Getting the Most Out of Electronic Crossmatch: *Trade-offs that matter*

Shelley Chang, M.D./Ph.D.
Transfusion Medicine Fellow
David Geffen School of Medicine at UCLA

Objectives

- Historical evolution of crossmatch method from serologic approaches to the rise of the electronic crossmatch (EXM)
- Benefits, limitations, and specific requirements of EXM
- EXM experience at our institution: Approach to further improve efficiency without compromising turnaround time

History of the Crossmatch

- Serologic crossmatch ("Matching" Hektoen in 1907) [1,2,3]
  - Saline direct agglutination test (Ottenberg in 1908)
  - AHG (Coombs in 1945), complement, albumin & enzymes
  - Methods: tube, rapid slide, capillary tubes, microtiter plates, solid, gel
- Antiglobulin testing with surrogate RBC's (1950's) [1,2,3]
  - Type and screen (T&S) method (Boral and Henry in 1977)
- Abbreviated XM (used for MTP's in 1978): [1,2,3]
  - Permit omission of AHG phase of XM if AB screen at AHG is nonreactive (FDA in 1984)
  - Immediate spin (IS) was cost-effective [4]
  - Advocated T&S with IS for qualified patients (AABB Standards, 1987)

1. Butch SH, Oberman HA. Transfus Med Rev. 1997 Oct;11(4):256-64.
2. Arslan, Onder. Transfusion Medicine Reviews, Vol 20, No 1 (January), 2006: pp 75-59.
3. Sandler SG, Abedalthagafi MM. Immunohematology. 2009;25(4):147-51.
4. Shulman IA, Nelson JM, Kent DR, et al. JAMA 1985;254:93–5.

History of the Crossmatch

- Limitations of IS XM as final check for ABO compatibility
- Options for detection of ABO incompatibility[2,3]:
- "Test methods" (AABB *Standards*, 1987), "Serologic" (AABB *Standards*, 1989)
- Electronic crossmatch (EXM) as alternative to IS XM for patients with no present or previous clinically significant antibodies[1]
- Use of electronic data to detect ABO incompatibilities (AABB *Standards*, 1993) [4]
- Adopted in 10 facilities internationally [5]
- Slow adaptation: software compatibility across information systems
- Prevalence of EXM among laboratories surveyed by CAP [6]:
  2.5% (2005), 13% (2007), 16.5% (2010)

1. Butch SH, et al. Transfusion. 1994;34:105-109.
2. Butch SH, et al. Transfus Med Rev. 1997 Oct;11(4):256-64
3. Shulman IA, et al. Arch Pathol Lab Med. 1989 Mar;113(3):270-2.
4. Widmann, FK, ed. Technical manual. 15th ed. Bethesda, MD: AABB, 1993:25.
5. Judd, JW. Vox Sanguinis. 1998; 74 (Suppl. 2): 409-417.
6. Downes KA, Shulman IA. Arch Pathol Lab Med. 2012;136(3):294-300.

Comparison between IS XM and EXM

- **Serologic IS XM:**
  - Unintentionally detected activity
    - Polyagglutinable donor red cells
    - Anti-A1 in individual with A2 or A2B
    - Other alloAB at room temperature
    - Rouleaux
    - Autoantibodies (e.g. Anti-I) cold
    - Anti-A or anti-B passively acquired
  - No representative plasma in massive transfusions
  - Delays in issue during acute hemorrhages
  - Potential false negative:
    - Prozone phenomenon in strong AB titer
    - A2B donors and group B recipients
- **EXM:**
  - Validation
  - Requires zero tolerance for errors in misidentification, mislabeling, data entry, and software interpretation of screen results
  - May still miss antibodies to low frequency antigens and early forming antibodies
  - Validation, staff training, software compatibility with LIS
  - Reimbursement

Butch SH, et al. Transfus Med Rev. 1997 Oct;11(4):256-64.
Judd WJ, et al. Transfusion. 1988 Jul-Aug;28(4):334-8.

