

RSV and the Older Adult

Much Ado About Something



RSV Tweetorial #5

Tweets

References

1/ 🍀 Going 3 for 3 🍀
#RSV #MedTweetorial 📖 #3
🔍 Focus on older adults & mRNA 📄
📈 #idweek2022 & #rsv2022 data

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- ✅ Answer the polls
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📌 Faculty disclosures & important info 📌

RSV and the OLDER ADULT

Much Ado About Something

FACULTY INFORMATION & DISCLOSURES

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📄 Hear ye, Hear ye ~Read all about it 📄

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RSV 3rd leading viral cause of 🏥 admissions in adults ≥65y of age

🚫 exist for prevention...yet

📄 mRNA-derived 📄 in clin trls use RSV genetic material to mimic infect. & stimulate immn response

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🔍 #RSV vaccine pipeline

📄 Many 📄 for older adults in development 📄

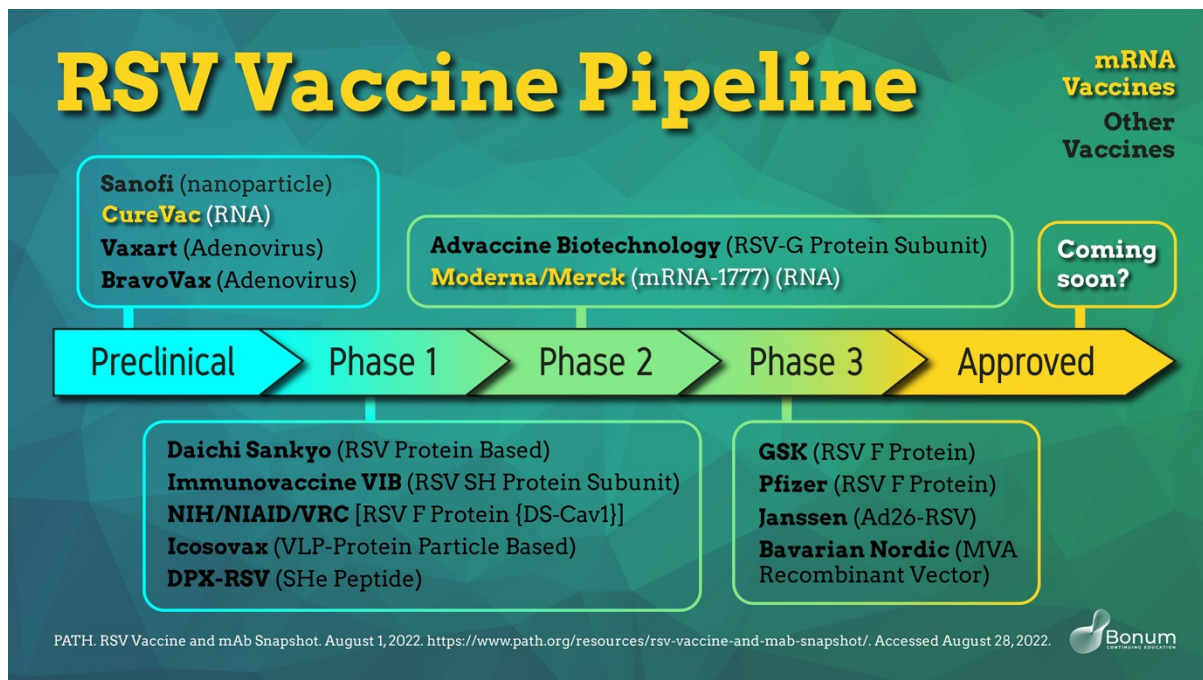
🎯 Protein-based

🎯 Nucleic acid

🎯 Live attenuated/chimeric

🎯 Recombinant vectors

📌 Diving into mRNA vaccines 📌



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● How do mRNA vaccines trigger immunity ?

