Completion of Treatment
Calculating Weeks of Treatment

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Disclosure

COVID 19 has taken over my work life so I'm borrowing the slides…..

Website link for calculating dates is an example. Similar tools available both online and offline.

Refer to **2016 Treatment of Drug Susceptible TB Guidelines** for more details: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf

Objectives

How to Calculate:

1. Expected Completion of Treatment (COT) date
2. Number of doses needed for regimen
3. Weeks of treatment received (dose counting)
4. Remaining number of doses & adjusted COT

Practice Makes Perfect!

Q: Is it adequate treatment?

Completion of Treatment (COT)

What is Completion of Treatment (COT)?

How do we calculate COT?

How do we apply it in the real world?

What is Treatment Completion?

Defines the number of doses ingested within a specified time frame (duration)

Duration depends on

- Drugs used
- Drug susceptibility test results of the isolate
- Patient's response to treatment
  - Smear results
  - Culture conversion
  - Xray results
  - Weight
  - Symptoms
- Site and extent of disease
- Patient comorbidities

What are the standard drugs for treating TB disease? (# pills, schedule)

INH	RIF	PZA	EMB
900 mg 2x or 3x wk (3)	600 mg 2x or 3x wk (2)	2x or 3x wk - (4) or (3) - (6) or (5) - (8) or (6)	2x or 3x wk - (4) or (3) - (6) or (5) - (8) or (6)
300 mg Daily (1)	600 mg Daily (2)	Daily -1 g (2) -1.5 g (3) -2 g (4)	Daily -800 mg (2) -1.2 g (3) -1.6 g (4)

Initial Phase: 8 weeks treatment (drug susceptible)

Full treatment period (usually 6 or 9 months)

When should treatment be extended?

Cavity on Xray **AND** positive sputum cultures at **2** months of therapy

If only one of the above, **consider** if. . .

- >10% below ideal body weight
- Being a smoker
- Diabetic
- HIV infection
- Other immunosuppressing condition
- Or having extensive disease on Xray

HIV infection not on ART (unusual situation)

2016 Treatment of Drug Susceptible TB Guidelines

Point to Remember

You often do not know how long the patient will need treatment until month 2 or 3

- Response to treatment
  - Culture conversion!
- Changes in treatment
- DST results

Patient Education & Communication

don't make promises you can't keep

How to Calculate:

1. **Expected Completion of Treatment (COT) date**
2. Number of doses needed for regimen
3. Weeks of treatment received (dose counting)
4. Remaining number of doses & adjusted COT

Weeks of treatment aka: the finish line

6 month = 26 weeks

9 month = 39 weeks

1 yr (12 month) = 52 weeks

Initial phase (8 weeks)

+

Continuation phase (18 weeks)

=

Total Treatment (26 weeks)

8 weeks

+

31 weeks

=

39 weeks

Date Duration Tool

Project expected date of completion (or end of Initial phase), if no missed doses:

http://www.timeanddate.com/date/dateadd.html

Tip: At end of treatment/initial phase, double check that enough calendar time has passed:

http://www.timeanddate.com/date/duration.html

For Precision, Look at Calendar

Calendar for Year 2017 (United States)

January

Su	Mo	Tu	We	Th	Fr	Sa
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

5◐ 12○ 19◑ 27●

February

Su	Mo	Tu	We	Th	Fr	Sa
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28				

3◐ 10○ 18◑ 26●

March

Su	Mo	Tu	We	Th	Fr	Sa
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

5◐ 12○ 20◑ 27●

April

Su	Mo	Tu	We	Th	Fr	Sa
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30						

3◐ 11○ 19◑ 26●

May

Su	Mo	Tu	We	Th	Fr	Sa
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

2◐ 10○ 18◑ 25●

June

Su	Mo	Tu	We	Th	Fr	Sa
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	

1◐ 9○ 17◑ 23● 30◐

July

Su	Mo	Tu	We	Th	Fr	Sa
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	31					

9○ 16◑ 23● 30◐

August

Su	Mo	Tu	We	Th	Fr	Sa
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

7○ 14◑ 21● 29◐

September

Su	Mo	Tu	We	Th	Fr	Sa
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30

6○ 13◑ 20● 27◐

How to Calculate:

1. Expected Completion of Treatment (COT) date
2. **Number of doses needed for regimen**
3. Weeks of treatment received (dose counting)
4. Remaining number of doses & adjusted COT

Weeks of Treatment = Dose counting (not calendar time)

Initial phase (8 weeks)

+

Continuation phase (18 weeks)

=

Total Treatment (26 weeks)

Equals how many doses??

2016 Treatment of Drug Susceptible Tuberculosis

Intensive Phase		Continuation Phase				
Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (Minimum Duration)	Range of Total Doses	Comments[c,d]	Regimen Effectiveness
INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182–130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.	Greater
INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	110–94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve.	
INH RIF PZA EMB	3 times weekly for 24 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	78	Use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse, and acquired drug resistance.	
INH RIF PZA EMB	7 d/wk for 14 doses then twice weekly for 12 doses[e]	INH RIF	Twice weekly for 36 doses (18 wk)	62	Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease. If doses are missed, then therapy is equivalent to once weekly, which is inferior.	Lesser

2016 Treatment of Drug Susceptible Tuberculosis

Calculating number of doses: example from a standard regimen

Initial phase (8 weeks)

Px frequency per week (dosage varies with frequency)	X	Week (duration)	=	Number doses
RIPE **5** days a week (daily dosage)	x	**8** weeks	=	**40** doses

Continuation phase (18 weeks)

INH/RIF **5** times a week (daily dosage)	x	**18** weeks	=	**90** doses

Total Treatment (26 weeks)

		26 weeks		130 doses

Calculating number of doses: example from a standard regimen

Initial phase (8 weeks)

Px frequency per week (dosage varies with frequency)	X	Week (duration)	=	Number doses
RIPE **5** days a week (daily dosage)	x	**8** weeks	=	**40** doses

Continuation phase (18 weeks)

INH/RIF **3** times a week (thrice weekly dosage)	x	**18** weeks	=	**54** doses

=

Total Treatment (26 weeks)

		26 weeks		**94 doses**

Calculating number of doses: example from a standard regimen

Initial phase (8 weeks)

	X	Week (duration)	=	Number doses
RIPE **7** days a week (daily dosage)	x	**2** weeks	=	**14** doses
RIPE **5** times a week (daily dosage)	x	**6** weeks	=	**30** doses

+

Continuation phase (18 weeks)

=

INH/RIF **3** times a week (thrice weekly dosage)	x	**18** weeks	=	**54** doses

Total Treatment (26 weeks)

		26 weeks		**98 doses**

Different regimens will have different total number of doses

Does your program have standard protocols with expected # of doses?

If you have eDOT, might do 7 days/week
DOT

How to Calculate:

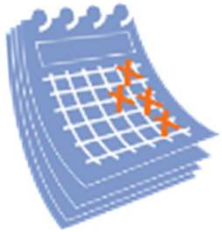
1. Expected Completion of Treatment (COT) date
2. Number of doses needed for regimen
3. **Weeks of treatment received (dose counting)**
4. Remaining number of doses & adjusted COT

Tools: Calendar Summary Table

Tools to Track Treatment

Each month calculate weeks of treatment received based on doses given. Helps to keep running summary of treatment.

Can use physical calendar



Can use monthly DOT log

- Ex: Texas TB-206

Can use excel

Tip for LTBI (self administered) count pills left in bottle at each office visit.