Requirements for Computer XM (EXM)

- **Laboratory Information Systems Criteria**
  1. Validated to dispense only ABO group/Rh type compatible red blood cells
  2. Notifies technologist ABO group/Rh type discrepancy is detected between donor unit and patient or if required information is missing.
  3. Stores the following information on a donor unit: Donor number, Component name, ABO group/Rh type, Confirmation of donor ABO group/Rh
  4. Stores the following information on a potential recipient: Two unique identifiers, ABO group/Rh type, Antibody screen results
  5. Method to verify correct entry of data prior to the release of blood
- **Recipient Requirements:**
  - ABO Group/Rh type confirmed on two occasions and agree
    - Second type: Retest same specimen, second separately drawn current sample, previous record at institution
  - No prior alloantibodies & negative antibody screen on current sample

Brooks JP, Fletcher CH. Transfusion. 2013 Feb;53(2):465-6.
Downes KA, Shulman IA. Pretransfusion testing. In: Fung MK, Grossman BJ, et al, eds. Technical Manual. 18th ed. Bethesda, MD: American Association of Blood Banks; 2014.

UCLA Check Type Policy

- A second independently drawn sample requested at T&S
  - Exempt: Historic type, Trauma (2nd BBID band), Outpatient (issued group O RBCs)
- 17 Years Check Type Experience at UCLA*
  - Review of ~400,000 T&S performed: 94 wrong blood in tube errors
  - 61 detected via type discrepancies
    - 40 detected via comparison with historic type
    - 21 detected via check type (7 incorrect initial TS; 14 incorrect 2nd specimen)
  - The 61 errors could have resulted in 27 ABO incompatible transfusions (1.6 transfusion/year) and 6 Rh incompatible transfusions (0.4 transfusion/year)
- Why Check Type?
  - **Pros:** Cost-effective (only ~$2.39 per checktype)
  - **Cons:** Potential inconvenience, delays, use of group O RBC units

UCLA Health System

* Figueroa et al. Am J Clin Pathol. 2006 Sep;126(3):1-5.

7

Electronic Crossmatch (EXM): The UCLA Experience

Impact of EXM on workload efficiency and turnaround time

UCLA Health System

8

Background

- An EXM policy was implemented in March 2013 in conjunction with a new hospital CPOE system
  - XM was performed at time of physician order and units were set aside for the patient
  - New CPOE resulted in increased duplicate orders
  - Many were never issued: ~30 units per day (840 units per month)

UCLA Health System

9

Unnecessary workload

- Given history of a robust check type policy since 1987 and EXM capabilities, we sought to further decrease inefficiencies and improve inventory management:
  - For patients who are eligible for EXM, orders are pended until actual issue requests were received. EXM and unit labeling is performed at time of issue request.
- However, it is unclear whether EXM performed at time of issue will impact the turnaround time as compared with EXM performed immediately at order.

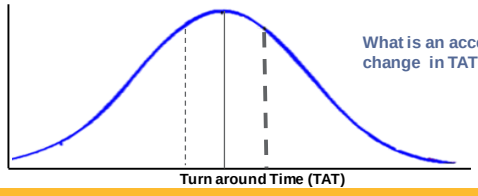
UCLA Health System

Turnaround Time (TAT)

UCLA quality metric:
Proportion of RBC units issued where TAT ≤ 12 min

Median ~12 min Actual
~15 min Clinically Acceptable

Median TAT operating room blood delivery is 14 min among fastest performing 10% hospitals*



What is an acceptable change in TAT?

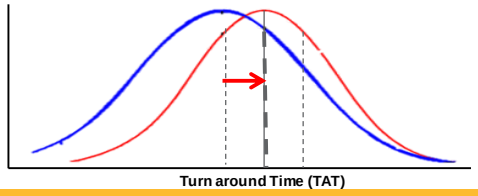
UCLA Health System

*Novis DA, Friedberg RC, Renner SW, et al. Operating room blood delivery turnaround time: a College of American Pathologists Q-Probes Study of 12,647 units of blood components in 466 institutions. Arch Pathol Lab Med 2002;126: 909-14.

