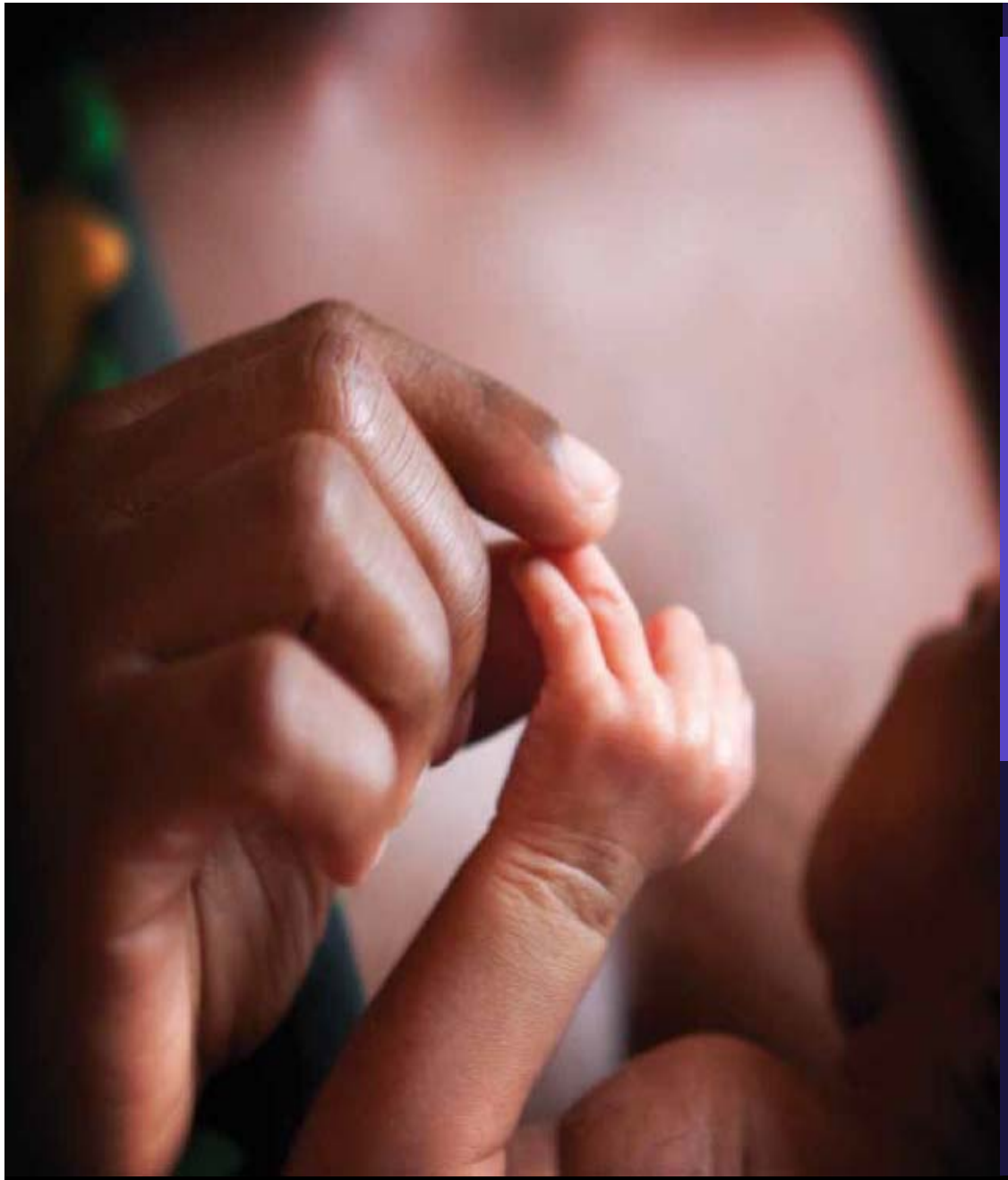
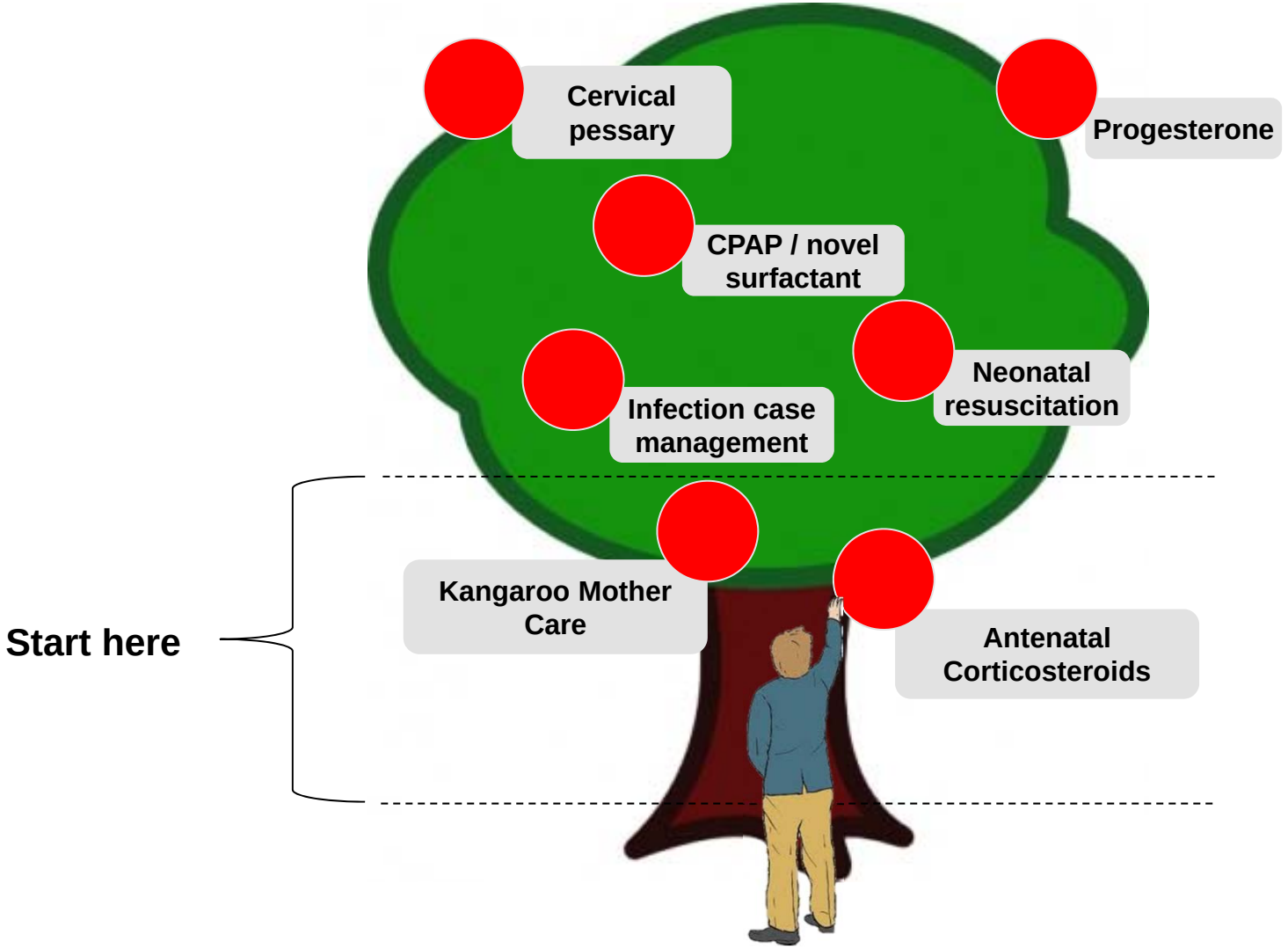


Antenatal Corticosteroids (ACS) for Fetal Maturation in Threatened Preterm Birth

Critical Path Discussion Draft

March 2013

Antenatal corticosteroids are among the “low hanging fruit” in the management of preterm labor and birth



Goal of the ACS group: Identify and act upon the critical path required to increase the uptake of ACS

Current context of antenatal corticosteroids (ACS)

Unmatched potential impact	Modeling suggests that ACS could save hundreds of thousands of premature infants annually at far lower cost than any other known intervention
Overlooked even among the overlooked	Prior to the UN Commission, the words “antenatal corticosteroids” or any derivation of it did not occur on the website of UNICEF or UNFPA
Relatively simple	ACS are an inexpensive, proven technology, used for decades across the wealthy world with little/no additional supply chain requirements. The right drug is already in many functioning hospitals!

