

Use of Nucleic Acid Amplification Tests in TB patients in California 2010-2012

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Objective: To describe, with surveillance data, how NAATs were used in TB patients in CA 2010-2012

TB NAAT background

- CDC recommendation: Use NAAT for diagnosis of pulmonary TB when the test result would alter case management or TB control activities¹
- NAAT can reliably detect *Mycobacterium tuberculosis* bacteria in specimens 1 or more weeks earlier than culture¹
- NAATs: high specificity, but modest and highly variable sensitivity, especially in smear-negative and extrapulmonary TB²

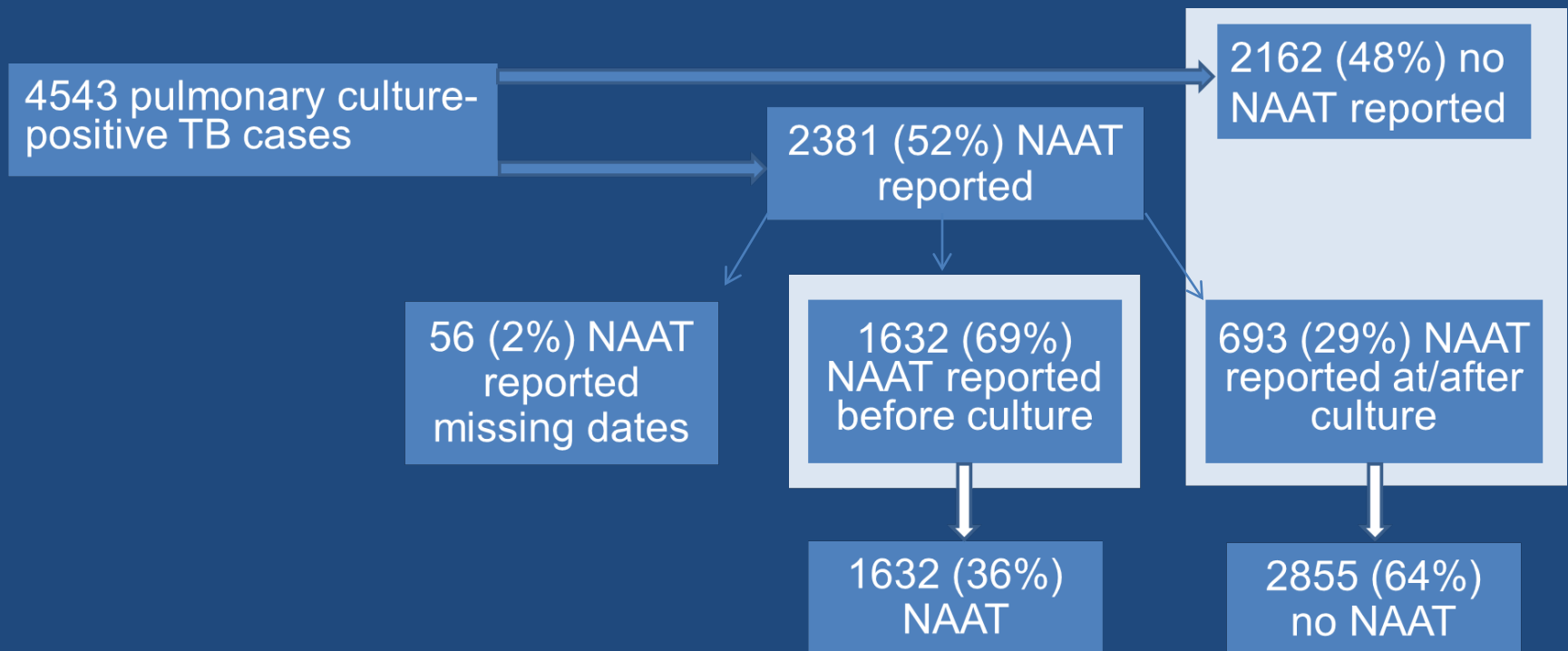
¹Updated Guidelines for the use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis, 2009. MMWR vol. 58, No. 1

²Pai M, Ramsay A, O'Brien R (2008) Evidence-Based Tuberculosis Diagnosis. PLoS Med 5(7): e156

Questions related to NAAT use

- How many pulmonary TB patients had NAAT?
- Can we determine, with surveillance data only, how NAATs were used to inform treatment decisions?

