Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

ACIP Adult RSV Work Group Considerations

Respiratory Syncytial Virus (RSV) in Adults

Use of RSV vaccines in adults aged 50–59 years

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Overview

- Review current recommendation for use of RSV vaccines in adults aged 60 years and older
- Summarize available safety and immunogenicity data on the use of RSVPreF3 vaccine in adults aged 50–59 years
- Share preliminary Adult RSV Work Group interpretations on the use of RSV vaccines in adults aged 50–59 years and upcoming policy decisions

Review of current ACIP recommendation for use of RSV vaccines in adults aged 60 years and older

In June 2023, ACIP and CDC recommended the first two RSV vaccines for older adults.

- RSVPreF3 (**Arexvy, GSK**) is a 1-dose adjuvanted ($AS01_E$) recombinant prefusion F protein (preF) vaccine.
- RSVpreF (**Abrysvo, Pfizer**) is a 1-dose recombinant preF vaccine.*

*The same vaccine formulation is FDA-approved and CDC-recommended for vaccination of pregnant persons for RSV prevention in infants. https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm

Vaccine Efficacy

- GSK's adjuvanted RSVPreF3 and Pfizer's RSVpreF vaccines both demonstrated significant efficacy against lower respiratory tract disease caused by RSV among older adults over at least two seasons.
  - Trials were underpowered to show efficacy in the oldest adults and in frail adults
  - Trials were underpowered to show efficacy against RSV hospitalization, although efficacy against symptomatic illness may indicate efficacy against more severe disease

- Acknowledging these limitations, the Work Group and ACIP felt that RSV vaccination had the potential to prevent considerable morbidity from RSV disease among older adults.

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/06-RSV-Adults-Melgar-508.pdf

Vaccine Safety

- Six cases of inflammatory neurologic events (including Guillain-Barré syndrome) were reported across trials in older adults within 6 weeks after RSV vaccination, compared with no cases within 6 weeks after placebo.
  - 3 cases after vaccination with GSK's RSVPreF3*
  - 3 cases after vaccination with Pfizer's RSVpreF

- Imbalance in the small number of atrial fibrillation events; more cases among vaccine recipients, compared with placebo recipients.

- It is unknown at this time whether these events occurred by chance, or whether RSV vaccination increases the risk of these events.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm

* Two of the 3 reported inflammatory neurologic events after vaccination with GSK's RSVPreF3 were reported as acute disseminated encephalomyelitis (ADEM) in participants that simultaneously received RSVPreF3 vaccine and standard dose seasonal influenza vaccine. The site investigator that initially reported the cases has since revised the diagnosis in both cases (from ADEM to hypoglycemia and dementia, and from ADEM to stroke). FDA's package insert for RSVPreF3 vaccine continues to list these as Serious Adverse Events.

ACIP deliberations leading to a recommendation on the use of RSV vaccine in adults 60 and older

- In June, the Adult RSV Work Group proposed:
  - A universal recommendation for RSV vaccination in adults 65 and older
  - RSV vaccination in adults aged 60–64 years, using shared clinical decision-making
- During ACIP deliberations an amendment was proposed and accepted for the following recommendation:
  - **Adults ages 60 years and older (both those 60–64 and 65 and older) may receive a single dose of RSV vaccine using shared clinical-decision making.**
- The shared clinical decision-making recommendation was intended to allow flexibility for providers and patients to consider individual risk for RSV disease and target RSV vaccination to those most likely to benefit.

ACIP Adult RSV Session. June 21, 2023. Webcast: https://www.youtube.com/watch?v=DunxtgBmRxI&list=PLvrpgiOILTQb6D9e1YZWpbUvzfptNMKx2&index=20

Chronic underlying medical conditions associated with increased risk of severe RSV disease

- Lung disease
- Cardiovascular disease
- Moderate or severe immune compromise
- Diabetes Mellitus
- Neurologic or neuromuscular conditions
- Kidney disorders
- Liver disorders
- Hematologic disorders
- Other conditions that might increase the risk for severe disease

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm

Other factors associated with increased risk of severe RSV disease

- Residence in a nursing home or other long-term care facility (LTCF)
- Frailty
- Advanced age

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm

Next steps: new data on the safety and immunogenicity of RSVPreF3 in adults aged 50–59 years

Today, GSK shared data demonstrating that the humoral immune response to a single dose of RSVPreF3 in adults 50–59 years is non-inferior to that in adults 60 and older.

