pshp ANNUAL ASSEMBLY

BRIDGING THE FUTURE OF PHARMACY 2022

PITTSBURGH, PA | NOVEMBER 2-5, 2022

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What the SHELD: Introduction and Implementation of Pre-exposure Prophylaxis with COVID-19 Monoclonal Antibody for Solid Organ Transplant Recipients

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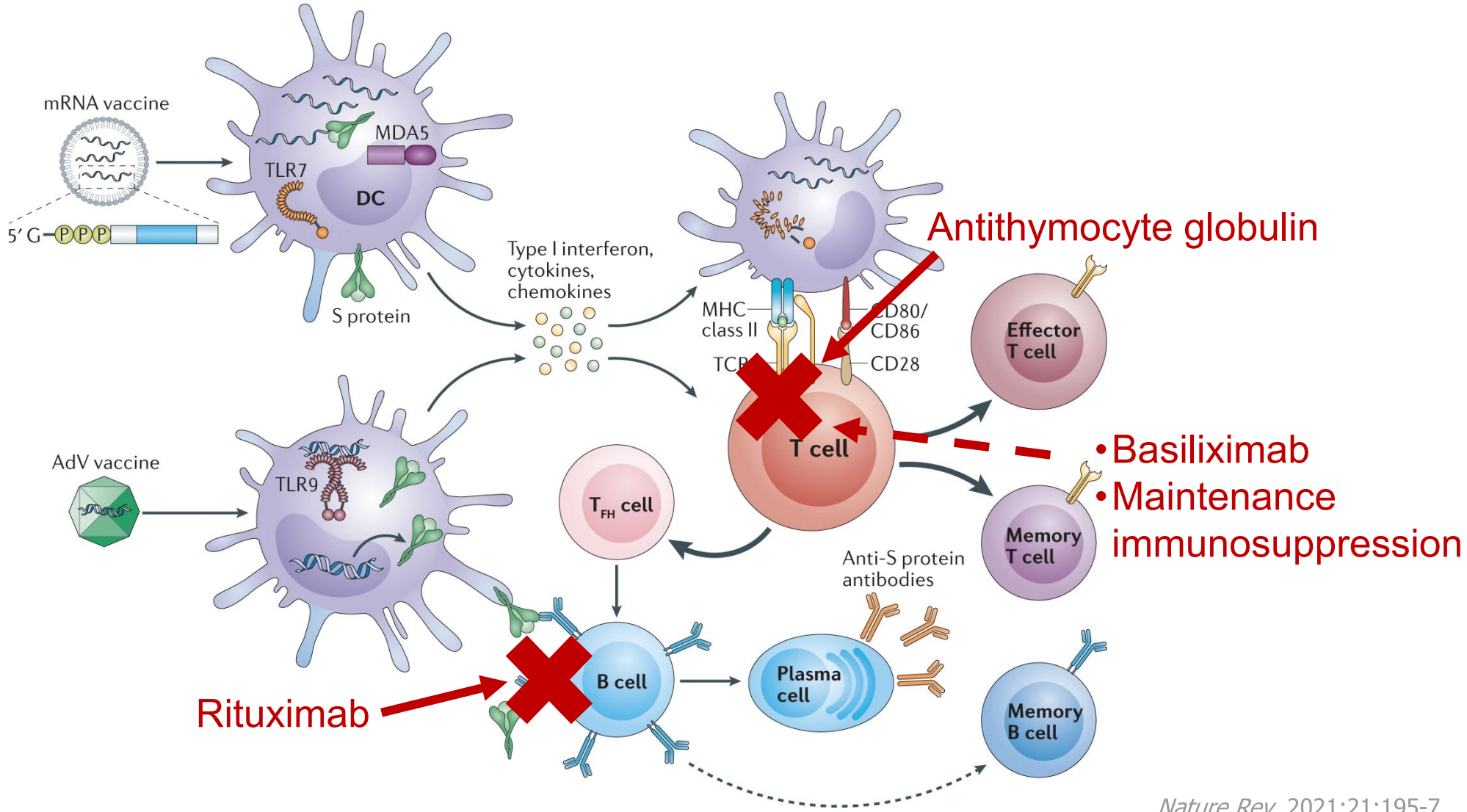
AHN

Objectives

- Explain diminished vaccine response in solid organ transplant recipients and role for pre-exposure prophylactic monoclonal antibody as protection against severe COVID-19
- Describe prioritization of highest risk patients upon initial availability of a new agent under Emergency Use Authorization (EUA)
- Discuss logistics for implementation of a new medication with Emergency Use Authorization (EUA) into hospital and clinic workflow, including administration, monitoring, and safety

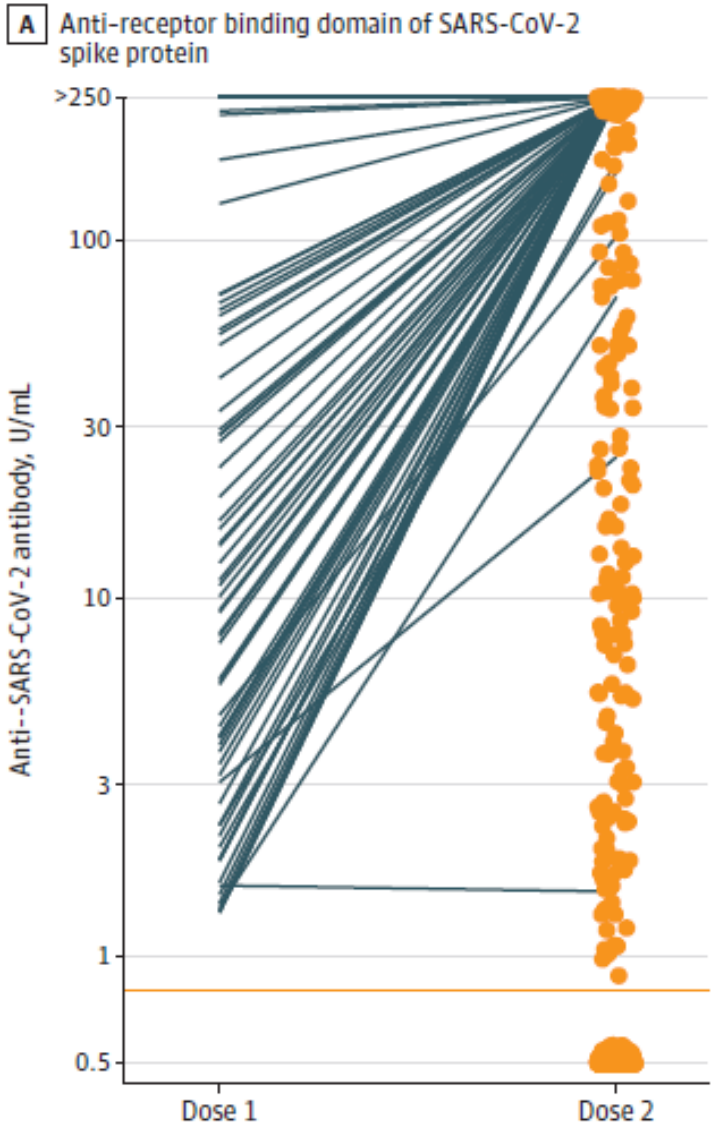
Vaccine Mechanism of Action (& immunosuppression impact)



Nature Rev. 2021;21:195-7.

COVID-19 Vaccine in SOT (antibody response)

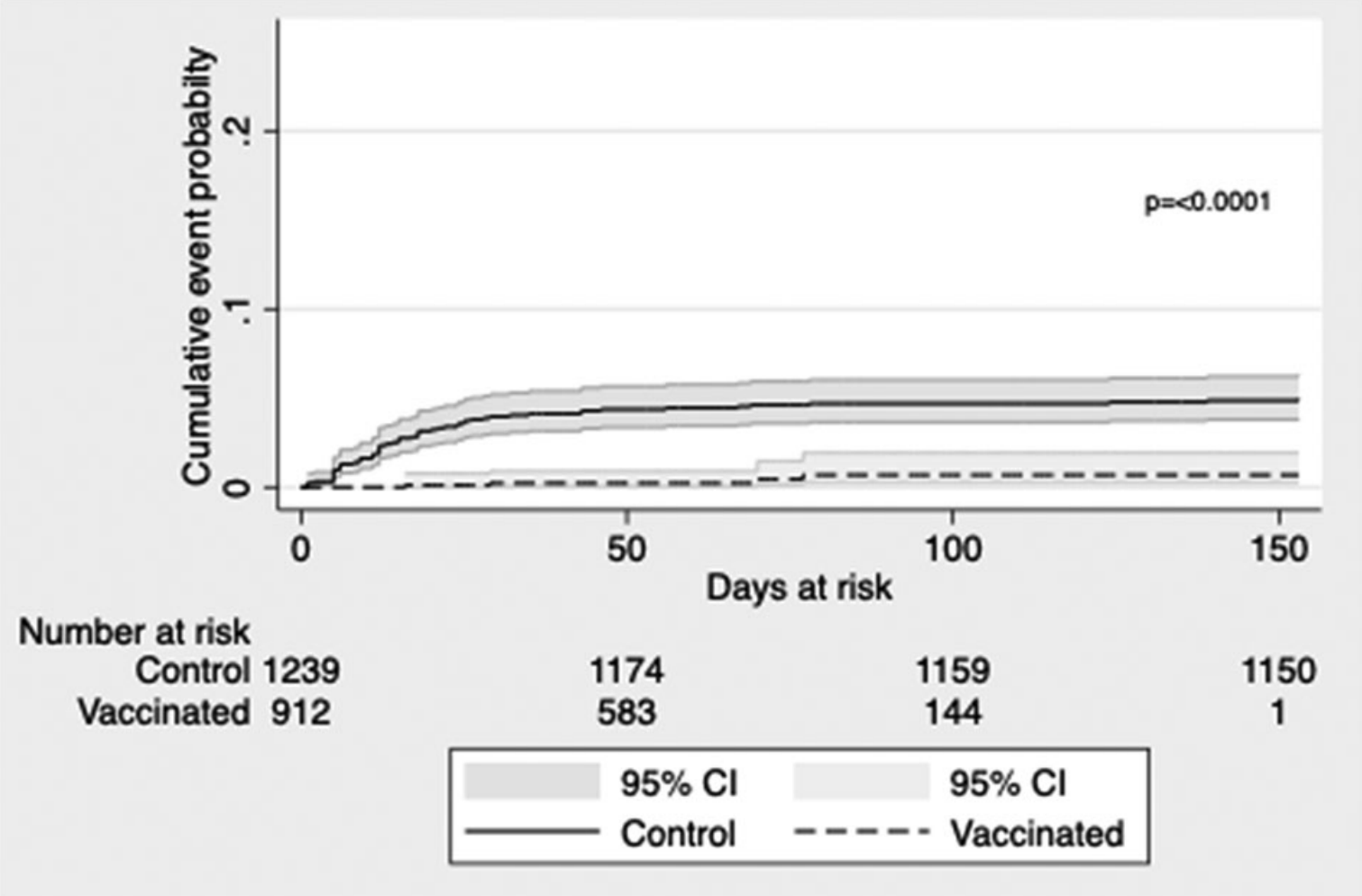
- n=658
- Antibody detected:
  - Dose 1: 15%
  - Dose 2: 54%



SOT = solid organ transplant

JAMA. 2021. DOI:10/1001/jama.2021.7489

COVID-19 Vaccine in SOT (clinical impact)



SOT = solid organ transplant

Transplant Infect Dis. 2021;23:e13705.