How many pulmonary TB patients had NAAT: NAAT report dates before or after culture?



How many pulmonary TB patients had NAAT?

- 52% of all pulmonary culture-confirmed TB patients had NAAT reported

BUT

- 36% had NAAT reported before culture

Assumptions: 29% of reported NAATs with report dates at/after culture were:

- Not used as rapid diagnostic tests*
- Did not influence treatment decision

* We are not considering use of NAATs for DST in these analyses

CDC recommends that NAAT be performed ...each patient with ...pulmonary TB ...
and for whom the test result would alter case management or TB control activities

How were NAATs used to:
alter case management or TB control?

- How were patients with NAAT different than those without?
- Did patients with NAAT start treatment earlier than those without?
- How rapidly were NAATs reported?
- Did NAAT turnaround time vary by lab type and jurisdiction?
- Did patients with positive NAATs start treatment earlier than those with negative NAATs?

Methods

- Study population:
 - Pulmonary culture-confirmed TB patients with a known AFB smear, reported to CA TB registry, 2010-2012
- Definitions
 - NAAT =NAAT reported before culture
 - No NAAT =NAAT not reported or NAAT reported at/after culture
 - Unless otherwise noted, time to treatment initiation=number of days between date of earliest specimen collection and date of treatment start, excluding patients who started treatment at or before specimen collection
 - NAAT TAT=time between specimen collection and NAAT report date
- Statistical analysis: frequencies compared across strata with chi-squared or Fisher's exact tests; median timeframes compared with Wilcoxon rank-sum tests

How were patients with NAAT different than those without NAAT?

Characteristic	NAAT N (%)	No NAAT N (%)	Total
Total	1632	2855	4487
Race/ethnicity			
White	128 (8)	231 (8)	359 (8)
Black	93 (6)	168 (6)	261 (6)
Hispanic	645 (40)	1003 (35)	1648 (37)
Asian/PI	762 (47)	1449 (51)	2211 (49)
Age			
Less than 65 yrs.	1183 (72)	1984 (69)	3167 (71)
65+	449 (28)	871 (31)	1320 (29)
Sputum smear			
Positive	1476 (90)	1496 (52)	2972 (66)
Negative	156 (10)	1359 (48)	1515 (34)
Chest x-ray findings			
Abnl w cavities	480 (31)	538 (20)	1018 (24)
Abnl no cavities	1091 (69)	2140 (80)	3231 (76)

How were patients with NAAT different than those without NAAT, cont.?

Characteristic	NAAT N (%)	No NAAT N (%)	Total
Total	1632	2855	4487
Co-morbidity			
Diabetes	479 (29)	687 (24)	1166 (26)
End stage renal dz	41 (3)	84 (3)	125 (3)
Immunosuppression	108 (7)	177 (6)	285 (6)
TNF antagonist rx	11 (0.7)	16 (0.6)	27 (1)
Post organ transplant	5 (0.3)	18 (0.6)	23 (0.5)
Primary reason evaluated for TB			
TB symptoms	1197 (73)	1779 (62)	2976 (66)
Abnormal CXR	290 (18)	618 (22)	908 (20)
Contact investigation	44 (3)	69 (2)	113 (3)
Targeted testing	26 (2)	44 (2)	70 (2)
Immigration med exam	18 (1)	134 (5)	152 (3)
Incidental lab result	45 (3)	164 (6)	209 (5)
HCW/admin/unk	11 (0.7)	46(2)	57 (1)

Compared to patients without NAAT, patients with NAAT were more likely

- Younger
- Hispanic
- Not Asian
- Sputum smear-positive

And to have:

- Cavities on chest radiograph
- Diabetes co-morbidity
- TB symptoms as the primary reason for TB evaluation

Did patients with NAAT start treatment earlier than those without NAAT?