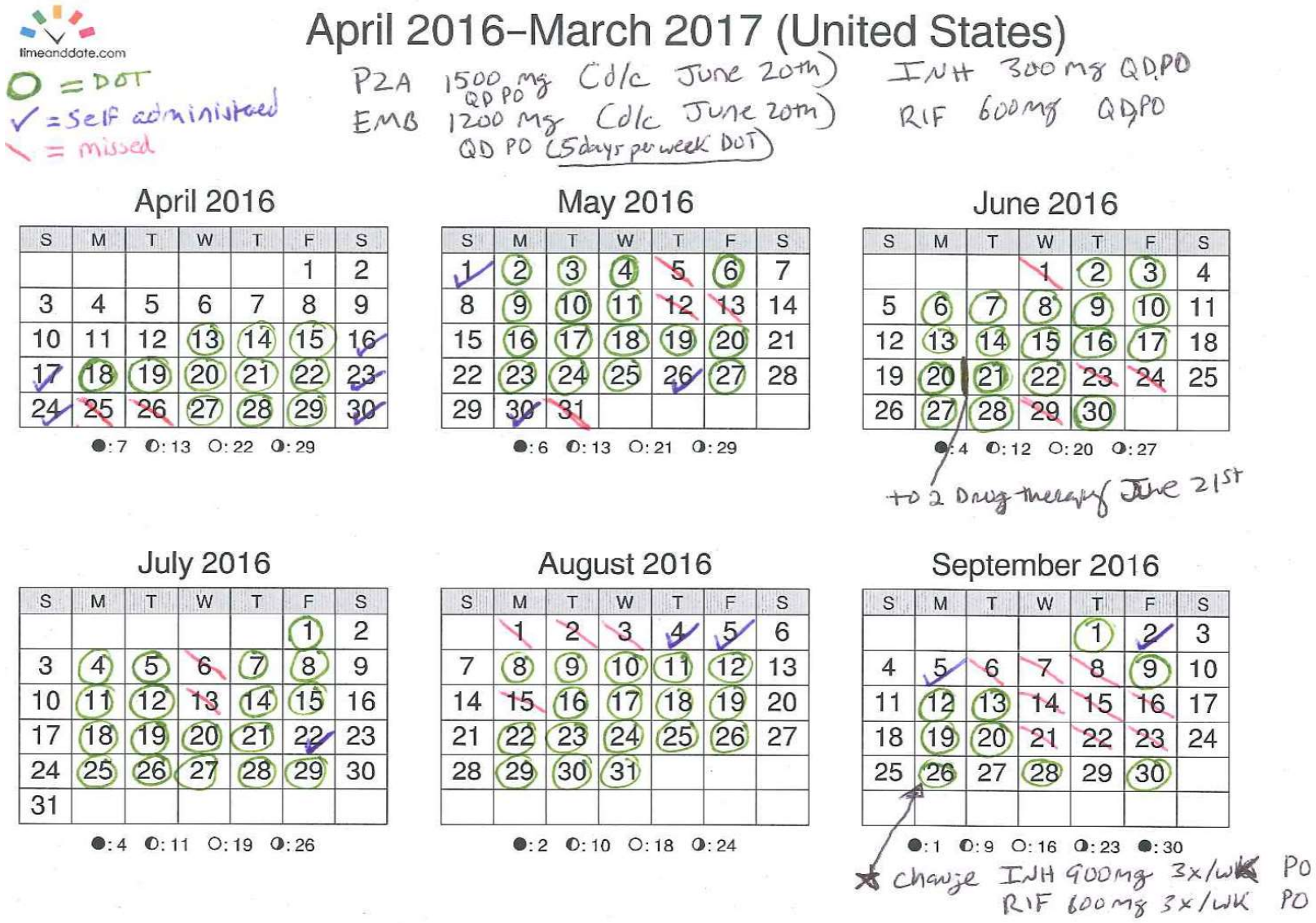
Date	DOT Adm	Self Adm	Dose Missed	DOT Provider's Initials	Client's Initials	Comments/Notes
/01/						
/02/						
/03						
/04/						
/05/						
/06/						
/07/						
/08/						
/09/						
/10/						
/11/						
/12/						
/13/						
/14/						
/15/						
/16/						

What does your program use?

May have Admin rules for counting

Many ways to track

Use what works for you & program!



1: Use a Calendar

Counting Apples and Oranges

To know where someone is in treatment

(weeks of treatment received)

Organize treatment summary by same prescribed dose and frequency. (Divide at change in Px).

For each separate section:

- Count number of **therapeutic** doses given
- Divide by prescribed frequency per week
- Equals number of weeks of treatment received
- Should be equal to or less than the number of weeks between the two dates

Add the number of weeks for each section for Total weeks completed

2: Summary Table

Example 1

Dates	Weeks (duration)	Doses administered	÷	Px (doses per week)	=	Weeks of Treatment *(total)*
1/6/16 to 1/25/16	2.9 wks	**20**	÷	RIPE **7** days/wk	=	**2.9** *(2.9)*
1/29/16 to 3/11/16	6.1 wks	**26**	÷	RIPE **5** days/wk	=	**5.2** *(8.1)*
3/14/16 To 4/15/16	4.6 wks	**13**	÷	Rif/INH(900mg) **3** days/wk	=	**4.3** *(12.4)*

Example 1

Dates	Weeks (duration)	Doses administered	÷	Px (doses per week)	=	Weeks of Treatment *(total)*
1/6/16 to 1/25/16	2.9 wks	**20**	÷	RIPE **7** days/wk	=	**2.9** *(2.9)*
1/29/16 to 3/11/16	6.1 wks	**26**	÷	RIPE **5** days/wk	=	**5.2** *(8.1)*
3/14/16 To 4/15/16	4.6 wks	**13**	÷	Rif/INH(900mg) **3** days/wk	=	**4.3** *(12.4)*

Things to look out for

Did they receive full 8 weeks PZA tx (# doses)?

Periods of monotherapy/under dosing?

Breaks in treatment

Figure 6.5
Algorithm for Management of
Initial Phase Treatment Interruptions

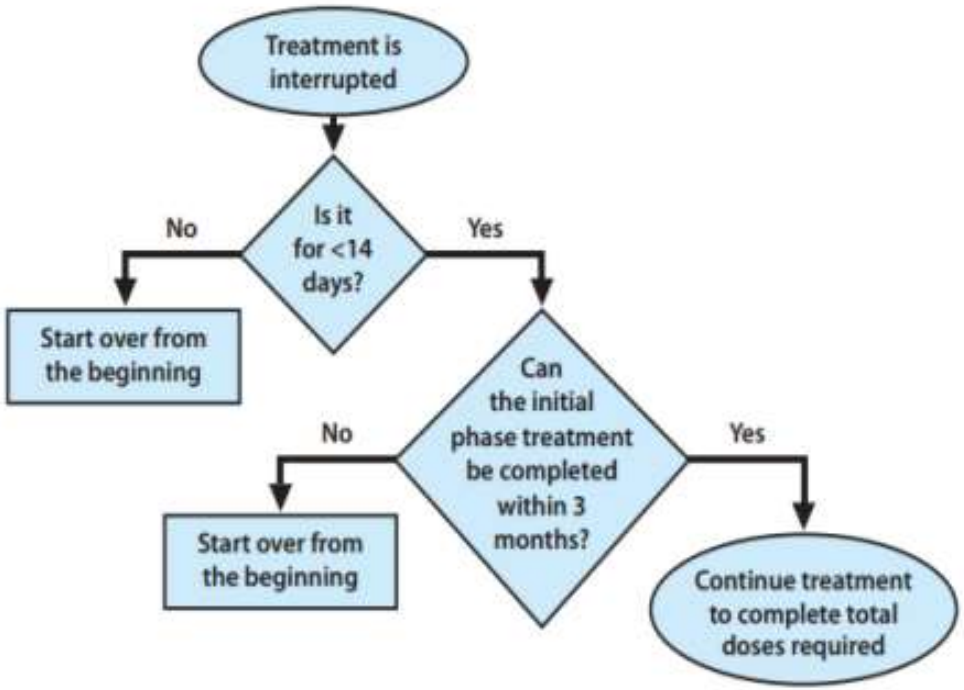
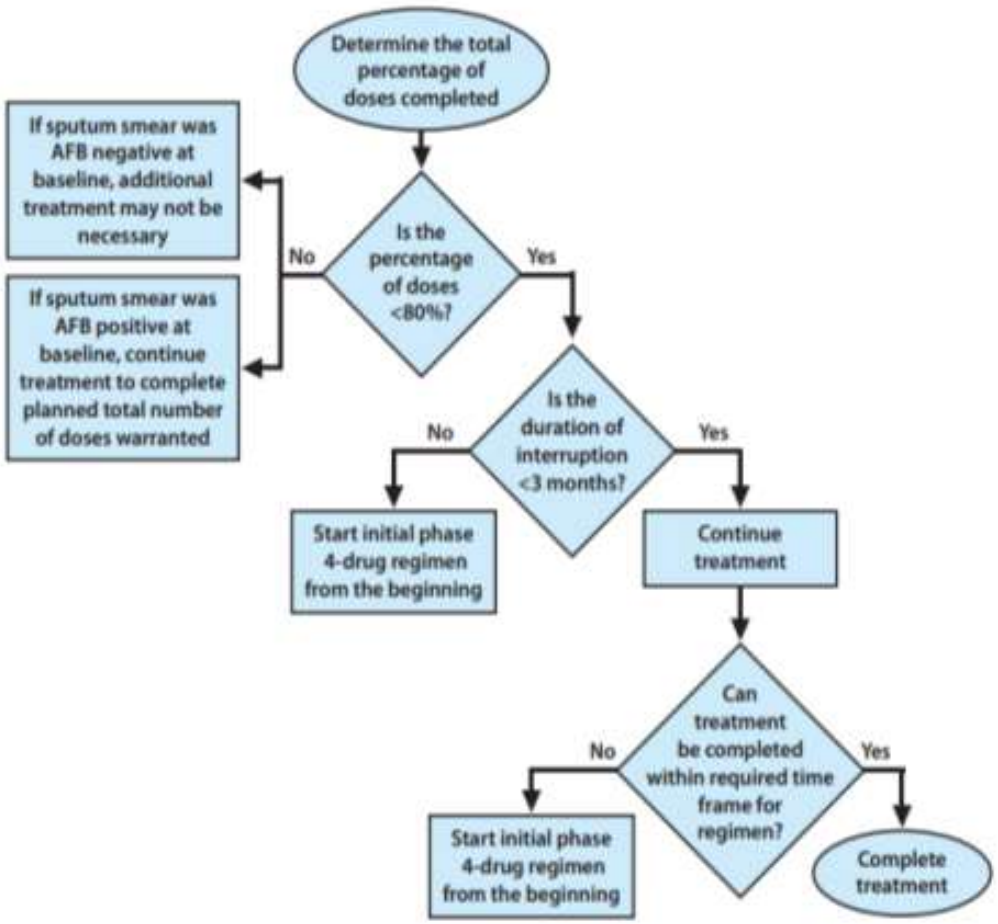


Figure 6.6
Algorithm for Management of
Continuation Phase Treatment Interruptions



http://www.cdc.gov/tb/education/corecurr/pdf/chapter6.pdf

Table 6. Management of Treatment Interruptions[a]