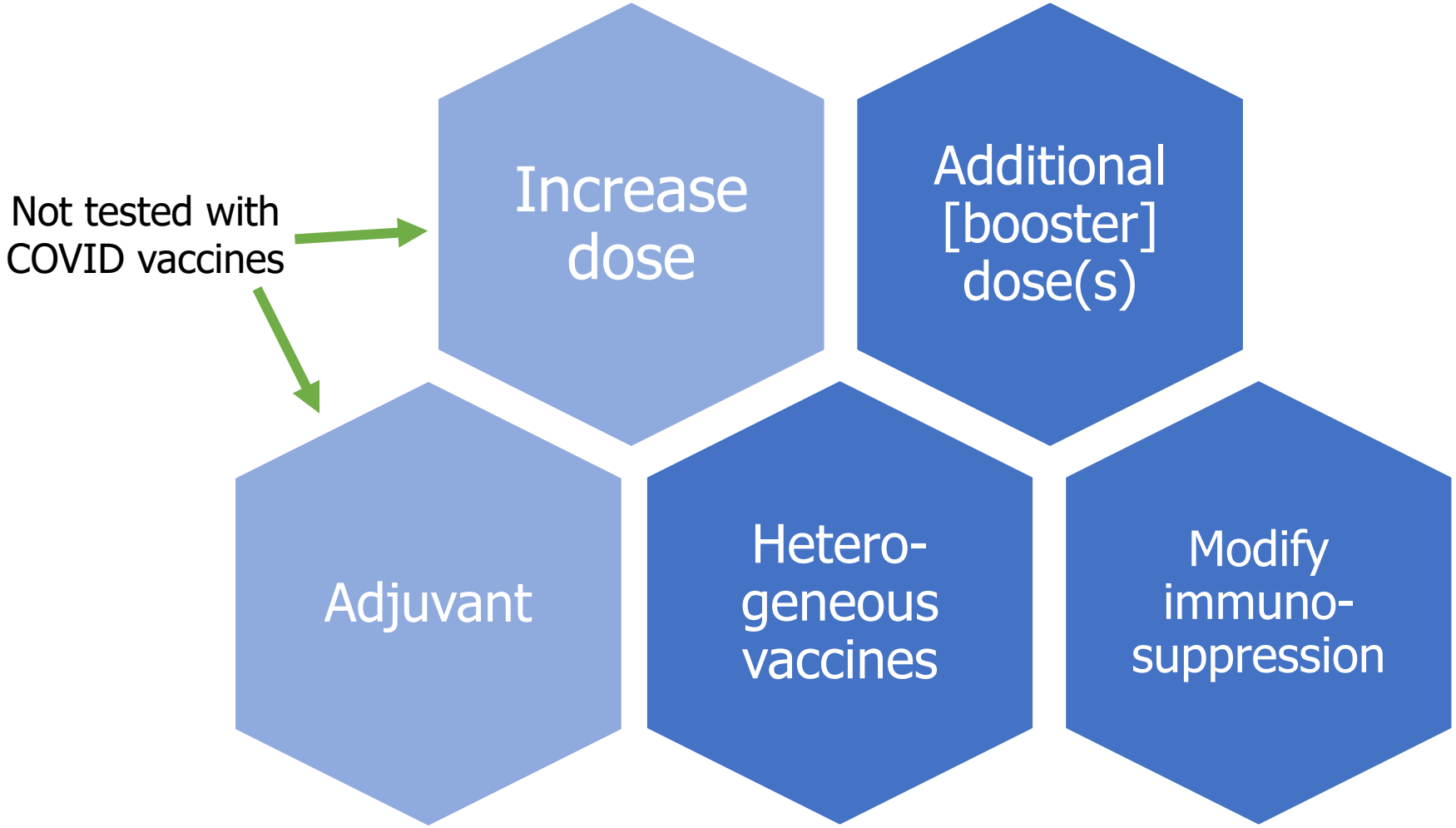
COVID-19 SOT Breakthrough Infections

	SOT (n=18,215)	**General population** (n=101 million)
Breakthrough infections	0.83%	0.0102%
Hospitalization	0.48%	0.00099%
Death	0.077%	0.00016%

SOT = solid organ transplant

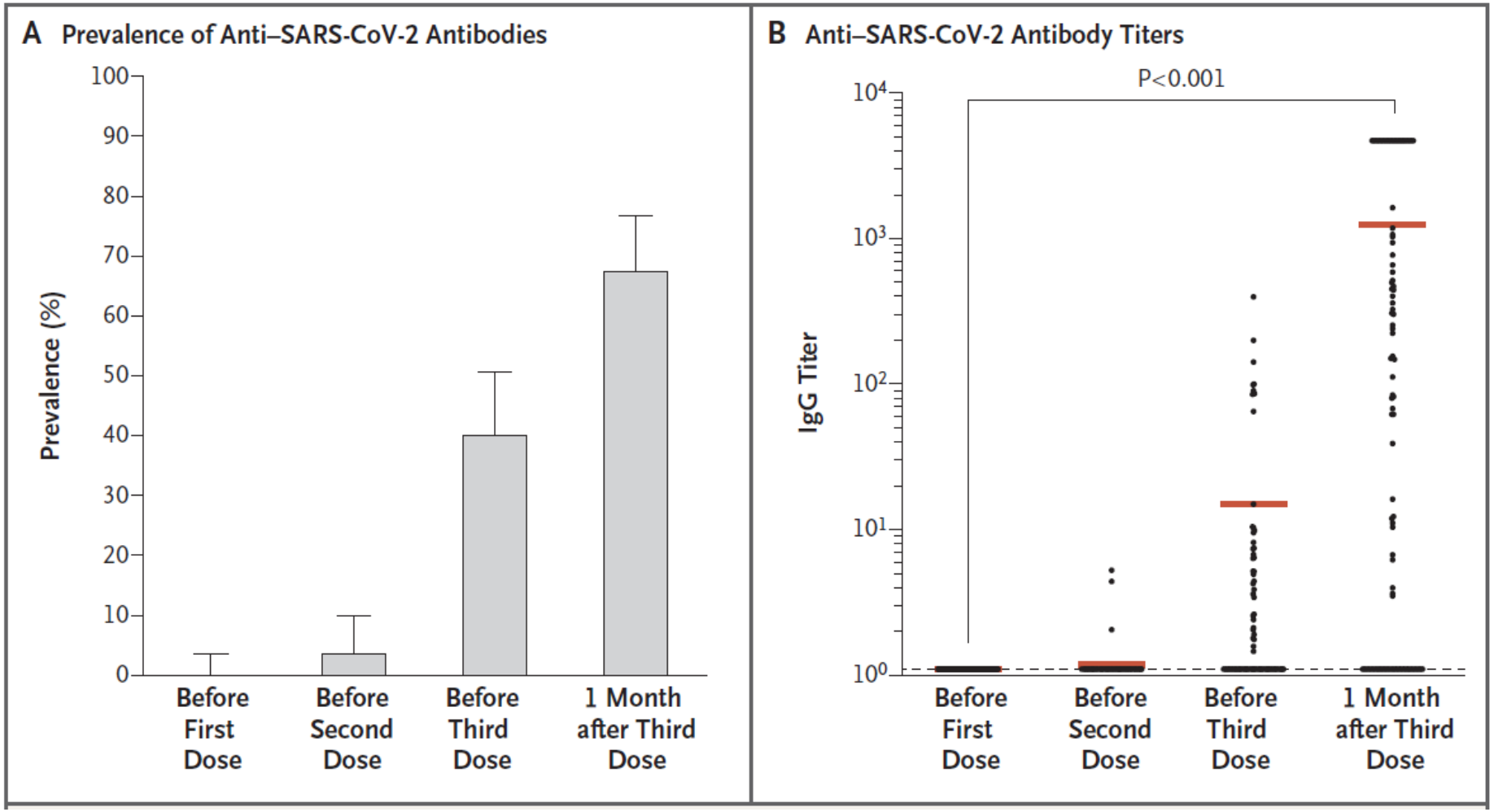
Transplantation. 2021;105(11):e265-6.

Strategies to Improve Vaccine Efficacy



Curr Opin Infect Dis. 2018;31:309-15.

