

# research



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## ORIGINAL RESEARCH Systematic analysis of the Global Burden of Disease Study 2019

### Global burden of type 2 diabetes in adolescents and young adults, 1990-2019

Xie J, Wang M, Long Z, et al

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**Study question** What is the global burden of type 2 diabetes in people aged 15-39 years, especially in less developed regions and countries?

**Methods** Data were from the Global Burden of Disease Study 2019 (Injuries and Risk Factors Collaborators). Age standardised incidence rate, age standardised disability adjusted life years (DALY) rate, and age standardised mortality rate were calculated based on a standard population. Joinpoint regression was used to estimate the secular trend from 1990 to 2019.

Proportional DALY attributable to different risk factors were also estimated.

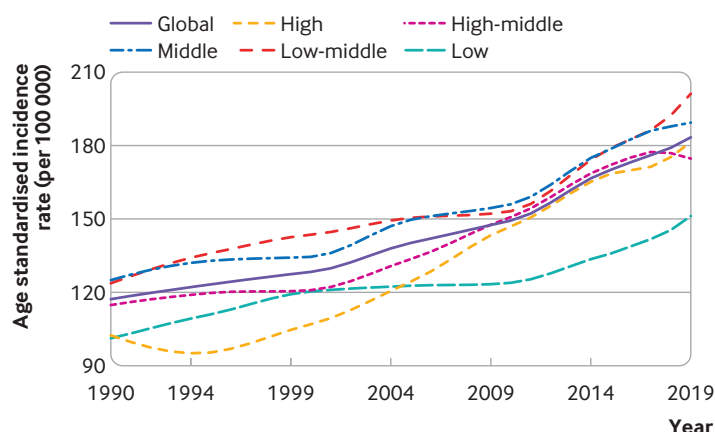
**Study answer and limitations** From 1990 to 2019, significant increases in age standardised incidence rate and age standardised DALY rate were found for type 2 diabetes in adolescents and young adults globally ( $P<0.001$ ). Age standardised incidence rate (per 100 000 population) increased from 117.22 (95% CI 117.07 to 117.36) in 1990 to 183.36 (183.21 to 183.51) in 2019, and age standardised DALY rate (per 100 000 population) increased from 106.34 (106.20 to 106.48) in 1990 to 149.61 (149.47 to 149.75) in 2019. The age standardised mortality

rate (per 100 000 population) was modestly increased, from 0.74 (0.72 to 0.75) in 1990 to 0.77 (0.76 to 0.78) in 2019. The greatest burdens were in countries with a low-middle and middle sociodemographic index. Women generally had higher mortality and DALY rates than men before age 30. A high body mass index was consistently found to be a leading risk factor worldwide, although the patterns of attributable risk factors varied across regions. The different types of diabetes were not available in many studies, and diagnosis criteria varied across studies. Children and adolescents aged <15 years were not included in the analysis.

**What this study adds** Early onset type 2 diabetes is a growing global health problem in adolescents and young adults, especially in countries with a low-middle and middle sociodemographic index. Effective measures to deal with type 2 diabetes at the global, regional, and national levels are needed. Weight control and management are essential to reduce the burden of early onset type 2 diabetes.

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No competing interests declared. Raw data can be obtained from <http://ghdx.healthdata.org/gbd-results-tool>.



Global burden of type 2 diabetes in people aged 15-39 years by sociodemographic index of country, 1990-2019

