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COVID Literature research & Summary

10/15/2021

1. Emergency surgery and non-operating room interventions during the pandemic period for COVID pts do not increase postoperative mortality
2. AstraZeneca estimated vaccine efficacy was 74.0%. 83% efficacious in the >65 yoa population
3. Vaccine associated cervical lymphadenopathy can mimic malignant lymphadenopathy and therefore might prove challenging to diagnose and manage correctly - more studies and reports are needed.
4. Vaccine-associated mRNA was not detected in milk samples collected 4 to 48 hours after vaccination of breastfeeding mothers.
5. more physical activity and less screen time were associated with better mental health for children
6. effectiveness of Pfizer against hospital admissions up until around 6 months was 90% after being fully vaccinated (including for delta variant)
7. Molnupiravir proved to be effective against COVID infections in a hamster model
8. Increases in Various inflammatory molecules were noted tin pts with  acute COVID-19 and Long COVID/PASC(post-acute syndrome COVID)
9. Excess deaths per 100,000 persons in 2020 among people of color were more than double of those in white/Asian male and females.
10. Six months after receipt of the second dose of the Pfizer vaccine, humoral response was substantially decreased, especially among men, among persons 65 years of age or older, and among persons with immunosuppression
11. Estimated incidence of myocarditis was 2.13 cases per 100,000 persons after mRNA vaccination; the highest incidence was among male patients between the ages of 16 and 29 years
12. Among symptomatic clinically stable outpatients with COVID-19, treatment with aspirin or apixaban compared with placebo did not reduce the rate of reduce major cardiopulmonary adverse outcomes over a 45-day treatment period. However, the study was terminated after enrollment of 9% of participants because of an event rate lower than anticipated
13. How about this GEM on Aspirin use - Aspirin use in healthy elderly persons did not prolong disability-free survival over a period of 5 years but led to a higher rate of major hemorrhage than placebo

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| ICHE - 9/11/2021 - safety of surgical and non-operating room procedures during COVID pandemic | * Little is known about the impact of COVID-19 on the outcomes of patients undergoing surgery and intervention. This study was conducted between 20 March and 20 May 2020 in six hospitals in Istanbul, and aimed to investigate the effects of surgery and intervention on COVID-19 disease progression, intensive care (ICU) need, mortality and virus transmission to patients and healthcare workers.
* Patients were examined in three groups:
	+ group I underwent emergency surgery,
	+ group II had an emergency non-operating room intervention, and
	+ group III received inpatient COVID-19 treatment but did not have surgery or undergo intervention.
* Mortality rates, mechanical ventilation needs and rates of admission to the ICU were compared between the three groups. During this period, patient and healthcare worker transmissions were recorded.
* In total, 1273 surgical, 476 non-operating room intervention patients and 1884 COVID-19 inpatients were examined.
* The rate of ICU requirement among patients who had surgery was nearly twice that for inpatients and intervention patients, but there was no difference in mortality between the groups.
* The overall mortality rates were 2.3% in surgical patients, 3.3% in intervention patients and 3% in inpatients. COVID-19 polymerase chain reaction positivity among hospital workers was 2.4%. Only 3.3% of infected frontline healthcare workers were anesthesiologists. No deaths occurred among infected healthcare workers.
* We conclude that emergency surgery and non-operating room interventions during the pandemic period do not increase postoperative mortality and can be performed with low transmission rates [https://www.cambridge.org/core/services/aop-cambridge-core/content/view/C8B5E23D9EA689C22C025A75180ACBB9/S0950268821002119a.pdf/are\_surgical\_and\_nonoperating\_room\_intervention\_safe\_in\_the\_covid19\_pandemic\_a\_retrospective\_study.pdf](https://urldefense.com/v3/__https%3A/www.cambridge.org/core/services/aop-cambridge-core/content/view/C8B5E23D9EA689C22C025A75180ACBB9/S0950268821002119a.pdf/are_surgical_and_nonoperating_room_intervention_safe_in_the_covid19_pandemic_a_retrospective_study.pdf__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8Dvfq_weYA$)
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| NEJM - 9/29/2021 - phase 3 safety and efficacy of AstraZeneca | * A total of 32,451 participants underwent randomization, in a 2:1 ratio, to receive AZD1222 (21,635 participants) or placebo (10,816 participants).
* AZD1222 was safe, with low incidences of serious and medically attended adverse events and adverse events of special interest; the incidences were similar to those observed in the placebo group. Solicited local and systemic reactions were generally mild or moderate in both groups.
