biophysical profile).
 - Prolongation past 39 weeks gestation is not recommended due to increased risk of stillbirth without anticipated neonatal benefit.
 - Monochorionic-Diamniotic Twins

- Elective delivery between 36-37 weeks in well-dated and uncomplicated monochorionic-diamniotic twin gestations.
- If the patient desires prolongation of pregnancy past 37 weeks, there must be evidence of normal fetal growth, amniotic fluid, umbilical artery Doppler studies, and twice weekly antenatal testing (at least one biophysical profile).
- Prolongation past 38 weeks gestation is not recommended due to increased risk of stillbirth without anticipated neonatal benefit.
- o Monochorionic-Monoamniotic Twins
 - Elective delivery at 32-34 weeks after administration of antenatal corticosteroids, as risk from complications of prematurity are likely less than the risk of fetal demise for ongoing pregnancies.
- Single-Twin IUFD
 - In monochorionic pregnancies, elective delivery at >34 weeks or at discovery if the IUFD occurs at a later gestational age.
 - In dichorionic pregnancies, elective delivery at 37 weeks.
- G. Prior Classical Cesarean Delivery
 - Definitions:
 - <u>Classical Cesarean Delivery</u>: A cesarean section with a vertical uterine incision that involves the upper muscular, contractile portion of the uterus.
 - o TOLAC: Trial of labor after cesarean section
 - Background
 - Greatest risk is uterine rupture in a subsequent pregnancy. Rupture risk is 4-9% if TOLAC attempted.
 - Uterine rupture may be associated with stillbirth, perinatal hypoxic brain injury, and maternal blood loss necessitating hysterectomy.
 - Rupture most often occurs as a complication during active labor, but can occur prior to labor.
 - Decision analyses balance RDS of newborn with preterm delivery against hypoxic ischemic encephalopathy and cerebral palsy after uterine rupture.
 - Timing of Delivery Guidelines (Level III)
 - Planned delivery via repeat cesarean section between 36-37 weeks without amniocentesis.

- H. Prior Myomectomy
 - Definition: <u>Myomectomy</u>: Surgical removal of uterine myomas
 - Background
 - Myoma prevalence is approximately 25%. After myomectomy, 55% of women become pregnant.
 - Shift in care over time from laparotomy to laparoscopic approach.
 - There is lack of high-quality evidence to accurately assess rupture risk.
 - Type of closure (single or multilayer) and use of electrocautery during myomectomy, as well as size and placement of fibroid, may influence rupture risk.
 - No risk associated with myomectomy of a pedunculated myoma
 - Recommendation is for cesarean delivery if the myometrium was significantly compromised, i.e. the uterine cavity was entered or nearly entered during prior myomectomy, or if a large number of myomas were removed.
 - In cases where the myometrium was not significantly compromised, the patient can be managed similar to women with a prior low transverse cesarean section including continuous fetal monitoring in labor, early access to obstetric anesthesia, and labor in units equipped to perform an emergent cesarean delivery should it become necessary.
 - Timing of Delivery Guidelines (Level III)
 - Planned delivery via cesarean section at 37-38 weeks with FLM documented by amniocentesis or at 38 weeks without amniocentesis
- I. Fetal Anomalies
 - Definition: <u>Ex Utero Intrapartum Treatment (EXIT)</u>: A procedure that maintains fetal oxygenation via the existing placental circulation at the time of cesarean delivery to allow for some procedure to be performed immediately on the fetus.
 - Background
 - \circ 2-3% of pregnancies are complicated by a fetal anomaly.

