MODELING THE COST-EFFECTIVENESS OF MATERNAL HIV RETESTING AND DUAL HIV/SYPHILIS TESTING

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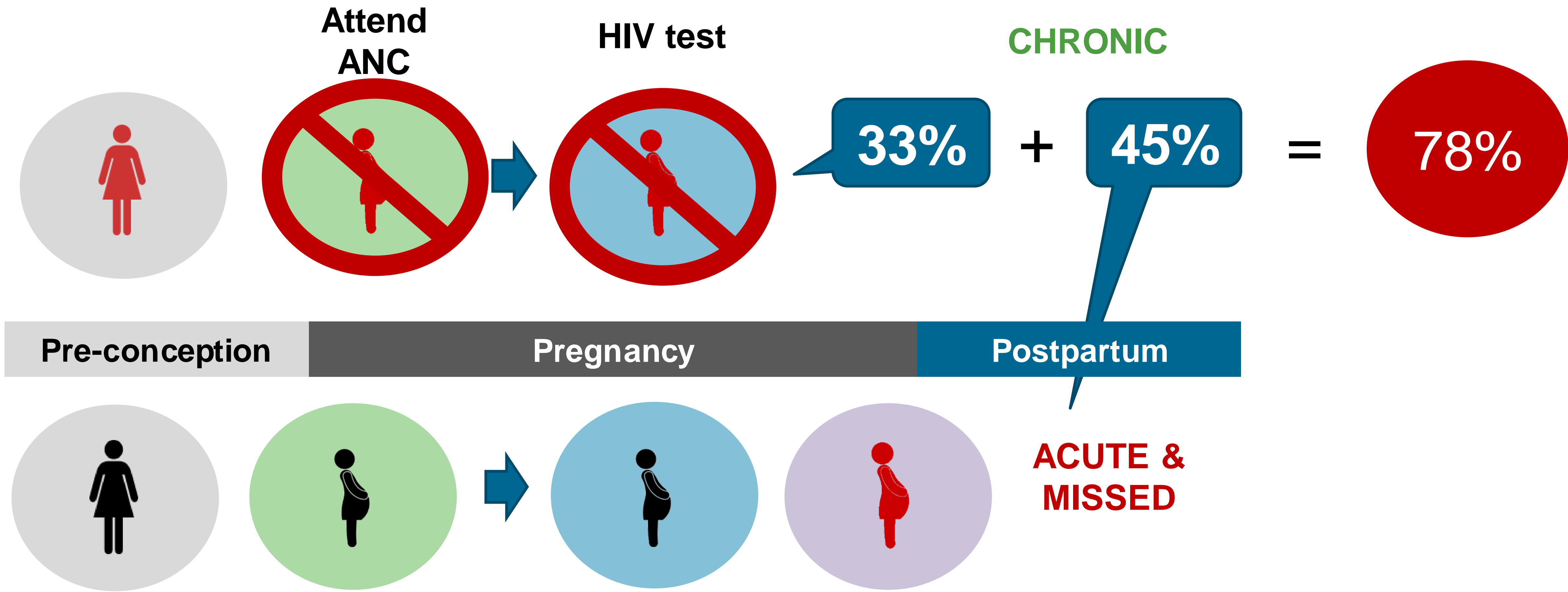
Universal HIV and syphilis screening during pregnancy are needed to achieve elimination of mother-to-child HIV transmission (MTCT) of both infections

MTCT

	HIV	Syphilis
Pregnant women	**1.4 M**	**930,000**
MTCT	**2-23%**	**11%**
Infants	**150,000** New infections (2015)	**102,000** Congenital infections (2012)

UNAIDS Global Plan, 2016; Wijesooriya NS, Lancet 2016; Johnson LF, JAIDS 2012.