COVID-19 Vaccine 3 doses in SOT

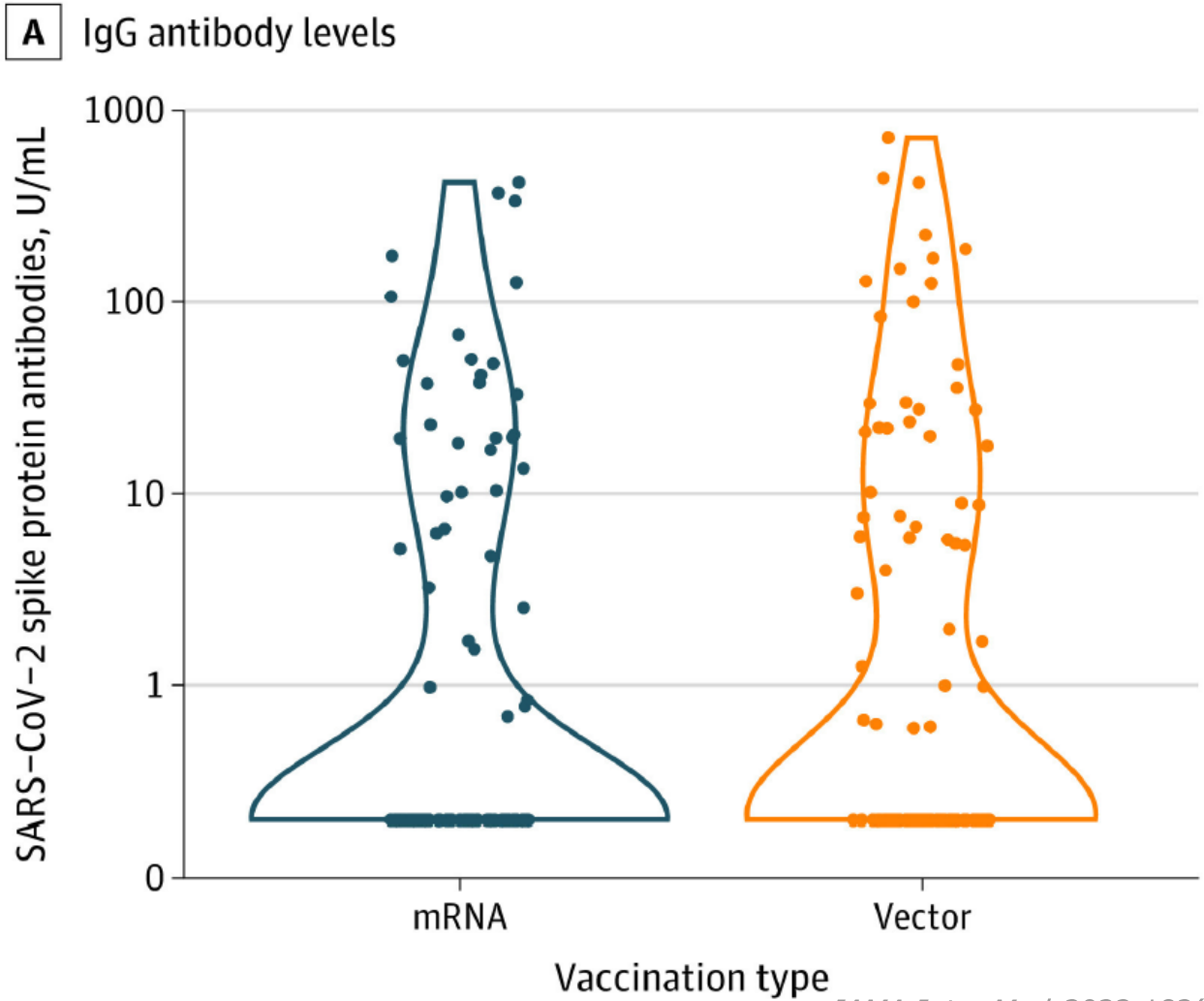


SOT = solid organ transplant

NEJM. June 2021;DOI:10.1056.

Heterogeneous Vaccines

- n=197, kidney transplant
- No antibody response to initial vaccine series (mRNA)
- After dose 3 (p=0.38):
  - mRNA: 35%
  - Adenovirus vector: 42%



JAMA Inter Med. 2022;182(2):1-8

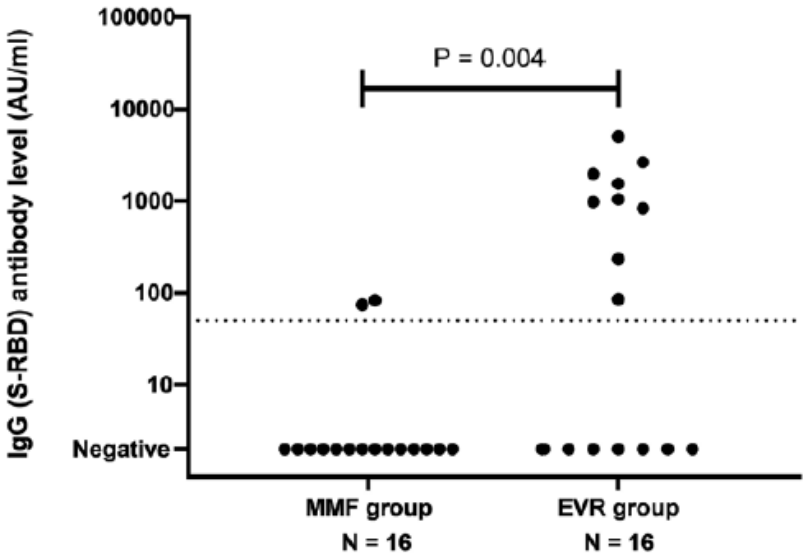
Modify Immunosuppression

	No. (%) by postvaccination antibody response			
	Dose 1− Dose 2−	Dose 1− Dose 2+	Dose 1+ Dose 2+	*P* value
No.	301 (46)	259 (39)	98 (15)	
Maintenance immunosuppression regimen				
Includes antimetabolite[h]	268 (57)	167 (35)	38 (8)	<.001[d]
Does not include antimetabolite[i]	33 (18)	92 (50)	60 (32)	

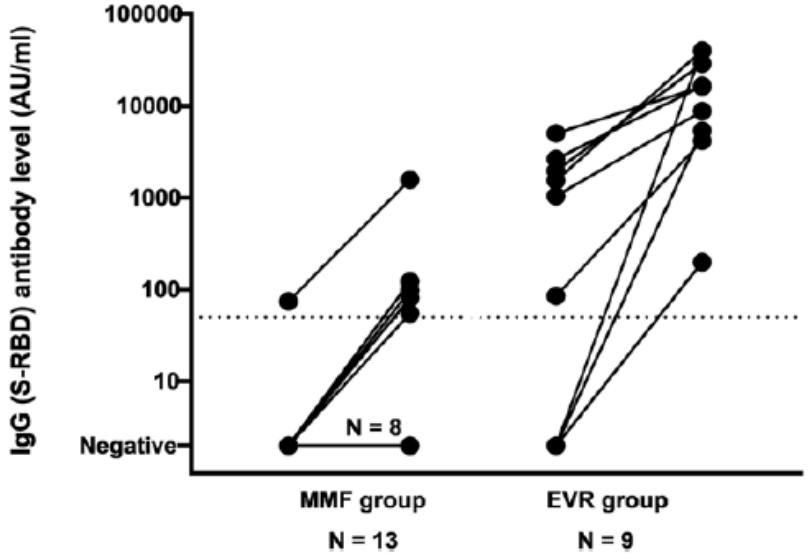
- Less response if on antimetabolite

- Greater antibody response with everolimus vs mycophenolate
  (kidney transplant, ≥65 yo)
  - 100% vs 38% after 3 doses

After 2 doses

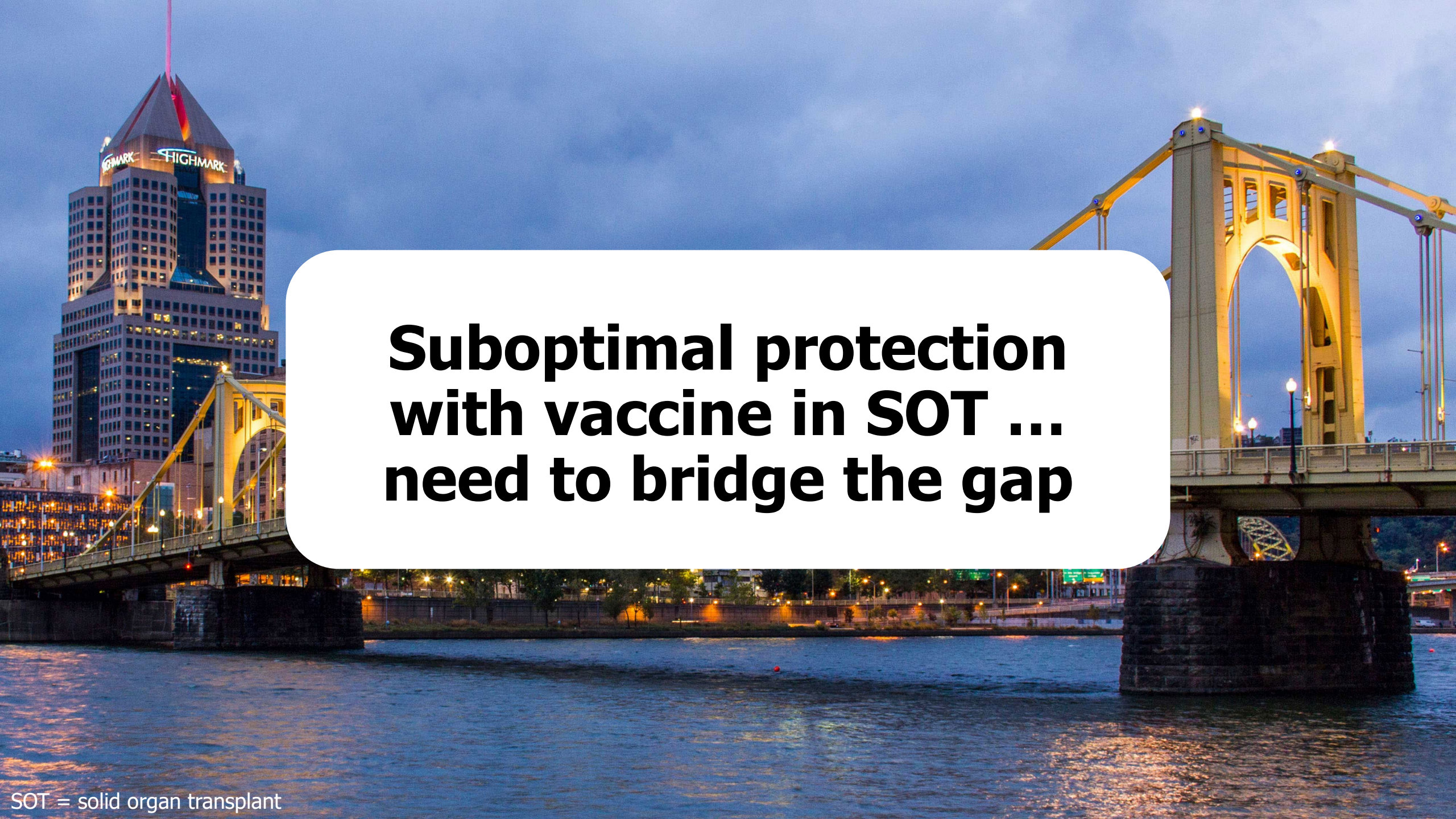


After 3 doses



SOT = solid organ transplant
yo = years old

JAMA. 2021. DOI:10/1001/jama.2021.7489
Transplantation. 2022;106:1615-21.