Document purpose

This document summarizes what we know about the critical path for ACS, making it simpler for local champions to drive local action.

Unless and until a broader group of stakeholders is aware of the opportunity and bottlenecks for ACS deployment, it will remain a missed opportunity.

Summary

Overview

Antenatal corticosteroids have been used since 1972 to accelerate fetal lung maturation in threatened pre-term birth. In high income countries, they are used in nearly 90% of cases where indicated, but in low income countries coverage rates are estimated at 5% (and have been assessed in 9 countries of SE Asia at 9-73%). Their low cost and high efficacy make them an attractive tool to save pre-term infants.

Summary of Findings

Product Definition	Dexamethasone is readily available and simple to administer via intramuscular injection.
Manufacturing	While betamethasone is commonly used in high income countries, dexamethasone is far easier to procure from multiple generics manufacturers globally, often at <$1/course.
Regulation	Corticosteroids for fetal lung maturation is registered in relatively few countries. Use in most countries is off-label, although recommended by obstetric societies and the WHO Priority Meds List
Initiating Local Coverage	Factors driving and preventing adoption of corticosteroids remain largely unknown in the developing world. Further research is required to understand the best approach to initiate local coverage.
Sustaining Local Coverage	The low cost, broad availability, and simplicity of use of corticosteroids will help facilitate the sustained coverage of these drugs to save lives once the practice is habitual.

Liggins accidentally discovered antenatal corticosteroids as a way to accelerate lung maturation in New Zealand in 1969

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

An accidental discovery in New Zealand

While conducting experiments on the onset of labor, and specifically using cortisol to induce labor in lambs, Sir Graham (Mont) Liggins observed one surprsing premature lamb:

"And I remember one morning, there was a lamb lying in a cage with its mother. A lamb that had been infused as a fetus with cortisol. And to my surprise this lamb was still breathing, not very healthy breathing, but **it was alive and breathing. It had no right to be**. It was so premature that its lungs should have been just like liver, and quite uninflatable. And this struck me as surprising …"

Liggins and Howie went on to conduct the first trials in humans, published in 1972, using a betamethasone, a molecule which crosses the placenta more easily than cortisol. They used a commercially available combination of betamethasone phosphate and betamethasone acetate, similar to the Schering products still sold today as Celestone Soluspan.

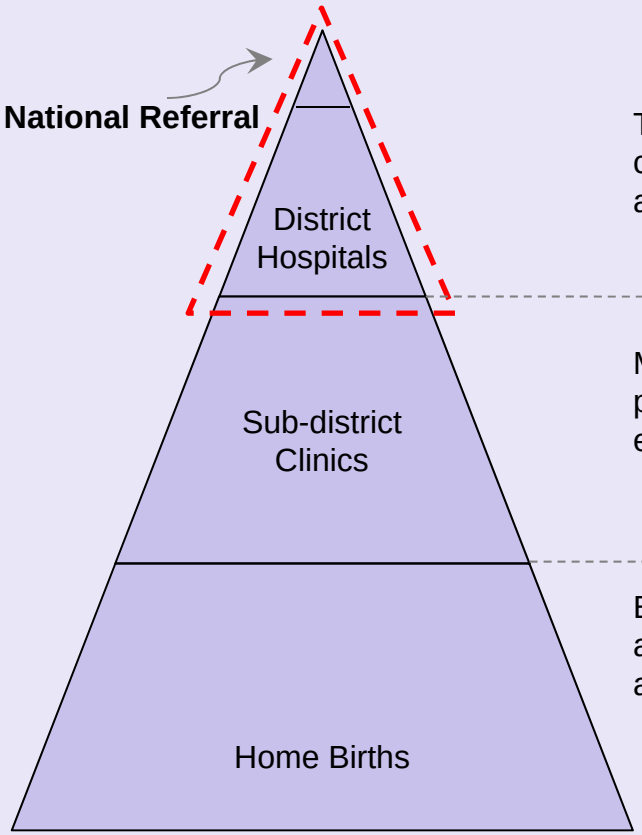
Ross Howie (L) and Graham (Mont) Liggins (R) circa 1972 when they first published on the effects of antenatal corticosteroids

Betamethasone and dexamethasone are the most widely studied and used antenatal corticosteroids today.

Sources: Reynolds L A, Tansey E M. (eds) (2005) prenatal corticosteroids for reducing morbidity and mortality after preterm birth. wellcome witnesses to twentieth century medicine, vol. 25. London: Wellcome Trust centre for the history of medicine at UCL.

This document will focus on ACS in high care settings, anticipating a trickle down across the continuum of care

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use



Focus of this document

Top level care: ACS efforts should focus at the top levels of care, where key opinion leaders can help to shape practice across a country, and potentially influence lower levels of care.

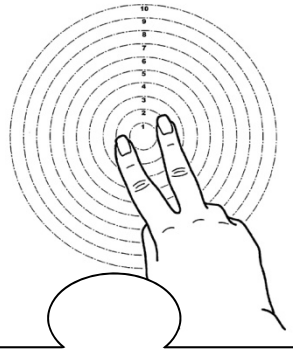
Middle level care: This is a likely area for future work, potentially carried forward by locals for locals through existing channels.

Botton level care: ACS are unlikely to be a home based care, and discussion of TBAs using this intervention in the near term are likely misplaced.

Proper use of ACS is part of a more complex set of 4+ interventions in threatened preterm labor

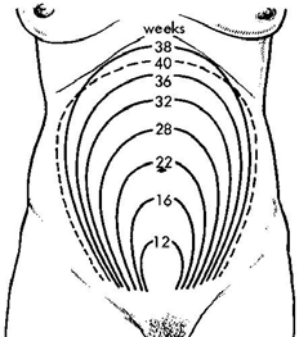
Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Confirmation of labor



1

Measurement of gestational age

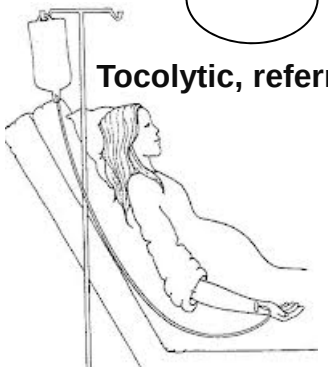


2

Administration of ACS

3

Tocolytic, referral, or both



4

1 Dx of preterm labor: Simple approaches to confirm preterm labor are inaccurate even in sophisticated settings

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Diagnosis of preterm labor

Most common methods
Less common, more expensive methods

Metric	Data Source	Limitation
Regular contractions	Woman's reporting	Difficult to differentiate from Braxton-Hicks contractions
Cervical dilation/effacement	Digital exam	Imprecise, especially under 3cm dilation
	Cervilenz	$30 device to measure cervical length
	Ultrasound	High cost, high skill approach with low coverage in LMICs
Fetal Fibronectin	Laboratory test	High cost, most helpful in ruling out preterm labor

Nearly half of all subjects diagnosed with preterm labor deliver at term in the wealthy settings (even without tocolytics). The ability to confidently predict preterm labor in lower skilled settings is even more limited.

