

# research



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## Using mobile health intervention to reduce cardiovascular disease risk

**ORIGINAL RESEARCH** Cluster randomised controlled trial

### A village doctor-led mobile health intervention for cardiovascular risk reduction in rural China

Zhang X, Wang S, Zhou X, et al; on behalf of the SMARTER Collaborative Group

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**Study question** How effective is a village doctor-led mobile health (mHealth) intervention in reducing cardiovascular risk among residents in rural China?

**Methods** 4533 participants aged  $\geq 35$  years, with no established atherosclerotic cardiovascular disease but a predicted 10 year risk of  $\geq 10\%$  and who owned a smart phone were enrolled from 127 villages. 2297 (64 villages) participants were randomised to the intervention group and 2236 (63 villages) to the control group. In addition to usual clinical care and basic public health services provided for the control group, the intervention group received a multifaceted mHealth intervention led by village doctors. The main

outcome was mean change in predicted 10 year risk of atherosclerotic cardiovascular disease from baseline to 12 months.

**Study answer and limitations** During the 12 month follow-up (completion rate 99.4%), the intervention group showed larger reductions than the control group in the 10 year risk of atherosclerotic cardiovascular disease ( $-6.3\%$  v  $-4.2\%$ ;  $P < 0.001$ ), as well as lifetime risk of atherosclerotic cardiovascular disease ( $-15.9\%$  v  $-11.0\%$ ;  $P < 0.001$ ), systolic blood pressure ( $-23.2$  mm Hg v  $-15.2$  mm Hg;  $P < 0.001$ ), diastolic blood pressure ( $-10.9$  mm Hg v  $-6.9$  mm Hg;  $P < 0.001$ ), fasting blood glucose ( $-0.9$  mmol/L v  $-0.5$  mmol/L;  $P = 0.008$ ), the proportion of daily smokers ( $-3.1\%$  v  $-0.6\%$ ; odds ratio 0.60, 95% confidence interval 0.43 to 0.84;  $P = 0.003$ ), and insufficient physical activity ( $-3.0\%$  v  $1.3\%$ ; odds ratio 0.63, 0.42 to 0.95;  $P = 0.03$ ). No significant differences were observed for change in non-high density lipoprotein cholesterol or proportion of participants with obesity. As the study did not cover all geographical regions in China, and the counties and villages were not

selected based on a random sampling strategy, the findings might not be representative of the entire country.

**What this study adds** A village doctor-led mHealth intervention is effective at reducing cardiovascular risk and improving control of behavioural and metabolic risk factors. This feasible approach could be scaled up in rural China and other under-resourced settings to improve health management based on the local primary healthcare system.

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**Study registration** [ClinicalTrials.gov](https://clinicaltrials.gov) NCT05645640.



CFOTO/SIPA/ALAMY

## COMMENTARY Technology can support personalised care

Cardiovascular disease is a leading cause of morbidity (40%) and mortality in China.<sup>1</sup> The increasing incidence of risk factors such as hypertension, diabetes, smoking, and poor diet, combined with an ageing population, results in a population with an increased 10 year risk of developing cardiovascular disease.<sup>2</sup>

In their study, Zhang and colleagues used a village doctor-led mobile health (mHealth) intervention for cardiovascular risk reduction in rural China.<sup>3</sup> The SMARTER (Strategy for cardiovascular disease prevention through tailored health Management and its effectiveness Assessment through a cluster Randomised Trial in individuals with Elevated Risk) study was a cluster randomised controlled trial that included 63 villages (2236 participants) in the control group—receiving usual care—and 64 villages (2297 participants) in the intervention group. In addition to usual care, the intervention group received a multifaceted intervention consisting of individual risk assessment by researchers to identify intervention targets, gradual goals based on doctor-participant

communication, short health education videos, monitoring and feedback by weekly reports to the doctors, and gamification for reporting goal progress to the participants. The main outcome was the change in predicted 10 year risk of atherosclerotic cardiovascular disease from baseline to 12 months.