- RNA directs antigen production
- Uses weak, live 🦠
- Delivered by vaccinia
- Boosted by adjuvant

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🌟 mRNA 📄 trigger immunity by → Encoding #RSV F protein in the mRNA → a carrier 🚚 transports it inside the cell → after cell uptake, an antigen is produced & displayed on the cell surface → which stimulates an immune response from T & B cells

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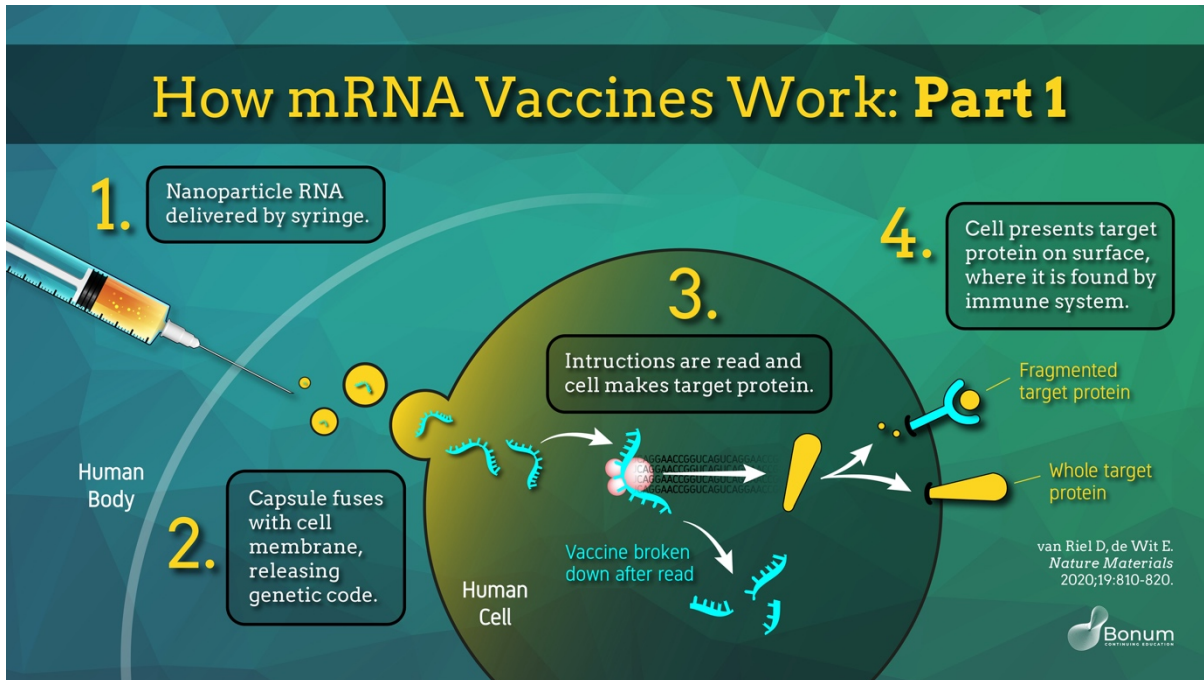
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- 🗣️ Here's how mRNA vaccines work:
- 🚚 Delivery of a transcript that encodes **1** or more immunogens into the host cell cytoplasm
- 📌 Immunogenic proteins translated intracellularly
- 📌 Incorporated into the cell membrane or secreted

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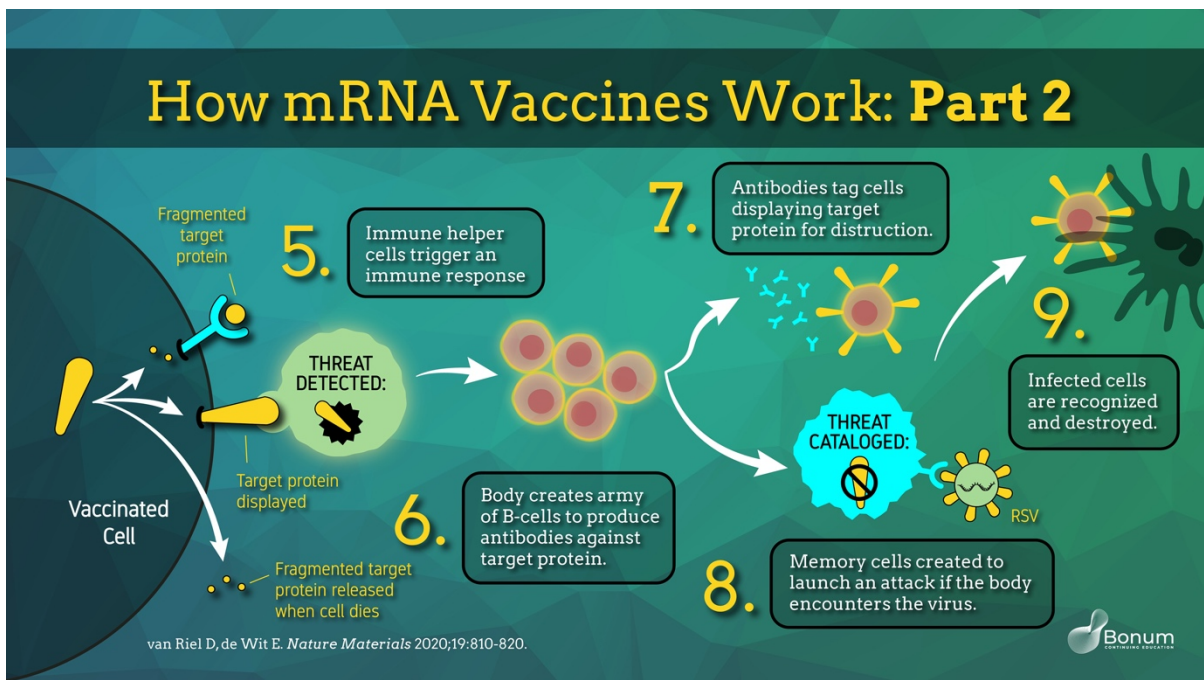