Shift in TAT

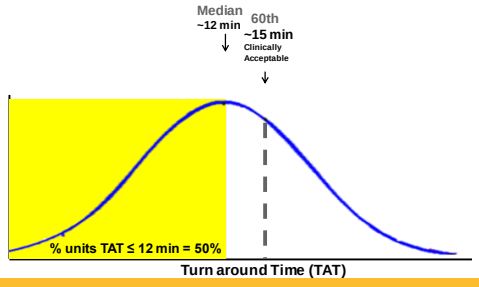
How does this impact our metric?

Median ~15 min Clinically Acceptable



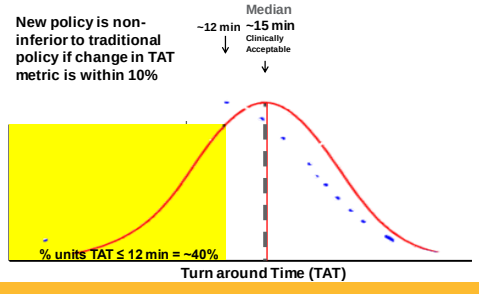
UCLA Health System

% units TAT ≤12 min



UCLA Health System

% units TAT ≤12 min



UCLA Health System

Impact of EXM at Issue Policy on TAT

- Assess whether the new EXM at issue policy is non-inferior to traditional EXM at order policy with regard to TAT
- 4 week before-and-after study design (Sept 2013)
- Proportion of EXM eligible RBC units issued at TAT ≤ 12 min*
  - Non-inferior margin of 10% compared with traditional XM at order policy
  - Excluded from TAT analysis: Massive transfusions & outpatient hematology-oncology clinics.
- Secondary outcomes:
  - Median TAT
  - Workload Efficiency: Crossmatch to issue (C:I) ratio
  - Formal complaints of delays in blood delivery

UCLA Health System

Improved Workload Efficiency

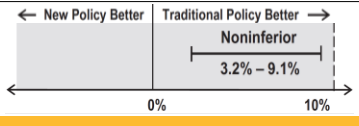
	Traditional Policy EXM at Order	New Policy EXM at Issue
Crossmatch (XM)	4389 units	3383 units
Issue	3523 units	3071 units
Unadjusted C:I ratio	1.25	1.10 *
Adjusted C:I ratio †	1.15	**1.00 ***

* Between-period differences in the C:I ratio, *P*<0.001
† C:I ratio adjusted for keep ahead units

UCLA Health System
Lin, D. M. et al (2014). Transfusion. PMID: 24863553

EXM Eligible RBC Units
% Issued in ≤ 12 min TAT

	Traditional Policy EXM at Order	New Policy EXM at Issue
Total No. Issued	2265 units	2223 units
% TAT ≤ 12 min	50%	43.9 %
Absolute Difference % [95% CI]	---	6.1% [3.2%-9.1%]



UCLA Health System
Lin, D. M. et al (2014). Transfusion. PMID: 24863553

EXM Eligible RBC Units
Median TAT (min)

Request Location	Traditional Policy EXM at Order	New Policy EXM at Issue	*P*
Inpatient	12 (IQR 7-24) N=1239	14 (IQR 9-25) N=1255	<0.001
Operating Room	13 (IQR 8-25) N=791	15 (IQR 9-29) N=722	0.004
Outpatient Hematology-Oncology	11 (IQR 7-25) N=192	11 (IQR 6-24) N=181	0.56
Emergency Department	18 (IQR 12-27) N=43	14 (IQR 10-23) N=65	0.18
Overall TAT	12 (IQR 7-25) N=2265	14 (IQR 9-26) N=2223	<0.001
Adjusted TAT†	13 (IQR 7-25) N=2073	14 (IQR 9-26) N=2042	<0.001

† Excludes outpatient heme-onc

UCLA Health System
Lin, D. M. et al (2014). Transfusion. PMID: 24863553

Impact of EXM at Issue Policy on Turnaround Time

- **Unissued XM'd units: ~10 RBC units/day (~300 units/month)**
- **Reduced XM workload by 10.5% [C:I ratio – 1:15 to 1:00]**
- **Non-inferior TAT**
- **No formal complaints**