- A small subset of pregnancies complicated by a fetal anomaly will require planning for location, mode, and timing of delivery.
- For most anomalies, there is no benefit to delivering in the late preterm or early term period.
- Specific anomalies carry ongoing risks to the fetus and/or mother. Fetal risks include fetal death, hemorrhage, and ongoing or worsening organ damage.
- o Benefits of late preterm or early term delivery
 - Avoidance of ongoing risk to fetus in utero.
 - Allowing for delivery in a controlled setting with coordination of a multidisciplinary team.
 - Allow for direct care of the neonate with organ injury.
- Risks of continued pregnancy near term
 - Risk of uterine rupture in women who have undergone invasive fetal intervention during pregnancy.
 - Preeclampsia/mirror syndrome if fetus has persistent hydrops.
 - Maternal hypertension in cases of fetal adrenal tumors.
 - Neonatal risk of unscheduled or unplanned delivery.
- Timing of Delivery Guidelines (Level IIII)
 - Vast majority of anomalies do not require early delivery
 - Among the small subset of anomalies that may benefit from late preterm or early term delivery, there is a large amount of variability regarding optimal management.
 - Each management plan requires individualization, often in conjunction with Maternal Fetal Medicine, Neonatology, and Pediatric Surgery.
 - Elective delivery between 34-39 weeks can be considered for:
 - Suspected worsening of fetal organ damage
 - Potential for fetal intracranial hemorrhage (ex. vein of Galen Aneurysm, neonatal alloimmune thrombocytopenia)
 - When delivery prior to labor is preferred (ex. planned EXIT procedure)
 - Previous fetal intervention
 - Concurrent maternal disease (ex. preeclampsia, chronic hypertension)
 - Potential for adverse maternal effect from fetal condition

- Known lethal anomalies
 - Delivery after 39 weeks is recommended.
- J. Oligohydramnios
 - Definition: <u>Oligohydramnios</u>: Maximum vertical pocket (MVP) <2 cm or an amniotic fluid volume of <5 cm.
 - Background
 - Oligohydramnios is associated with an increase in nonreactive nonstress tests, fetal heart rate decelerations, fetal intolerance of labor, stillbirth, 5-minute Apgar scores <3, and meconium aspiration.
 - Optimal definition of oligohydramnios has not been determined; no evidence that one method is a better predictor of adverse neonatal outcome than the other.
 - Maximum vertical pocket has higher specificity in the preterm period and would lead to lower rates of delivery.
 - Timing of Delivery Guidelines (Level III)
 - Appropriate for gestational age
 - 34-36 weeks- Maternal hydration followed by repeat fluid evaluation 2-12 hours later. If no improvement, recommendation is for intensive fetal monitoring with delivery in the setting of non-reassuring fetal testing.
 - >37 weeks- elective delivery
 - Presence of comorbidities (chronic hypertension, documented placental disease, or IUGR)
 - <u>></u>34 weeks- elective delivery
- K. Diabetes
 - Definitions: <u>Macrosomia</u>- Birthweight greater than 4000 grams.
 - Background
 - Risks associated with diabetes related to disease type and presence/severity of end organ involvement.
 - Maternal risks (mostly with pre-gestational diabetes)
 - Worsening diabetic retinopathy
 - Nephropathy
 - Gastroparesis
 - Hypertensive disorders (including preeclampsia)
 - Cardiovascular disease (including congestive heart failure and ischemic coronary syndrome)
 - Ketoacidosis

- o Fetal risks
 - Spontaneous abortion
 - Congenital anomalies (directly proportional to hemoglobin A1c in first trimester)
 - Intrauterine growth restriction
 - Macrosomia
 - Intrauterine fetal demise
- o Delivery risks
 - Shoulder dystocia
 - Brachial plexus injury
- Neonatal risks
 - Hypoglycemia
 - Polycythemia
 - Hypocalcemia
 - Hyperbilirubinemia
 - Cardiac dysfunction secondary to septal hypertrophy
 - Respiratory distress syndrome
- Timing of pulmonary maturation is related to degree of glucose control
- Timing of Delivery Guidelines (Level I)
 - Pregestational diabetes
 - Well controlled- Delivery prior to 39 weeks is not recommended
 - Poorly controlled- 37-39 weeks after documented fetal lung maturity by amniocentesis
 - Gestational diabetes
 - Well controlled (by diet or medication)- Delivery prior to 39 weeks is not recommended
 - Poorly controlled- 37-39 weeks after documented fetal lung maturity by amniocentesis
- L. Intrauterine Growth Restriction
 - Definitions:
 - Intrauterine Growth Restriction (IUGR): An estimated fetal weight (EFW) less than the 10th percentile for gestational age.
 - <u>Small for Gestational Age</u> (SGA): Infants with birth weight less than the 10th percentile, representing small but normally grown infants (constitutionally small).
 - Background
 - Approximately 70% of infants with a birth weight less than the 10th percentile represent constitutionally small infants, and are not at risk for adverse perinatal outcomes.