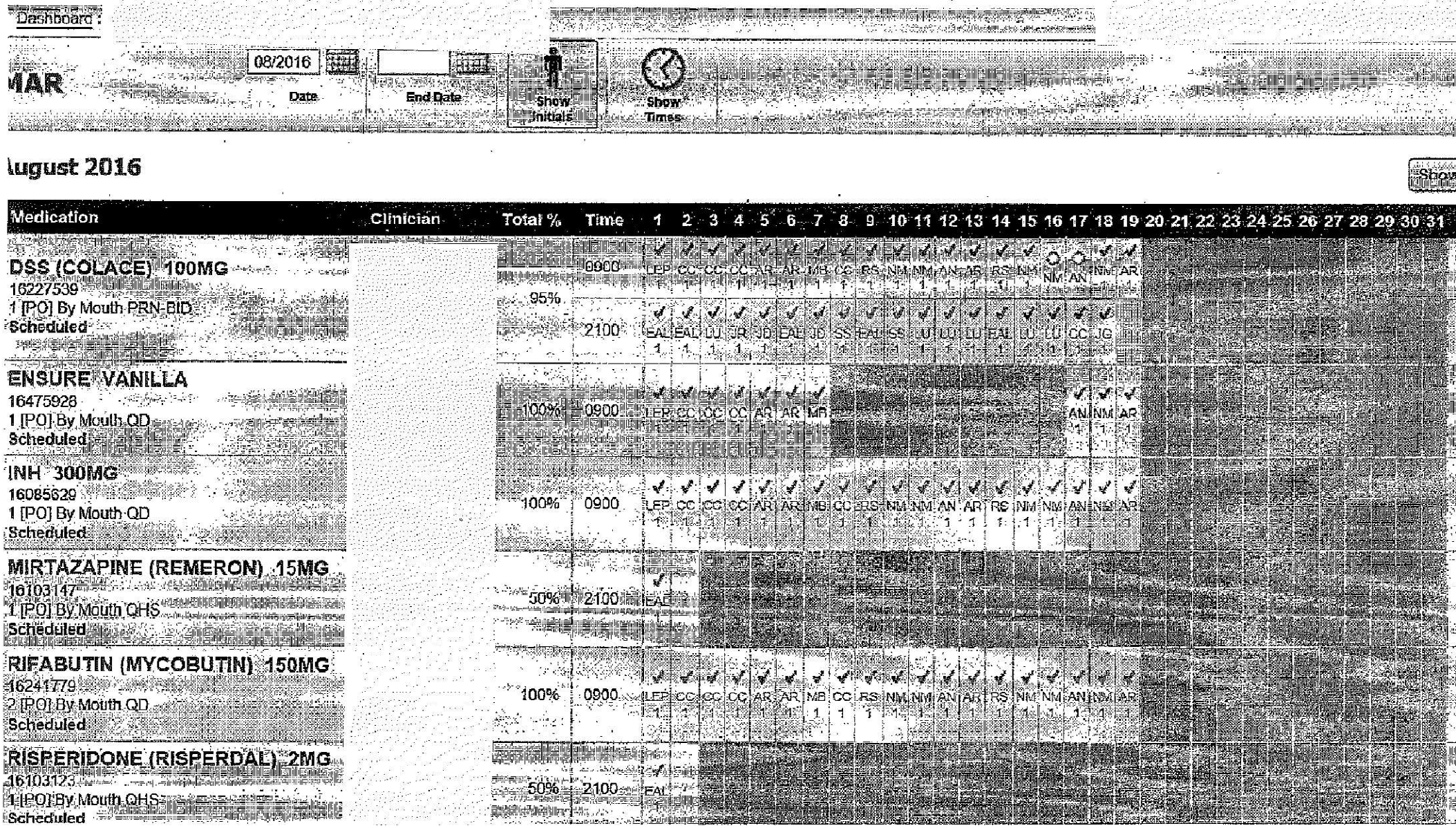
Time Point of Interruption	Details of Interruption	Approach
During intensive phase	Lapse is <14 d in duration	Continue treatment to complete planned total number of doses (as long as all doses are completed within 3 mo)
	Lapse is ≥14 d in duration	Restart treatment from the beginning
During continuation phase	Received ≥80% of doses and sputum was AFB smear negative on initial testing	Further therapy may not be necessary
	Received ≥80% of doses and sputum was AFB smear positive on initial testing	Continue therapy until all doses are completed
	Received <80% of doses and accumulative lapse is <3 mo in duration	Continue therapy until all doses are completed (full course), unless consecutive lapse is >2 mo If treatment cannot be completed within recommended time frame for regimen, restart therapy from the beginning (ie, restart intensive phase, to be followed by continuation phase)[b]
	Received <80% of doses and lapse is ≥3 mo in duration	Restart therapy from the beginning, new intensive and continuation phases (ie, restart intensive phase, to be followed by continuation phase)

Abbreviation: AFB, acid-fast bacilli.

[a] According to expert opinion, patients who are lost to follow-up (on treatment) and brought back to therapy, with interim treatment interruption, should have sputum resent for AFB smear, culture, and drug susceptibility testing.

[b] The recommended time frame for regimen, in tuberculosis control programs in the United States and in several European countries, is to administer all of the specified number of doses for the intensive phase within 3 months and those for the 4-month continuation phase within 6 months, so that the 6-month regimen is completed within 9 months.

2016 Treatment of Drug Susceptible Tuberculosis



How many weeks of treatment were given in August?