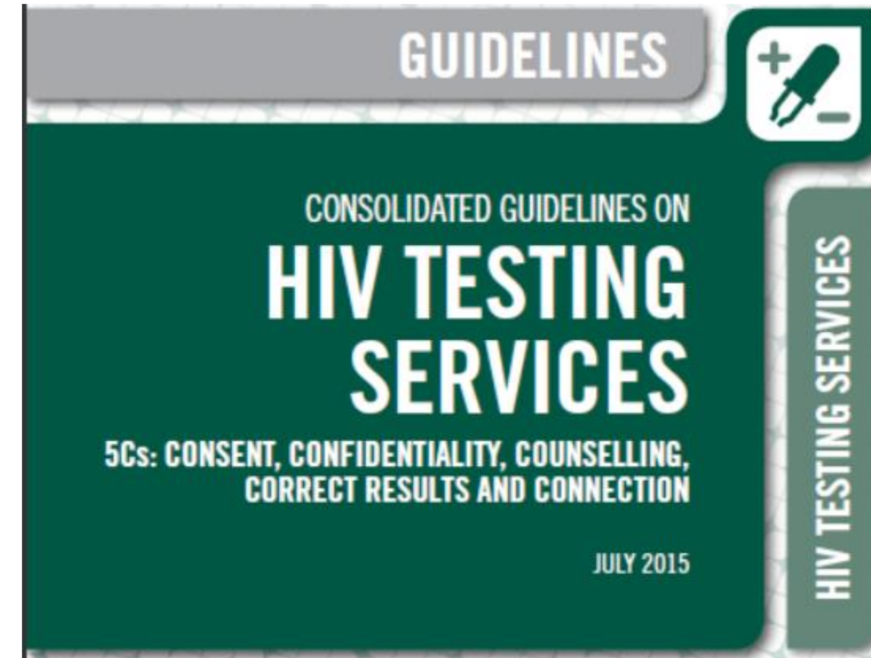
MTCT rates for HIV are underestimated due to acute maternal infections



Njuguna IN, AIDS Patient Care and STDs 2016.

Guidance on timing of retesting lacks specificity

Retesting criteria	Concentrated epidemic	Generalized epidemic
3rd trimester, labor, or postpartum		✓
Serodiscordant couple	✓	
Member of key population	✓	



Effective maternal treatment to prevent MTCT for both infections, but HIV screening rates higher

Maternal HIV and syphilis testing coverage, Tanzania*

	Syphilis	Additional for HIV
Attend ANC	100	
Tests available	43	83
Effective coverage	15	65

Attrition	Attend ANC → Tests available	Tests available → Effective coverage
syphilis	57%	28%
HIV	17%	18%

% (y-axis: 0–100)

■ Syphilis ▨ Additional for HIV

UNAIDS Global Plan, 2016; Alexander JM, Obstet Gynecol 1999.
**Adapted from Fig 3: Baker U, Int J Obstet Gynecol 2015.*

Objectives

Using a Markov decision analytic model to evaluate economic and health impact of

1) **Maternal HIV retesting** during pregnancy and postpartum in Kenya and South Africa
2) **Dual HIV/syphilis testing** into ANC in Kenya
   - *Model also incorporates retesting for syphilis/HIV retesting in ANC and HIV*

- *Models for Ukraine, Colombia, [South Africa], under development*

Maternal HIV retesting scenarios

Scenario	Late pregnancy or delivery	Postpartum			
		6 weeks (early)	14 weeks	6 months (mid)	9 months (late)
1	✓				
2		✓			
3				✓	
4	✓	✓			
5	✓			✓	
6	✓	✓	✓	✓	✓

Initial HIV testing at 1st ANC assumed under the base case and all retesting scenarios.

Markov decision-analytic cohort model for **HIV**

Stage n

A_n: HIV-

B_n: HIV+ Ag+/Ab- nART

C_n: HIV+ Ag+/Ab- ART

D_n: HIV+ Ab+ uk_nART

E_n: HIV+ Ab+ k_nART

F_n: HIV+ Ab+ ART

Stage n+1

A_{n+1}: HIV-

B_{n+1}: HIV+ Ag+/Ab- nART

C_{n+1}: HIV+ Ag+/Ab- ART

D_{n+1}: HIV+ Ab+ uk_nART

E_{n+1}: HIV+ Ab+ k_nART

F_{n+1}: HIV+ Ab+ ART

Stage n+2

A_{n+2}: HIV-

B_{n+2}: HIV+ Ag+/Ab- nART

C_{n+2}: HIV+ Ag+/Ab- ART

D_{n+2}: HIV+ Ab+ uk_nART

E_{n+2}: HIV+ Ab+ k_nART

F_{n+2}: HIV+ Ab+ ART

6 Maternal disease states

A: HIV-
B: HIV+ recent infection, no ART
C: HIV+ recent infection, ART
D: HIV+ chronic infection, no ART (unknown status)
E: HIV+ chronic infection, no ART (known status)
F: HIV+ chronic infection, ART