* Overall estimated vaccine efficacy was 74.0% (95% confidence interval [CI], 65.3 to 80.5; P<0.001) and estimated vaccine efficacy was 83.5% (95% CI, 54.2 to 94.1) in participants 65 years of age or older. High vaccine efficacy was consistent across a range of demographic subgroups. In the fully vaccinated analysis subgroup, no severe or critical symptomatic Covid-19 cases were observed among the 17,662 participants in the AZD1222 group; 8 cases were noted among the 8550 participants in the placebo group (<0.1%). The estimated vaccine efficacy for preventing SARS-CoV-2 infection (nucleocapsid antibody seroconversion) was 64.3% (95% CI, 56.1 to 71.0; P<0.001). SARS-CoV-2 spike protein binding and neutralizing antibodies increased after the first dose and increased further when measured 28 days after the second dose
* [https://www.nejm.org/doi/full/10.1056/NEJMoa2105290?query=featured\_coronavirus](https://urldefense.com/v3/__https%3A/www.nejm.org/doi/full/10.1056/NEJMoa2105290?query=featured_coronavirus__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DsKvgw_vQ$)
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| ICHE - 9/16/2021 - lymphadenopathy after COVID vaccine | * The incidence of vaccine-associated cervical lymphadenopathy referrals was 14.8 per cent (*n* = 13).
* Five patients (38.5 per cent) had abnormal-looking enlarged and rounded nodes with increased vascularity.
* Only seven patients (53.9 per cent) reported full resolution within an average of 3.1 ± 2.3 weeks
* Coronavirus disease vaccine associated cervical lymphadenopathy can mimic malignant lymphadenopathy and therefore might prove challenging to diagnose and manage correctly
* [https://www.cambridge.org/core/journals/journal-of-laryngology-and-otology/article/cervical-lymphadenopathy-following-coronavirus-disease-2019-vaccine-clinical-characteristics-and-implications-for-head-and-neck-cancer-services/EDFDC7E23E32A7246679127CDC16F441](https://urldefense.com/v3/__https%3A/www.cambridge.org/core/journals/journal-of-laryngology-and-otology/article/cervical-lymphadenopathy-following-coronavirus-disease-2019-vaccine-clinical-characteristics-and-implications-for-head-and-neck-cancer-services/EDFDC7E23E32A7246679127CDC16F441__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8Dur9CJl6g$)
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| JAMA - 10/1/2021 - mRNA vaccines and breastmilk | * A total of 7 breastfeeding mothers (mean [SD] age, 37.8 [5.8] years) volunteered for this study ([Table](https://urldefense.com/v3/__https%3A/jamanetwork.com/journals/jamapediatrics/fullarticle/2781679%2Apld210013t1__;Iw!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DtivGa3kA$)). Their children ranged in age from 1 month to 3 years.
* Post-vaccination milk samples were collected 4 to 48 hours after administration of the BNT162b2 (n = 5) or mRNA-1273 (n = 2) vaccines.
* Analysis of 13 human milk samples collected 24 hours after vaccination, including multiple time points (4 to 48 hours) from a single participant, revealed that none of the samples showed detectable levels of vaccine mRNA in any component of the milk
* Vaccine-associated mRNA was not detected in 13 milk samples collected 4 to 48 hours after vaccination from 7 breastfeeding individuals
* [https://jamanetwork.com/journals/jamapediatrics/fullarticle/2781679](https://urldefense.com/v3/__https%3A/jamanetwork.com/journals/jamapediatrics/fullarticle/2781679__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DsHdwQ-iA$)
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| JAMA - 10/1/2021 - Childrens physical activity and mental health related to screen time.  | * Among the 1000 children included in the analysis (mean [SD] age, 10.8 [3.5] years; 517 [52.6%] boys; 293 [31.6%] American Indian/Alaska Native, Asian, or Black individuals or individuals of other race; and 233 [27.8%] Hispanic/Latino individuals), 195
* (20.9%) reported at least 60 minutes of physical activity every day.
* Children reported a mean (SD) of 3.9 (2.2) d/wk with at least 60 minutes of physical activity and 4.4 (2.5) h/d of recreational screen time. COVID-19 stressors were significantly associated with higher total difficulties for both younger (β coefficient, 0.6; 95% CI, 0.3-0.9) and older (β coefficient, 0.4; 95% CI, 0.0-0.7) groups.
* After accounting for COVID-19 stressors, engaging in 7 d/wk (vs 0) of physical activity was associated with fewer externalizing symptoms in younger children (β coefficient, −2.0; 95% CI, −3.4 to −0.6).