- Humoral immune response* at day 31 after a single dose of RSVPreF3 in adults 60 and older compared to:
  - **Adults 50–59, healthy** (**without prespecified conditions** associated with increased risk of severe RSV disease)
    OR
  - **Adults 50–59, at-increased-risk** (**AIR, with conditions** associated with increased risk of severe RSV disease)
    - AIR conditions included: COPD resulting in activity restricting symptoms or use of long-term medication, chronic cardiovascular disease, diabetes mellitus type 1 or 2, chronic kidney disease, and chronic liver disease
- Cellular immune response appeared similar across groups, but was not statistically evaluated
- Safety profile of RSVPreF3 in adults 50–59 years similar to profile in 60 and older

*The primary immunogenicity analysis of non-inferiority of the healthy and at-increased risk (AIR) 50–59 year-old group versus the established vaccine age group of 60 and older was based on geometric mean titer ratios and seroresponse rates. Data provided by GSK.

What do these new data mean for future policy?

- The non-inferiority data suggest that RSVPreF3 vaccine efficacy in (immunocompetent) adults aged 50–59 years with and without chronic medical conditions that increase risk of RSV disease will be similar to efficacy demonstrated among adults 60 years and older.

- The Work Group notes that **if FDA licensure is granted** for use of RSVPreF3 in **adults aged 50–59 years**, then ACIP will likely need to make a policy recommendation on:
  - Whether RSV vaccination should be recommended in this age group?
  - And if so, should the recommendation be the same as in adults aged 60 years and older, i.e. shared clinical decision-making, or is a different type of recommendation preferred?

Additional work group interpretations of immunogenicity data in adults aged 50–59 years

- Persons with immunocompromising conditions were excluded from this trial (and prior trials). This is a group likely to benefit from RSV vaccination across the age-spectrum.

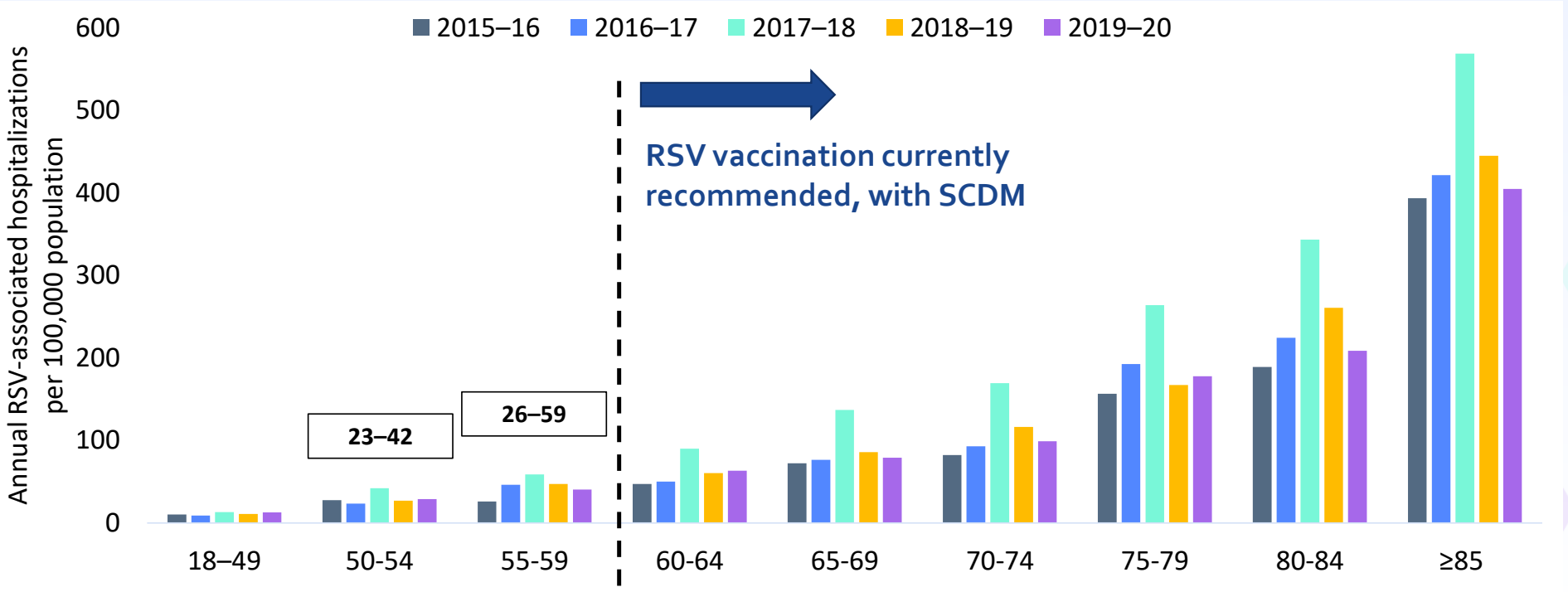
- Would have preferred efficacy data in this age group, noting that there is no immunologic correlate of protection against RSV disease.