9 Maternal pregnancy/postpartum stages
Pregnancy onset – 12 months postpartum

1 week time step

Maternal and infant model parameters

	Kenya	South Africa
Pregnant women	1.6 million	1.2 million
Attend 1st ANC (%)	96%	80%
Gestational age at 1st ANC (weeks)	26	18
Maternal HIV	6.3%	22.5%
Maternal HIV incidence (per person-week)	.000269 -.000331	.00022-.0009
Test kit stock out	5%	5%
Test acceptance	83.3%	98%
MTCT per week, recent maternal infection	0.05 – 2.5	.0005 – 0.025
MTCT per week, chronic maternal infection	.005 - 0.025	.005 - 0.025
ART initiation	82%	98%
Reduction in MTCT with infant ARVs	80%	80%
Reduction in MTCT due to maternal VL suppression	82.9%	82.9%

MTCT risk based on:
Recent vs chronic infection
Maternal ART
Infant ARV
Breastfeeding

Costs and cost-effectiveness

Incremental costs (2017 USD)

- Time and motion studies; published literature
- Labor, supplies, medication
  - HIV related
    - HIV testing*
    - Infant ARVs
    - Maternal ART
    - Maternal PrEP
    - Infant ARVs
  - Syphilis related (dual model only)
    - Syphilis testing
    - Maternal penicillin

Cost-effectiveness

- Global burden of disease (GBD)
  - Convert infant infections/adverse birth outcomes into DALYs (WHO GBD)
  - Disability weights for syphilis, HIV, and AIDS (UW IHME GBD)
- DALYs = sum of years lived with disability (YLDs) and years of life lost (YLLs)
- Incremental cost-effectiveness ratio (ICER)=

  *[costs of retesting**– costs of base case scenario]*

  *[DALY retesting**– DALY under base case scenario]*

- **Cost-effective** if ICER < $500/DALY averted

*Time and motion studies, **dual testing rather than retesting in dual model*

Retesting in late pregnancy best single retesting scenario

Retesting scenario	Infant infections averted	% of potential max. benefit achieved	Infant deaths averted	Total DALYs	DALYs averted
Kenya					
1: Late pregnancy/delivery	3,981	**26%**	587	4,954,799	212,571
2: 6 week MCH visit	3,087	21%	455	5,002,522	164,848
3: 6 month MCH visit	1,268	8%	187	5,099,670	67,700
4: Late pregnancy/delivery and 6 week MCH visit	5,325	35%	785	4,883,058	284,312
5: Late pregnancy/delivery and 6 month MCH visit	4,785	32%	706	4,911,889	255,481
6: Late pregnancy/delivery and ~every 3 months PP	6,759	45%	997	4,806,469	360,900
South Africa					
1: Late pregnancy/delivery	8,847	**32%**	1,318	4,215,123	433,841
2: 6 week MCH visit	3,549	13%	529	4,474,901	174,062
3: 6 month MCH visit	1,656	6%	247	4,567,747	81,217
4: Late pregnancy/delivery and 6 week MCH visit	10,049	37%	1,497	4,156,187	492,776
5: Late pregnancy/delivery and 6 month MCH visit	9,872	36%	1,471	4,164,854	484,110
6: Late pregnancy/delivery and ~every 3 months PP	11,676	43%	1,740	4,076,404	572,559

**% of infant infections that could be prevented with retesting*

All maternal HIV retesting scenarios are cost-effective

Retesting scenario	Incremental costs	ICER (per DALY averted)
Kenya		
1: Late pregnancy/delivery	$5,078,140	$23.89
2: 6 week MCH visit	$4,984,413	$30.24
3: 6 month MCH visit	$4,431,325	$65.46
4: Late pregnancy/delivery and 6 week MCH visit	$8,825,058	$31.04
5: Late pregnancy/delivery and 6 month MCH visit	$8,786,722	$34.39
6: Late pregnancy/delivery and ~every 3 months PP	$17,802,649	$49.33
South Africa		
1: Late pregnancy/delivery	$5,665,657	$13.06
2: 6 week MCH visit	$5,705,289	$32.78
3: 6 month MCH visit	$5,462,835	$67.26
4: Late pregnancy/delivery and 6 week MCH visit	$9,568,103	$19.42
5: Late pregnancy/delivery and 6 month MCH visit	$9,998,821	$20.65
6: Late pregnancy/delivery and ~every 3 months PP	$18,589,238	$32.47