ACS are likely to be overprescribed wherever they are used, and most believe the cost/benefit merits their overuse within reason

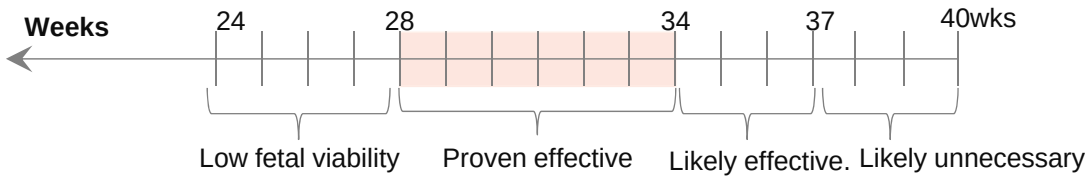
Sources: Cervilenz.com; March of dimes; Hologic.com; King JF et al. Beta mimetics to control preterm labor. Br. J Obstetrics Gynaecol 85:211: 1988

2 Measurement of gestational age: Tools offer limited accuracy, but are accurate enough to safely use ACS

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Many national guidelines recommend ACS from 24-37 weeks gestational age:
The cost/benefit of the drug merits use even if there is suspicion of preterm birth

Measurement Method	Estimated Accuracy
Ultrasound Limited availability, highest accuracy in 1st trimester	±1wks
Last Menstrual Period Not useful in cases where LMP unknown	±2wks
Fundal Height Low cost, viable solution	±3wks



The ability to determine gestational is unlikely to curtail ACS use. Even the crudest measurement of 27–37 weeks should merit use.

Sources: Blencowe et al. Born too soon global action report, Chapter 2, 2012

4 Tocolytics may delay delivery by up to 48 hours, improving ACS effect, but are not a required component

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Common Tocolytics

☐ Often preferred due to lower side effect profile
☐ Higher risks of side effects

Drug	Class	Dose	Route	Approx Price
Nifedipine*	Ca-Blocker	10-20mg+	Oral	$0.01 (MSH)
MgSO4	Myosin inhibitor	6g+	IV	$1.14 (MSH)
Atosiban	Oxytocin Antagonist	6.75mg+	IV	$43.20 (Wex)
Indomethacin	NSAID	50-100mg+	Oral/Rectal	$1.37 (Retail)
Salbutamol	Beta-Mimetic	10-100mcg+	IV	$0.17 (MSH)
Terbutaline	Beta-Mimetic	250mcg+	IV	$2.50(UKMi)
Ritodrine**	Beta-Mimetic	50mcg/min+	IV	$80.00 (UKMi)

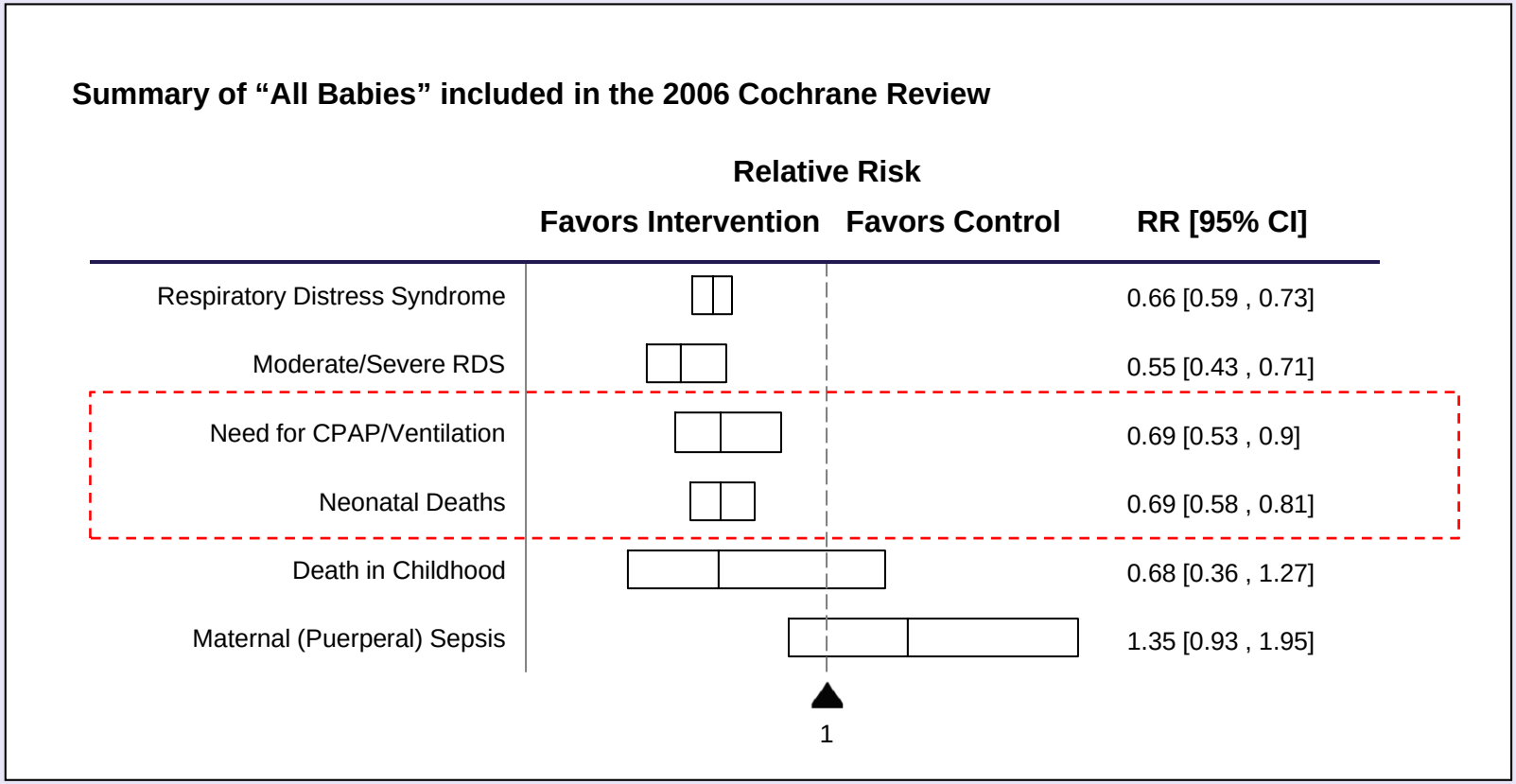
*Nifedipine is the only drug listed as a tocolytic on the WHO Essential Medicines List
**Although ritodrine carries greater risk and lower efficacy than several other drugs, it remains the only FDA approved tocolytic, illustrating how common off-label usage is in obstetrics

For mothers in early labor with no contraindications, tocolytic administration may improve ACS effect. However, tocolytics signficiantly complicate the care algorithm. ACS can still be helpful in the absence of tocolytics.

Sources: Wex et al. Atosiban versus betamimetics in the treatment of preterm labour in Germany: an economic evaluation. *BMC Pregnancy and Childbirth 2009*, 9:23; MSH International Drug Price Indicator Guide 2010. ; http://www.ukmi.nhs.uk/NewMaterial/html/docs/atosiban.pdf

Meta-analysis shows preemies treated with corticosteroids are less likely to develop RDS, need CPAP, or die

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use



Sources: Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database of Systematic Reviews* 2006,Issue3.Art.No.:CD004454. DOI:10.1002/14651858.CD004454.pub2.