UCLA Health System

Lin, D. M. et al (2014). Transfusion. PMID: 24863553

Follow-up Audit at 6-months Post-implementation

- Outcome: Proportion of EXM eligible RBC issued - TAT ≤ 12 min
- *Composite performance*: orders during period immediately post-implementation plus at 6 month audit
- Composite performance post-implementation was compared with traditional XM at order policy period
- Non-inferiority margin pre-specified at 10%

UCLA Health System

20

Follow-up Audit: Workload Efficiency

	Traditional XM	Post-EXM Immediate	Post-EXM Composite Immediate & 6 mo
Adjusted Crossmatch to Issue (C:I) ratio †	**1.15 ***	**1.00**	**1.02 ***

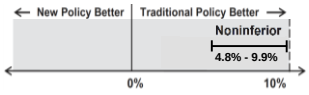
*Between-period differences in the C:I ratio, *P*<0.001
† C:I ratio adjusted for keep ahead units

UCLA Health System

D M Lin, et al. Abstract Presentations from the AABB Annual Meeting, Philadelphia, PA, October 25-28, 2014. Transfusion. 2014 Sep;54 Suppl 2:15A-268A. PMID: 25220542

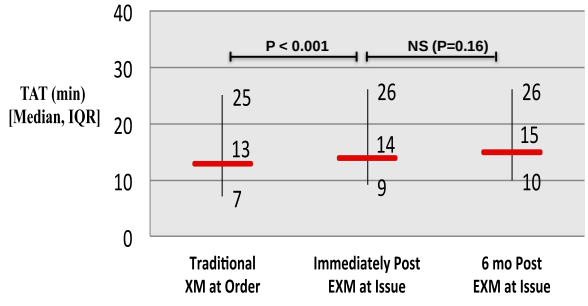
Follow-up Audit: % issued at ≤12 min TAT

	Traditional XM	EXM Policy Immediate	EXM Policy Composite Immediate & 6-mo
Total Orders	2265 units	2223 units	4402 units
% TAT ≤ 12 min	50%	43.9%	42.7%
Absolute Difference % [95% CI]	--Ref--	6.1% [3.2%-9.1%]	7.4% [4.8%-9.9%]



UCLA Health System D M Lin, et al. Abstract Presentations from the AABB Annual Meeting, Philadelphia, PA, October 25-28, 2014. Transfusion. 2014 Sep;54 Suppl 2:15A-268A. PMID: 25220542

Follow-up Audit: Median TAT (min)



UCLA Health System D M Lin, et al. Abstract Presentations from the AABB Annual Meeting, Philadelphia, PA, October 25-28, 2014. Transfusion. 2014 Sep;54 Suppl 2:15A-268A. PMID: 25220542

Summary: Endurance of EXM at Issue Policy at 6-months follow up

- ✓ EXM at issue policy showed sustained reduction in crossmatch workload efficiency
  - Significant reduction in C:I ratio from 1.15 to 1.02
- ✓ Proportion issued under 12 min TAT remains inside pre-specified 10% acceptable non-inferiority margin
- ✓ Median TAT increased by 2 min to 15 min and remains just above published benchmark of 14 min for the fastest performing 10% of hospitals in the US

UCLA Health System D M Lin, et al. Abstract Presentations from the AABB Annual Meeting, Philadelphia, PA, October 25-28, 2014. Transfusion. 2014 Sep;54 Suppl 2:15A-268A. PMID: 25220542

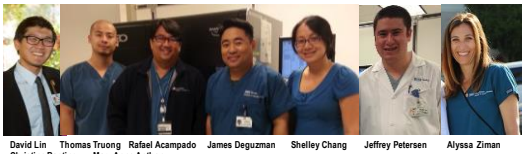
Our Experience with EXM

- Challenges:
  - Appropriate triage at time of order by technologists
  - Clear communication of expectations with clinicians
  - Shift in workflow from time of order (routine) to time of issue (STAT)
- Benefits:
  - Reduces technologist workload, specimen exposure, and specimen volume from patients
  - Reinforces the check type policy
  - Bypass inefficiencies associated with duplicate/excess XM orders
  - Improve inventory management
  - Eliminates serologic crossmatch and unnecessary discrepancy workups in patients with clinically insignificant antibodies (ie. Colds)