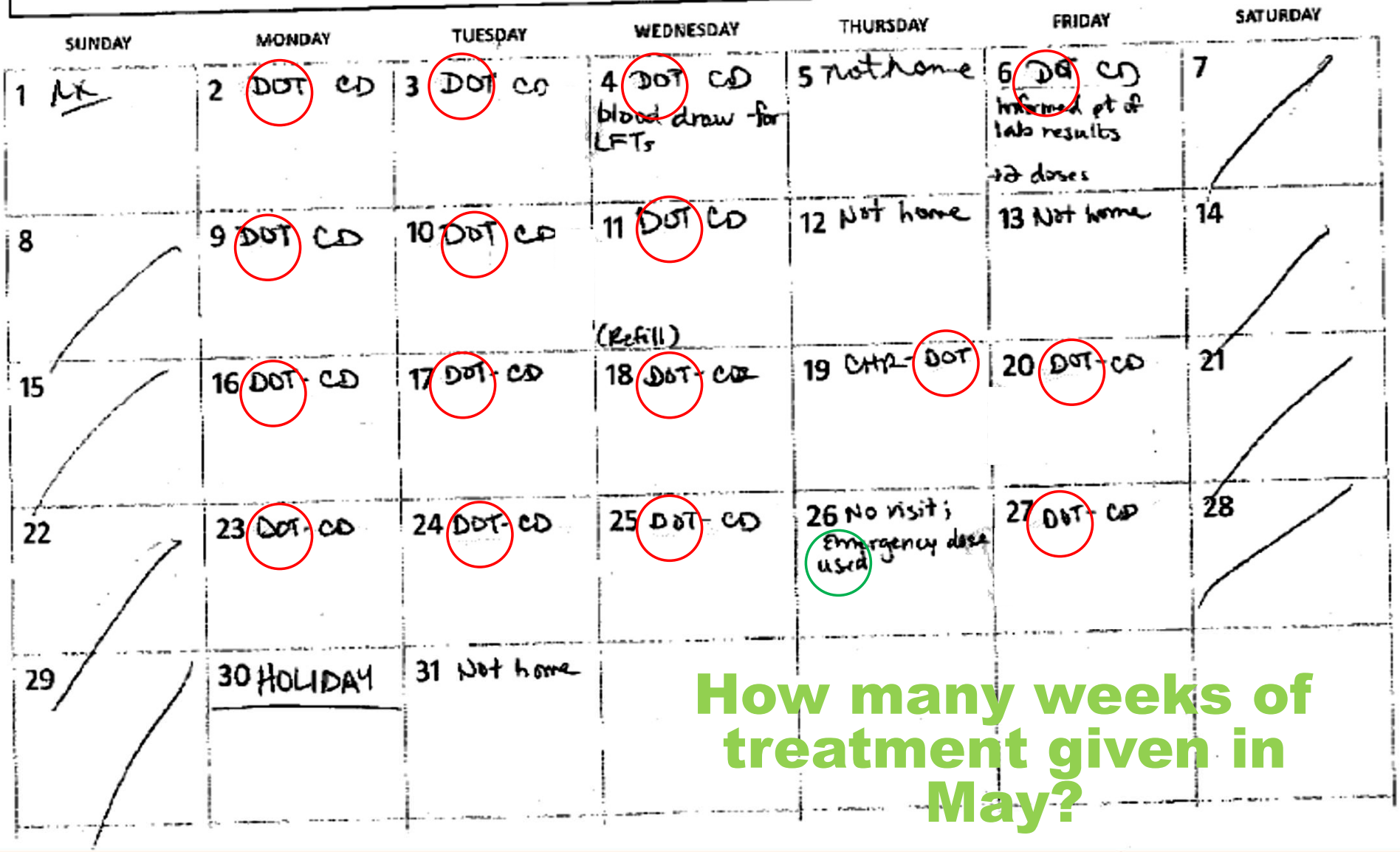
TB Directly Observed Therapy

Patient: **DOB:** **Age:** **Sex:**

Name	02/13/2016	02/12/2016	02/11/2016	02/10/2016	02/09/2016	02/08/2016	02/05/2016	02/04/2016
Drugs Prescribed		Ethambutol HCl 400 MG 4 tablets once a day, Isoniazid 300 MG 1 tablet once a day, Pyrazinamide 500 MG 4 tablets once a day, Rifabutin 150 MG 2 capsules once a day	Ethambutol HCl 400 MG 4 tablets once a day, Isoniazid 300 MG 1 tablet once a day, Pyrazinamide 500 MG 4 tablets once a day, Rifabutin 150 MG 2 capsules once a day	Ethambutol HCl 400 MG 4 tablets once a day, Isoniazid 300 MG 1 tablet once a day, Pyrazinamide 500 MG 4 tablets once a day, Rifabutin 150 MG 2 capsules once a day	Ethambutol HCl 400 MG 4 tablets once a day, Isoniazid 300 MG 1 tablet once a day, Pyrazinamide 500 MG 4 tablets once a day, Rifabutin 150 MG 2 capsules once a day	Ethambutol HCl 400 MG 4 tablets once a day, Isoniazid 300 MG 1 tablet once a day, Pyrazinamide 500 MG 4 tablets once a day, Rifabutin 150 MG 2 capsules once a day	Ethambutol HCl 400 MG 4 tablets once a day, Isoniazid 300 MG 1 tablet once a day, Pyrazinamide 500 MG 4 tablets once a day, Rifabutin 150 MG 2 capsules once a day	Ethambutol HCl 400 MG 4 tablets once a day, Isoniazid 300 MG 1 tablet once a day, Pyrazinamide 500 MG 4 tablets once a day, Rifabutin 150 MG 2 capsules once a day
Rifampin	-	-	-	-	-	-	-	-
Rifabutin	-	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Isoniazid	-	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pyrazinamide	-	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ethambutol HCl	-	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Vitamin B-6	-	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rifapentine	-	-	-	-	-	-	-	-
Moxifloxacin	-	-	-	-	-	-	-	-
Cycloserine	-	-	-	-	-	-	-	-
Ethionamide	-	-	-	-	-	-	-	-
Levofloxacin	-	-	-	-	-	-	-	-
Linezolid	-	-	-	-	-	-	-	-
Streptomycin	-	-	-	-	-	-	-	-
Prednisone	-	-	-	-	-	-	-	-
Other								
None Reported	No	No	No	No	No	No	No	No
Bruising/Bleeding	No	No	No	No	No	No	No	No
Fever/Chills	No	No	No	No	No	No	No	No
Loss of Appetite	No	No	No	No	No	No	No	No
Nausea/Vomiting	No	No	No	No	No	No	No	No
Headache	No	No	No	No	No	No	No	No
Abdominal Pain	No	No	No	No	No	No	No	No
Joint Pain	No	No	No	No	No	No	No	No
Numbness/Tingling	No	No	No	No	No	No	No	No
Jaundice/Dark Urine	No	No	No	No	No	No	No	No
Rash/Hives	No	No	No	No	No	No	No	No
Fatigue	No	No	No	No	No	No	No	No

TB 4-drug therapy, carried out with direct observational therapy (DOT)
1) Pyrazinamide (PZA) – 1500 mg oral daily (500 mg tablets x 3)
2) Ethambutol (EMB) – 1200 mg oral daily (400 mg tablets x 3)
3) Isoniazid (INH) – 300 mg oral daily (300 mg tablet x 1)
4) Rifampin (RIF) – 600 mg oral daily (300 mg capsules x 2)
*Adjunctive medication: Pyridoxine 50 mg oral daily (50 mg tablet x 1)

May 2016



How many weeks of treatment given in May?

timeanddate.com

April 2016–March 2017 (United States)

O = DOT
✓ = self administered
\ = missed

PZA 1500 mg QD PO (dc June 20th)
EMB 1200 mg QD PO (dc June 20th) (5 days per week DOT)
INH 300 mg QD PO
RIF 600 mg QD PO

April 2016

S	M	T	W	T	F	S
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30

●: 7 ◐: 13 ○: 22 ◑: 29

May 2016

S	M	T	W	T	F	S
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

●: 6 ◐: 13 ○: 21 ◑: 29

June 2016

S	M	T	W	T	F	S
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

●: 4 ◐: 12 ○: 20 ◑: 27

+ to 2 Drug therapy June 21st

July 2016

S	M	T	W	T	F	S
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

●: 4 ◐: 11 ○: 19 ◑: 26

August 2016

S	M	T	W	T	F	S
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

●: 2 ◐: 10 ○: 18 ◑: 24

September 2016

S	M	T	W	T	F	S
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	

●: 1 ◐: 9 ○: 16 ◑: 23 ●: 30

★ change INH 900mg 3x/wk PO
RIF 600mg 3x/wk PO

October 2016

S	M	T	W	T	F	S
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	31					

◐: 9 ○: 16 ◑: 22 ●: 30

Create a summary table of treatment

Example 2

Dates	Weeks (duration)	Doses administered	÷	Px (doses per week)	=	Weeks of Treatment *(total)*
4/13/16 to 6/20/16	<10 wks	**40**	÷	RIPE **5** days/wk	=	**8** *(8)*
6/21/16 to 9/20/16	13 wks	**46**	÷	RIF 600mg & INH 300mg **5** days/wk	=	**9.2** *(17.2)*
9/26/16 to 10/17/16	3+ wks	**9**	÷	Rif 600mg & INH 900mg **3** days/wk	=	**3** *(20.2)*

Example 2

Dates	Weeks (duration)	Doses administered	÷	Px (doses per week)	=	Weeks of Treatment *(total)*
4/13/16 to 6/20/16	<10 wks	**40**	÷	RIPE **5** days/wk	=	**8** *(8)*
6/21/16 to 9/20/16	13 wks	**46**	÷	RIF 600mg & INH 300mg **5** days/wk	=	**9.2** *(17.2)*
9/26/16 to 10/17/16	3+ wks	**9**	÷	Rif 600mg & INH 900mg **3** days/wk	=	**3** *(20.2)*

How to Calculate:

1. Expected Completion of Treatment (COT) date
2. Number of doses needed for regimen
3. Weeks of treatment received (dose counting)
4. **Remaining number of doses & adjusted COT**