* For older children, engaging in 1 to 6 and 7 d/wk (vs 0) of physical activity was associated with lower total difficulties (β coefficients, −3.5 [95% CI, −5.3 to −1.8] and −3.6 [95% CI, −5.8 to −1.4], respectively), fewer externalizing symptoms (β coefficients,  −1.5 [95% CI, −2.5 to −0.4] and −1.3 [95% CI, −2.6 to 0], respectively), and fewer internalizing symptoms (β coefficients, −2.1 [95% CI, −3.0 to −1.1] and −2.3 [95% CI, −3.5 to −1.1], respectively).
* More screen time was correlated with higher total difficulties among younger (β coefficient, 0.3; 95% CI, 0.1-0.5) and older (β coefficient, 0.4; 95% CI, 0.2-0.6) children. There were no significant differences by sex
* More physical activity and less screen time were associated with better mental health for children
* [https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2784611](https://urldefense.com/v3/__https%3A/jamanetwork.com/journals/jamanetworkopen/fullarticle/2784611__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DvO_kkolA$)
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| LANCET - 10/4/2021 - effectiveness of Pfizer, 6 months after vaccination | * Between Dec 14, 2020, and Aug 8, 2021, of 4 920 549 individuals assessed for eligibility, we included 3 436 957 (median age 45 years [IQR 29–61]; 1 799 395 [52·4%] female and 1 637 394 [47·6%] male).
* For fully vaccinated individuals, effectiveness against SARS-CoV-2 infections was 73% (95% CI 72–74) and
* Against COVID-19-related hospital admissions was 90% (89–92).
* Effectiveness against infections declined from 88% (95% CI 86–89) during the first month after full vaccination to 47% (43–51) after 5 months.
* Among sequenced infections, vaccine effectiveness against infections of the delta variant was
	+ high during the first month after full vaccination (93% [95% CI 85–97]) but declined to
	+ 53% [39–65] after 4 months. Effectiveness against other (non-delta) variants the first month after full vaccination was also high at 97% (95% CI 95–99), but waned to 67% (45–80) at 4–5 months.
* Vaccine effectiveness against hospital admissions for infections with the delta variant for all ages was high overall (93% [95% CI 84–96]) up to 6 months
* Effectiveness of Pfizer against hospital admissions up until around 6 months was 90% after being fully vaccinated
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| JID - 7/2021 - Molnupiravir inhibits replication in Hamsters  | * The emergence of SARS-CoV-2 variants of concern (VoCs) has exacerbated the COVID-19 pandemic.
* Currently available monoclonal antibodies and vaccines appear to have reduced efficacy against some of these VoCs. Antivirals targeting conserved proteins of SARS-CoV-2 are unlikely to be affected by mutations arising in VoCs and should therefore be effective against emerging variants.
* We here investigate the efficacy of Molnupiravir, currently in phase 2 clinical trials, in hamsters infected with Wuhan strain or B.1.1.7 and B.1.351 variants.
* Molnupiravir proved to be effective against infections with each of the variants and therefore may have potential combating current and future emerging VoC
* [https://academic.oup.com/jid/article/224/5/749/6318434](https://urldefense.com/v3/__https%3A/academic.oup.com/jid/article/224/5/749/6318434__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DurmyNR_Q$)
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| Cardiovascular Diabetology - 8/23/2021 - Persistent Clotting protein in Long COVID individuals | * We show that plasma samples from Long COVID/PASC still contain large anomalous (amyloid) deposits (microclots). We also show that
* these microclots in both acute COVID-19 and Long COVID/PASC plasma samples are resistant to fibrinolysis (compared to plasma from controls and T2DM), even after trypsinisation. After a second trypsinization, the persistent pellet deposits (microclots) were solubilized.
* We detected various inflammatory molecules that are substantially increased in both the supernatant and trapped in the solubilized pellet deposits of acute COVID-19 and Long COVID/PASC, versus the equivalent volume of fully digested fluid of the control samples and T2DM.
* Of particular interest was a substantial increase in α(2)-antiplasmin (α2AP), various fibrinogen chains, as well as Serum Amyloid A (SAA) that were trapped in the solubilized fibrinolytic-resistant pellet deposits
* [https://cardiab.biomedcentral.com/articles/10.1186/s12933-021-01359-7](https://urldefense.com/v3/__https%3A/cardiab.biomedcentral.com/articles/10.1186/s12933-021-01359-7__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DuTp8uhBA$)
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| Annals of IM - 10/5/2021 - racial and ethnic disparities in excess deaths due to COVID | * An estimated 2.88 million deaths occurred between March and December 2020. Compared with the number of expected deaths based on 2019 data,
* 477 200 excess deaths occurred during this period, with
	+ 74% attributed to COVID-19.