References

- Arslan O. Electronic crossmatching. Transfus Med Rev 2006;2D:75-9.
- Blackwelder WC. "Proving the null hypothesis" in clinical trials. Control Clin Trials 1982;3:345-53.
- Butch SH, Judd WJ, Steiner EA, et al. Electronic verification of donor-recipient compatibility: the computer crossmatch. Transfusion 1994;34:105-9.
- Brooks JP, Fletcher CH. ABO checking should be performed in the same institution as computer crossmatch. Transfusion. 2013 Feb;53(2):465-6.
- Butch SH, Oberman HA. The computer or electronic crossmatch. Transfus Med Rev. 1997 Oct;11(4):256-64.
- D' Agostino RBD, Massaro JM, Sullivan LM. Non-inferiority trials: design concepts and issues—the encounters of academic consultants in statistics. Stat Med 2003;22:169-86.
- Downes KA, Shulman IA. Pretransfusion testing practices in North America, 2005-2010: an analysis of the College of American Pathologists Interlaboratory Comparison Program J-survey data, 2005-2010. Arch Pathol Lab Med. 2012;136(3):294-300.
- Downes KA, Shulman IA. Pretransfusion testing. In: Fung MK, Grossman BJ, et al, eds. Technical Manual. 18th ed. Bethesda, MD: American Association of Blood Banks; 2014.
- Figueroa PI, Ziman A, Wheeler C, Gornbein J, Monson M, Calhoun L. Nearly two decades using the check-type to prevent ABO incompatible transfusions: one institution's experience. Am J Clin Pathol. 2006 Sep;126(3):422-6.
- Henaff AL, Giraudeau B, Baron G, et al. Quality of reporting of noninferiority and equivalence randomized trials. JAMA 2006;295:1147-51.
- Judd WJ, Steiner EA, O'Donnell DB, Oberman HA. Discrepancies in reverse ABO typing due to prozone. How safe is the immediate-spin crossmatch? Transfusion. 1988 Jul-Aug;28(4):334-8.
- Lin, D. M., et al. (2014), Measuring trade-offs that matter: assessing the impact of a new electronic cross-match policy on the turnaround time and the cross-match workload efficiency. Transfusion. doi: 10.1111/trf.12725
- Mazepa MA, et al. Pathology consultation on electronic crossmatch. Am J Clin Pathol. 2014 May;141(5):618-24.
- Novis DA, Friedberg RC, Renner SW, Meier FA, Walsh MK. Operating room blood delivery turnaround time: a College of American Pathologists Q-Probes Study of 12,647 units of blood components in 466 institutions. Arch Pathol Lab Med 2002;126:909-914.
- Sandler SG, Abedalthagafi MM. Historic milestones in the evolution of the crossmatch. Immunohematology. 2009;25(4):147-51.
- Shulman IA, Nelson JM, Kent DR, et al. Experience with a cost-effective crossmatch protocol. JAMA 1985;254:93–5.
- Shulman IA, Kent D. Safety in transfusion practice. Is it safe to eliminate the major crossmatch for selected patients? Arch Pathol Lab Med. 1989 Mar;113(3):270-2.
- Widmann, FK, ed. Technical manual. 15th ed. Bethesda, MD: AABB, 1993:25.

Acknowledgements



David Lin Thomas Truong Rafael Acampado James Deguzman Shelley Chang Jeffrey Petersen Alyssa Ziman
Christine Banting Mary Anne Anthony

Special Thanks:

•**Transfusion Medicine Service Staff, Supervisors, and Specialists:** Bethany Porter, Amy Fang, Bridget Wallace, Rebecca Jeffery, Shih-Mao Teng, Marvic Visico

•**Medical Directors:** Dr. Dawn Ward, Dr. Dennis Goldfinger, and Dr. Alyssa Ziman