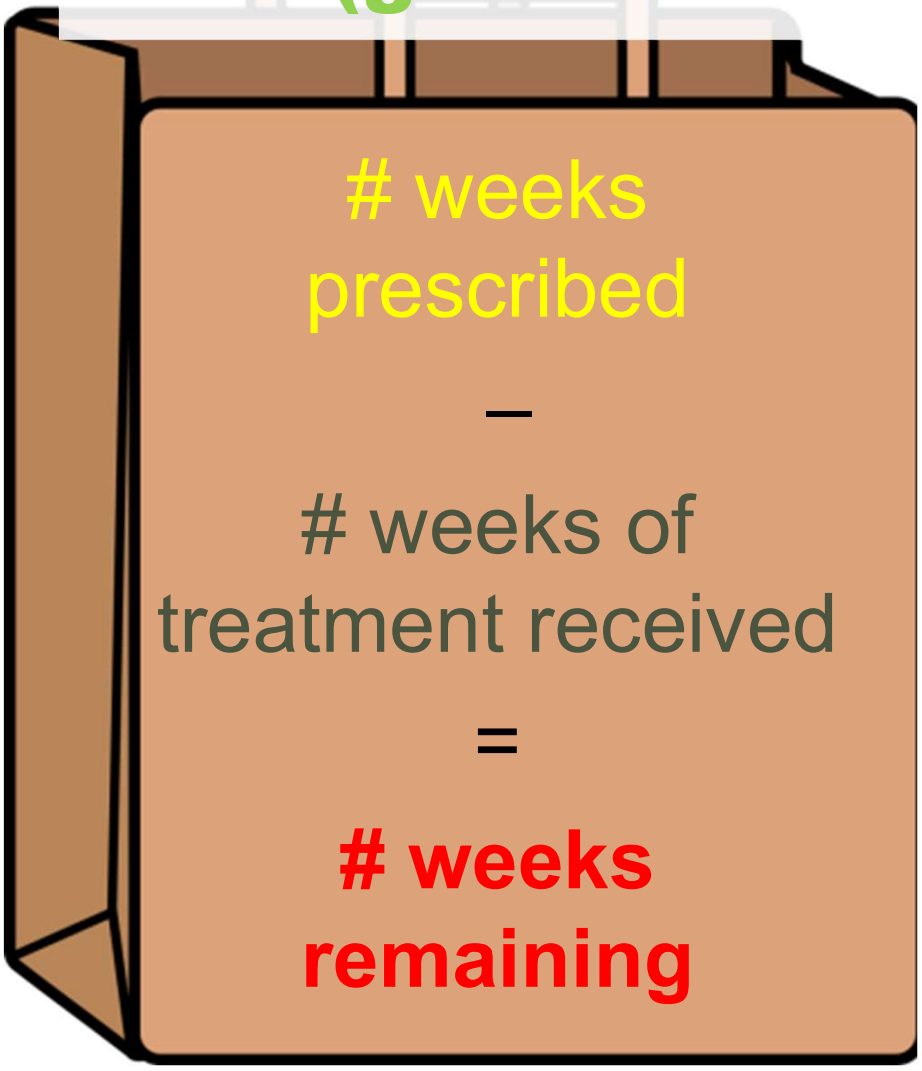
Calculating Revised COT

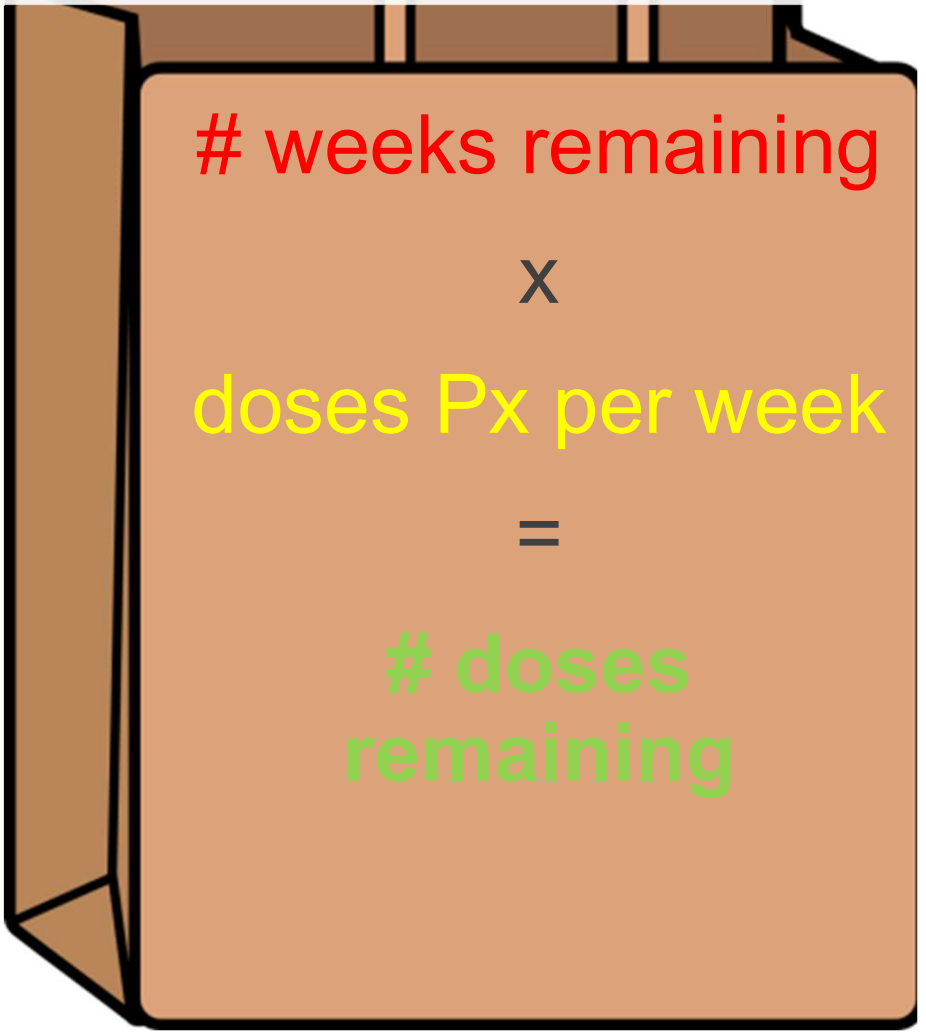
Option 1: tag on missed doses to end

- If no missed doses, no need to adjust!
- Example: missed 2 doses in initial phase due to holidays. None missed in continuation phase. Adjust on calendar

Calendar based adjustments

- **Option 2: add remaining weeks to date (good for lots of missing doses!)**





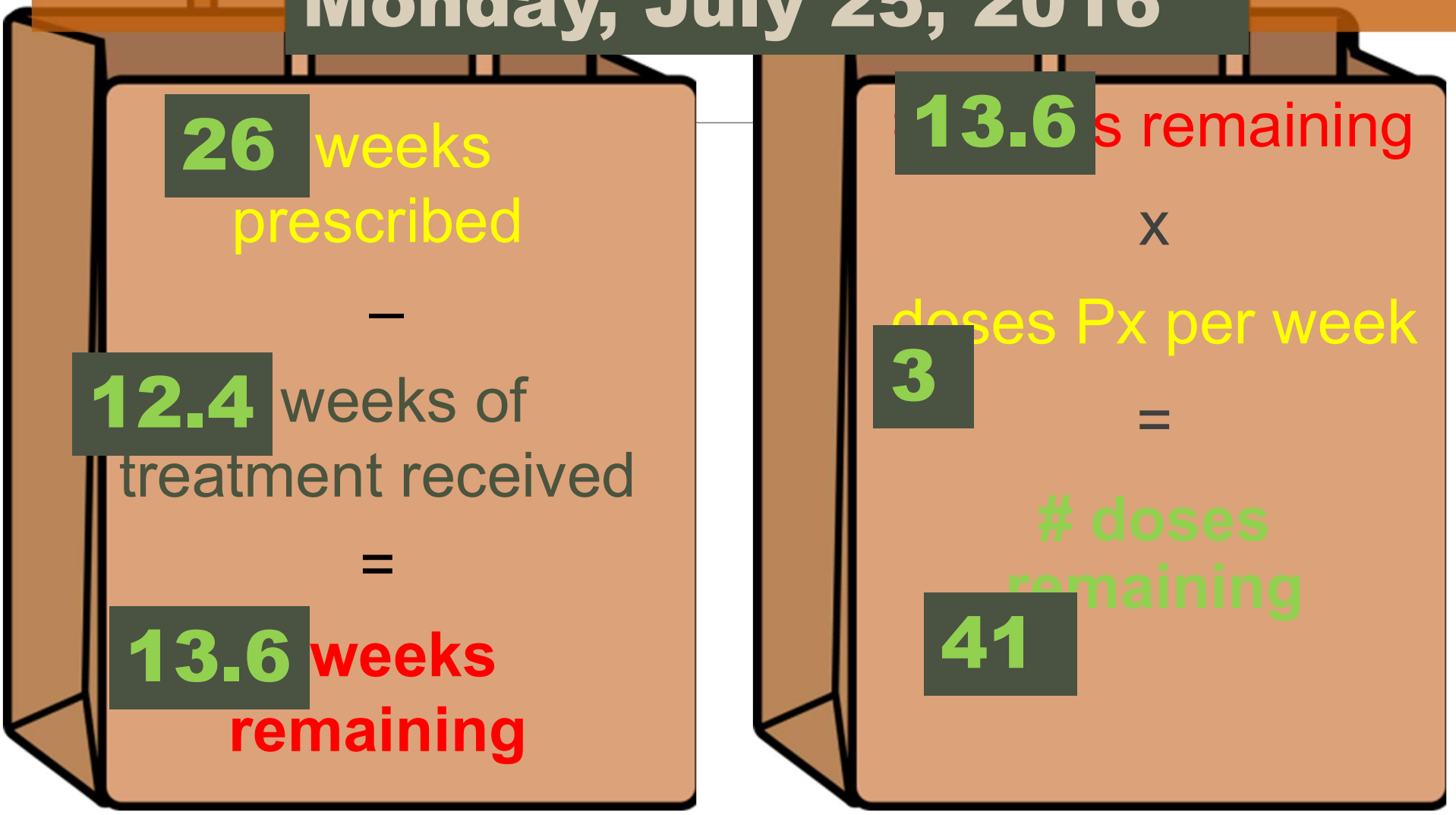
Projecting out remaining doses and COT date

Example 1

Dates	Weeks (duration)	Doses administered	÷	Px (doses per week)	=	Weeks of Treatment *(total)*
1/6/16 to 1/25/16	2.9 wks	**20**	÷	RIPE **7** days/wk	=	**2.9** *(2.9)*
1/29/16 to 3/11/16	6.1 wks	**26**	÷	RIPE **5** days/wk	=	**5.2** *(8.1)*
3/14/16 To 4/15/16	4.6 wks	**13**	÷	Rif/INH(900mg) **3** days/wk	=	**4.3** *(12.4)*