* Age-standardized excess deaths per 100 000 persons among Black, American Indian/Alaska Native (AI/AN), and Latino males and females were more than double those in White and Asian males and females.
* Non–COVID-19 excess deaths also disproportionately affected Black, AI/AN, and Latino persons. Compared with White males and females, non–COVID-19 excess deaths per 100 000 persons were 2 to 4 times higher in Black, AI/AN, and Latino males and females, including deaths due to diabetes, heart disease, cerebrovascular disease, and Alzheimer disease.
* Excess deaths in 2020 resulted in substantial widening of racial/ethnic disparities in all-cause mortality from 2019 to 2020
* There were profound racial/ethnic disparities in excess deaths in the United States in 2020 during the COVID-19 pandemic, resulting in rapid increases in racial/ethnic disparities in all-cause mortality between 2019 and 2020
* [https://www.acpjournals.org/doi/10.7326/M21-2134](https://urldefense.com/v3/__https%3A/www.acpjournals.org/doi/10.7326/M21-2134__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8Du2DBvD8w$)
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| NEJM - 10/6/2021 - waning immune humoral response to mRNA vaccines after 6 months. | * The study included 4868 participants, with 3808 being included in the linear mixed-model analyses. The level of IgG antibodies decreased at a consistent rate, whereas the
* neutralizing antibody level decreased rapidly for the first 3 months with a relatively slow decrease thereafter. Although IgG antibody levels were highly correlated with neutralizing antibody titers (Spearman’s rank correlation between 0.68 and 0.75), the regression relationship between the IgG and neutralizing antibody levels depended on the time since receipt of the second vaccine dose.
* Six months after receipt of the second dose, neutralizing antibody titers were substantially lower
	+ among men than among women (ratio of means, 0.64; 95% confidence interval [CI], 0.55 to 0.75),
	+ lower among persons 65 years of age or older than among those 18 to less than 45 years of age (ratio of means, 0.58; 95% CI, 0.48 to 0.70), and
	+ lower among participants with immunosuppression than among those without immunosuppression (ratio of means, 0.30; 95% CI, 0.20 to 0.46)
* Six months after receipt of the second dose of the BNT162b2 vaccine, humoral response was substantially decreased, especially among men, among persons 65 years of age or older, and among persons with immunosuppression
* [https://www.nejm.org/doi/full/10.1056/NEJMoa2114583?query=featured\_coronavirus](https://urldefense.com/v3/__https%3A/www.nejm.org/doi/full/10.1056/NEJMoa2114583?query=featured_coronavirus__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DvmtrnCCw$)
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| NEJM - 10/6/2021 - Myocarditis after Pfizer vaccine in Israel | * Among 304 persons with symptoms of myocarditis,
* 21 had received an alternative diagnosis. Of the remaining 283 cases,
	+ 142 occurred after receipt of the BNT162b2 vaccine; of these cases,
	+ 136 diagnoses were definitive or probable. The clinical presentation was judged to be
	+ mild in 129 recipients (95%);
	+ one fulminant case was fatal. The overall risk difference between the first and second doses was 1.76 per 100,000 persons (95% confidence interval [CI], 1.33 to 2.19), with the largest difference among male recipients between the ages of 16 and 19 years (difference, 13.73 per 100,000 persons; 95% CI, 8.11 to 19.46).
* As compared with the expected incidence based on historical data, the standardized incidence ratio was 5.34 (95% CI, 4.48 to 6.40) and was highest after the second dose in male recipients between the ages of 16 and 19 years (13.60; 95% CI, 9.30 to 19.20). The rate ratio 30 days after the second vaccine dose in fully vaccinated recipients, as compared with unvaccinated persons, was 2.35 (95% CI, 1.10 to 5.02); the rate ratio was again highest in **male recipients between the ages of 16 and 19 years (8.96; 95% CI, 4.50 to 17.83), with a ratio of 1 in 6637.**
* The incidence of myocarditis, although low, increased after the receipt of the BNT162b2 vaccine, particularly after the second dose among young male recipients. The clinical presentation of myocarditis after vaccination was usually mild.
* The incidence of myocarditis, although low, increased after the receipt of the BNT162b2 vaccine, particularly after the second dose among young male recipients. The clinical presentation of myocarditis after vaccination was usually mild.