Suboptimal protection with vaccine in SOT … need to bridge the gap

SOT = solid organ transplant

Tixagevimab-Cilgavimab (Evusheld™)

- Long-acting monoclonal antibodies vs COVID-19
- FDA EUA December 2021
  - **Immunocompromised**
  - Unable to receive vaccine (i.e. anaphylaxis)
- Initially 150 mg (1.5 mL) per antibody per dose
  - Later updated to 300 mg (3 mL), 2 vials
- IM injections in 2 sites (preferably gluteal muscles)
- Patient to be monitored for 1 hour following
- Protection for ~6 months

FDA = Food and Drug Administration
EUA = emergency use authorization
IM = intramuscular

EVUSHELD™ [package insert]. AstraZeneca 2022

Tixagevimab-Cilgavimab for Prevention

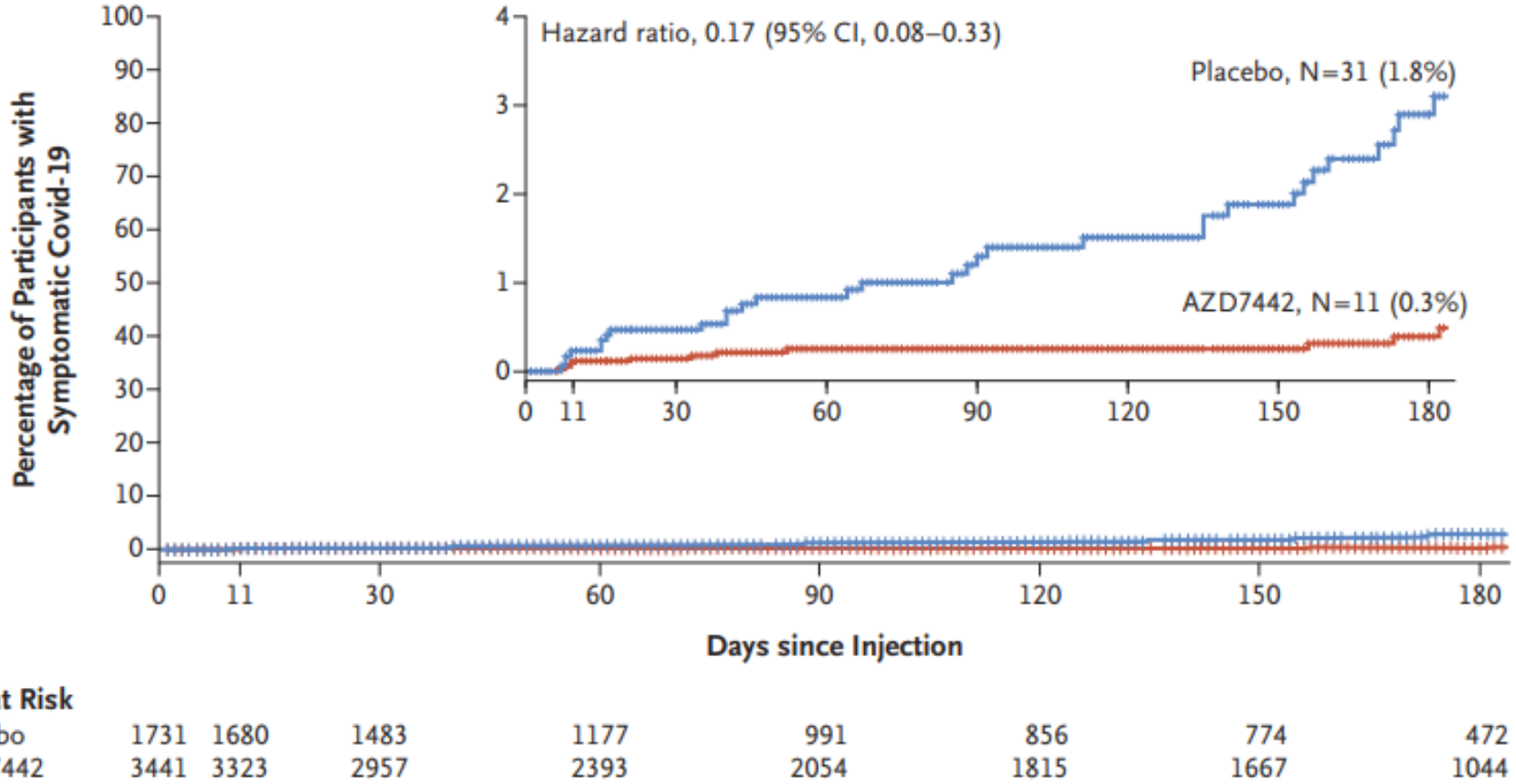
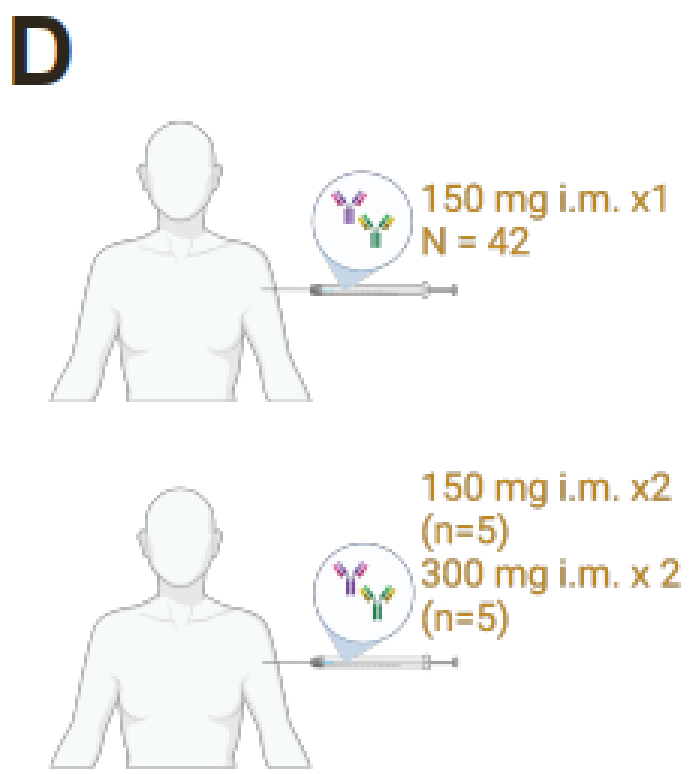
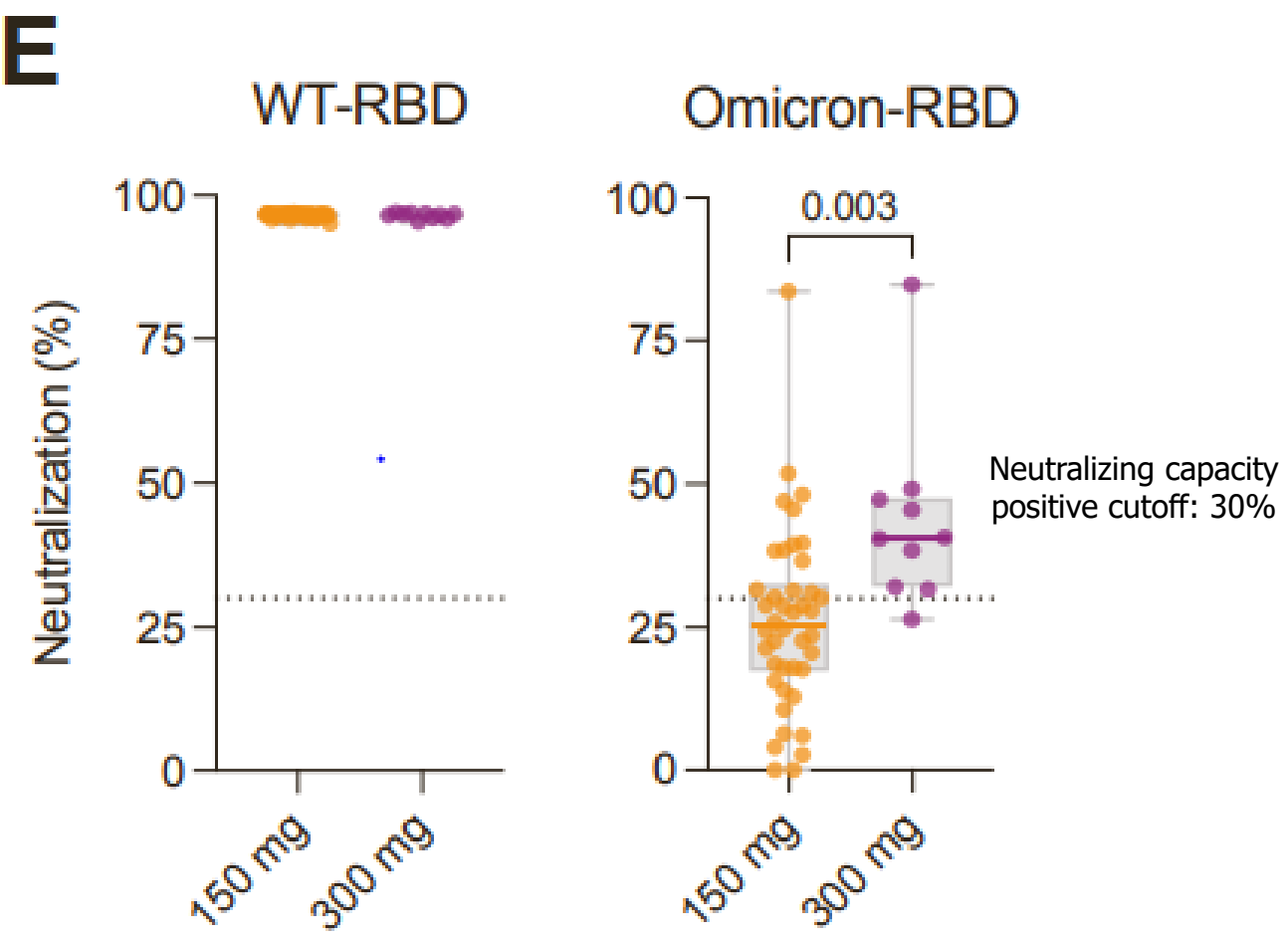


Figure 2. Time to First SARS-CoV-2 RT-PCR–Positive Symptomatic Illness.