Partial dosing is beneficial to neonates, even if a full dose cannot be completed before birth

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Relative risks with 1 versus 0 doses of betamethasone in infants 24-34 wks
N=125

Outcome	RR [CI]
Need for vasopressors	0.35 [0.14,0.85]
Rate of IVH	0.42 [0.19,0.92]
Neonatal Death	0.31 [0.11,0.86]

Relative risks using partial doses of dexamethasone in infants <1kg
N=124

Steroid dose	1 versus 0	2 versus 0	3-4 versus 0
RDS	0.6 (0.2 to 2.3)	0.1 (0.0 to 0.7)	0.2 (0.1 to 0.5)
Surfactant	1.0 (0.3 to 3.4)	0.4 (0.1 to 1.7)	0.2 (0.1 to 0.5)
PDA	3.7 (1.0 to 13.4)	0.5 (0.1 to 2.0)	0.4 (0.2 to 1.1)
IVH[1]	0.4 (0.1 to 1.6)	2.1 (0.4 to 11.2)	0.2 (0.0 to 0.5)
CLD & death	0.7 (0.2 to 2.6)	0.2 (0.0 to 0.9)	0.4 (0.1 to 1.1)

Note: Data from seven infants not included secondary to early death. RDS = Respiratory Distress Syndrome, PDA = patent ductus arteriosus ; IVH = Intraventricular hemorrhage; CLD = Chronic lung disease

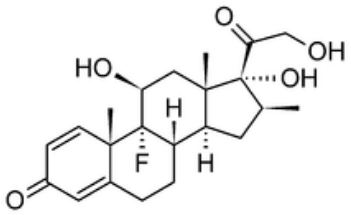
Even partial doses of ACS save lives when labor cannot be delayed to accommodate a full dose

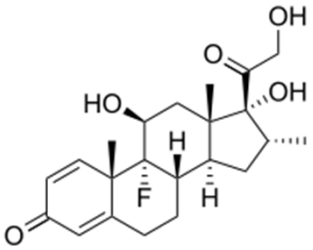
Sources: Salhab W et al. Partial or complete antenatal steroids treatment and neonatal outcome in extremely low birth weight infants 1000 g: Is There a Dose-Dependent Effect? *Journal of Perinatology* (2003) 23, 668–672.; Elimian A. Antenatal corticosteroids: Are incomplete courses beneficial? obstetrics & gynecology: 2003

There are several corticosteroids available, but beta-and dexamethasone are most common for lung maturation

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endor sement | Initiate local coverage | Sustain local use

Dosing for betamethasone vs. dexamethasone





Drug	Betamethasone (Phosphate+Acetate)	Dexamethasone
Dose /Injection	12 mg	6 mg
No of Injections	2	4
Interval btwn injections	24hrs	12hrs
Total Amount	24 mg	24 mg
Avg Price/24mg (India)	No Known Indian Supplier	$0.51 (10 brands)
Injectable form on WHO Essential Medicines List?	No	Yes

Sources: ACOG, RCOG, NIH, DrugsUpdate.com, 18th essential medicines List WHO 2011

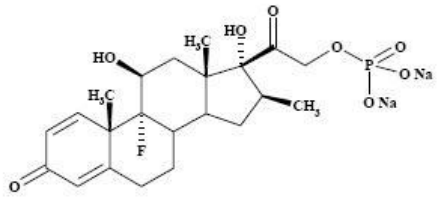
The betamethasone used for fetal indications is a very specific suspension of two salts

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endor sement | Initiate local coverage | Sustain local use

Liggins initially combined the betamethasone forumulations with the hope of maximizing the drug's efficacy using a single injection per day

Betamethasone sodium phosphate

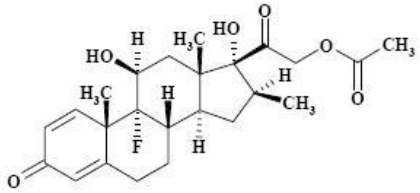
Relatively short half life (and therefore fast acting)



+

Betamethasone acetate

Relatively long half life (and therefore long acting)



Recent (2007 and 2009) data in sheep suggests that there may be some advantage to this approach, with a combination of both formulations outperforming either formulation alone.

Sources: Jobe et al. Betamethasone for Lung maturation: testing dose and formulation in fetal sheep. Am J Obstet Gynecol. 2007 November ; 197(5): 523.e1–523.e6. ; blackwell publishing Commentary on Betamethasone

There are only two known manufacturers of this acetate suspension in phosphate, and both are relatively expensive

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

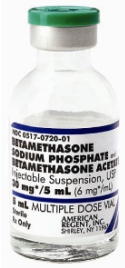
Celestone Soluspan has suffered supply shortages

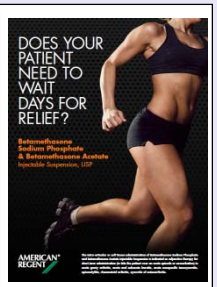
Wholesale: ~$40
Retail: ~$75

According to the US FDA:
"Celestone Soluspan injection **may not be commercially** available because, under a consent decree between FDA and the manufacturer, it is being made available in certain instances of medical necessity only. The reasons for its unavailability are not safety or effectiveness considerations associated with the drug product in general, but specific to the manufacturer…

…**Schering ceased manufacture of Celestone injection in March 2004**, and it was moved from the prescription drug product list to the ``Discontinued Drug Product List'' section of the Orange Book"

American Regent has been marketing a generic since 2010





Wholesale: ~$40
Retail: ~$75

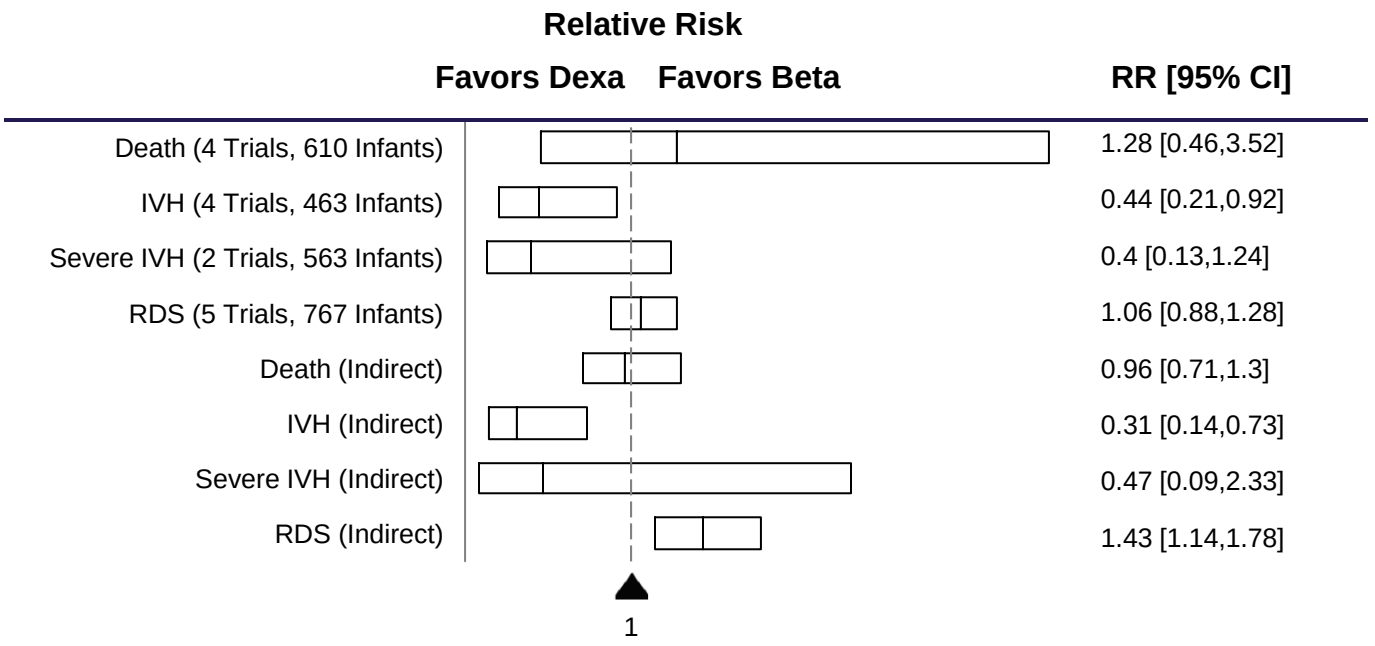
- Is "AB" rated by the FDA , indicating that a study has been is submitted demonstrating bioequivalence (in this case to Celestone).
- AB drugs can be substituted at the pharmacy without the advice of a doctor, but obstetricians aren't necessarily comfortable with a brand other than Celestone, as Celestone uses a specific milling process which may not be replicated in other drugs
- American Regent's product does not carry an indication for fetal use. The obstetric market for this product is too small any likely carries too much perceived risk to be interesting to manufacturers