Dual HIV/syphilis models scenarios

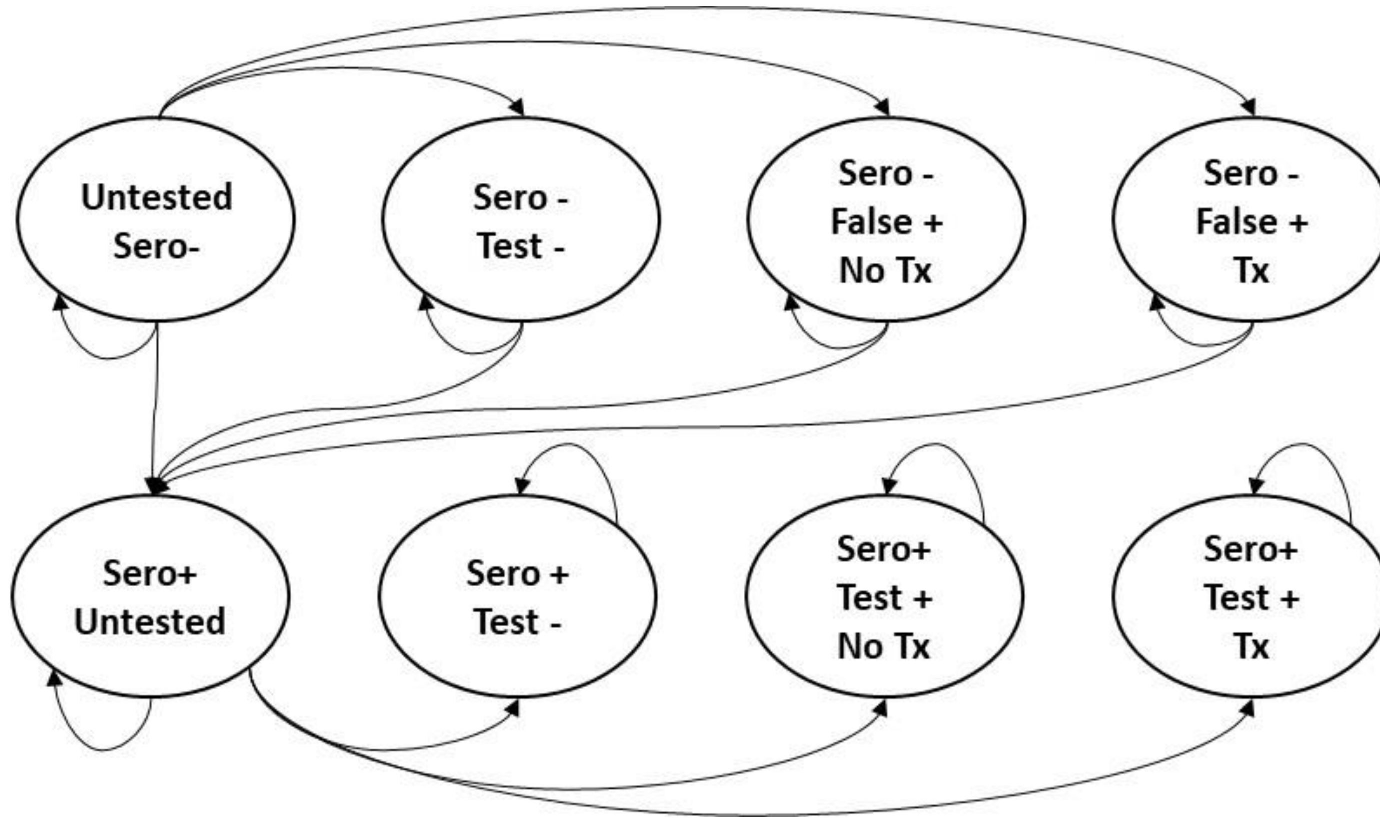
- HIV and syphilis modeled separately

Model scenarios	1st ANC syphilis	1st ANC HIV	Late ANC syphilis	Late ANC HIV
1) Base case (individual tests)	RPR/TPHA	Rapid	-	-
2) Dual* 1st ANC	Dual	Dual	-	-
3) Retest (individual tests)	RPR/TPHA	Rapid	RPR/TPHA	Rapid
4) Retest dual*	Dual	Dual	Dual	Dual