* [https://www.nejm.org/doi/full/10.1056/NEJMoa2109730?query=featured\_coronavirus](https://urldefense.com/v3/__https%3A/www.nejm.org/doi/full/10.1056/NEJMoa2109730?query=featured_coronavirus__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DsIK9yiEg$)
	+ Among patients in a large Israeli health care system who had received at least one dose of the BNT162b2 mRNA vaccine, the estimated incidence of myocarditis was 2.13 cases per 100,000 persons; the highest incidence was among male patients between the ages of 16 and 29 years. Most cases of myocarditis were mild or moderate in severity
	+ [https://www.nejm.org/doi/full/10.1056/NEJMoa2110737?query=featured\_coronavirus](https://urldefense.com/v3/__https%3A/www.nejm.org/doi/full/10.1056/NEJMoa2110737?query=featured_coronavirus__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DtXpmJ5Ag$)
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| JAMA - 10/11/2021 - antithrombotic therapy in COVID | * On June 18, 2021, the trial data and safety monitoring board recommended early termination because of lower than anticipated event rates; at that time,
* 657 symptomatic outpatients with COVID-19 had been randomized (median age, 54 years [IQR, 46-59]; 59% women). The median times from diagnosis to randomization and from randomization to initiation of study treatment were 7 days and 3 days, respectively.
* Twenty-two randomized participants (3.3%) were hospitalized for COVID-19 prior to initiating treatment.
* Among the 558 patients who initiated treatment, the adjudicated primary composite end point occurred in 1 patient (0.7%) in the aspirin group, 1 patient (0.7%) in the 2.5-mg apixaban group, 2 patients (1.4%) in the 5-mg apixaban group, and 1 patient (0.7%) in the placebo group.
* The risk differences compared with placebo for the primary end point were 0.0% (95% CI not calculable) in the aspirin group, 0.7% (95% CI, –2.1% to 4.1%) in the 2.5-mg apixaban group, and 1.4% (95% CI, –1.5% to 5.0%) in the 5-mg apixaban group. Risk differences compared with placebo for bleeding events were 2.0% (95% CI, –2.7% to 6.8%), 4.5% (95% CI, –0.7% to 10.2%), and 6.9% (95% CI, 1.4% to 12.9%) among participants who initiated therapy in the aspirin, prophylactic apixaban, and therapeutic apixaban groups, respectively, although none were major. Findings inclusive of all randomized patients were similar
* Among symptomatic clinically stable outpatients with COVID-19, treatment with aspirin or apixaban compared with placebo did not reduce the rate of a composite clinical outcome. However, the study was terminated after enrollment of 9% of participants because of an event rate lower than anticipated
* [https://jamanetwork.com/journals/jama/fullarticle/2785218](https://urldefense.com/v3/__https%3A/jamanetwork.com/journals/jama/fullarticle/2785218__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DsKahM22Q$)
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| NEJM - 10/18/2021 - Effect of aspirin in disability-free survival | * A total of 19,114 persons with a median age of 74 years were enrolled, of whom 9525 were randomly assigned to receive aspirin and 9589 to receive placebo. A total of 56.4% of the participants were women, 8.7% were nonwhite, and 11.0% reported previous regular aspirin use.
* The trial was terminated at a median of 4.7 years of follow-up after a determination was made that there would be no benefit with continued aspirin use with regard to the primary end point.
* The rate of the composite of death, dementia, or persistent physical disability was 21.5 events per 1000 person-years in the aspirin group and 21.2 per 1000 person-years in the placebo group (hazard ratio, 1.01; 95% confidence interval [CI], 0.92 to 1.11; P=0.79).
* The rate of adherence to the assigned intervention was 62.1% in the aspirin group and 64.1% in the placebo group in the final year of trial participation.
* Differences between the aspirin group and the placebo group were not substantial with regard to the secondary individual end points of death from any cause (12.7 events per 1000 person-years in the aspirin group and 11.1 events per 1000 person-years in the placebo group), dementia, or persistent physical disability.
* The rate of major hemorrhage was higher in the aspirin group than in the placebo group (3.8% vs. 2.8%; hazard ratio, 1.38; 95% CI, 1.18 to 1.62; **P<0.001)**
* Aspirin use in healthy elderly persons did not prolong disability-free survival over a period of 5 years but led to a higher rate of major hemorrhage than placebo
* [https://www.nejm.org/doi/full/10.1056/NEJMoa1800722?query=featured\_home](https://urldefense.com/v3/__https%3A/www.nejm.org/doi/full/10.1056/NEJMoa1800722?query=featured_home__;!!ECp5tQ!wBINeD6UEjN6tsqGDV-IajyIV8h_LxomNbSgcKqZBKy5SUvBNvhmc4vh8DsyuupIJw$)
 |