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- 🌟 mRNA vaccine immunity created
- 🎯 protein displayed
- Immune response triggered
- B-cells produce antibodies vs target protein
- Antibodies tag 🎯 cells for destruction
- 🧠 Memory cells created
- 🚫 Infected cells detected & destroyed



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 Benefits of mRNA-based 

-  Induces innate & adaptive immune response
-  Safe for use in immunocompromised pts
-  Does not integrate into the genome
-  No live components
-  Rapid, scalable, cost-effective production
-  Cell-free manufacture






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 Disadvantages of mRNA-based vaccines 

-  Poor stability
-  Ultra-cold storage req'd
-  Duration of response, may involve multiple  for efficacy
-  Req delivery vehicles w/o toxicity or immunogenicity for passage through cell membrane

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Types of mRNA-based vaccines:

-  Conv, nonreplicating (small size, simple, encodes only immunogen of interest)
-  Self-replicating (inc code for RNA-dep RNA polymerase 4 self-amplification & components in non-replicating constructs) ++ immune response

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 What are the most common delivery systems for mRNA vaccines ?

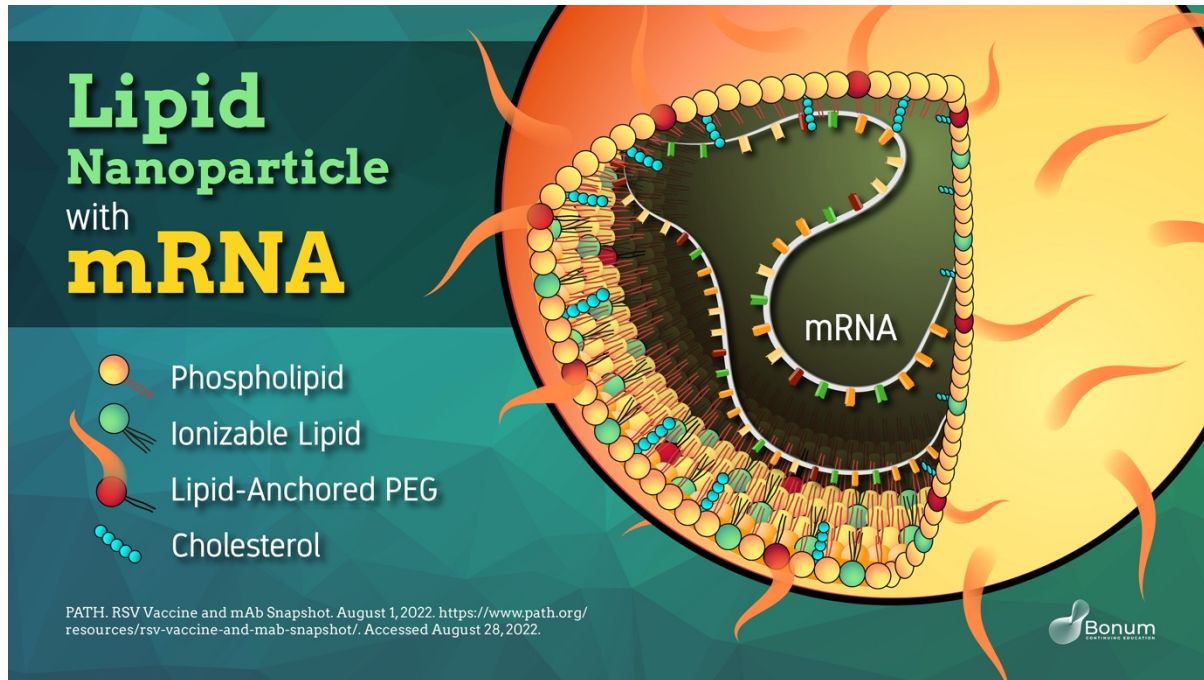
- Stem cells
- Lipid nanoparticles
- Cationic dendrimer
- Carrier erythrocytes