- If risk conditions are being prioritized, then those under 50 are also at risk and immuno-bridging (and ideally efficacy) studies in at-risk adults under 50 would also provide important information.

Work Group considerations on the use of RSV vaccines in adults aged 50–59 years

RSV disease is a public health problem in adults aged 50–59 years. However, the rate of RSV-associated disease in the general population of adults 50–59 years is less than the rate in adults 60 and older.

Adjusted RSV-associated hospitalization rates* per 100,000 adults ≥18 years by 5-year age group and year, RSV-NET, 2015–2016 to 2019–2020



*Unpublished data from RSV-NET. Rates are adjusted for the frequency of RSV testing during recent prior seasons and the sensitivity of RSV diagnostic tests.

Persons with certain risk conditions are at increased risk of severe RSV disease, even at younger ages.

Prevalence of certain medical conditions* among non-pregnant adults with RSV-associated hospitalizations (RSV-NET, 2014–2015 to 2017–2018 and 2022–2023) and among the general population (National Center for Health Statistics†, 2022) by age group

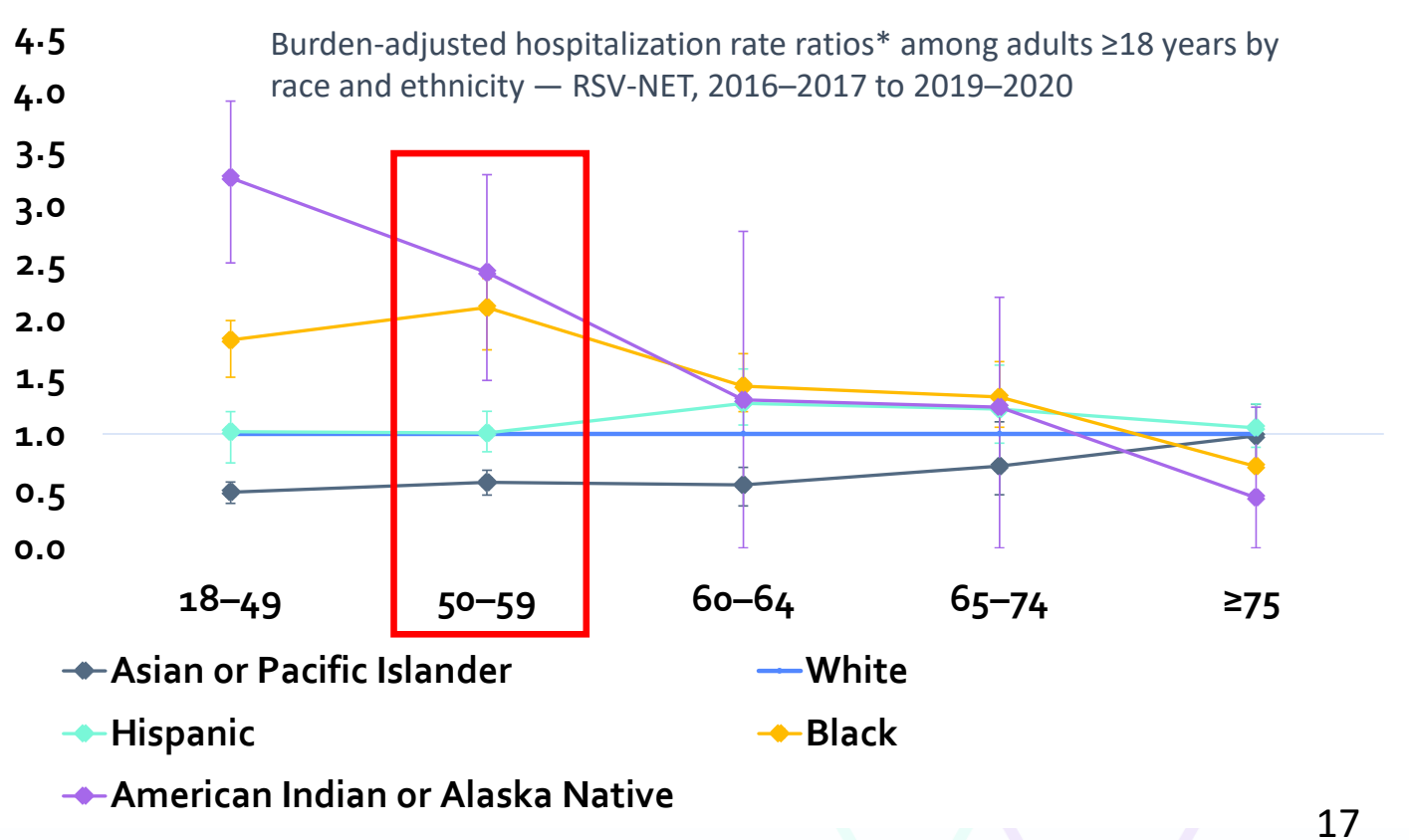
Condition	50–64 years			≥65 years		
	General population % (95% CI)	RSV-NET % (95% CI)	RSV-NET/ Pop	General population % (95% CI)	RSV-NET % (95% CI)	RSV-NET/ Pop
Coronary artery disease	5.0 (4.4, 5.6)	18.9 (16.9, 21.0)	3.8	15.3 (14.4, 16.2)	31.3 (29.1, 33.6)	2.0