- Approximately 30% have true IUGR and are at risk for complications including increased rates of perinatal mortality, meconium staining, emergency cesarean delivery, low Apgar scores, and low umbilical cord pH.
- Findings associated with increased risk of fetal hypoxemia/academia in IUGR fetuses:
 - Biophysical profile score <4
 - Repetitive decelerations
 - Nonreactice nonstress test
 - Oligohydramnios
 - Absent or revere flow in the umbilical artery
 - Reversal of flow in the ductus arteriosus
- Timing of Delivery Guidelines (Level III)
 - Singleton Gestation
 - Delivery regardless of gestational age
 - Persistent abnormal fetal surveillance suggesting imminent fetal jeopardy
 - Patients with severe preeclampsia or other maternal condition complicated by IUGR when maternal benefit from delivery outweighs fetal benefit of pregnancy continuation.
 - Delivery between 34-37 weeks
 - Biophysical profile score <4
 - Oligohydramnios
 - Repetitive fetal heart rate decelerations
 - Absent or reversed end diastolic flow in the umbilical artery
 - Delivery between 36-37 weeks
 - Elevated umbilical artery Dopplers
 - Delivery between 38-39 weeks
 - IUGR fetuses with normal Doppler studies and normal amniotic fluid volume (with twice weekly antenatal testing)
 - \circ Twins
 - Delivery regardless of gestational age
 - Persistent abnormal fetal surveillance suggesting imminent fetal jeopardy
 - Patients with severe preeclampsia or other maternal condition complicated by IUGR when maternal benefit from delivery outweighs fetal benefit of pregnancy continuation.
 - Dichorionic twins with isolated IUGR- 36-37 weeks
 - Monochorionic-diamniotic twins with isolated IUGR-32-34 weeks

- M. Intrahepatic Cholestasis of Pregnancy
 - Definition: Intrahepatic Cholestasis of Pregnancy (ICP): Condition characterized by increased total serum bile acid concentrations and generalized pruritis.
 - Background:
 - Maternal outcomes are generally favorable
 - ICP is associated with increased risks of preterm labor, meconium staining, respiratory distress syndrome, and fetal death.
 - Fetal demise is seen in approximately 1-3% of patients with ICP, and rarely occurs prior to 36 weeks.
 - There are no antenatal tests that have been shown to predict the risk of fetal demise.
 - Timing of Delivery Guidelines (Level III)
 - Delivery at 37 weeks after fetal lung maturity documented by amniocentesis or at 38 weeks without amniocentesis

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Appendix 1a:

Summary of Clinical Practice Guideline: Indications for Late Preterm and Early-Term Delivery

Condition	Timing of Delivery Guideline	Alternative Timing of
Previous Stillbirth	>30 wooks	37-38 6/7 wooks with
	<u>-</u> 33 weeks	documented FLM
Placenta Accreta	34-35 weeks	
Stable Placenta Previa (No	36-37 weeks with documented FLM	
Co-morbidities)	38 weeks without FLM	
Stable Placenta Previa	36-37 weeks without FLM	
(With Co-morbidities)		
Vasa Previa (Cervical	36 weeks	
length >2.5cm)		
Vasa Previa (Cervical	34-35 weeks	
length <2.5cm)		
Severe gestational	>34 weeks (for dx made >34 weeks)	
HTN/preeclampsia		
Mild gestational	≥37 weeks	
HTN/preeclampsia		
Dichorionic Twins	38 weeks	38-39 weeks with
		reassuring antenatal testing
Monochorionic Diamniotic	36-37 weeks	37-38 weeks with
Twins		reassuring antenatal testing
Monoamniotic Twins	32-34 weeks	
Single-Twin IUFD		
Monochorionic Twins	≥34 weeks	
Dichorionic Twins	37 weeks	
Prior Classical Cesarean	36-37 weeks	
Prior Myomectomy	37-38 weeks with documented FLM	
	38 weeks without FLM	
Fetal Anomalies (See	34-39 weeks	
guideline for details)		
Lethal fetal anomalies	≥39 weeks	
Oligohydramnios (AGA)	≥37 weeks	
	(34-36 weeks- Maternal hydration with repeat	
	AFI in 2-12 hrs; intensive monitoring if oligo	
	persists)	
Oligohydramnios (IUGR or	>34 weeks	
co-morbitities)		
Diabetes- Pregestational	>39 weeks	
(Well-Controlled)	-	
Diabetes- Pregestational	37-39 weeks with documented FLM	
(Poorly-Controlled)		
Diabetes- Gestational	≥39 weeks	
(Well-Controlled)		
Diabetes- Gestational	37-39 weeks with documented FLM	