Timing of diagnostic tests and treatment initiation



240 (15%) patients with NAAT vs.
320 (11%) patients without NAAT
started treatment presumptively
(at/before specimens were collected)
P-value=0.0019

Timing of diagnostic tests and treatment

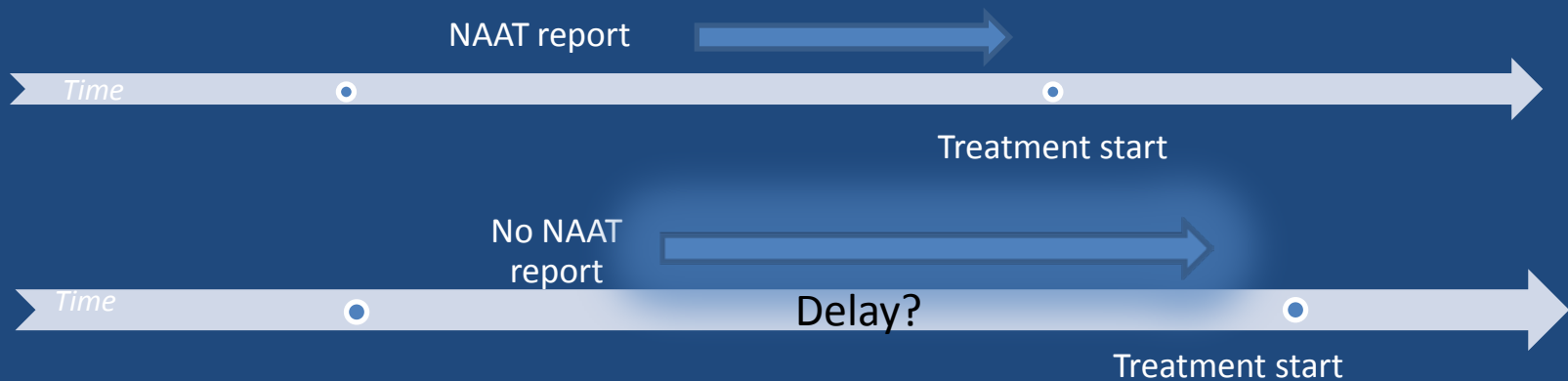


Smear-positive patients*
98% with NAAT started treatment before culture reported vs.
75% without NAAT

Smear-negative patients*
81% with NAAT started treatment before culture reported vs.
38% without NAAT

*excluding patients starting treatment at/before specimen collection
P-value <0.0001

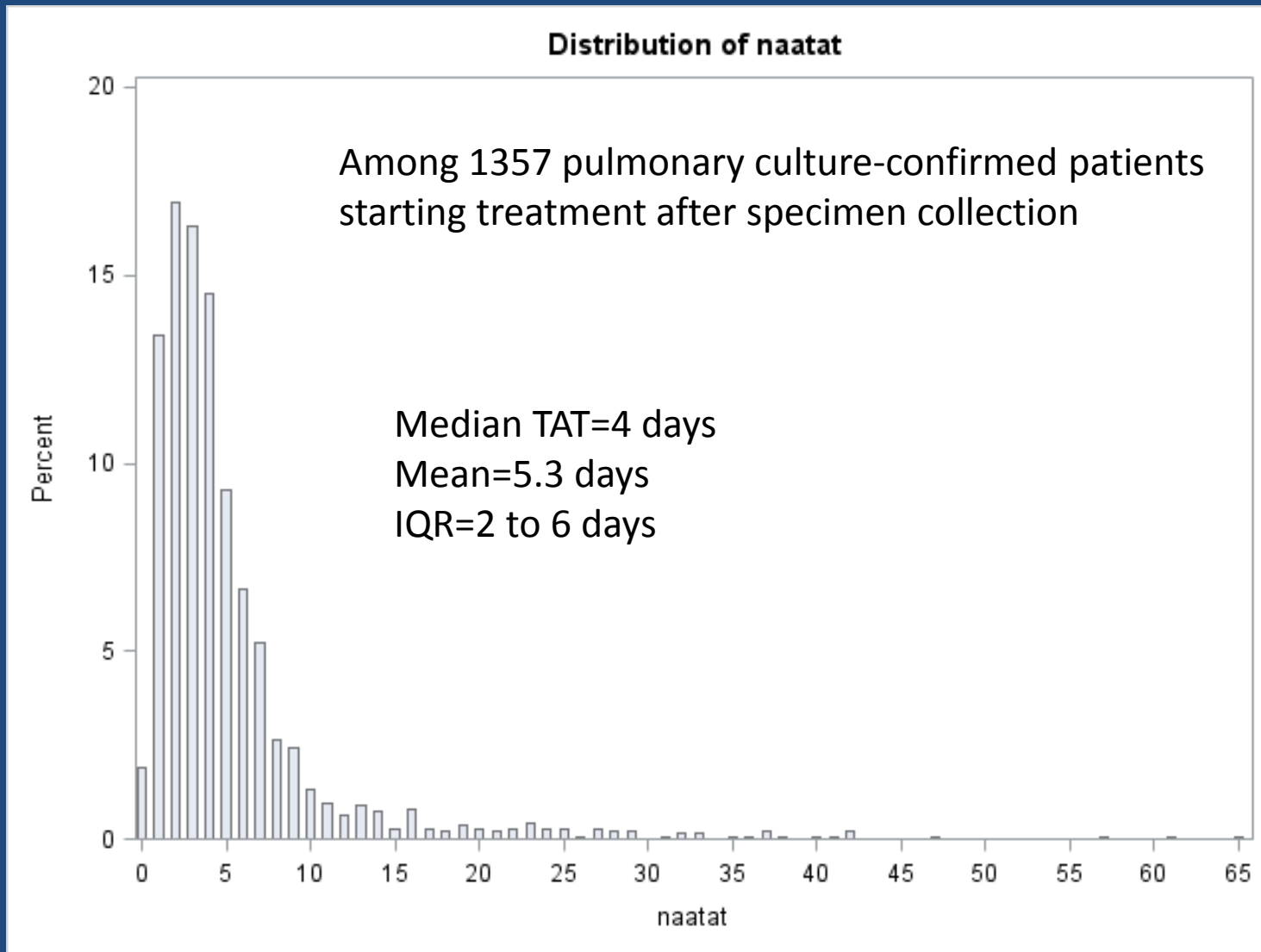
Did patients with NAAT start treatment earlier than those without NAAT?