Sources: American Regent; : http://edocket.access.gpo.gov/2006/E6-178.htm, http://www.pharmacychecker.com/compare-drug-prices-online-pharmacies/Celestone+Soluspan-6+mg&252ml/19697/32083

There is insufficient evidence to show superior efficacy between betamethasone and dexamethasone

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Meta analysis of the effectiveness of beta and dexa from 2008 Cochrane Review



Sources: Brownfoot et al. Different corticosteroids and regimens for accelerating fetal lung maturation for women at risk of preterm birth (Review). The cochrane library 2008, Issue 4

A 6mg presentation of dexamethasone would be ideal, but does not exist– 4mg ampoules are common in many settings

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Usable Option

4mg ampoules are most common

The WHO and most essential medicines lists specify 4 mg/ml in 1-ml ampoule

Advantages: Ubiquitous
Disadvantages: Caregivers would need to open and draw from two 1ml-ampoules with sterile technique, likely discarding 25% of the product at each dosing as they draw 6mg of drug from two containers of 4mg each that cannot be resealed

Alternative Option

A 6mg dose would be best

Single dose vials or ampoules of 6mg are not currently produced.

No 6mg Package Exists

Advantages: Ideal size for each 6mg dose
Disadvantages: Not in production, would likely need to be a custom product

Alternative Option

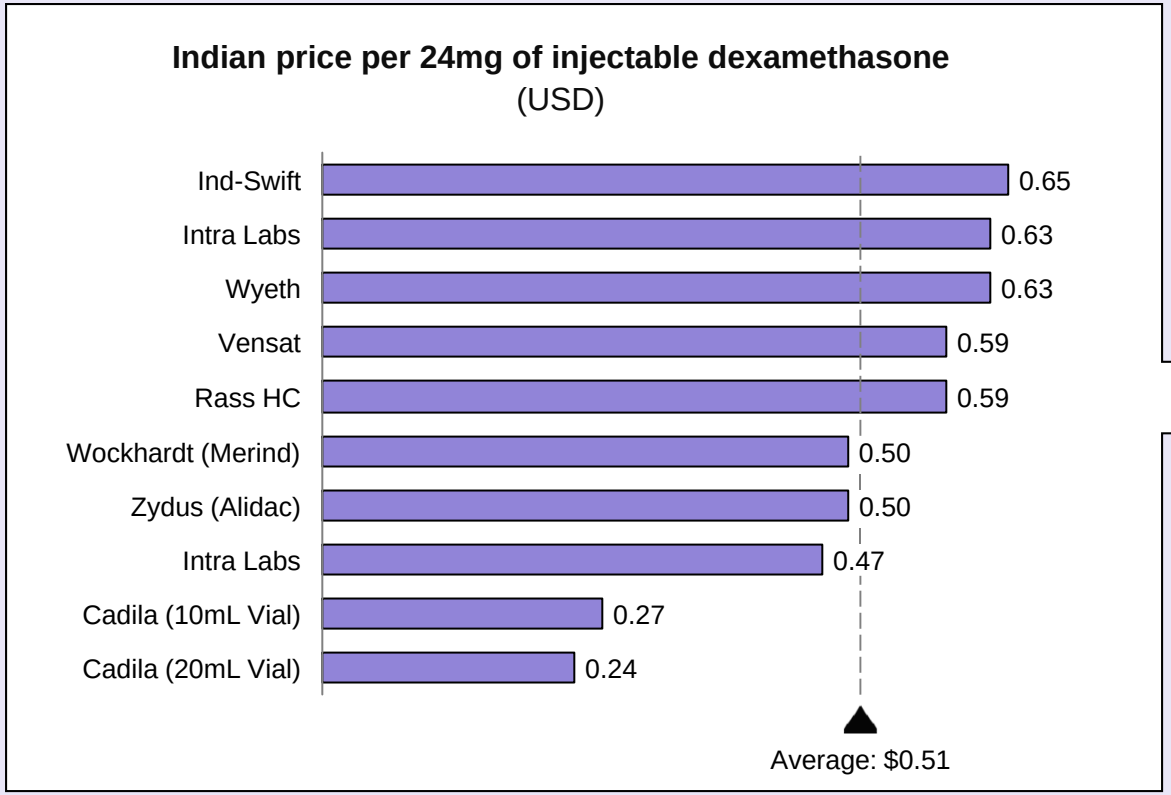
Larger, multi-dose vials exist

Multi-dose vials are available from 2-30mL and concentrations from 4-10mg/ml

Advantages: Lower wastage, better price per dose
Disadvantages: As in the 1ml ampoule option, caregivers would need to calculate and measure dosing carefully. There are additional risks of contamination and spread of infection.

Indian generic vendors offer affordable pricing per 24mg of injectable dexamethasone

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use



Product cost seems unlikely to be a primary barrier to product adoption

Source: http://www.drugsupdate.com

Only Schering has a license to market antenatal corticosteroids, and only in a few countries

Injectable <u>betamethasone</u> is more typically registered for:

- 6 Allergic states
- 5 Dermatological diseases
- 3 Endocrine disorders
- 2 Gastrointestinal Diseases
- 4 Hematologic disorders
- 2 Neoplastic diseases
- 3 Renal Diseases
- 3 Ophthalmic diseases
- 4 Respiratory diseases
- 9 Rheumatic disorders

But not fetal lung maturation!

Injectable <u>dexamethasone</u> is more typically registered for:

- 7 Endocrine disorders
- 10 Rheumatic disorders
- 7 Dermatological disorders
- 9 Allergic states
- 10 Ophthalmic diseases
- 3 Gastrointestinal diseases
- 5 Respiratory diseases
- 3 Neoplastic diseases
- 5 Hematologic disorders
- And more!

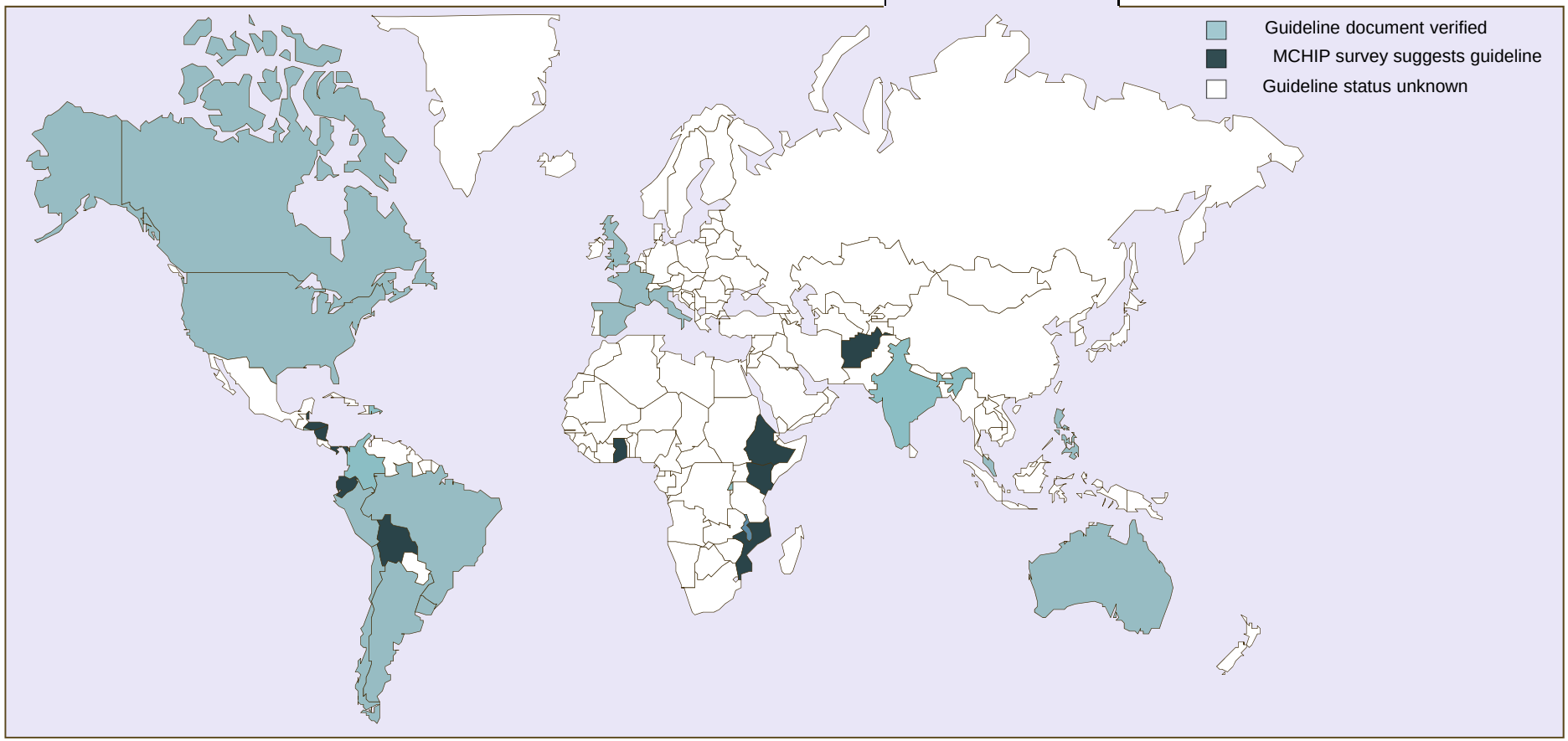
But not fetal lung maturation!