COPD	6.2 (5.5, 6.9)	35.4 (32.9, 37.9)	5.7	9.8 (9.1, 10.5)	33.2 (30.1, 35.5)	3.4
Diabetes mellitus	13.8 (12.9, 14.7)	37.7 (35.1, 40.4)	2.7	20.1 (19.1, 21.1)	31.8 (29.6, 34.1)	1.6
Asthma	9.1 (8.4, 9.9)	28.6 (26.3, 31.0)	3.1	8.0 (7.3, 8.6)	17.6 (15.8, 19.4)	2.2
Obesity	37.6 (36.2, 38.9)	46.4 (43.7, 49.0)	1.2	30.4 (29.2, 31.6)	28.4 (26.1, 30.8)	0.9

*Clinical data were collected for all patients with laboratory-confirmed RSV hospitalizations during the 2014–2015 to 2017–2018 seasons, and for an age- and site-stratified random sample of patients with laboratory-confirmed RSV hospitalizations during the 2022–2023 season. Displayed percentages were weighted for the probability of selection.

†National Center for Health Statistics. United States, 2022. National Health Interview Survey. Generated interactively: Oct 17, 2023 from https://wwwn.cdc.gov/NHISDataQueryTool/SHS_adult/index.html

There is an important equity component when considering the use of RSV vaccine among adults aged 50–59 years.

- In adults aged 50–59 years, **hospitalization rates are higher** among Black and American Indian/Alaska Native adults than among White adults.



*Unpublished data from RSV-NET. Rates are adjusted for the frequency of RSV testing during recent prior seasons and the sensitivity of RSV diagnostic tests. Black, White, American Indian/Alaska Native and Asian/Pacific Islander people were categorized as non-Hispanic

Work Group preliminary considerations on the policy question (part 1)