- Confirmatory testing assumptions
  - *Rapid HIV or dual HIV reactive: sequential rapid HIV test*
  - *RPR reactive: TPHA*
  - *Dual syphilis reactive: no confirmatory test*

**SD Bioline*

Markov decision-analytic cohort model for **syphilis**



6 Maternal disease states

A: Syphilis seronegative (not tested)
B: Syphilis seronegative (tested)
C: Syphilis seropositive (false positive, not treated)
D: Syphilis seropositive (false positive, treated)
E. Syphilis seropositive (not tested)
F. Syphilis seropositive (tested, not treated)
G. Syphilis seropositive (tested, treated)

1 week time step

Additional maternal and infant syphilis model parameters (Kenya)

	Parameter
Maternal syphilis	1.2%
Maternal syphilis incidence rate (per person-year)	.008
Test coverage (base case)	73%
Maternal treatment, lab testing	50%
Maternal treatment, dual testing	67%
Stillbirth, untreated	0.6%
Stillbirth, treated	0.1%
Neonatal death, untreated	0.2%
Neonatal death, treated	0%
Congenital syphilis, untreated	0.4%

Preliminary dual testing model results

Scenario	Total infant HIV infections	Infant HIV infections averted	Total congenital syphilis infections	Congenital syphilis infections averted	Total infant deaths	Infant deaths averted	Total DALYs	DALYs Averted
1) Base case	21,668	-	2,076	-	68,230	-	5,508,112	-
2) Dual* 1st ANC	21,668	-	1,633	442	67,377	853	5,461,473	46,638
3) Retest (individual tests)	17,684	3,985	2,076	-	67,031	1,199	5,295,320	212,791
4) Retest dual*	17,684	3,985	1,633	442	66,337	1,893	5,248,682	259,430

Preliminary dual testing model results

Scenario	Total cost (USD)	HIV costs	Syphilis costs	Incremental costs (USD)	ICER (per DALY averted)
1) Base case	$44,384,291	$42,474,474	$1,909,818	-	-
2) Dual* 1st ANC[1]	$43,708,987	$41,828,227	$1,880,760	-$675,305	-$14.48**
3) Retest (individual tests)	$51,218,791	$47,541,783	$2,203,900	$6,834,500	$32.12*
4) Retest dual[1]	$51,590,647	$49,370,746	$2,219,901	$7,206,356	$27.78*

- Dual test at first ANC is cost-saving
- Retesting strategies (individual and dual) both cost-effective

Assume 96% HIV and 4% syphilis programmatic costs under dual test
** Cost effective: < $500/DALY averted; ** Cost-savings. All costs in 2017 USD.*

Limitations

- Model does not:
  - Explicitly model infants (just women), but infant health outcomes modeled
  - Incorporate maternal protection for infection after treatment for the other infection
- Model may be sensitive to uncertainty in some model parameters
  - MTCT rates
  - Efficacy/adherence of infant ARV prophylaxis
- Cost-effectiveness threshold of $500/DALY is relatively new

Conclusions

Maternal HIV retesting

- All scenarios cost-effective in Kenya and South Africa
- Retesting in late pregnancy most cost-effective single retesting strategy
- Incremental benefits (and costs) with >1 retesting strategy
- Retesting may not be cost-effective in lower prevalence settings (stay tuned)

Dual testing

- Integration in ANC is cost-saving in Kenya
  - Cost-effective with maternal HIV retesting
- May increase coverage for maternal syphilis testing and treatment in some settings
  - Reduces congenital syphilis
  - May prevent maternal HIV acquisition and MTCT of HIV

Discussion

Maternal HIV retesting

- May be warranted in some settings (consider age and risk factors*)
- Need empiric data/metrics on maternal retesting

Dual testing

- High coverage of screening, and early detection and treatment of maternal infections necessary for dual EMTCT
- In Kenya
  - Costs shared and lower for HIV programs than siloed programming
  - No direct health benefit for HIV, but indirect benefits of syphilis treatment may be possible

Next steps…
Finalize parameters with in-country contacts
Compare model results from different settings

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