Outside a very short list of countries, antenatal use for lung maturation is an un-licensed use. This is not known to be a barrier to usage.

Source: Celestone soluspan package insert , Pfizer package insert

50+ guidelines exist for the use of ACS, across at least 31 countries, although not all have been verified

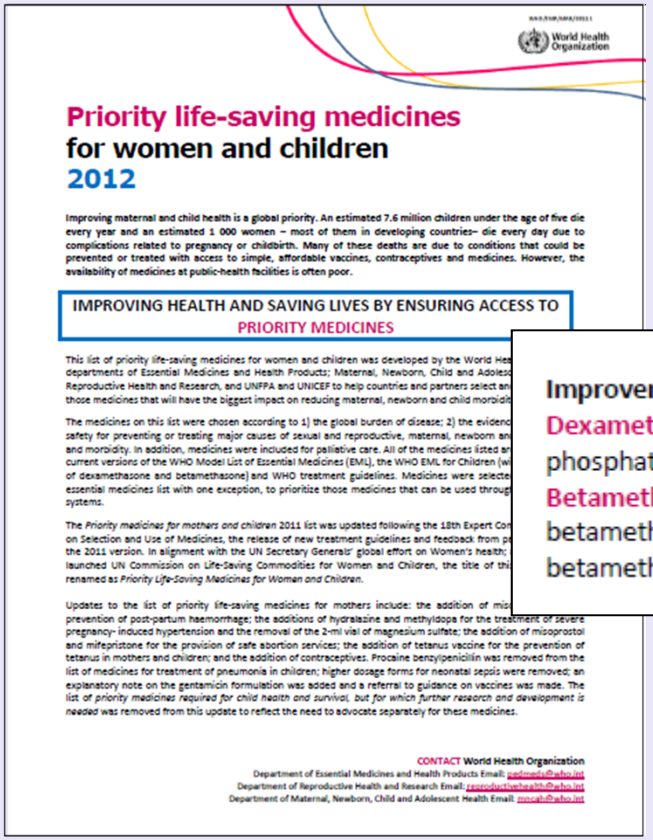
Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use



Source: Unpublished MCHIP Survey 2011, Global Network national guideline search 2008

Betamethasone and dexamethasone are listed on the 2012 WHO list of Priority Medicines for Mothers and Children

Define the intervention → Prove efficacy & effectiveness → Define the product → Manufacture → Gain regulatory approval/endorsement → Initiate local coverage → Sustain local use



World Health Organization

Priority life-saving medicines for women and children 2012

Improving maternal and child health is a global priority. An estimated 7.6 million children under the age of five die every year and an estimated 1 000 women – most of them in developing countries– die every day due to complications related to pregnancy or childbirth. Many of these deaths are due to conditions that could be prevented or treated with access to simple, affordable vaccines, contraceptives and medicines. However, the availability of medicines at public-health facilities is often poor.

IMPROVING HEALTH AND SAVING LIVES BY ENSURING ACCESS TO PRIORITY MEDICINES

This list of priority life-saving medicines for women and children was developed by the World Hea departments of Essential Medicines and Health Products; Maternal, Newborn, Child and Adolesc Reproductive Health and Research, and UNFPA and UNICEF to help countries and partners select an those medicines that will have the biggest impact on reducing maternal, newborn and child morbidit

The medicines on this list were chosen according to 1) the global burden of disease; 2) the evidenc safety for preventing or treating major causes of sexual and reproductive, maternal, newborn an and morbidity. In addition, medicines were included for palliative care. All of the medicines listed ar current versions of the WHO Model List of Essential Medicines (EML), the WHO EML for Children (wi of dexamethasone and betamethasone) and WHO treatment guidelines. Medicines were selecte essential medicines list with one exception, to prioritize those medicines that can be used throug systems.

The *Priority medicines for mothers and children* 2011 list was updated following the 18th Expert Co on Selection and Use of Medicines, the release of new treatment guidelines and feedback from p the 2011 version. In alignment with the UN Secretary Generals' global effort on Women's health; launched UN Commission on Life-Saving Commodities for Women and Children, the title of thi renamed as *Priority Life-Saving Medicines for Women and Children*.

Updates to the list of priority life-saving medicines for mothers include: the addition of mis prevention of post-partum haemorrhage; the additions of hydralazine and methyldopa for the treatment of severe pregnancy- induced hypertension and the removal of the 2-ml vial of magnesium sulfate; the addition of misoprostol and mifepristone for the provision of safe abortion services; the addition of tetanus vaccine for the prevention of tetanus in mothers and children; and the addition of contraceptives. Procaine benzylpenicillin was removed from the list of medicines for treatment of pneumonia in children; higher dosage forms for neonatal sepsis were removed; an explanatory note on the gentamicin formulation was added and a referral to guidance on vaccines was made. The *list of priority medicines required for child health and survival, but for which further research and development is needed* was removed from this update to reflect the need to advocate separately for these medicines.

CONTACT World Health Organization
Department of Essential Medicines and Health Products Email: pedmeds@who.int
Department of Reproductive Health and Research Email:
Department of Maternal, Newborn, Child and Adolescent Health Email: mncah@who.int

Improvement of fetal lung maturity

Dexamethasone: injection 4 mg dexamethasone phosphate (as disodium salt) in 1-ml ampoule *or*

Betamethasone: injection 6 mg/ml (3 mg/ml betamethasone sodium phosphate + 3 mg/ml betamethasone acetate) in an aqueous vehicle