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🚚 mRNA vaccines req sophisticated transport systems to cross negatively charged ⚡ cell membranes

- ◆ These 🚚 vehicles must protect mRNA from enzyme digestion & enable uptake by host cell
- ◆ Lipid nanoparticles (LNP) are most common carriers



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- 🚚 LNPs optimized for
- ⬆️ impv'd cellular uptake
- 👏 endosomal release
- ⚡ mRNA expression
- 🏠 rapid metabolism/excretion & safety

Characterized by

- 📍 low # of mRNA copies
- 📍 located in interior core of 🚚 carrier LNP
- 🚚 some del agents acts like adjuvant

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mRNA-1354

- ➡️ #RSV 📄 encoding for the prefusion F glycoprotein
- ◆ Phase 3 RCTs
- ☀️ Interim data from ph1 trial in ages 65-79y showed 🙌 single vaccination boosted neutralizing antibodies against RSV-A by 14-fold and RSV-B by 10-fold

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🟢 What was the most common adverse event w/ the mRNA-1345 vaccine?
?

- 🤒 Fever
- 🤯 Headache
- 💪 Myalgia
- 📍 Site pain

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mRNA-1354 Phase 1 analysis, the most common AEs lasting 1-4 days were:

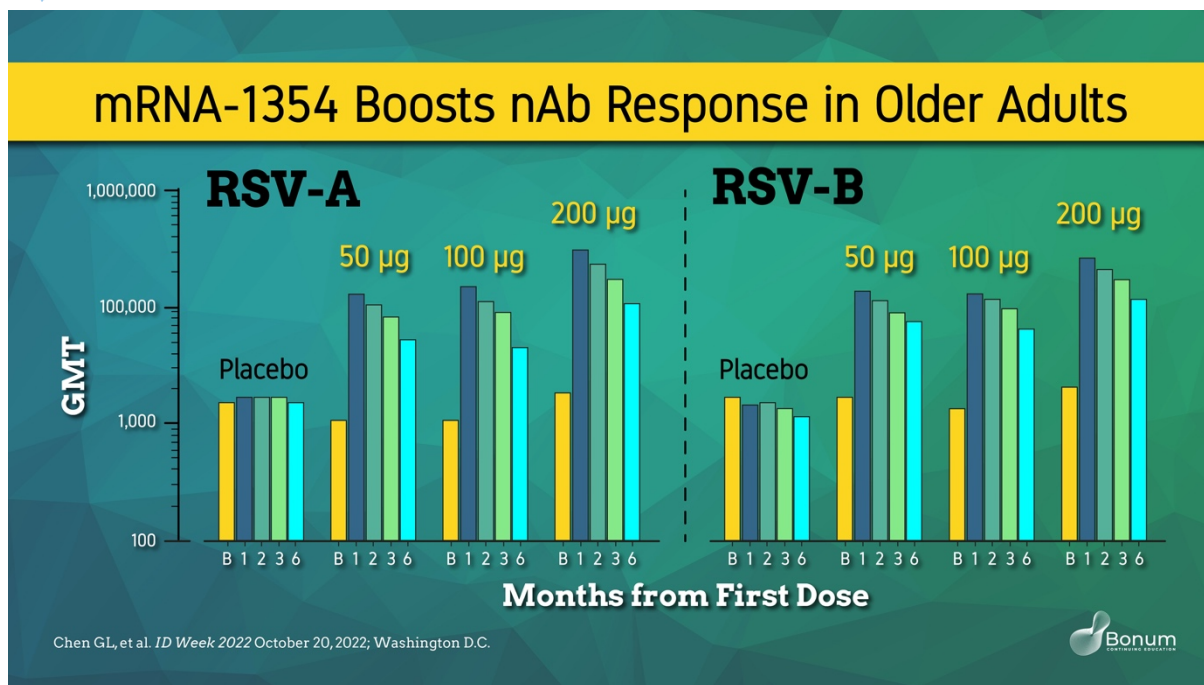
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- ✓ site pain (66.2% vs 12.7% for PBO)
- ✓ headache 🤒
- ✓ fatigue 🥱
- ✓ myalgia 💪