NEJM. 2022;386(23):2188-2200.

Tixagevimab-Cilgavimab vs Omicron

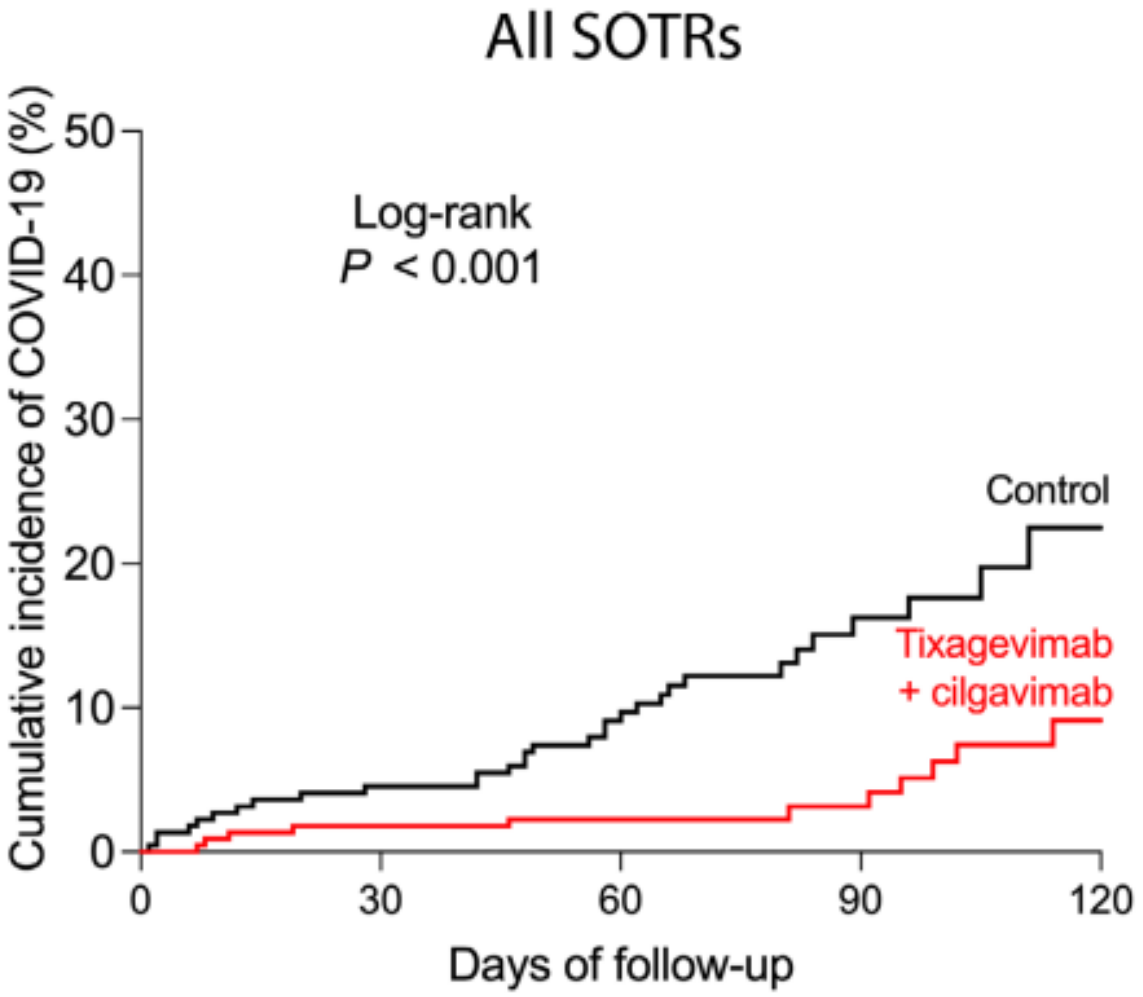




WT = wild type
RBD = receptor binding domain

Cancer Cell. 2022;40:590-1.

Tixagevimab-Cilgavimab in SOT



SOT = solid organ transplant
SOTR = solid organ transplant recipient

AJT. 2022;Online ahead of print.

Tixagevimab-Cilgavimab Criteria

SOT = solid organ transplant

CDC Recommendation, 2022

- Adults and adolescents (aged ≥12 years and weighing ≥40 kg) who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, AND who:
  - Are **moderately to severely immunocompromised** and may have an inadequate immune response to COVID-19 vaccination;

  OR
  - Are not able to be fully vaccinated with any available COVID-19 vaccines due to a history of severe adverse reactions to a COVID-19 vaccine or any of its components.

https://www.covid19treatmentguidelines.nih.gov

EUA Limitations

- NOT for treatment of COVID-19, or post-exposure prophylaxis of COVID-19
- NOT a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.
  - Individuals for whom COVID-19 vaccination is recommended, including individuals with moderate to severe immune compromise who may derive benefit from COVID-19 vaccination, should receive COVID-19 vaccination.
- Must be administered at least two weeks after COVID-19 vaccination

EVUSHELD™ [EUA]. AstraZeneca 2022

Immunocompromised defined by EUA

- Active treatment for solid tumor and hematologic malignancies
- SOT + immunosuppression
- CAR T-cell or HSTC (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (people with HIV and CD4 cell counts <200/mm^3, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
- Active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)

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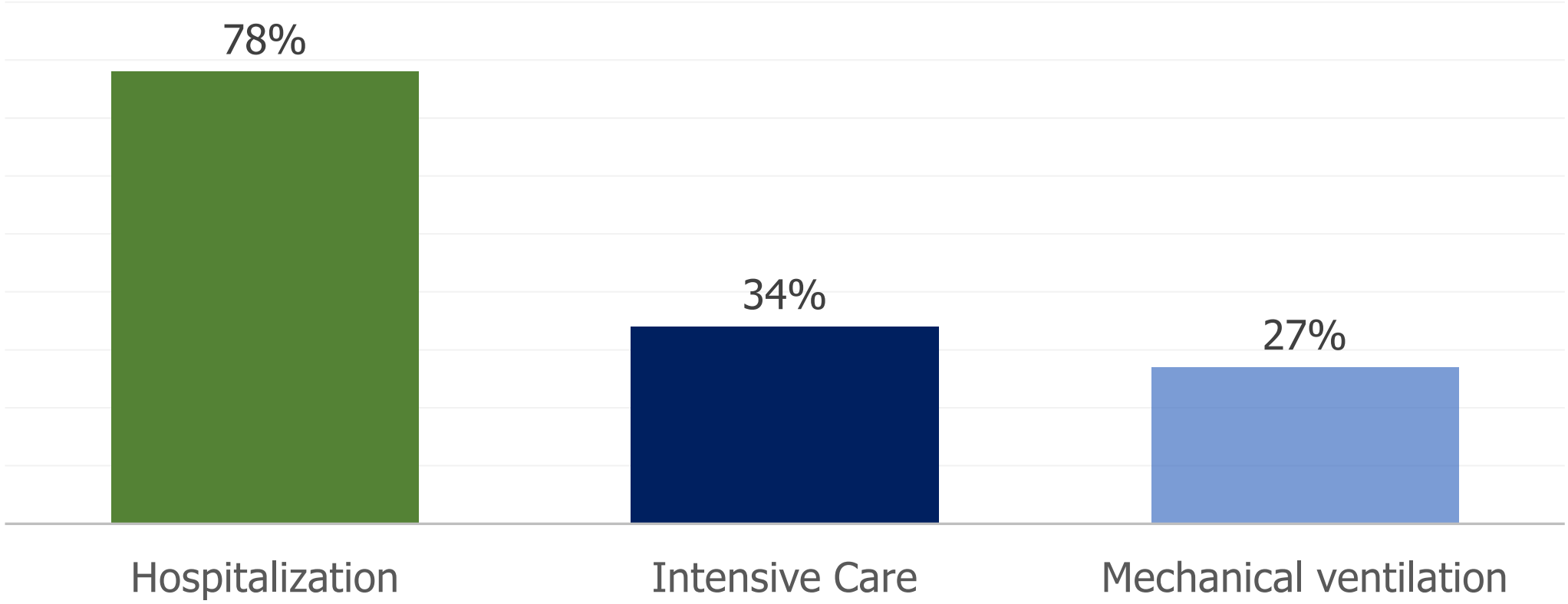
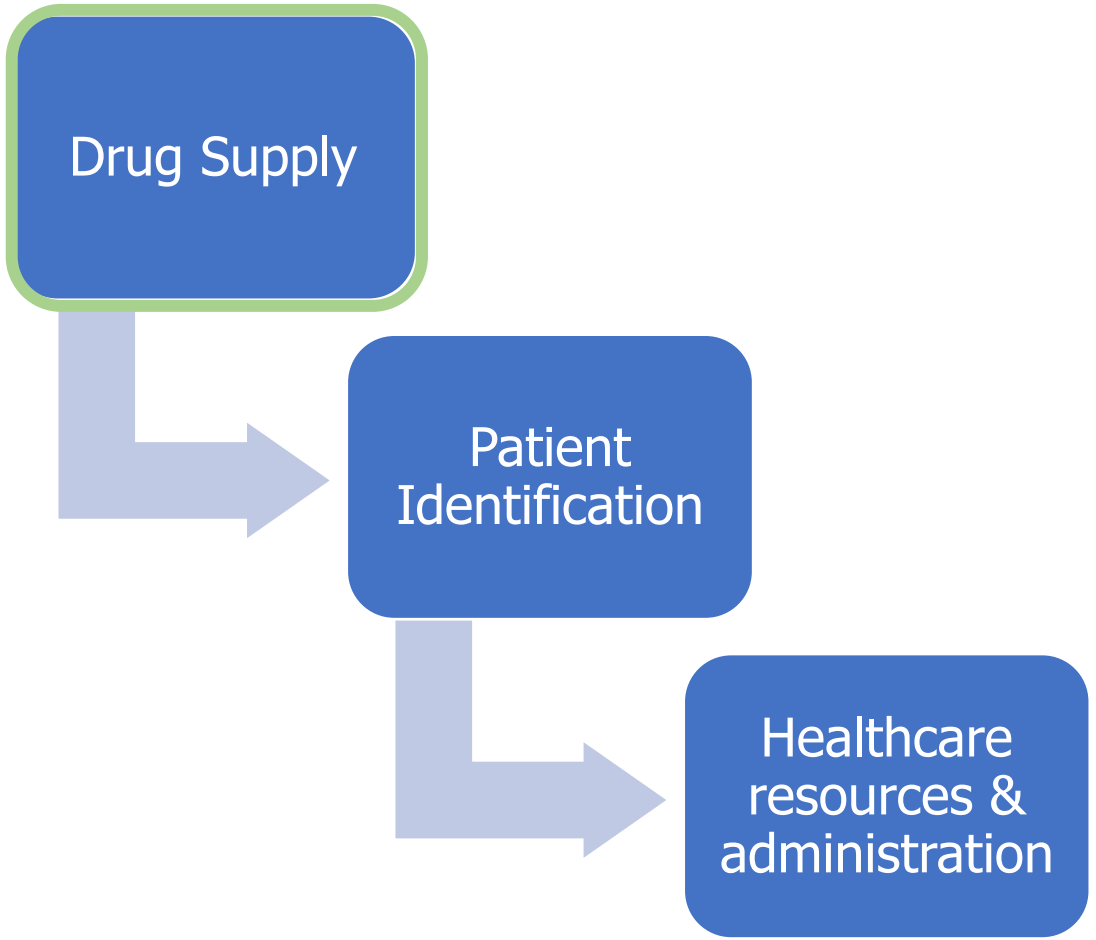
COVID-19 Outcomes in 482 SOTRs from >50 transplant centers (March 1, 2020-April 15, 2020)