Group	NAAT Median time* (N)	No NAAT Median time* (N)	P-value for Wilcoxon rank sums test
All *	3.0 (1357)	13.0 (2410)	<0.0001
Smear-positive*	2.0 (1224)	4.0 (1233)	<0.0001
Smear-negative*	14.0 (133)	25.0 (1177)	<0.0001

*Time (days) between date of earliest specimen collection and treatment initiation
Pulmonary culture-positive TB cases initiating treatment after specimen collection

How rapidly were NAATs reported?



Did NAAT turnaround time vary by laboratory type?

Laboratory	NAAT median TAT ¹	P-value ²
Public health	2 days	
Commercial	3 days	0.008
Other	2 days	0.05

¹NAAT turnaround time (working days between date of NAAT specimen collection and NAAT report, median)

²Wilcoxon rank-sum comparison of median NAAT TAT with NAAT TAT for public health lab

Did NAAT turnaround time vary by jurisdiction?

Health department	NAAT, N (% total pts with NAAT)	NAAT TAT median days excluding wkend
A	12 (0.7)	7.0
B	37 (2)	1.0
C	49 (3)	8.0
D	266 (16)	2.0
E	519 (32)	3.0

Varying NAAT TATs suggest that

Accessibility to NAAT varied by local health jurisdiction

For patients with NAAT, how did NAAT results inform treatment decisions?