Use date calculator to project end

Monday, July 25, 2016



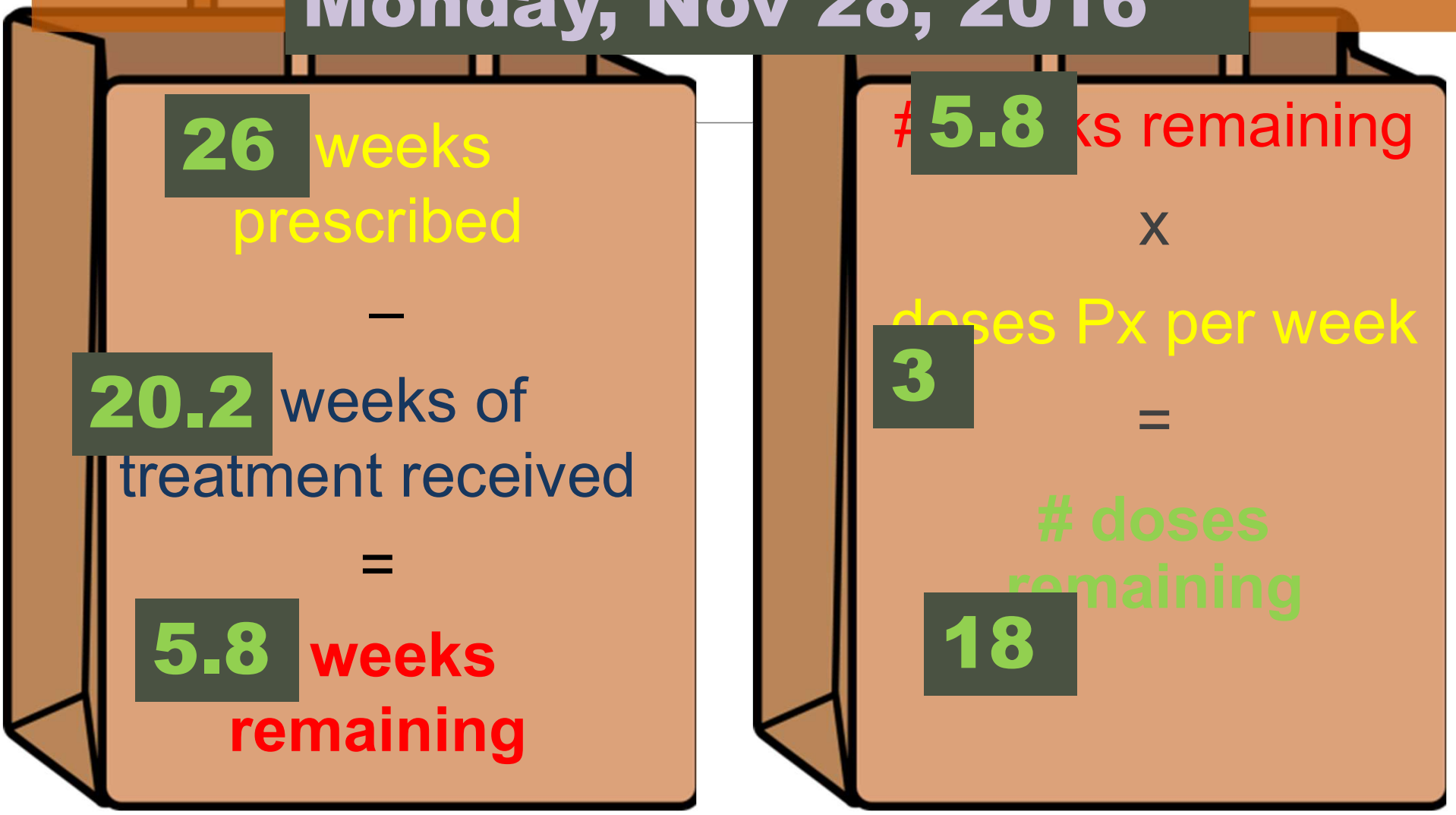
Example 1 Continued

Example 2

Dates	Weeks (duration)	Doses administered	÷	Px (doses per week)	=	Weeks of Treatment *(total)*
4/13/16 to 6/20/16	<10 wks	**40**	÷	RIPE **5** days/wk	=	**8** *(8)*
6/21/16 to 9/20/16	13 wks	**46**	÷	RIF 600mg & INH 300mg **5** days/wk	=	**9.2** *(17.2)*
9/26/16 to 10/17/16	3+ wks	**9**	÷	Rif 600mg & INH 900mg **3** days/wk	=	**3** *(20.2)*

Use date calculator to project end

Monday, Nov 28, 2016



Example 2 Continued

Q: Is it adequate treatment?

Full 8 weeks of PZA?

Under dosed or periods of monotherapy?

- Weight?

Gaps in treatment?

What were DST's?

What was Xray?

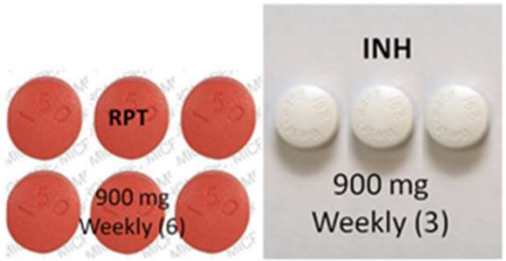
What were smear results?

When did patient culture convert?

Any significant comorbidities?

Site of Disease?

What about Latent TB Infection?

Regimens for Treating LTBI (dosage shown based on adults weighing ≥ 50 kg)	Length of Treatment Number of Doses Number of Pills	$*
	Isoniazid and Rifapentine once a week for 12 weeks by DOT (12 doses, 108 pills) *Preliminary results for RPT/INH:*	$76
	Rifampin Every day for 4 months (120 doses, 240 pills)	$110
	Isoniazid Every day for 9 months (270 doses, 270 pills) *Fewer than 60% complete full course*	$30

*Estimated cost based on possible 340B prices, excluding DOT and lab costs

TABLE 3. Recommendations for regimens to treat latent tuberculosis infection

Priority rank*	Regimen	Recommendation (strong or conditional)	Evidence (high, moderate, low, or very low)
Preferred	3 mos isoniazid plus rifapentine given once weekly	Strong	Moderate
Preferred	4 mos rifampin given daily	Strong	Moderate (HIV negative)†
Preferred	3 mos isoniazid plus rifampin given daily	Conditional	Very low (HIV negative)
		Conditional	Low (HIV positive)
Alternative	6 mos isoniazid given daily	Strong§	Moderate (HIV negative)
		Conditional	Moderate (HIV positive)
Alternative	9 mos isoniazid given daily	Conditional	Moderate

Abbreviation: HIV = human immunodeficiency virus.

* *Preferred:* excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness; *alternative:* excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.

† No evidence reported in HIV-positive persons.

§ Strong recommendation for those persons unable to take a preferred regimen (e.g., due to drug intolerability or drug-drug interactions).

Two months of rifampin plus pyrazinamide are not recommended for treatment of LTBI because of the hepatotoxicity risk. However, in persons treated empirically for TB disease with isoniazid, rifampin, and pyrazinamide for 2 months, this regimen will effectively treat LTBI in persons subsequently determined to have LTBI rather than TB disease.

https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6901a1-H.pdf

TABLE 4. Dosages for recommended latent tuberculosis infection treatment regimens

Drug	Duration	Dose and age group	Frequency	Total doses
Isoniazid* and rifapentine†	3 mos	**Adults and children aged ≥12 yrs** Isoniazid: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum Rifapentine: 10–14.0 kg, 300 mg 14.1–25.0 kg, 450 mg 25.1–32.0 kg, 600 mg 32.1–49.9 kg, 750 mg ≥50.0 kg, 900 mg maximum **Children aged 2–11 yrs** Isoniazid*: 25 mg/kg; 900 mg maximum Rifapentine†: see above	Once weekly	12
Rifampin¶	4 mos	**Adults:** 10 mg/kg **Children:** 15–20 mg/kg** **Maximum dose:** 600 mg	Daily	120
Isoniazid* and rifampin¶	3 mos	**Adults** Isoniazid*: 5 mg/kg; 300 mg maximum Rifampin¶: 10 mg/kg; 600 mg maximum **Children** Isoniazid*: 10–20 mg/kg††; 300 mg maximum Rifampin¶: 15–20 mg/kg; 600 mg maximum	Daily	90
Isoniazid*	6 mos	**Adults:** 5 mg/kg **Children:** 10–20 mg/kg†† **Maximum dose:** 300 mg	Daily	180
		Adults:15 mg/kg **Children:** 20–40 mg/kg†† **Maximum dose:** 900 mg	Twice weekly§	52
	9 mos	**Adults:** 5 mg/kg **Children:** 10–20 mg/kg†† **Maximum dose:** 300 mg	Daily	270
		Adults: 15 mg/kg **Children:** 20–40 mg/kg†† **Maximum dose:** 900 mg	Twice weekly§	76

12 weeks = 12 doses within 16 weeks

4 months= 120 doses within 6 months

6 months tx within 9 months

9 months tx within 12 months

* Isoniazid is formulated as 100-mg and 300-mg tablets.
† Rifapentine is formulated as 150-mg tablets in blister packs that should be kept sealed until use.
§ Intermittent regimens must be provided via directly observed therapy (i.e., a health care worker observes the ingestion of medication).
¶ Rifampin (rifampicin) is formulated as 150-mg and 300-mg capsules.
** The American Academy of Pediatrics acknowledges that some experts use rifampin at 20–30 mg/kg for the daily regimen when prescribing for infants and toddlers (**Source:** American Academy of Pediatrics. Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018:829–53).
†† The American Academy of Pediatrics recommends an isoniazid dosage of 10–15 mg/kg for the daily regimen and 20–30 mg/kg for the twice-weekly regimen.

A patient on the 12 week regimen just took their 4th dose and told you they are moving in a month. How many doses are left? Which of the following would you do?

A) You have four weeks to complete 8 more doses. Just double them up to completed 12 doses

B) Give the patient the rest of their meds to self administer

C) Do an interjurisdictional transfer to the new health department

D) Educate the patient on the importance of completing treatment and tell them to find a new doctor after they arrive

IJN

http://www.tbcontrollers.org/resources/interjurisdictional-transfers/#.V-lxDYgrKM8

A three year old household contact tests positive for TB infection. After being ruled out for TB disease, which regimen do you expect her to be on?

a) Isoniazid and rifapentine once weekly (DOT)

b) Rifampin daily for 4 months

c) INH DOT twice a week (can give during DOT of the index case)

DST's came back and the index case is INH resistant. The child has had 4 doses of weekly INH & Rifapentine. How much treatment does she have left?

- Even though she's had 4 weeks of INH & Rifapentine, she has to restart with Rifampin (as long as it's susceptible).