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- 📌 mRNA-1354 boosts #RSV nAb Responses in Older Adults
- 💠 Peak GMFRs over BL @ 1mo were 9.9-16.6 for RSV-A & 5.3-12.6 for RSV-B
- B
- 💠 Peak nAB declined thru M6 but higher than initial BL for all doses
- 💠 GMFRs over BL @ 6mo were 3.1-5.8 for RSV-A and 2.9-5.5 for RSV-B



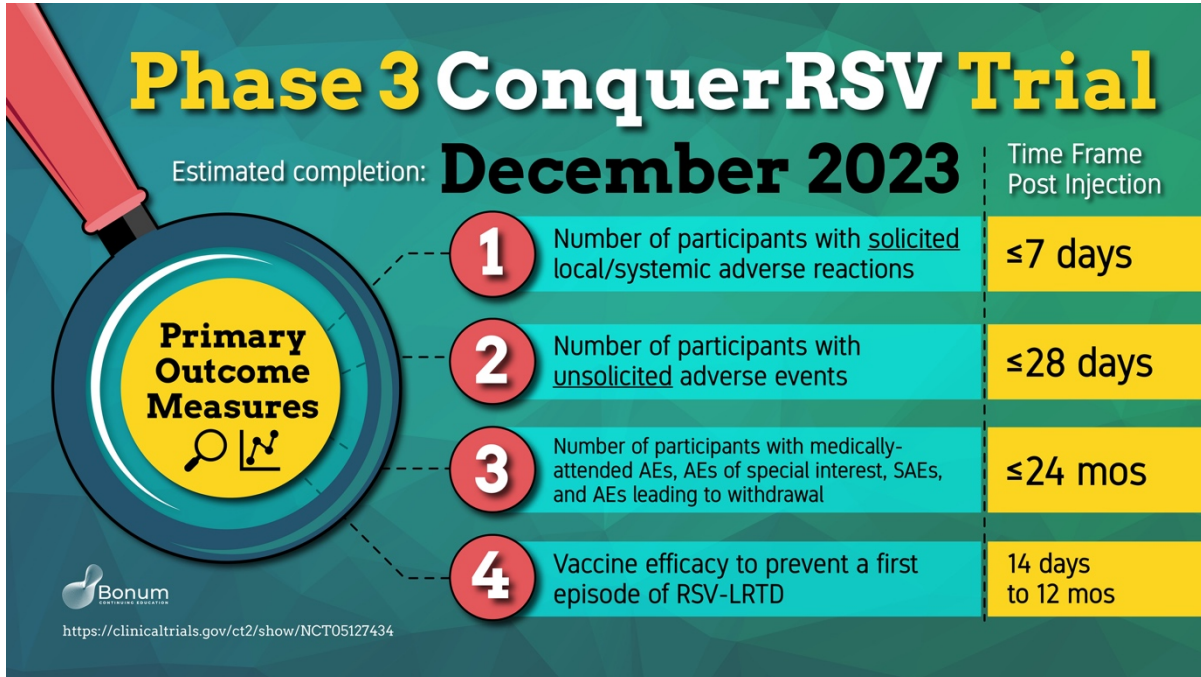
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mRNA-1354 gained @FDA Fast Track Status 🏃

★ Ph3 ConquerRSV trial est. to complete in Dec 2023 📅 Now recruiting
 34,000 adults aged ≥60y



Phase 3 ConquerRSV Trial

Estimated completion: **December 2023**

Time Frame Post Injection

Primary Outcome Measures	Time Frame Post Injection
1 Number of participants with <u>solicited</u> local/systemic adverse reactions	≤7 days
2 Number of participants with <u>unsolicited</u> adverse events	≤28 days
3 Number of participants with medically-attended AEs, AEs of special interest, SAEs, and AEs leading to withdrawal	≤24 mos
4 Vaccine efficacy to prevent a first episode of RSV-LRTD	14 days to 12 mos

<https://clinicaltrials.gov/ct2/show/NCT05127434>

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SUMMARY | mRNA vaccines:

- 🔑 Elicit robust CD4+ and CD8+ T-cell responses
- 🔑 Req's delivery vehicle to get into the cell
- 🔑 No live components, safe for immunocompromised pts

Claim your CME credit by completing the post-survey and evaluation. Link provided 🖱️

[🔗 here](#)
Or: <http://bit.ly/3hPnlG4>

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