### What did the authors find?

The decrease in 10 year risk of atherosclerotic cardiovascular disease was significantly larger in the intervention group (from 18.0% to 11.7%) compared with the control group (from 17.8% to 13.6%). These results are in line with existing scientific evidence on this topic.<sup>4</sup> An interesting, though expected, observation was that people in the control group also showed a relevant decrease in the 10 year risk. These participants were assessed at baseline for risk factors, and the village doctors acted appropriately, resulting in improved regular care. This finding underlines the importance of a more personalised approach to prevention.

A strength of the offered intervention is its multifaceted nature. mHealth or eHealth applications offer novel opportunities for the prevention, monitoring, and management of cardiovascular risk factors.<sup>5-7</sup> For example, gamification has proved to be more effective than clinic

based prevention programmes.<sup>8</sup> In the SMARTER study, both participants and doctors were actively engaged; participants were encouraged to adopt healthier lifestyles, whereas doctors were nudged to optimise clinical decision making, such as prescribing medication. Nudging in this context has been proved to be an effective method to make better decisions that comply with evidence based guidelines and patient safety.<sup>9</sup> Indeed, the intervention showed a positive effect on the prescription behaviour of the village-led doctors and on adherence to medication. In addition, physical activity increased significantly in the intervention group compared with control group, and therefore there might be a relation between those outcomes.<sup>10,11</sup> However, it could be argued that including more recent mHealth innovations (eg, multimodal objective sensing, prediction modelling, clinical decision support systems, dynamically tailored coaching, or embodied conversational agents) could further benefit health and behavioural outcomes. The use of (real time) data for example not only provides greater insight into the dynamics of health behaviour but also allows for more dynamically tailored mHealth,<sup>12</sup> which are more effective in promoting health behaviours with sustained long term effects.<sup>13</sup>