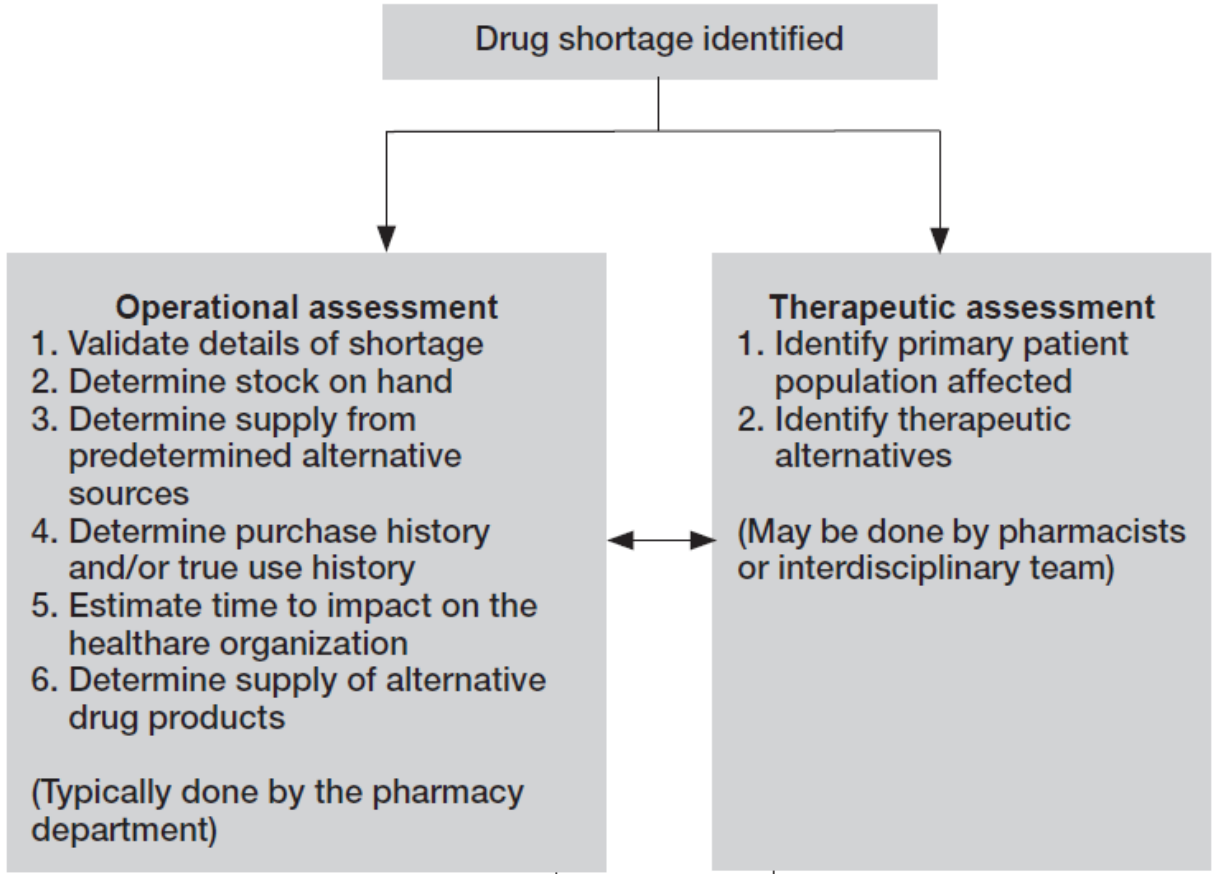
Clin Infect Dis 2021;73(6):e1397–401.

Planning for Distribution



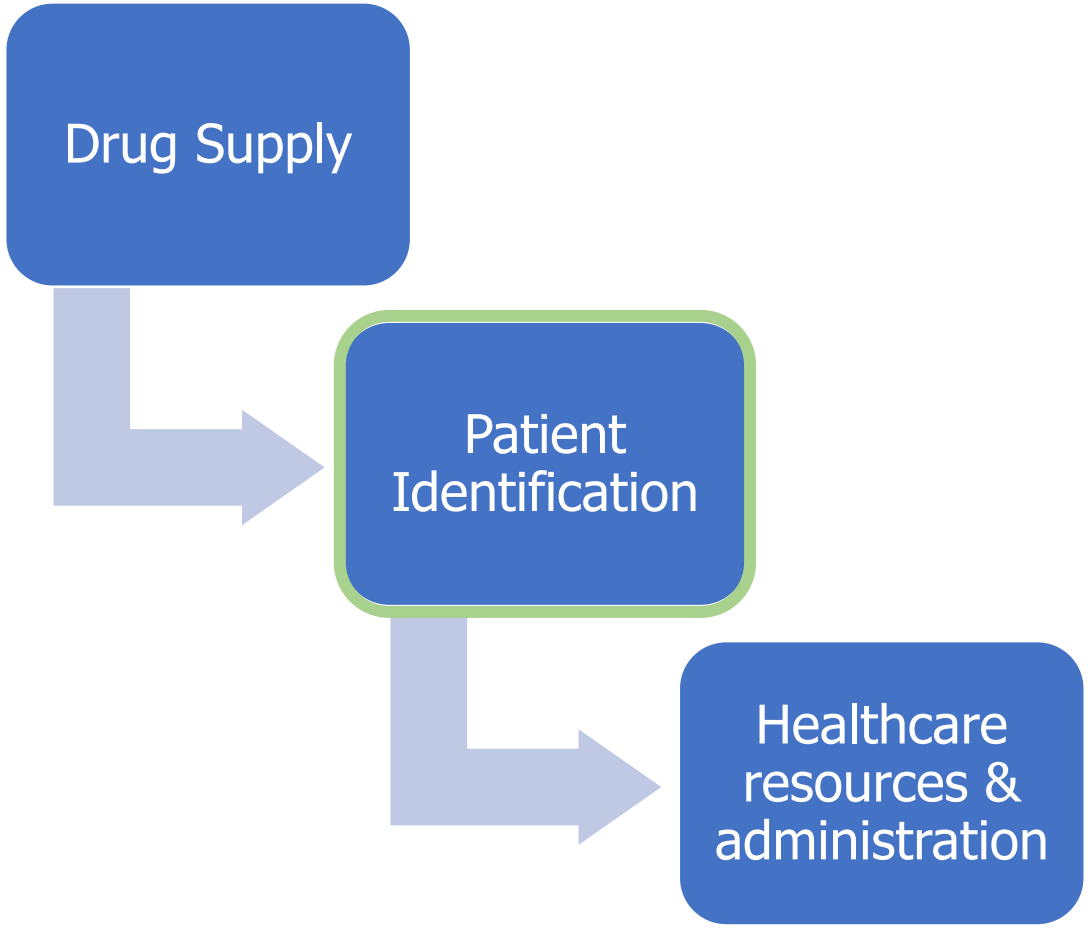
Limited Resource Distribution

Figure 1. Process for decision-making in the management of drug product shortages.



ASHP guidelines for drug distribution and control.