Part 2: Case Studies

Applying COT to the Real World

May you live in interesting times

Interesting case study #1

March 15: 49 yr old US born, homeless, binge drinker, no ETOH “since December”. DM for over 12 years. Presented to hospital with c/o 3 months of fatigue, anorexia, and malaise. Headache started in jail about six or eight weeks ago. Also started to have reduction in hearing. Headache lasted for a month, and now has significant hearing loss. Increased SOB over 3 or 4 weeks, cough 2 weeks with blood tinged sputum. Intermittent night sweats and fevers of about 100.5.

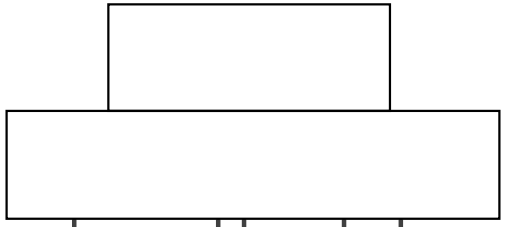
Q: What are the hospital's next steps?

Airborne Isolation

Chest x-ray/CT scan: CT showed profuse miliary-like nodules bilaterally

Sputum collection x3, at least eight hours apart.

- 3/15 00:45: smear neg
- 3/15 13:10: smear neg
- 3/15 15:00: smear neg
- 3/15 15:15: smear neg
- 3/16 08:45: smear neg
- 3/16 14:25: smear neg
- 3/17 17:05: smear neg



3/20 Lingula wash pathology: Few acid fast organisms with irregular and beaded appearance.

Q: Any advice for lab collection?

A1: Order a NAA

A2: Space the sputum collections over 8 hours

What are the hospital's next steps? (continued)

Work up for possible CNS involvement

- MRI "abnormal"
- CSF smear neg.

Baseline labs:

- **Q: which labs do you expect them to focus on?**
- A1: LFT's: normal. ALT/AST: 40/68 (Range 15-46/13-69)
- A2: HbA1C: 6.4

Notify Health Department of patient with possible TB

Q: What is the role of the HD during hospitalization?

Reporting

Coordinating with hospital for discharge and continuity of care

Interview patient for discharge planning and contact investigation

Q: Is there anything in the initial summary that would be a cause for concern?

A: Patient reports 3 months of symptoms, during which time he reports being incarcerated.

Hospital Care Plan

3/15: started meds. Weight 145 lbs (66kg)

- Isoniazid 300 mg PO QD
- Rifampin 300 mg PO BID
- Pyrazinamide 1500 mg PO QD
- Ethambutol 1000 mg PO QD

Q: Would you make any changes to this regimen on discharge?

A1: Ethambutol **1200** mg PO QD

A2: Rifampin **600 mg PO QD.** *Splitting doses is not recommended.*

Hospital Discharge Planning

Hospital worked with home jurisdiction for discharge planning:

ETOH: refused rehab

Housing: wanted to return to home area, however three family members all declined to let him stay with them. His plan was to live in a cave. PHN assessed the location of the cave, which requires climbing down from a mesa. They did not consider it a safe location for them to deliver DOT.

Solution: Agreed to stay in hospital's jurisdiction where housing was available through local county TB program. Housed in motel with no shared airspace.

Discharge Date: 4/2. Does he need to be on airborne isolation?

Facts to consider:

- Started RIPE 3/15.
- Sputums smear neg x3, at least 8 hrs apart. (continued to be smear neg).
- Improvement of symptoms, including decreased cough, feels better, improved hearing (subjective).

Guidelines for Home and Hospital Isolation of Infectious Tuberculosis Patients: http://www.heartlandntbc.org/assets/products/guidelines_home_hospital_infectious_patients.pdf

Guidance on Release from Hospital Tuberculosis Isolation[a]

Diagnostics:	Clinical Impression:	Under Airborne Isolation (AII) and discharging to:	Patient must meet all criteria:
Sputum **AFB Smear Positive** ***AND*** **NAAT Positive**	Active TB Disease	**Home**—**No** high risk individuals or individuals without prior exposure	• Follow-up plan has been made with local TB program and DOT has been arranged[b] • Started on standard TB treatment • All household members, who are not immunocompromised, have been previously exposed to the person with TB • Patient is willing to not travel outside the home until negative sputum smear results are received • No infants or children younger than 5 years of age or persons with immunocompromising conditions are present in the household who have not been evaluated and started on appropriate treatment
		Home—**WITH** high risk individuals OR **High-Risk/Congregate Setting**	Patients with infectious TB should NOT be allowed to return to a setting with high risk individuals. The patient can be *discharged* and is considered non-infectious if: • Three consectutive negative sputum smears from sputum collected in 8 - 24 hour intervals (at least one early morning specimen) ***AND*** • Started on drug regimen and tolerating for AT LEAST 2 weeks or longer ***AND*** • Symptoms have improved
Sputum **AFB Smear Negative** (or No Sputum AFB Smear Done) ***AND*** **NAAT Positive**	High likelihood of TB	**Home**—with/without high risk individuals OR **High-Risk/Congregate Setting**	• Three consecutive negative sputum smears from sputum collected in 8 to 24 hour intervals (at least one early morning specimen) • Started on standard TB treatment and tolerating for AT LEAST 5 days • A plan has been made to follow-up on culture results • No infants or children younger than 5 years of age or persons with immunocompromising conditions are present in the household who have not been evaluated and started on appropriate treatment
Sputum **AFB Smear Negative** ***AND*** **NAAT Negative**	High likelihood of TB	**Home**—with/without high risk individuals OR **High-Risk/Congregate Setting**	

AFB *- Acid-fast bacilli* ***AII*** *- airborne infection isolation* ***DOT*** *- Directly Observed Therapy* ***DST*** *- Drug Susceptibility Testing* ***MDDR*** *- Molecular Detection of Drug Resistance* ***MDR*** *- Multi-drug resistant* ***NAAT*** *- Nucleic Acid Amplification Test* ***TB*** *- Tuberculosis* ***XDR*** *- Extensively-drug resistant*

[a]Pulmonary Tuberculosis

[b]The hospital and/or treating clinician should contact the local health department prior to release of a patient with confirmed active TB disease.

Guidance on Release from Hospital Tuberculosis Isolation[a]

Diagnostics:	Clinical Impression:	Under Airborne Isolation (AII) and discharging to:	Patient must meet all criteria:
Sputum **AFB Smear Negative** ***AND*** **NAAT Negative**	TB is unlikely	**Home**—with/without high risk individuals OR **High-Risk/Congregate Setting**	• Three consecutive negative sputum smears from sputum collected in 8 to 24 hour intervals (at least one early morning specimen) • A plan has been made to follow-up on culture results • A diagnosis other than TB is identified or is likely
Sputum **AFB Smear Positive** ***AND*** **NAAT Negative** **A second NAAT should be considered to confirm**	High likelihood of TB	**Home**—with/without high risk individuals OR **High-Risk/Congregate Setting**	• Three consecutive negative sputum smears from sputum collected in 8 to 24 hour intervals (at least one early morning specimen) • Started on standard TB treatment and tolerating for AT LEAST 5 days • A plan has been made to follow-up on culture results • No infants or children younger than 5 years of age or persons with immunocompromising conditions are present in the household who have not been evaluated and started on appropriate treatment
	TB is unlikely		• Three consecutive negative sputum smears from sputum collected in 8 to 24 hour intervals (at least one early morning specimen) • A plan has been made to follow-up on culture results • A diagnosis other than TB is identified or is likely
Confirmed or **Strongly Suspected** MDR or XDR Diagnosed via: DST, MDDR, GeneXpert, or MTB/RIF Assay	N/A	**Home**—with/without high risk individuals OR **High-Risk/Congregate Setting**	• Three consecutive negative sputum smears from sputum collected in 8 to 24 hour intervals (at least one early morning specimen) ***AND*** • Started on adequate DR-TB drug regimen and tolerating for AT LEAST 2 weeks (14 daily doses) or longer ***AND*** • At least 2 consecutive negative sputum cultures without a subsequent positive culture

References:

1. Centers for Disease Control and Prevention. *Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings.* MMWR: December 30, 2005; Volume 54 (RR17).
2. Centers for Disease Control and Prevention. *Controlling Tuberculosis in the United States.* MMWR: November 4, 2005; Volume 54 (RR12s).

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HEARTLAND NATIONAL TB CENTER
THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT TYLER
2303 Southeast Military Drive
San Antonio, Texas
1-800-TEX-LUNG www.HeartlandNTBC.org

Outpatient care

Discharged on 4/2.

On 5 days/week DOT out of motel. Given food cards for incentives. Cannot buy alcohol with the food cards.

On Friday, 4/5, patient was not present at motel. Manager stated that he saw him walking down the road with his O2.

Q: What would you do?

Monday Morning: Phone Call

Showed up at brother's house on Saturday, 4/6. Brother called as public health had been looking for him. Patient reports that he began to walk home and slept overnight "in the forest". Hitched rides. Arrived without O2.

Social admit to community health center/hospital, as he had no place to stay and required continued treatment. RIPE restarted (only missed one day).

Tuesday

AST/ALT of 338/268. (Range 15-46/13-69)

- Calculate x's normal:
- 7.3x/3.9x
- Alcohol associated AST>ALT

Q: What would you do?

All TB meds stopped.

Consult done with reference physician by treating doctor.