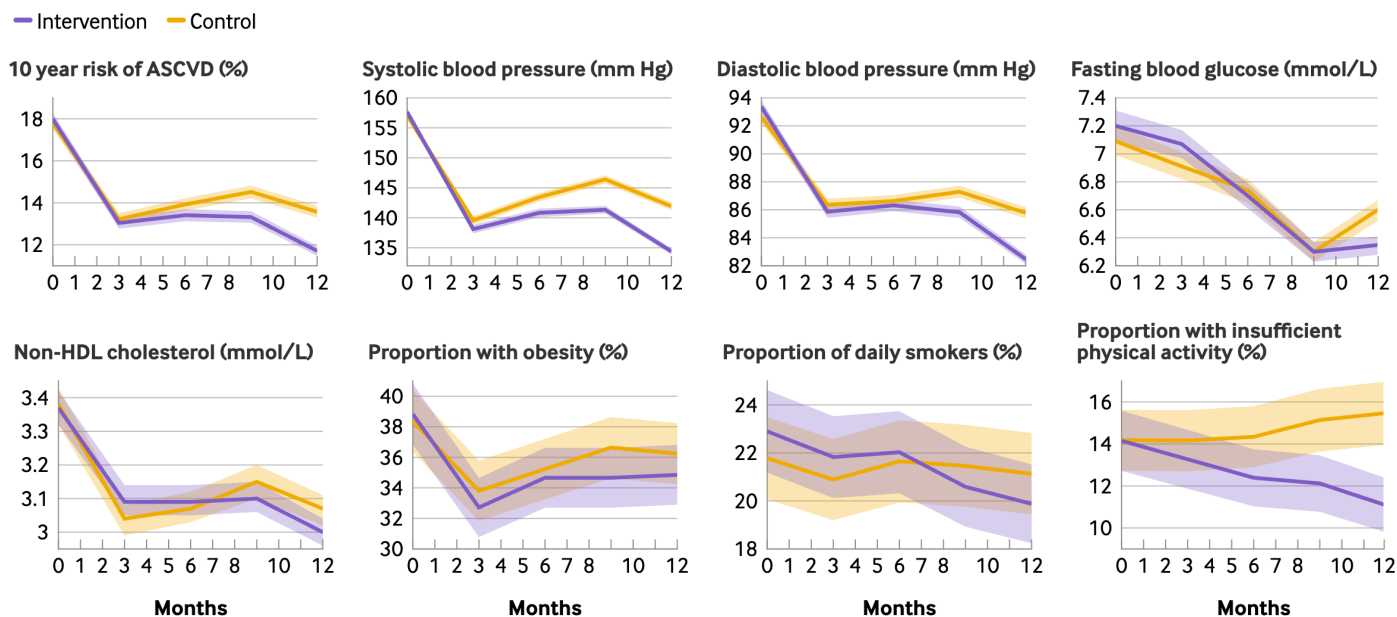
In the doctor-led intervention, the

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Trends in control of cardiovascular risk factors during follow-up in participants assigned to village doctor-led mobile health intervention on cardiovascular risk reduction or to usual clinical care and basic public health services. Shaded areas represent 95% confidence intervals. SMARTER=Strategy for cardiovascular disease prevention through tailored health Management and its effectiveness Assessment through a cluster Randomised Trial in individuals with Elevated Risk. An interactive version of this graphic is available at <https://public.flourish.studio/visualisation/22895185>



village doctor had to perform (additional) tasks, including the forwarding of health education videos to participants and providing gifts, such as washing powder, to patients if they achieved their health promotion goals. Doctors worldwide are overburdened by the relatively large proportion of people at increased risk of cardiovascular diseases.<sup>14,15</sup> Besides the technological possibilities for reducing doctors' workload, future interventions might also benefit from optimising implementation in the healthcare processes. Such implementation strategies should focus on identifying important

stakeholders, structures, and processes within daily practice.<sup>16</sup> Comprehensive training on integrating digital care into standard practice is also essential. Not only the findings of the SMARTER study but also those of previous research highlight the lack of adequate training for doctors on how to apply digital health interventions in current standard of care.<sup>17,18</sup>

#### Next steps

A strong point of Zhang and colleagues' study was the large representative sample of rural Chinese residents, which enhances the generalisability and applicability of

### Further research could focus on more technology supported personalised care and efficient implementation in daily practice

the findings to this population. The extent to which these results can be extrapolated beyond rural China remains debatable. Further research should also be performed in other healthcare systems, and with outcome measures that also provide insight into intervention mechanisms, efficiency, cost effectiveness, and use in daily practice, to gain further evidence for scalability.

In summary, Zhang and colleagues developed an innovative mHealth management strategy that significantly reduced the 10 year risk of atherosclerotic cardiovascular disease in rural China. We eagerly await possible 10 year results of this trial to gain insight into the lasting effects of the intervention on cardiovascular outcomes. Further research could focus on more technology supported personalised care and efficient implementation in daily practice. In this way we could move from a doctor-led to a more participant centred intervention to deal with societal healthcare challenges.

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# Descriptive epidemiology of dementia in the US

ORIGINAL RESEARCH Population based study

## Incidence and prevalence of dementia among US Medicare beneficiaries, 2015-21

Blass B, Ford CB, Soneji S, et al

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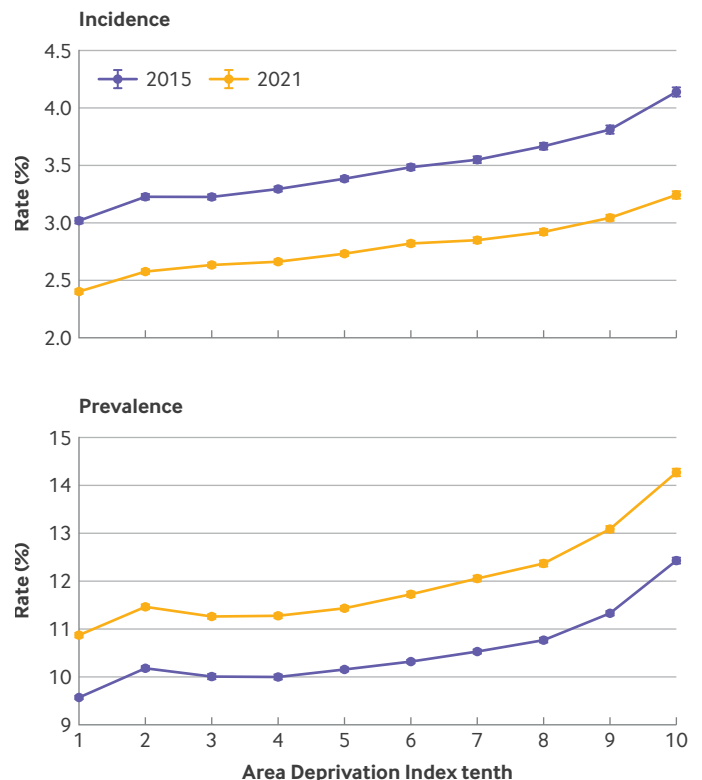
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**Study question** What are the nationwide incidence and prevalence of dementia from 2015 to 2021 among US Medicare beneficiaries?