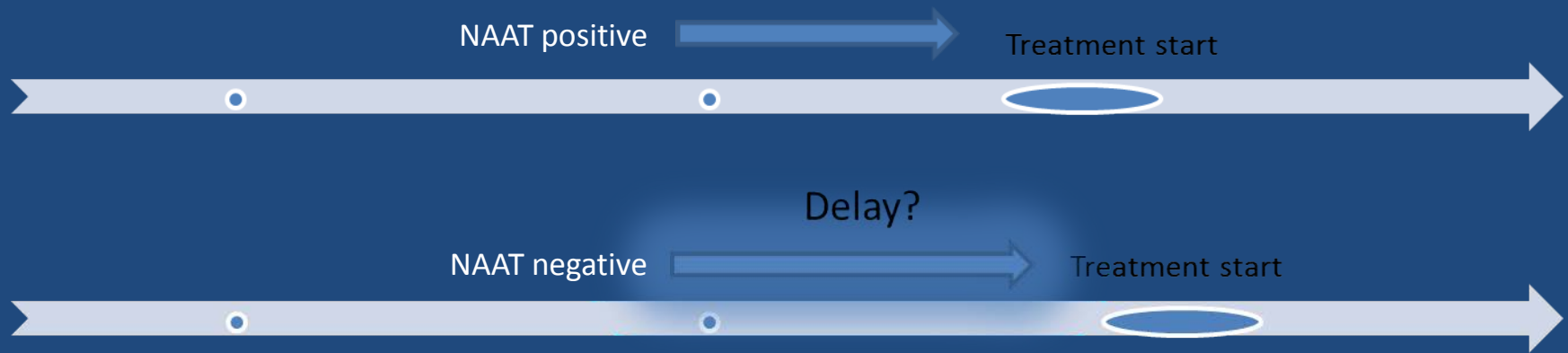
Population

- NAAT reported before culture
- treatment initiated after specimens collected
- treatment initiated after NAAT reported

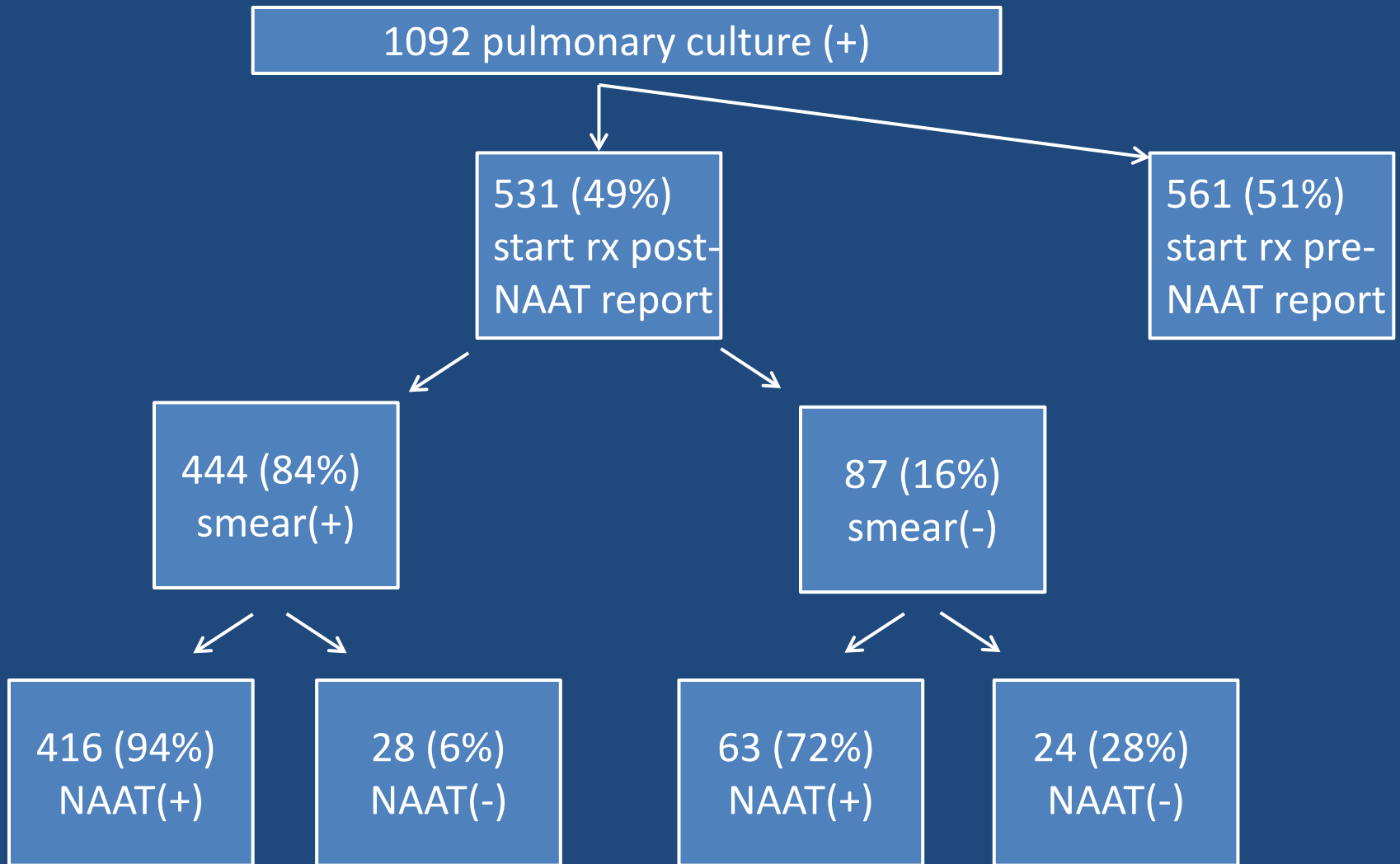
How many patients started treatment after NAAT report?