Planning for Distribution



Therapeutic Assessment of Risk

- Patient population groups:
  - Congenital or Acquired Immunodeficiency
  - Hematologic Malignancies
  - Solid Tumors
  - Solid Organ Transplant
- Risk categories for implementation

Category 1	Category 2	Category 3	Category 4
Highest risk immunocompromised patients→ Lowest risk immunocompromised patients			
Treat within the first month of tix/cil availability	Treat within first 3 months of availability	Treat within first 6 months of availability	EUA eligible, but initially deprioritized for higher risk pts

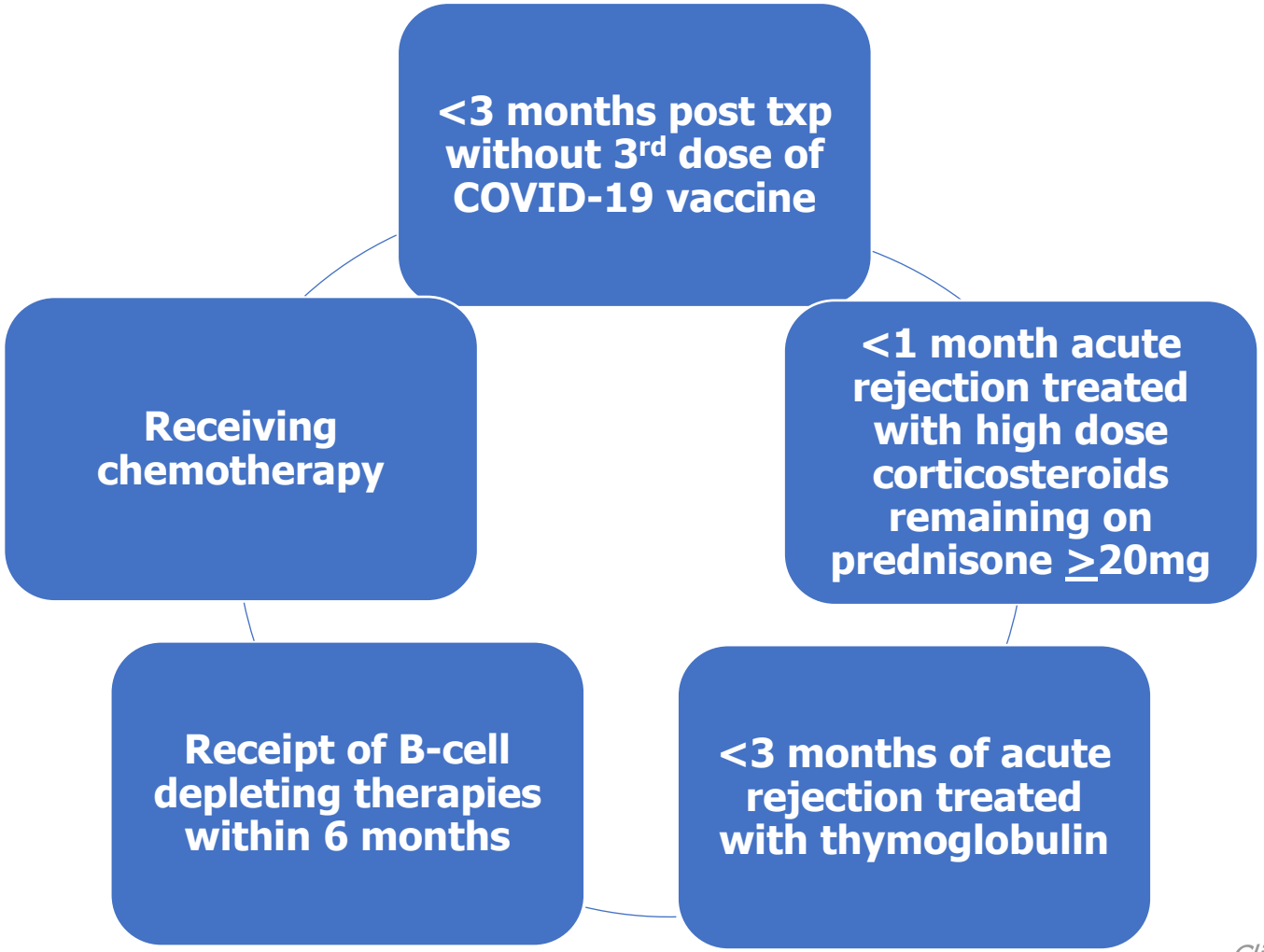
Nebraska Medicine. Evusheld™ Patient Prioritization Matrix

Single Center COVID-19 outcomes in SOTRs by organ transplant type

	Kidney	Liver	Other
Sample size (N)	40	17	9
Average age (years)	53.6	57.2	55.2
Sex (% male)	75	52.9	66.7
Median LOS (days)	6	9.5	6
Readmissions (%)	22.5	11.8	66.7
Deaths (%)	10	0	11.1

Am J Transplant. 2021; 21 (suppl 3).

Example Tixagevimab-Cilgavimab Utilization criteria in SOT

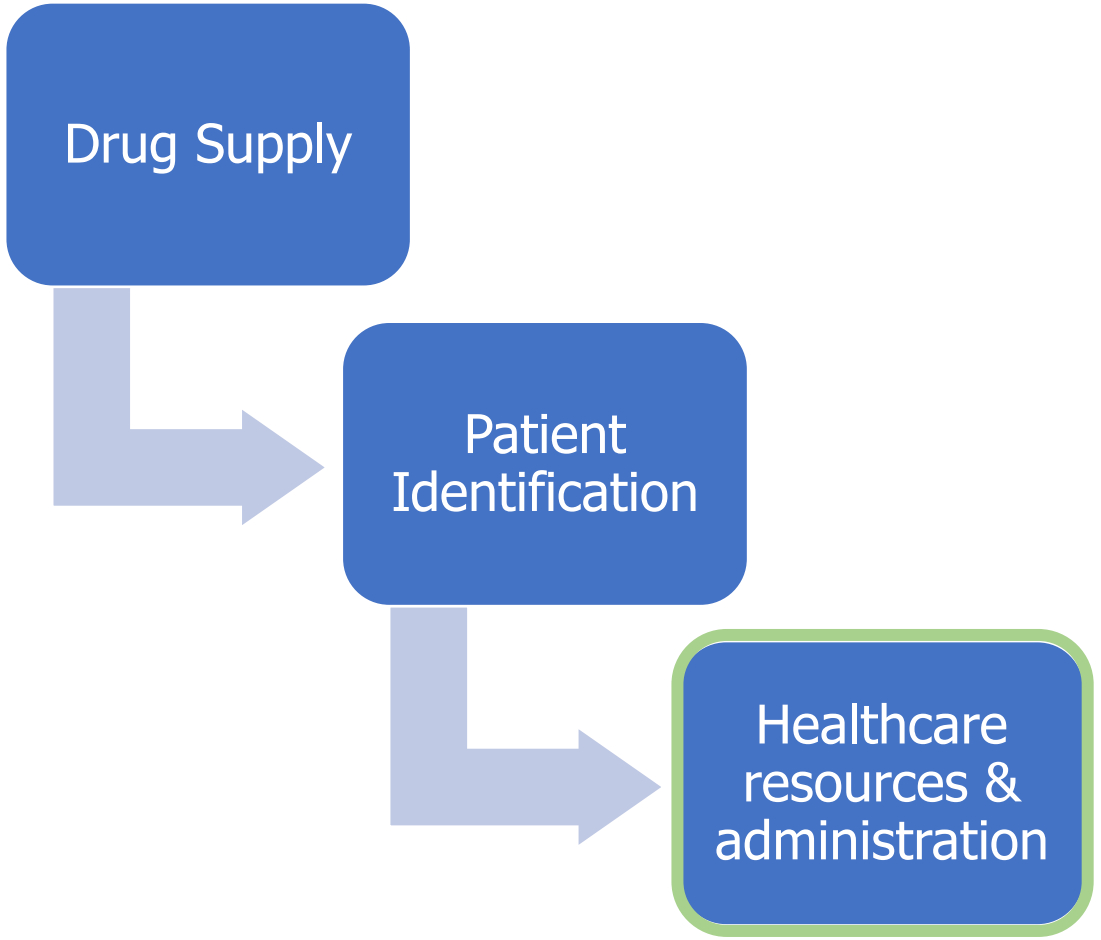


Clin Transplantation. 2022;36:e14661.

AHN SOT Target population

- Abdominal transplant recipients who received Thymoglobulin in the past 3-6 months
  - Phase 1: Index admission, within 6 months
  - Phase 2: Within 1 year
  - Phase 3: Those with other risk factors and within our post transplant cohort
- Heart transplant recipients within 1 year and those who received Thymoglobulin or Rituximab

Planning for Distribution



Getting stakeholders involved

High risk populations

- Infectious Disease*
- Solid organ transplant
- Bone marrow transplant
- Rheumatology
- Oncology
- Allergy/Immunology

Multidisciplinary Teams

- Leadership
- Physicians
- Pharmacy
- Nursing
- Information technology

IT build (In-patient and out-patient)

- Orderable
- Administration
- Emergency medicine order set
- Inventory
- Billing

Supplies for storage and administration

- Refrigeration and temperature monitoring devices
- Alcohol swabs
- Needles
- Syringes
- Band-Aids
- Hypersensitivity kits versus crash carts

Training process

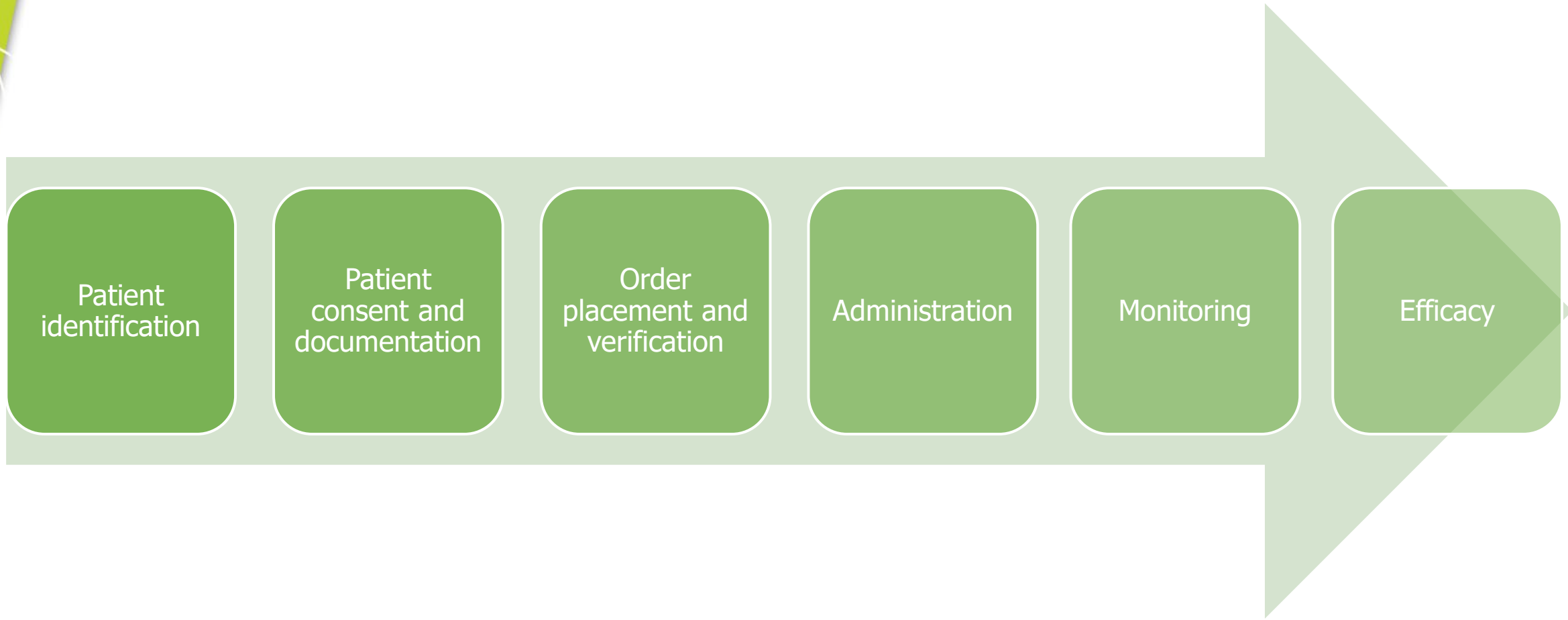
- In-patient versus out-patient nursing
- Pharmacy staff on delivery and verification
- Physician and mid-level providers