**Methods** This was a retrospective, nationwide, cross sectional study of US Medicare beneficiaries between 2015 and 2021. The main outcomes were incidence and prevalence of dementia. These metrics were also calculated in key subgroups defined by age, sex, race/ethnicity, and neighbourhood socioeconomic status.

**Study answer and limitations** A total of 5 025 039 incident cases of dementia were documented in 2015-21. The overall age and sex standardised incidence decreased from 3.5% to 2.8% in this period, and prevalence increased from 10.5% to 11.8%. Male beneficiaries had a higher age standardised incidence than did female beneficiaries (3.5% v 3.4% in 2015; 2.9% v 2.6% in 2021). Incidence was highest for black beneficiaries (4.2% in 2015; 3.1% in 2021). The study was limited by including only data from fee-for-service (traditional) Medicare beneficiaries and lacking information on Medicare Advantage beneficiaries, as well as by its reliance on routinely collected dementia diagnoses, which probably do not concord perfectly with gold standard diagnostic practices.

**What this study adds** The incidence of dementia as diagnosed in routine clinical care in the US decreased between 2015 and 2021. Despite decreases in dementia incidence, prevalence continues to rise, with dementia diagnosed in nearly 2.9 million traditional Medicare beneficiaries (around 12%) in 2021. At the same time, a greater burden of disease was observed in marginalised and low resource communities, highlighting the importance of policy approaches to promote equitable dementia care.



Incidence and prevalence rates of dementia, 2015 and 2021, per 1000 person years, by Area Deprivation Index (ADI) tenths, with 10 indicating greatest degree of socioeconomic deprivation

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Population estimates of dementia have, in recent decades, become of national interest to policy makers, politicians, and the wider community. In their study, Blass and colleagues report estimates of the incidence and prevalence of dementia in the US Medicare fee-for-service health insurance system for people aged 66 years and older.<sup>1</sup> Consistent with findings from cross generational cohort studies,<sup>2,3</sup> they found that age standardised incidence of dementia declined from 3.5% in 2015 to 2.8% in 2021 and prevalence increased from 10.5% to 11.8% owing to population ageing. Clear differences existed between subgroups by race/ethnicity and deprivation, but interpreting these differences is not simple using this dataset alone.

Studies that rely on routine data have both strengths and limitations. These include the nature, availability, and configuration of services, who accesses them and how, and how these are recorded, as well as how all can vary across time and between specific communities. This can drive numbers in different directions. The study is based on Medicare fee-for-service claims and does not include Medicare Advantage plans. Non-uniform enrolment and retention of beneficiaries in Medicare fee-for-service by income, race/ethnicity, and underlying health conditions make interpretation of the findings less than straightforward. At face value, the narrowing gap in incidence of dementia by race/ethnicity may suggest that inequalities are decreasing. Conversely, it could be driven, wholly or in part, by growing inequalities in access to healthcare. By 2021, 43% of Medicare beneficiaries, up from 31% in 2015, had enrolled in or switched to Medicare Advantage. People who switched were more likely to be from Hispanic or black minorities and to be in the lower strata of income and education within those groups.<sup>4-7</sup> Compared with their white counterparts, black and Hispanic Medicare Advantage beneficiaries had fourfold to fivefold higher rates of enrolment in special needs plans, indicating severe chronic disease or institutional care.<sup>4</sup> These inequalities suggest that black and



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### The need to tackle life course inequalities and inequities for ethnic minorities and socially deprived communities is vital

Hispanic beneficiaries who were at higher risk of dementia were more likely to opt out of fee-for-service during the study period. This shift may account for, or overestimate, the narrowing gap in dementia incidence by race/ethnicity. Hispanic beneficiaries had the highest and fastest growing enrolment in Medicare Advantage and special needs plans,<sup>4-7</sup> which might explain the lower incidence of dementia in those of them who remained with fee-for-service compared with their white counterparts in 2021.