(Poorly-Controlled)		
Singleton IUGR	Delivery regardless of GA -Persistent abnormal fetal surveillance -Severe preeclampsia or other maternal condition 34-37 weeks -Biophysical profile score ≤4 -Oligohydramnios -Repetitive fetal heart rate decelerations -Absent or reversed end diastolic flow in the umbilical artery	
	36-37 weeks	
	Lievaled unbilical aftery Doppiers	
	38-39 weeks	
	-IUGR with normal Dopplers and AFI	
	Delivery regardless of GA -Persistent abnormal fetal surveillance -Severe preeclampsia or other maternal condition	
	36-37 weeks	
	-Dichorionic twins with isolated IUGR	
	32-34 weeks	
Cholestasis of Pregnancy	37 weeks with documented FLM	
	38 weeks without FLM	
Alloimmunization- Mild	37-38 weeks	
anemia		
Alloimmunization- Severe anemia/Multiple fetal transfusions	34-38 weeks, (Individualize each case)	
FLM-Fetal Lung Maturity		1
IUGR- Intrauterine Growth Re	striction	

Appendix 2 Full search terms

("Labor, Induced"[Mesh] OR ((time factors[mesh] OR timing[tw]) AND (pregnan*[tw] OR labor[tw] OR delivery[tw])) OR (induced[tw] AND (delivery[tw] OR labor[tw]))) AND (stillbirth[tw] OR fetal demise[tw] OR fetal death[tw] OR Placenta Accreta[tw] OR placenta previa[tw] OR vasa previa[tw] OR pre-eclampsia[tw] OR preeclampsia[tw] OR multiple gestation[tw] OR prior classical Cesarean[tw] OR myomectomy[tw] OR fetal anomal*[tw] OR oligohydramnios[tw] OR cholestasis[tw] OR alloimmunization[tw] OR diabet*[tw]) AND retrospective[tw]

The initial search was performed on March 5, 2013 and resulted in 786 articles. The following standard filters culled the data to 513 articles: abstract and full-text available, humans and English. This cohort was further refined on title alone to include 55 articles. Exclusion criteria included case reports, editorials and letters, and research performed outside of Western Europe and North America. To be included, titles needed to indicate that the article addressed timing of delivery, outcomes, complications or delivery within the gestational age the CPG includes. Titles were also rejected if the article mainly addressed spontaneous preterm labor. Abstracts of articles further reduced the articles to a final number of 35. Of these 35 full articles for review, 20 gave recommendations for optimal time of delivery.

Appendix 3

Evaluating the Evidence: Studies and Recommendations

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force.

I Evidence obtained from at least one properly designed randomized controlled trial

II-A Evidence obtained from well-designed controlled trials without randomization

II-B Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group

II-C Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Recommendations were graded in the following categories:

Level A: The recommendation is base on good and consistent scientific evidence. **Level B**: The recommendation is base on limited or inconsistent scientific evidence. **Level C**: The recommendation is based on expert opinion or consensus.