Consent process

- In Pennsylvania, consenting patient to treatment is out of the scope of the pharmacist.
  - Medication education is within the scope of pharmacist, so risk/benefit discussion can take place with pharmacist prior to consent documentation

- Consent must be obtained and documented by a qualified practitioner
  - Physician Assistant, Physician, Nurse Practitioner

Iterations of work flow



Inpatient

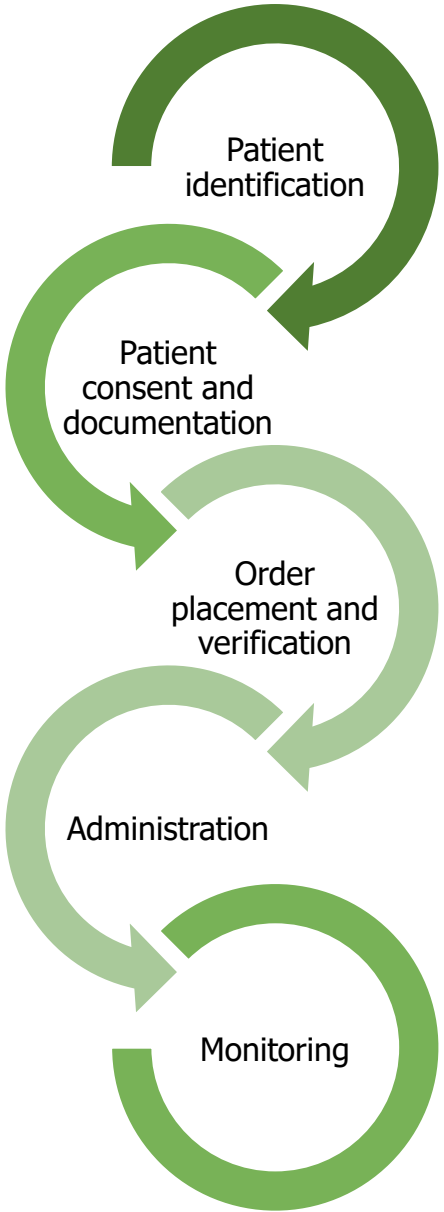
All kidney post-transplants on the day of discharge

Provider status required for consent
Documentation required prior to ordering

Reserved to pharmacists only

Nursing education

1 hour of monitoring with emergency orders available



Outpatient

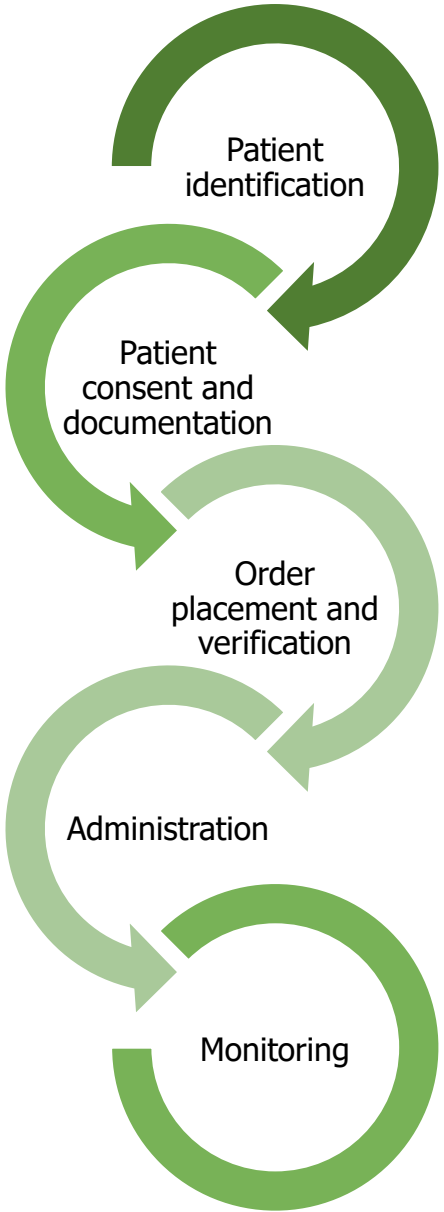
All kidney transplant recipients within 1 year of transplant

Provider status required for consent
Day prior to clinic to help facilitate workflow

Reserved to pharmacists only

Nursing education

1 hour of monitoring with emergency box/ standing orders



Heart Transplant

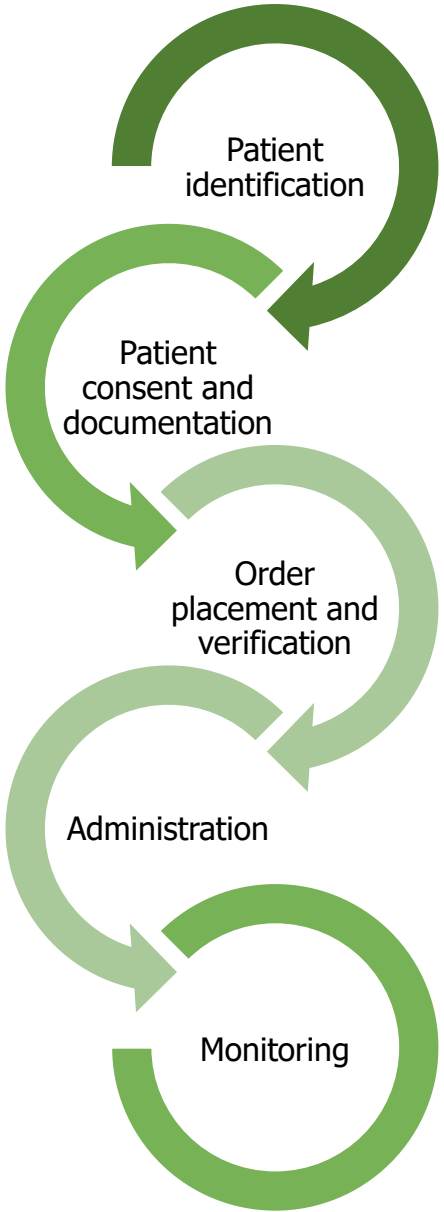
All heart transplant recipients

Provider status required for consent
Cath Lab

Reserved to pharmacists only

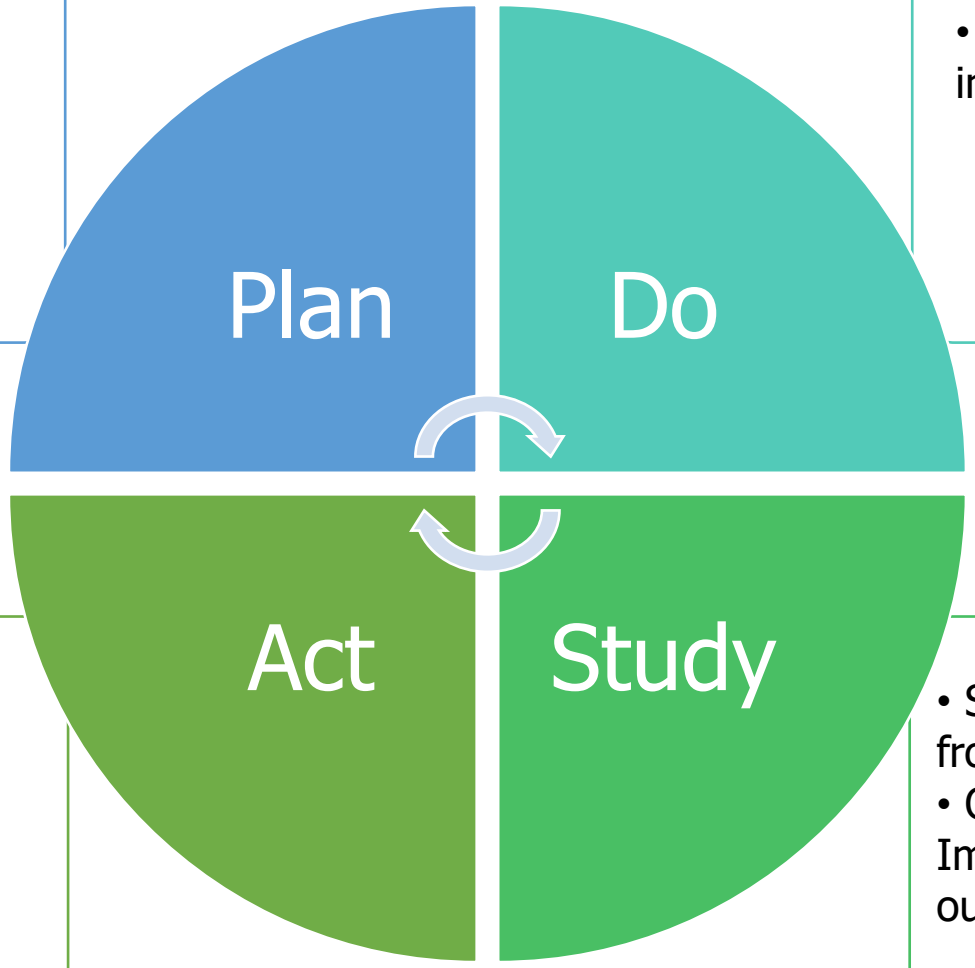
Nursing education

1 hour of monitoring with emergency box/ standing orders



On-going Process Improvement

- Weekly stakeholder meetings
- Department meetings for implementation



- Administration
- Weekly changes in work flow base

- Updates in workflow based off of experience
  - Inventory
  - Billing
  - Information technology

- Solicit feedback from front line
- Quality Improvement for outcomes

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