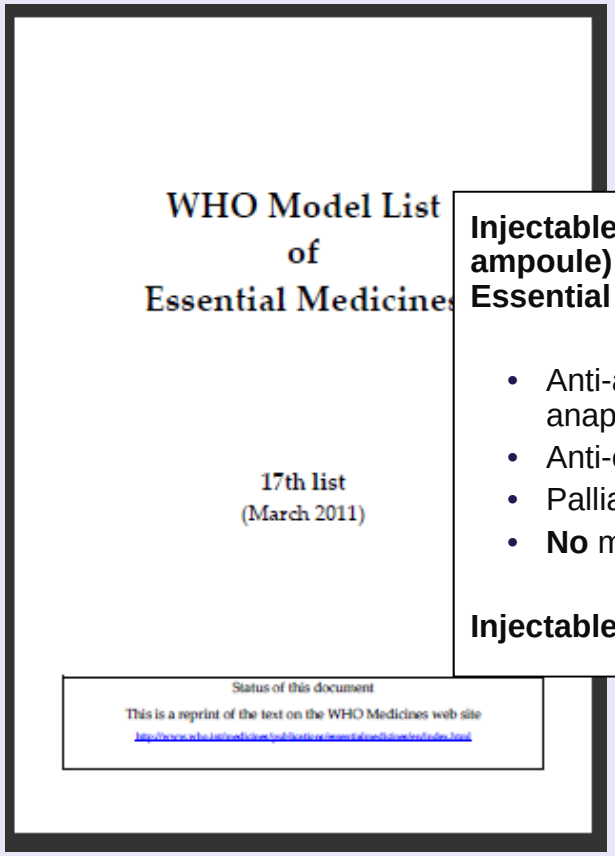
The priority medicines guideline may help win country endorsement of antenatal corticosteroids in the future but does not carry the weight of the WHO EML

Betamethasone and dexamethasone for fetal lung maturation are the only medicines on the priority medicines list not on the WHO Essential Medicines List

Source: Priority Medicines for mothers and children. WHO 2012 (http://apps.who.int/medicinedocs/documents/s19290en/s19290en.pdf)

Dexamethasone is listed on the 2011 WHO Essential Medicines List, but not (yet) for fetal indications

Define the intervention → Prove efficacy & effectiveness → Define the product → Manufacture → Gain regulatory approval/endorsement → Initiate local coverage → Sustain local use


WHO Model List
of
Essential Medicines

17th list
(March 2011)

Status of this document
This is a reprint of the text on the WHO Medicines web site

Injectable dexamethasone (4mg/ml in 1 ml ampoule) is listed on the 2011 WHO Essential Medicines List for:

- Anti-allergy & medicines use in anaphylaxis
- Anti-emetic
- Palliative care
- **No** mention of fetal lung maturation

Injectable Betamethasone is not listed.

An application to add fetal indications for dexamethasone is underway

Source: WHO. 18th List of essential medicines, 2011.

National Medicines Lists of the multiple countries show dexa is present, but not listed for fetal indications

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Presence of ACS in several National Essential Medicines Lists

Country	Year	Injectable Dexa	Injectable Beta	Fetal Indication
Ghana	2004	Y	N	N
Uganda	2007	Y	N	N
Brazil	2010	Y	PO4+Ac	Y
Pakistan	2007	Y	N	N
Bangladesh	2008	Y	N	N
Nepal	2009	Y	N	N
China	2009	Y	N	N
India	2011	Y	PO4 Only	N
Philippines	2008	Y	N	N
Malawi	2009	5mg/ml-5ml	N	N
Mozambique	?	Unknown	Unknown	Unknown

Dexamethasone should be present in national formularies, but is not indicated for fetal maturation.

This is consistent with the WHO Model EML

Source: National essential medicines lists online at http://www.who.int/selection_medicines/country_lists/en/index.html

We have relatively little data about current coverage rates or barriers to adoption in the developing world

Define the intervention → Prove efficacy & effectiveness → Define the product → Manufacture → Gain regulatory approval/endorsement → Initiate local coverage → Sustain local use

1 **Barriers as identified in May 2011 MCHIP survey of 19 countries**

Country	Surveyed	Barriers Identified via Survey
Ghana	Y	No response
Uganda	N	
Brazil	N	
Pakistan	N	
Bangladesh	Y	No Uniform guideline, inadequate information
Nepal	Y	Not in the policy
China	N	
India	N	
Philippines	N	
Malawi	N	
Mozambique	Y	Lack of trained personnel and lack of dissemination

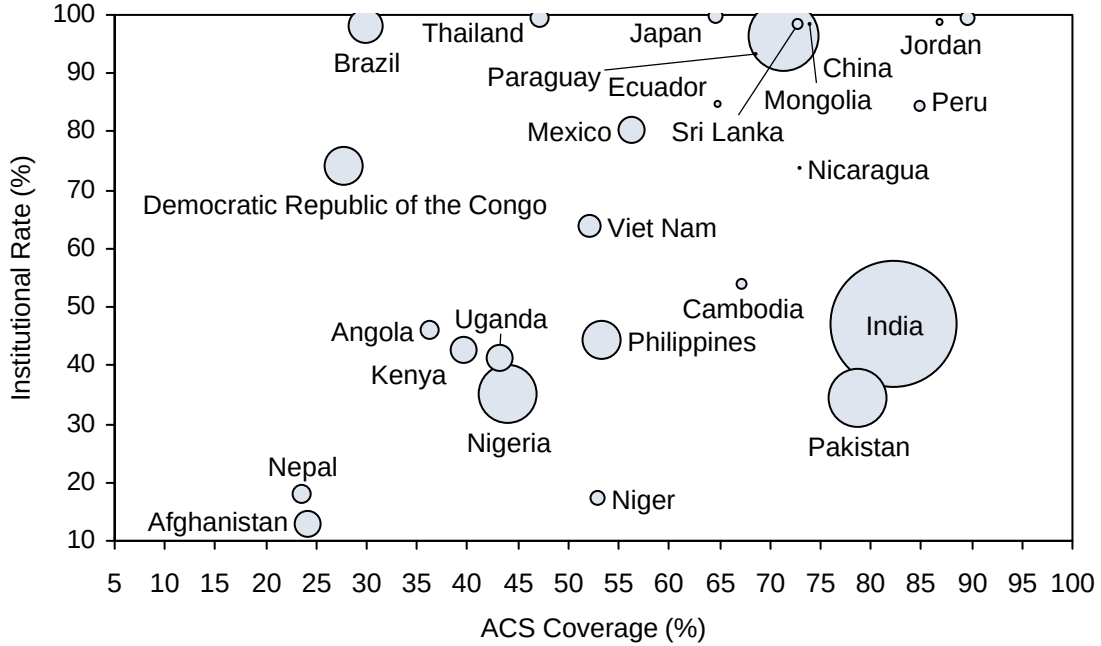
More detailed information on local barriers is required to initiate/increase coverage

2 **WHO Study of 300,000+ hospital deliveries to be analyzed for publication in coming months (see next slide)**

WHO MCS survey data suggests that even in high volume facilities, ACS usage is low in many countries