Sources:

http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm http://www.acog.org/Resources%20And%20Publications/Department%20Publications/Reading %20the%20Medical%20Literature.aspx http://guideline.gov/index.aspx

			Condition	Give	Type of	Notes - If no recommendation given, the reason
Identifiers	Title	Authored By	Addressed	recommendation?	Article	why is included first
	Expectant management of severe preeclampsia and preeclampsia superimposed on chronic hypertension between 24 and 34 weeks'	Vigil-De Gracia P, Montufar-			Retrospective cohort 129	Beyond the scope -Standard of care in this hospital was delivery at 34 wks for severe preeclampsia as an indication alone but the focus of the results was on poor outcomes if the pregnancy was expectantly managed to
PMID: 12593889	gestation.	Rueda C, Ruiz J.	Preeclampsia	No	women	this point- my focus is beyond the scope of this study.
PMID: 15458915	ACOG Practice Bulletin #56: Multiple gestation: complicated twin, triplet, and high-order multifetal pregnancy.	American College of Obstetricians and Gynecologists Committee on Practice Bulletins- Obstetrics	Multiple gestation	Νο	Guideline from American Congress of Obstetricians and Gynecologists	Not enough evidence to make recommendation- Offers the information that 38 weeks for twins is the nadir of perinatal mortality, but stops short of a recommendation, citing not enough evidence for improved outcome with induction at this age.
PMID: 22185537	Perinatal outcome after ultrasound diagnosis of anhydramnios at term.	Visvalingam G, Purandare N, Cooley S, Roopnarinesingh R, Geary M.	Oligohydramnios	No	Review of the literature; expert opinion	Beyond the scope- Focus of study was perinatal outcome after anhydramnios at term, neither condition applicable to my guideline

Appendix 4, Part 1: Articles that made no recommendation

PMID: 12781410	Pregnancy outcome after laparoscopic and laparoconverted myomectomy.	Soriano D, Dessolle L, Poncelet C, Benifla JL, Madelenat P, Darai E.	Myomectomy	No	Retrospective cohort 106 women	Beyond the scope- Focus of study was pregnancy outcomes, not timing of delivery.
PMID: 22341806	Pregnancy outcomes after transvaginal myomectomy by colpotomy.	Rovio PH, Heinonen PK.	Myomectomy	No	Prospective case control	Observational study, without recommendations. Does not apply to my indications as these pregnancies were all delivered without complication at term
PMID: 12389673	Severe pre- eclampsia remote from term: what to expect of expectant management.	Blackwell SC, Redman ME, Tomlinson M, Berry SM, Sorokin Y, Cotton DB.	PreEclampsia	No	Retrospective cohort study at a single hospital, 142 women	Beyond the scope- Outcome of study was latency period between diagnosis and delivery, not on optimal timing of delivery. Beyond the scope of the trial.
PMID: 22071052	Perinatal outcome in pregnancies complicated by isolated oligohydramnios diagnosed before 37 weeks of gestation.	Melamed N, Pardo J, Milstein R, Chen R, Hod M, Yogev Y.	Oligohydramnios	Νο	Retrospective cohort 108 pregnancies	Beyond the scope- Focus of study was perinatal outcome after diagnosis of low fluid, and study suggests (but does not <i>recommend</i>) that most of the problems with low amniotic fluid are actually due to iatrogenic preterm delivery, and not secondary to the low fluid itself.
PMID: 18327870	Risk factors associated with preterm birth according to gestational age at birth.	Ofori BD, Le Tiec M, Bérard A.	Preterm birth	No	Three case- control analyses	Beyond the scope- this is an epidemiological case-control study looking at risk factors associated with preterm birth, and describes them while accounting for cofounding factors.

PMID: 22939722	Impact of chorionicity on risk and timing of intrauterine fetal demise in twin pregnancies.	McPherson JA, Odibo AO, Shanks AL, Roehl KA, Macones GA, Cahill AG.	Multiple gestation and stillbirth	No	Retrospective cohort of 2161 twin pregnancies	study, noting the frequency of the second twin's demise if one demise occurs- results show that monochorionic twins are at much higher risk of double fetal demise. They do not make recommendations about delivery beyond "these data can provide some guidance when counseling women" with twin pregnancies about outcomes. Recommendation data could be extrapolated.
PMID: 17014813	Maternal-fetal conditions necessitating a medical intervention resulting in preterm birth.	Ananth CV, Vintzileos AM.	Preterm birth	No	Population- based retrospective cohort study	Beyond the scope- This is a descriptive study, looking at <i>reasons</i> babies are born early, which include many of my indications. No recommendations were put forth by the authors, and indeed the study was not attempting to answer my study question. Institution-specific- the authors start with the premise that late-preterm and early term birth is associated with
	Nonspontaneous	Gyamfi- Bannerman C,				higher fetal morbidity, and they want to see whether such briths in their institution are evidence-based or non- evidence based. The study ends up being a social commentary, suggesting that phyicians are more likely to deliver older, wealther women early if they want to be delivered early. However, they do question the validity of most of the indications our guideline covers, and it appears they would disagree with our findings- not
	late preterm	Fuchs KM,			Retrospective	because they mounted evidence against these indications,
	birth: etiology	Young OM,			cohort 2693	but because they don't believe the existing literature
PMID: 22035950	and outcomes.	Hoffman MK.	Preterm birth	No	women	supports us.