#### Understanding socioeconomic inequalities

As the marginalised minorities are under-represented in Medicare fee-for-service, true inequalities by area deprivation index are likely to be larger than those reported. Better health monitoring, greater awareness, and diagnosis at an earlier stage could also drive numbers up for the more advantaged groups, further masking socioeconomic inequalities. The geographical variation in estimates of incidence/prevalence is likewise compounded by factors such as regional clustering of the under-represented groups<sup>4,5</sup> and differences in access, quality of care, and attitudes towards diagnosis and treatment. Without accounting for these factors, estimates derived from routine data and insurance claims cannot be taken at face value.

An important policy implication is to ensure that under-representation of marginalised groups in data does not create blind spots that lead to further marginalisation in provision of services for those in greatest need. Dementia estimates have been reported in a range

of data sources,<sup>2,3</sup> including routine data, geographically representative cohorts, volunteer cohorts, and national panels such as the Health and Retirement Study. Numbers of people estimated to be living with dementia are now sensitive metrics.

#### Going forward

Estimates are used globally or nationally for forward planning in almost every proposal for research funding from policy to molecule and to justify investment into the search for a range of potential benefits—from upstream prevention, risk reduction, and effective treatments for proposed underlying causes, to symptomatic approaches, carer research, and later stage support and care. This study highlights a further need. Routine data are subject to diagnostic fashions. Robust descriptive dementia epidemiology requires sustained attention to how we estimate dementia in ageing populations, anchoring through population representative studies and deep dives into unrepresented populations. Comparisons across time must be made using stable methods, along with understanding changes in the biological underpinning of expressed dementia (including protective factors).

The implications of the findings added to those already published, for the US and beyond, are clear. Decline in the occurrence of dementia is not experienced universally. Disadvantage matters, and the need to tackle life course inequalities and inequities for ethnic minorities and socially deprived communities is vital. All the risk factors identified in the Lancet Commission are associated with clustering in such communities.<sup>8</sup> The findings highlight not just the need for improvement in services for people living with dementia in communities where higher incidence and prevalence might be expected, but also the need to implement policies for improvement in risk factor profiles across populations from early life onwards. Politicians and many others are calling for early detection without clear evidence of benefit. Reducing life course inequalities is probably the greatest intervention that any society can do to push morbidity from its risk factors and the syndromal presentation back as close to late life death as possible.

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**Drug treatments for mild or moderate covid-19**

Ibrahim S, Siemieniuk RAC, Oliveros MJ, et al  
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**Study question** How do the effects of drug treatments for mild or moderate (ie, non-severe) covid-19 compare?

**Methods** This systematic review and bayesian network meta-analysis involved a search of several databases and included randomised clinical trials identified between 1 December 2019 and 28 June 2023. Pairs of reviewers independently conducted screening and data abstraction. Risk of bias was assessed using a modification of the Cochrane risk of bias 2.0 tool, and the certainty of the evidence using the

grading of recommendations assessment, development, and evaluation (GRADE) approach. For each outcome, following GRADE guidance, drug treatments were classified in groups from the most to the least beneficial or harmful.

**Study answer and limitations** Of 259 trials enrolling 166 230 patients, 187 (72%) investigating 40 different drug treatments were included in the analysis. Compared with standard care, two drugs probably reduce hospital admission: nirmatrelvir-ritonavir (25 fewer per 1000 (95% credible interval 28 fewer to 20 fewer), moderate certainty) and remdesivir (21 fewer per 1000 (28 fewer to 7 fewer), moderate certainty). Compared with standard care, only lopinavir-ritonavir increased adverse effects leading to discontinuation. The main limitation of the

evidence was serious imprecision. This review did not consider drug specific adverse events.

**What this study adds** Nirmatrelvir-ritonavir and remdesivir probably reduce hospital admission for mild or moderate covid-19, whereas molnupiravir and systemic corticosteroids may reduce hospital admission. Several drugs, including molnupiravir and systemic corticosteroids, probably reduce symptom duration while nirmatrelvir-ritonavir and remdesivir may not.

**Funding, competing interests, and data sharing** This study was supported by the Canadian Institutes of Health Research (grant MM1-174897). The authors report no other competing interests. No additional data available.