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

ACS use, institutional delivery rate and annual preterm births

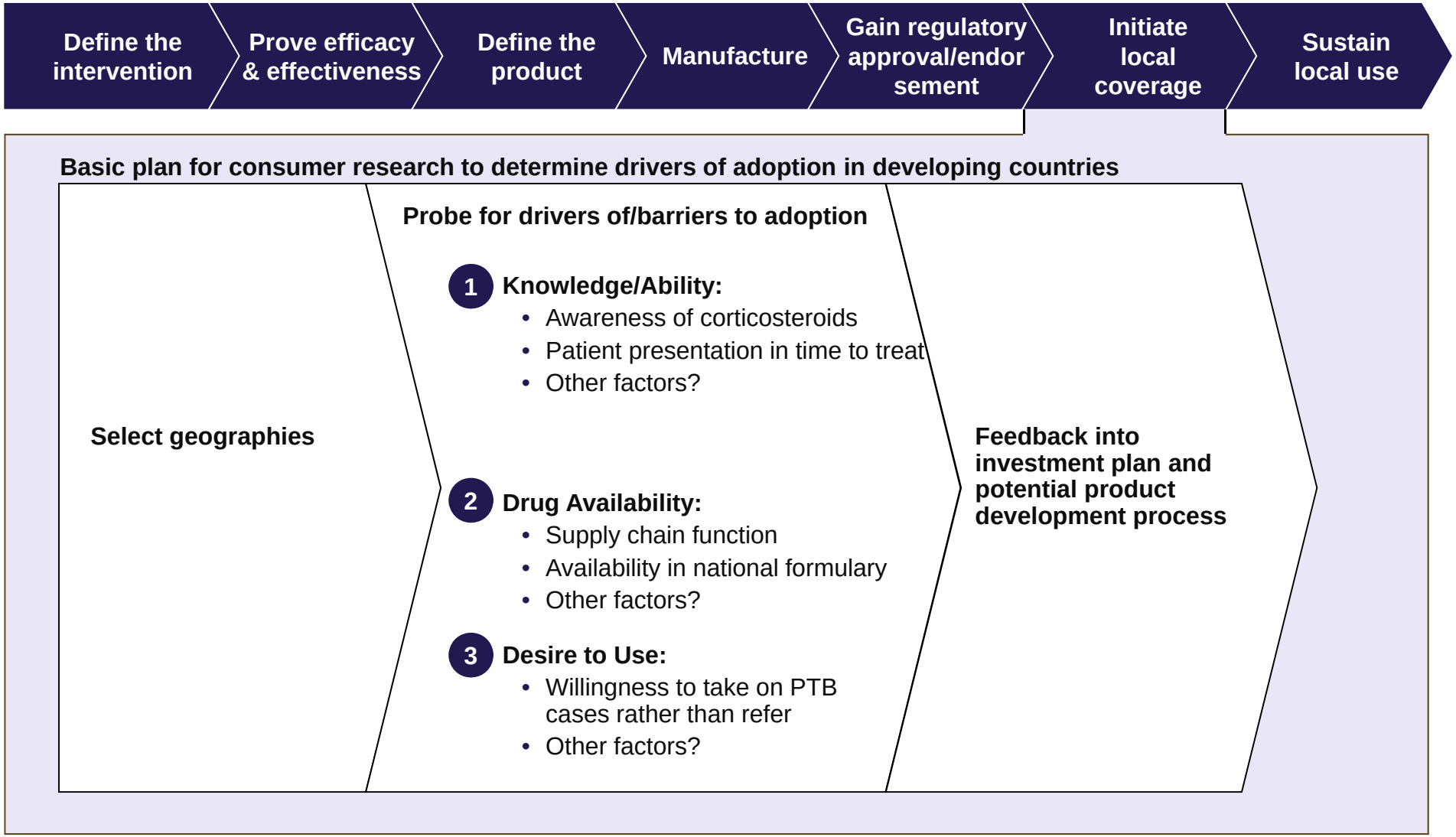


Circle area corresponds to total annual preterm births

Notes:

- ACS coverage rates are preliminary figures from WHO MCS Survey, 2011
- Hospitals surveyed had >1000 births annually
- Coverage rate is defined as % of live births 24-34wks GA with childbirth taking place after 3hrs in hospital
- No data is available on the type of ACS used, protocol, or completion of dosing

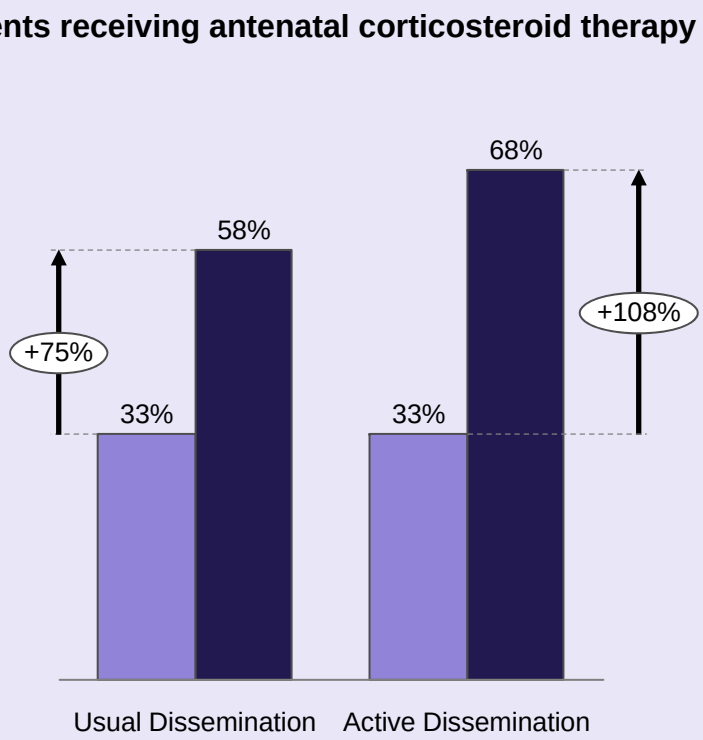
Our next steps should be to talk to caregivers to determine usage rates and drivers of their behaviors



In US Hospitals, active dissemination was important in accelerating the use of antenatal corticosteroids

Define the intervention | Prove efficacy & effectiveness | Define the product | Manufacture | Gain regulatory approval/endorsement | Initiate local coverage | Sustain local use

Percentage of eligible patients receiving antenatal corticosteroid therapy



Usual dissemination:
(n= 14 tertiary care institutions)

Publication of the recommendations of an NIH consensus conference and endorsement by the American College of Obstetricians and Gynecologists.

Active dissemination:
(n= 13 tertiary care institutions)

Usual dissemination plus a year-long educational effort led by an influential physician and nurse coordinator at each facility, consisting of grand rounds, a chart reminder system, group discussion of case scenarios, monitoring and feedback"

Source: Leviton et al. Methods to encourage the use of antenatal corticosteroid therapy for fetal maturation. JAMA 1999.

Active dissemination has also proven effective for changing obstetric care outside the United States

Define the intervention → Prove efficacy & effectiveness → Define the product → Manufacture → Gain regulatory approval/endorsement → Initiate local coverage → Sustain local use

A behavioral intervention to improve obstetrical care in Argentina and Uruguay

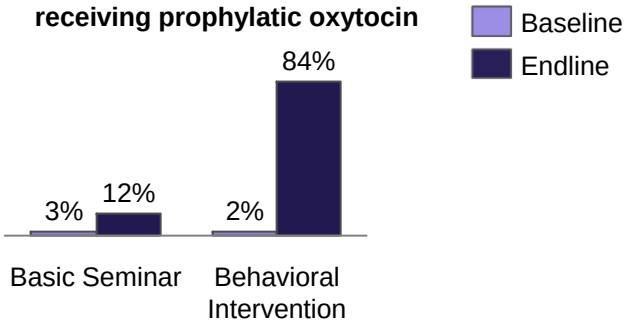
Basic Seminar:
(n= 9 hospitals)

Basic seminar on AMTSL, selective use of episiotomy, and use of the WHO Reproductive Health Library as a source of evidence based interventions

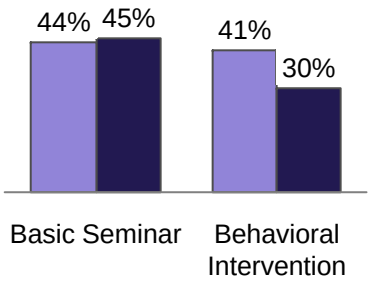
Behavioral intervention
(n= 10 hospitals)

Basic seminar plus a promotion of key opinion leaders, interactive workshops, training of manual skills, one on one academic detailing visits, reminders, and feedback.

Percentage of eligible patients receiving prophylatic oxytocin



Episiotomy rate



Uptake will hinge upon active dissemination programs within target regions.

Source: Althabe et al. A Behavioral intevention to improve obstetrical Care. New England journal of medicine. 2008

Next Steps

Determine country-level needs and remedies

Gather country-level data

- Identify the countries of highest priority
- Determine the level of rigor required to act
- Determine the networks to be tapped
- Conduct a survey

Inventory common barriers

- Aggregate results from survey
- Identify common bottlenecks that can be addressed centrally (eg EML) vs locally (eg behavior change)

Develop common solutions

- Match the needs identified above to the strengths of the Born Too Soon Care Team members
- Disseminate findings to collaborating partners