Beyond the scope-This ia an observational and descriptive

	The value of the short-term fetal heart rate					
PMID: 18715432	variation for timing the delivery of growth-retarded fetuses.	Serra V, Moulden M, Bellver J, Redman CW.	Intrauterine growth restriction	No	Retrospective cohort 257 fetuses	No guts - "Timing the delivery of the most preterm and small fetuses remains a difficult task." And to be fair, their evidence could be used to support either side.

									Level of			
								Quality	Evidence			
					Give	What is	Agree with	of	if		Article	
No.	ID	Title	Authored By	Condition Addressed	recommendation?	recommendation?	CPG?	Evidence	guideline	Type of Article	Number	Notes
												In uncomplicated twin gestations, delivery at between 36 and 37 weeks' gestation was no
13	PMID: 10879335	Optimal gestational age for twin delivery.	Udom-Rice I, Inglis SR, Skupski D, Adams D, Chervenak FA.	Multiple gestation	Yes	At or after 38 wks	Yes	II-B		Retrospective cohort of 329 twin deliveries	13	associated with a reduction in neonatal complications compared with deliveries at or after 38 weeks' gestation.
		,	Southwest									The data do not support a policy of elective delivery before 36 weeks' gestation in monochorionic twin pregnancies
		Prospective risk of late stillbirth in monochorionic	Thames Obstetric Research	Multiple		At an after				Retrospective cohort of 3005		which agrees with our finding that places optimal
14	22302586 PMID:	cohort study. Previous stillbirth, late preterm, and	(STORK).	gestation	Yes	At or after 36 wks	No	II-B		pregnancies Review of the literature.	14	36-37 weeks. The paper finds n
15	21962631	early-term birth.	Silver RM.	Prior stillbirth	Yes	39 wks	Yes	II-A		including	15	support earlier

Appendix 4: Part 2, Articles that made recommendations

16	PMID: 21962629	Management of late preterm and early-term pregnancies complicated by mild gestational hypertension/pre- eclampsia.	Sibai BM.	Gestational hypertension	Yes	At or after 37 wks	Yes	1		retrospective trials	16	delivery than afte 39 weeks, but does suggest that in cases of extreme materna distress, earlier delievery with evidence of pulmonary maturity is acceptable. This RCT finds good data to support induction at or after 37 wks for mild/stable preeclampsia, but finds no data to support either expectant management or earlier delivery in patient with complications. Fo our purposes, the data supports our recommendation Elective delivery by caesarean section in
17	Not in PubMed	Placenta praevia, placenta praevia accreta and vasa praevia: diagnosis and management	Royal College of Obstetricia and Gynecologists	Previa and accreta	Yes	Previa- 38wks; accreta- 36- 37wks	Yes for accreta, yes for previa	I	Level A	Guideline from Royal College of Obstetricia and Gynecologists	17	asymptomatic women is not recommended before 38 weeks of gestation for