**Study registration** This review was not registered. The protocol is publicly available in the supplementary material online.

	Admission to hospital	Mortality	Mechanical ventilation	Adverse events‡	Venous thrombo-embolism	Clinically important bleeding	Length of hospital stay	Time to symptom resolution
Baseline risk*	0.03 per 1000	0.003 per 1000	0.02 per 1000	-	0.008 per 1000	0.003 per 1000	-	9 days
Minimal important difference†	10 per 1000	10 per 1000	15 per 1000	20 per 1000	20 per 1000	20 per 1000	1 day	1 day
(Hydroxy)chloroquine	-1.97 (-11.61 to 11.38)	0.15 (-1.03 to 1.59)	8.72 (-4.34 to 28.73)	10.09 (-2.84 to 23.95)			-0.610 (-2.180 to 0.570)	-0.690 (-1.810 to 0.560)
Colchicine	-5.88 (-14.17 to 4.47)	-1.08 (-1.87 to 0.24)§	-8.08 (-13.96 to 3.45)§	0.75 (-7.39 to 11.78)			0.500 (-1.500 to 2.510)	-1.570 (-3.190 to 0.390)
Corticosteroids (systemic)	-15.99 (-23.93 to -2.63)	0.17 (-1.48 to 1.98)	-3.53 (-12.38 to 11.02)	-0.01 (-14.28 to 14.53)				-3.480 (-5.320 to -1.050)
Fluvoxamine	7.44 (-16.41 to 4.56)	-0.75 (-2.11 to 1.72)	-3.37 (-12.32 to 11.49)	36.68 (-6.66 to 79.88)				-0.090 (-2.910 to 3.600)
IL-6 receptor antagonists		213.37 (-3.0 to 996.99)						
Ivermectin	-4.02 (-11.4 to 5.35)	-0.69 (-1.64 to 0.59)	-6.52 (-12.14 to 1.12)	5.74 (-1.1 to 16.07)			-0.400 (-1.800 to 0.950)	-0.690 (-1.660 to 0.370)
JAK inhibitors		-0.66 (-2.0 to 1.53)	-12.46 (-17.53 to -2.98)					
Lopinavir-ritonavir	-2.57 (-16.79 to 20.62)	1.11 (-0.49 to 3.81)	2.81 (-10.45 to 27.33)	41.46 (15.1 to 68.29)			1.770 (0.340 to 3.190)§	4.440 (-0.580 to 12.540)¶
Molnupiravir	-9.82 (-16.66 to -2.28)	-2.23 (-2.78 to -1.19)	-10.96 (-17.36 to 1.69)	-0.5 (-8.59 to 6.08)				-2.340 (-3.450 to -1.070)
Nirmatrelvir-ritonavir	-24.99 (-27.86 to -20.19)	-2.25 (-2.8 to -1.15)	-0.92 (-12.37 to 17.65)	-5.6 (-18.05 to 8.63)			-0.500 (-2.620 to 1.430)	0.200 (-2.960 to 4.420)
Remdesivir	-20.93 (-27.79 to -6.69)	-0.71 (-1.75 to 0.87)	-5.82 (-12.53 to 3.0)	9.3 (-5.8 to 25.4)			0.640 (-1.040 to 2.340)	-0.560 (-2.890 to 2.370)
VV116		313.73 (-3.0 to 997.0)		-13.07 (-39.58 to 14.62)				0.360 (-3.800 to 6.590)

Among most beneficial      Intermediate benefit      Not convincingly different than standard care      Harmful

High/moderate certainty  
 Low certainty  
 Very low certainty  
 No evidence

High/moderate certainty				
Low certainty				
Very low certainty				
No evidence				

\*Expected risk of each outcome with standard care. Numbers in coloured cells are estimated risk differences (95% CI) per 1000 patients or mean difference (95% CI) in days when compared with standard care  
 † Minimal important differences were used to support judgments of imprecision  
 ‡ This outcome was analysed as a risk difference due to low number of events  
 § Best estimate of effect was obtained from direct evidence  
 ¶ Best estimate of effect was obtained from indirect evidence

**Summary of effects of selected drug treatments compared with standard care for mild and moderate covid-19. IL-6=interleukin-6; JAK=Janus kinases**

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