Plan to reintroduce TB meds (RIF/INH/PZA) one at a time with EMB when AST/ALT < 2xs normal. LFT's monitored before adding next med.

Fast Forward

LFT's stabilized. TB meds reintroduced. On all four drugs 4/26.

Last had RIPE 4/8=17 days off meds.

Reminder: Started RIPE 3/15 in hospital.

Q: Which date is used as reporting start of treatment (for surveillance)?

A: 3/15. The date first ingested RIPE

Q: Which date is used for dose counting?

A: 4/26. ≥ 14 day lapse during initial phase.

Table 6. Management of Treatment Interruptions[a]

Time Point of Interruption	Details of Interruption	Approach
During intensive phase	Lapse is <14 d in duration	Continue treatment to complete planned total number of doses (as long as all doses are completed within 3 mo)
	Lapse is ≥14 d in duration	Restart treatment from the beginning
During continuation phase	Received ≥80% of doses and sputum was AFB smear negative on initial testing	Further therapy may not be necessary
	Received ≥80% of doses and sputum was AFB smear positive on initial testing	Continue therapy until all doses are completed
	Received <80% of doses and accumulative lapse is <3 mo in duration	Continue therapy until all doses are completed (full course), unless consecutive lapse is >2 mo If treatment cannot be completed within recommended time frame for regimen, restart therapy from the beginning (ie, restart intensive phase, to be followed by continuation phase)[b]
	Received <80% of doses and lapse is ≥3 mo in duration	Restart therapy from the beginning, new intensive and continuation phases (ie, restart intensive phase, to be followed by continuation phase)

Abbreviation: AFB, acid-fast bacilli.

[a] According to expert opinion, patients who are lost to follow-up (on treatment) and brought back to therapy, with interim treatment interruption, should have sputum resent for AFB smear, culture, and drug susceptibility testing.

[b] The recommended time frame for regimen, in tuberculosis control programs in the United States and in several European countries, is to administer all of the specified number of doses for the intensive phase within 3 months and those for the 4-month continuation phase within 6 months, so that the 6-month regimen is completed within 9 months.

2016 Treatment of Drug Susceptible Tuberculosis

Fast Forward continued

During extended stay with continued interventions, eventually agreed to go to in-patient rehab in another state. Transferred care 5/3 through interjurisdictional process.

Q: What is the interjurisdictional process in your health department? Who do you contact? How do you track transfers in, and transfers out?

http://www.tbcontrollers.org/resources/interjurisdictional-transfers

Fast Forward x2

None of the cultures grew MTB (sputum, CSF, bronch wash). Only had pathology report that looked like TB.

Improved on treatment: x-ray, respiratory, and auditory symptoms. Considered culture negative case, with questionable CNS involvement.

Due to possible CNS involvement, recommended 9 months of treatment. No drug sensitivities available, however epidemiology of area is for pansensitive TB.

Finishing Treatment

6/4: Transferred back to AZ to continue rehab in another facility, which was in a new jurisdiction.

10/26: Returned home. Family accepted him back home while social services worked with him on finding low income housing. Continuing classes on outpatient basis. Staying sober.

Q: How many weeks of his 9 month (39 weeks) course of treatment has he completed?

SUMMARY OF TREATMENT: 5 TRANSFERS, 4 HD'S

Dates	Treatment	# Doses	Weeks of Treatment
3/15-4/8	RIPE 7 days/wk	24	
4/9-4/25	Held meds due to AST. Reintroduced one by one	0:partial only	
4/26-6/10	RIPE 7 days/wk	38	
6/12-8/15	RIF 600 mg & INH 900 mg 2x/wk	18	
8/19-10/25	RIF 600 mg & INH 900 mg 3x/wk	30	

Q: If the treatment is for 9 months, how many more doses (and weeks) are left on three times a week regimen?

A: 39 – 24.4 = 14.6 weeks. 14.6 weeks x 3 = 44 more doses.

Q: On receiving transfer, what would you alert the treating provider regarding treatment history?

A: Did not receive full course of PZA. If PZA is not given for the full 8 weeks of the initial phase, will need at least 9 months of treatment. He is already receiving 9 months. May need to extend treatment.

Interesting case study #2

6/15: 65 year old US born female with type 2 DM, HTN, asthma, hx of LTBI with 9 months INH treatment in 1977. Presented with 1 -2 months of cough, with fatigue and muscle aches. Medical record shows blood tinged sputum, which patient denies. CT in ER showed "RUL cavitary mass contiguous to the R hilum & multiple bilateral pulmonary nodules."

6/17 BAL done. Doctor doubts that it is TB, but gives orders to "remain on airborne isolation until results are back."

Labs sent to outside facility

6/18: sputums collected 6/15 reported as 3+ and 4+. NAA ordered on bronch specimen. RIPE started.

6/19: NAA (equivalent test) detected MTB

Date collected	Time	Specimen	Smear	Culture	NAA
6/15	16:00	sputum	3+	MTB	
6/15	18:25	sputum	4+	MTB	
6/16	7:05	sputum	4+	MTB	
6/17	11:05	bronch	3+	MTB	MTB
6/20	17:15	sputum	4+	MTB	
6/24	5:03	sputum	4+	MTB	
6/25	10:45	sputum	4+	MTB	
6/27	9:40	sputum	4+	MTB	MTB
6/28	10:00	sputum	4+	MTB	
7/2	11:15	sputum	4+	MTB	
7/2	9:15	sputum	4+	MTB	
7/5	8:30	sputum	3+	MTB	

Discharge Planning

Discharged home on 7/6.

- Smears from 7/5 are 3+.
- On daily RIPE since 6/18.
- Improved symptoms, but still ill. Epidemiology for pansensitive TB. She lives with husband and adult son.

Q: Does she need to continue on airborne isolation?

Q: Does she need to continue on airborne isolation?

A: Continue until 3 consecutive smear negative sputums are collected at least 8 hours apart, at least one early morning specimen.

Date collected	Smear	Culture
6/15	4+	MTB
7/5	3+	
7/9	neg	
7/10	2+	
7/10	2+	
7/12	neg	
7/15	1+	
7/16	rare	
7/17	rare	

6/18: RIPE started

7/17: results come back: PANSEN (INH/RIF/EMB/PZA/Strep)

2 month: Still smear positive. Clinically and radiology doing well.

Q: When was culture conversion?

3 month: Still smear positive. Repeat susceptibilities automatically done.

4 month: finally smear neg. Close to culture conversion? Repeat susceptibilities PANSEN.

Delayed Sputum Conversion

Q: What are her risk factors for delayed sputum conversion?

A: DM, with cavity and 4+ smears at start of treatment

Q: When there are delays in response to treatment, what can be done?

A: Look at treatment regimen. Is the dosage correct for the patient's weight? For DM and heavy burden of disease, recommend daily (5 days/wk) DOT, not intermittent therapy.

A: Look at clinical response to therapy, and the trend of lab results. If they were underweight, is their weight improving? How is their appetite? How is their energy level? Is there any reason to suspect drug resistance?

A: Think about taking drug levels.

Q: How long of treatment would you expect?

Completion of Treatment!

Letter of Completion of Treatment

Follow up needed?

- MDR: monitor for 2 years post treatment
- INH or RIF resistance: individualize follow up
- Satisfactory response to standard treatment: routine f/u not necessary. Patient to report symptoms.

Date:_____

Dear_____

Congratulations! You have completed _____ weeks of antituberculosis therapy as of _____. For this reason we are not making any further routine clinic appointments for you.

However, no treatment is perfect and we will keep your records in case you should develop symptoms of possible tuberculosis in the future, such as weakness, tiredness, cough that hangs on, unexplained loss of 10 pounds or more, sweating at nights, etc.

Please keep this letter with your important papers so that if you need to see another doctor you will have accurate information about the treatment you have received.

Sincerely,

_____

Dear Doctor:
This patient has received treatment for tuberculosis as indicated below. In the event of symptoms compatible with reinfection, an x-ray and several bacteriological examinations are of paramount importance.
Original diagnosis_____
Treatment from ___/___/___ to ___/___/___
Drugs used: ____ INH 300mg, ____ RIF 600 mg, ____PZA ____ mg ____EMB ____ mg,
Other_____

One Last Interesting Example

5/1: Thursday afternoon, received call from HD in another state. They had report of possible TB from their local VA. 72 year old Arizona resident (US born WM) with "AFB identified" in a biopsy of right lung mass done on 4/21. Faxed records: Pathology showed caseating granulomas and rare acid fast organism on stain. Had a cavitary chest xray in RUL on same date. Presented with weight loss, fatigue, SOB, cough, and hemopytsis. No TST or IGRA noted in records. No sputums were included in records. Has return appointment on Monday and plans to take Greyhound for four hours to his doctor.

Q: What would you do?

One last Interesting Example (continued)

Coordinated with HD in other state to have the follow up appointment postponed until cleared for travel on Greyhound. His VA provider discussed with patient over phone plan for AZ HD to clear him for travel.

Status of original sample unclear.

AZ HD contacted patient and had patient collect sputums Friday, Saturday, and Sunday. Sent to AZ State lab with request for NAA.

Smear 3+, 3+, 4+. NAA did NOT detect MTB.

Cleared for travel as presumed atypical mycobacteria. Grew out MAC in culture.

Congratulations!

You've completed this session!

THANK YOU TO MS. STAFFORD FOR THE USE OF HER SLIDES!!!!

Any Questions?