18	PMID: 16801956	The impact of the interaction between increasing gestational age and obstetrical risk on birth outcomes: evidence of a varying optimal time of delivery.	Nicholson JM, Kellar LC, Kellar GM.	Hypertension and diabetes	Yes	HTN 39wks, DM 40-41	Yes	II-B		Retrospective cohort study at a single hospital 1995- 2003	18	or before 36–37 weeks of gestatio for suspected placenta accreta. Their data supported our recommendation for Optimal Time to Delivery for these two conditions, and they searched the literature to corroborate their findings.
		gestations: timing of indicated late preterm and early-term births in uncomplicated dichorionic, monochorionic, and								Expert opinion		Includes an expert-focused review of the literature and expert opinion, as well as a simple decision-tree, and agrees with our
19	21962627	twins	Newman KB, Unal FR	restation	Ves	At 38 wks	Ves	ш		the literature	19	literature
20	PMID: 22855972	Multiple Pregnancy: The Management of Twin and Triplet Pregnancies in the Antenatal Period.	National Collaborating Centre for Women's and Children's Health (UK).	Multiple	Yes	At 38 wks	Yes		Level A	Guideline from National Collaborating Centre for Women's and Children's Health	20	This guideline reveiwed all the literature surrounding multiple gestations to an exhaustive degre They had 195
20	22033372	i chou.		Bestation	105	, it 50 with	. 05	•	<i></i>	neurth	20	11109 1100 100

placenta praevia,

	PMID:	Hypertension in Pregnancy: The Management of Hypertensive Disorders During	National Collaborating Centre for Women's and Children's			At or after			Level	Clinical practice guideline from Royal College of Obstetricians and		references and fully covered all reasonable clinica questions. This is another exhaustive guideline on management of hypertension in pregnancy. Includes a full systematic review of the literature and covers all management
21	22220321	Pregnancy.	Health (UK).	Hypertension	Yes	38 wks	Yes	I	A	Gynaecologists	21	questions. The papers pulls together a review of the literature, and apparently used an expert-
		The role of amniotic fluid								Boviow of the		focused approach similar to
	PMID:	indicated preterm				At or after				literature:		supported our
22	21962628	delivery. Optimal timing and mode of	Moore TR.	Oligohydramnios	Yes	34 wks	Yes	111		expert opinion	22	conclusion. The paper acknowledges the
		delivery after cesarean with								Practice guideline, Society of		paucity of randomized
		incision or myomectomy: a								Obstetricians and		but "gleans" from the available
23	PMID: 21962624	review of the data.	Landon MB, Lynch CD.	Prior uterine incision	Yes	At or after 39 wks	Yes	II-A	Level B	Gynaecologists of Canada	23	research the best
			_,						_			
											review of the literature to come up with the guideline.	
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	PMID:	Perinatal mortality and neonatal morbidity rates among twin pairs at different gestational ages: optimal delivery timing at 37 to 38	Hartley RS, Emanuel I,	Multiple					Population- based retrospective 10 year		The paper suggests that induction of labor should be routinely considered for twins at 37 to 38	
24	11228502	weeks' gestation.	Hitti J.	gestation	Yes	37-38 wks	Yes	II-A	window	24	weeks' gestation. The paper specifically excludes twins	
		Perinatal mortality and mode of delivery in monochorionic diamniotic twin pregnancies ≥ 32 weeks of gestation: a multicentre	Hack KE, Derks JB, Elias SG, van Mameren FA, Koopman- Esseboom C,						Multicenter retrospective		with twin-to-twin transfusion syndrome, but given that caveat makes a clear recommendation that agrees with our paper (which also does not	
25	PMID: 21585628	retrospective	Mol BW, et	Multiple	Voc	NOT before	Voc	II_R	cohort study	25	address TTTT	
23	21202028	Timing delivery of	aı.	Intrauterine	125	37-38	res	11-D	Literature review and	23	The research supports delivery by 37 to 38 week for singleton IUG	
26	21962625	restricted fetus.	Galan HL.	restriction	Yes	34-36 TIUP	Yes	II-B	consensus	26	pregnancies with	

They did a full

Monoamniotic twin pregnancy: a review of	Litosotuso		co-twin IUGR fetus, chorionicity also impacts timing of delivery but delivery should occur by 34-36 weeks. Quote the multiple observational studies whose results contradict each other directly. Recommend, using ambilvant language, that it "appears prudent
27 16401210 practice. Dickinson JE. gestation Yes 32-34 wks Yes II-A	review	27	weeks. Concluded the time to delivery will be anomaly- specific, but do
Indicated preterm PMID: birth for fetal Case- 28 21962626 anomalies. Craigo SD. Fetal anomalies Yes dependant Yes I Timing of	Literature review, RCT review and expert opinion consensus	28	make specific recommendation for different anomalies based on their research Used as a main
indicated late preterm and early-term birth PMID: in chronic medical Catalano PM, Case- 29 21962630 complications: Sacks DA. Diabetes Yes dependant Yes I	Literature review, RCT review and expert opinion consensus	29	source for recommendation the ACOG Practice Bulletin, and agreed that their