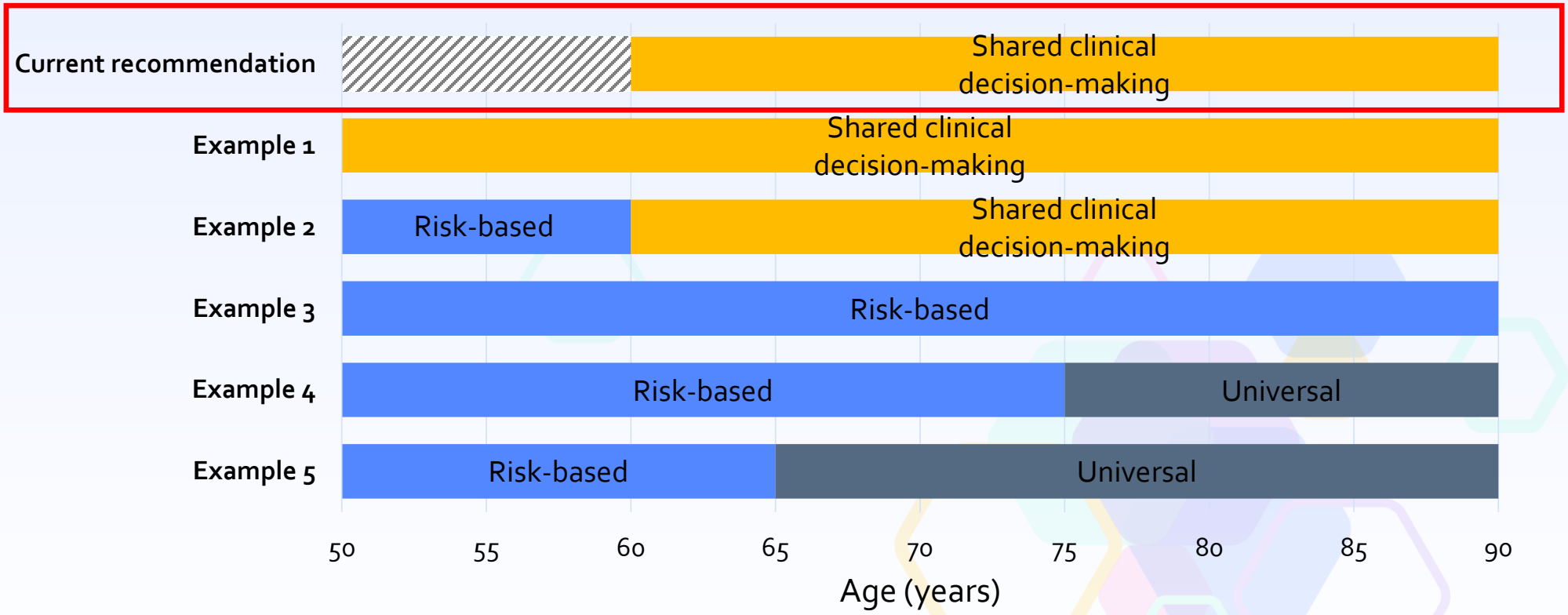
- Work Group is considering multiple policy options.
- **Upcoming data on the implementation of shared clinical decision-making, safety, and effectiveness (if available) will be important** to determine future preferred policy options, both among adults 50–59 years and among those 60 and older.
- The Work Group continues to believe that a focus on those at highest risk of severe RSV disease is warranted while awaiting post-marketing surveillance data.

Work Group preliminary considerations on the policy question (part 2)

- Work Group members broadly agree that use of RSV vaccine among certain adults aged 50–59 years is likely to have public health benefit.
  - Members particularly acknowledge the equity concern of a recommendation for this age group.
- In addition, they note that if FDA licenses this product for adults 50–59 years, but there is NO recommendation made, insurance will not cover use in this age group, potentially furthering existing disparities.

- The current priority of the Work Group is to **ensure access** to vaccination among adults 50–59 (and those ≥60) who are at substantially **increased risk of severe RSV disease and likely to benefit most.**

Example *potential* policy options



Next steps for the Work Group

- Over the next few months, the Work Group will review **post-marketing data** on the use of RSV vaccines in adults 60 and older as they become available, including:
  - Vaccine **uptake**, stratified by demographic characteristics and risk conditions
  - Vaccine **safety** surveillance

- The Work Group will consider the implementation and implications of shared clinical decision-making

Next steps for the Work Group

- The Work Group will then develop an updated policy question for RSV vaccination in adults through review of:
  - Updated **GRADE** of evidence profile for use of GSK's **RSVPreF3** in adults
  - Updated **cost effectiveness analysis** (CEA) of use of **RSVPreF3** in adults
  - Updated **Evidence to Recommendations** framework for adult **RSV vaccination**

- The Work Group will also begin reviewing **safety and efficacy of a new RSV vaccine (Moderna's mRNA-1345)** for use in adults 60 and older

Questions for ACIP

1. What additional data are needed prior to ACIP voting on updated recommendations for RSV vaccination in adults aged ≥50 years?

2. Other questions from ACIP?

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