- Of 1092 pulmonary culture-confirmed TB cases starting treatment after NAAT specimen collected
 - 531 (49%) started treatment after NAAT report
 - 561 (51%) started treatment before NAAT report

Did NAAT results impact treatment initiation times?

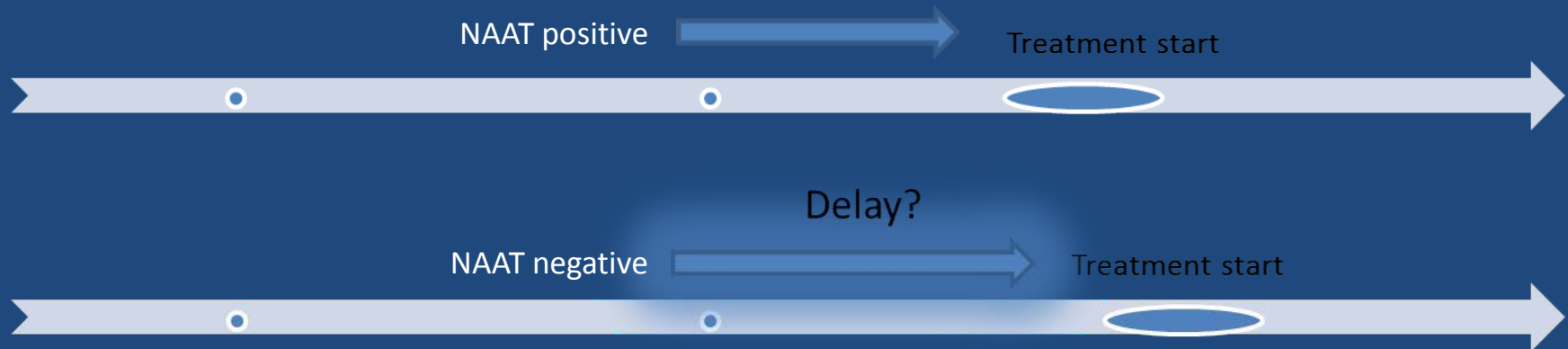


Timing of treatment and smear status NAAT-positives vs. NAAT-negatives



*starting treatment after specimens collected for NAAT

Did patients with positive NAATs start treatment earlier than those with negative NAATs?



Group	NAAT positive Median time *(N)	NAAT negative Median time* (N)	P-value for Wilcoxon rank sums test
All	1.0 (479)	8.0 (52)	<0.0001
Smear-positive	0.0 (416)	5.0 (28)	<0.0001
Smear-negative	2.0 (63)	15.0 (24)	0.0024

*Time (days) between date NAAT reported and treatment initiation
Pulmonary culture-positive TB cases initiating treatment after NAAT report

Limitations

- Chart review was not performed so not all factors contributing to treatment decision were known
- Type of NAAT was not collected so we could not assess the use of different NAATs

Conclusions

- 36% pulmonary culture (+) TB patients had NAAT used for diagnosis prior to culture
- NAATs reported at/after culture suggest additional training to improve reporting accuracy
- Patients with NAAT were more likely to have clinical indicators of TB than patients without
- Time to treatment initiation was shorter in patients with NAAT compared to patients without NAAT
- NAAT TAT varied by local health jurisdiction, suggesting differential access to NAAT
- Patients with positive NAATs started treatment earlier than those with negative NAATs

Next steps:

The California TB Control Branch is

- Implementing enhanced training on NAAT reporting
- Encouraging the use of NAAT for diagnosis of TB

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Extra slide

NAAT sensitivity in pulmonary culture-confirmed TB patients in CA 2010-2012

- Smear positives = 94% (95% CI=93-95)
- Smear negatives =70% (95% CI=63-77)