		diabetes.										data supported the ACOG finding
	PMID:	Indicated preterm birth for placenta							Level	Literature		Given the paucity of good RCTs in this area, the paper pulled together all the known studies based on a systematic review of the literature t make the recommendation Of all the papers, this one used the best methodology and graded the literature
30	21962623	accreta.	Belfort MA. American College of Obstetricians	Accreta	Yes	34-35 week	Yes	II-A	В	review	30	appropriately. They do not offer evidence to support this position, but they do offer a
21	PMID:	ACOG Practice Bulletin No. 102: management of	and Gynecologists Committee on Practice Bulletins-	Drior stillbirth	Voc	At or after	Voc		Level	Guideline from American Congress of Obstetricians and	21	recommendation which is considered the standard of practice in the field of OPCYN
31	19300347	stilipirth.	Obstetrics	Prior stillbirth	res	39WKS	Yes	111	C	Gynecologists	31	TIEID OF OBGYN.

		ACOG Practice										Quoted 2 papers, one randomized controlled trial and one publisher
		Bulletin. Clinical	American									algorithm based
		Management	College of									on retrospective
		Guidelines for	Obstetricians									review. Neither
		Obstetrician-	and							Guideline from		addressed timing
		Gynecologists.	Gynecologists							American		of delivery as the
		Number 60,	Committee							Congress of		focus of their
		March 2005.	on Practice							Obstetricians		research, but the
	PMID:	Pregestational	Bulletins-	Pregestational					Level	and		practice bulletin
32	15738045	diabetes mellitus.	Obstetrics	diabetes	Yes	By due date	Yes	I.	А	Gynecologists	32	draws inferences.

Appendix 4, Part 3: Simplified presentation of articles that gave recommendation									
Identifiers	Condition Addressed	What is recommendation?	Agree with CPG?	Quality of Evidence	Evidence Level	Article Type			
21962629	Gest HTN	≥ 37 wks	Yes	I		Analysis (sec) of RCT			
RCOG	Previa	38wks	Yes	I	Level A	Guideline			
RCOG	Acreta	36-37wks	Yes	I	Level A	Guideline			
22220321	HTN	≥ 38 wks	Yes	I	Level A	Guideline			
21962624	Prior ut incs	≥ 39 wks	Yes	II-A	Level B	Guideline			
19300347	Prior stillbirth	≥ 39 wks	Yes	III	Level C	Guideline			
15738045	Pregest DM	By due date	Yes	I	Level A	Guideline			
22855972	Mult gest	38 wks	Yes	I	Level A	Guideline			
21962631	Prior stillbirth	≥ 39 wks	Yes	II-A		Lit review/expert consensus			
21962627	Mult gest	38 wks	Yes	III		Lit review/expert consensus			
21962628 21962625	Oligohydramnios Growth restriction	≥ 34 wks 37-38 singleton;	Yes Yes	III II-B		Lit review/expert consensus Lit review/expert consensus			
21962625	Growth restriction	34-36 TIUP				Lit review/expert consensus			
21962626	Fetal anomalies	Case-dependant	Yes	I		Lit review/expert consensus			
21962623	Accreta	34-35 wks	Yes	II-A	Level B	Lit review/expert consensus			
16401210	Mult gestation	32-34 wks	Yes	II-A		Literature review Literature review, RCT review and			
21962630	DM	Case-dependant	Yes	I		expert opinion consensus			
10879335	Mult gest	≥ 38 wks	Yes	II-B		Retrospective cohort			
22302586	Mult gest	≥ 36 wks	Yes	II-B		Retrospective cohort			
16801956	HTN	39wks	Yes	II-B		Retrospective cohort			
16801956	DM	40-41 wks		II-B		Retrospective cohort			
21585638 11228502	Multiple gest Mult gest	32 wks 37-38 wks	Yes Yes	II-B II-A		Retrospective cohort Retrospective population			