# Awake prone positioning and covid-19

## ORIGINAL RESEARCH Systematic review and meta-analysis of randomised trials

### Efficacy of awake prone positioning in patients with covid-19 related hypoxaemic respiratory failure

Weatherald J, Parhar KKS, Al Duhailib Z, et al

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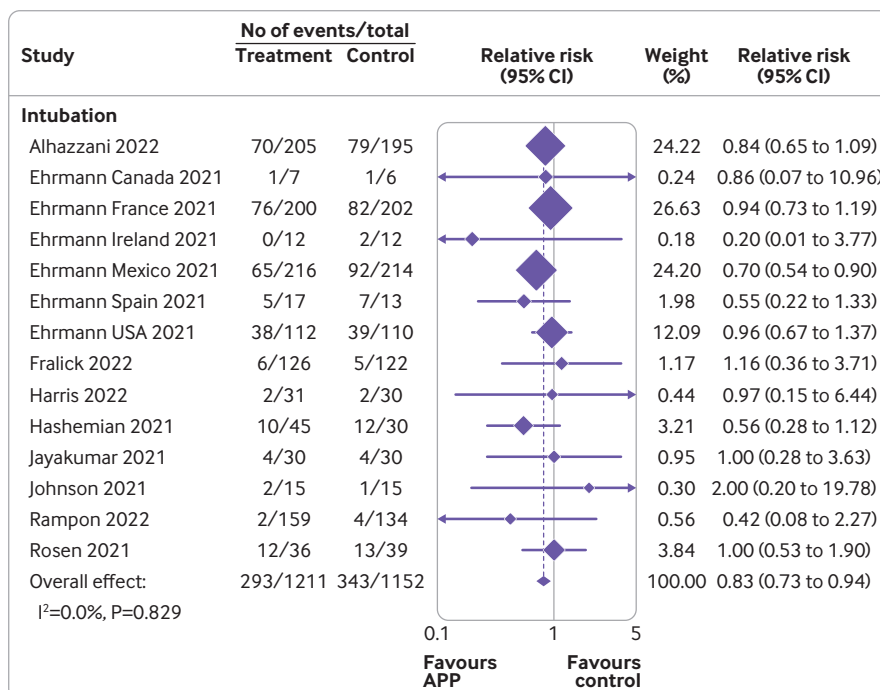
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**Study question** What is the efficacy and safety of awake prone positioning compared with usual care in non-intubated adults with hypoxaemic respiratory failure due to covid-19?

**Methods** This systematic review and meta-analysis assessed randomised trials comparing awake prone positioning with usual care in adults with covid-19 related hypoxaemic respiratory failure. The primary outcome was endotracheal intubation. Secondary outcomes were mortality, ventilator-free days, intensive care unit and hospital length of stay, escalation of oxygen modality, change in oxygenation and respiratory rate, and adverse events. The primary analysis used a random effects meta-analysis. Secondary bayesian analyses were performed for the endotracheal intubation and mortality outcomes.

**Study answer and limitations** 17 trials (2931 patients) were included. Awake prone positioning reduced the risk of endotracheal intubation compared with usual care (crude average 24.2% v 29.8%, relative risk 0.83, 95% confidence interval 0.73 to 0.94; high certainty) but had little to no effect on mortality (15.6% v 17.2%, 0.90, 0.76 to 1.07; high certainty) or other secondary outcomes. On average, awake prone positioning resulted in 55 fewer intubations per 1000 patients (95% confidence interval 87 to 19 fewer intubations). Adverse events related to awake prone positioning were uncommon. The secondary bayesian analysis supported the primary results, suggesting a high probability of benefit for endotracheal intubation and a low probability of benefit for mortality. A limitation was that assessment of subgroups at trial level, not individual participant level, may have underpowered these analyses.

**What this study adds** Awake prone positioning compared with usual care reduces the risk of endotracheal intubation in adults with hypoxaemic respiratory failure due to covid-19 but evidence for the effect on mortality or other outcomes was inconclusive.



Forest plot for awake prone positioning compared with usual care for intubation in adults with hypoxaemic respiratory failure due to covid-19. Intubation was assessed at 28 days in the Ehrmann trials, any time during hospital admission in the Johnson and Fralick trials, 30 days in the Alhazzani, Rosén, and Harris trials, and 14 days in the Rampon trial. Jayakumar and Hashemian trials did not specify times

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Study registration PROSPERO CRD42022314856.



GABRIEL KUCHTA/GETTY IMAGES

## COMMENTARY Prone positioning reduces intubation for patients with hypoxaemia

In their paper, Weatherald and colleagues offer the most up-to-date evidence synthesis evaluating the use of awake prone positioning in adults with covid-19 related hypoxaemia,<sup>1</sup> finding that awake prone positioning reduced the risk of endotracheal intubation but not mortality. Their systematic review and meta-analysis was performed more than 40 years after a 1976 study observed that prone positioning improved oxygenation in five patients who were mechanically ventilated for acute respiratory distress syndrome (ARDS).<sup>2</sup> A year later another study described similar effects in five patients with ARDS who were mechanically ventilated and also found that prone positioning allowed intubation to be deferred in one patient who was breathing spontaneously.<sup>3</sup> In subsequent clinical trials, prone positioning was found to reduce mortality in patients with moderate-to-severe ARDS who were mechanically ventilated, particularly in trials that targeted a duration of prone positioning for more than 12 hours daily.<sup>4,5</sup>

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### The reduction in intubation was driven mainly by trials that achieved longer duration of prone positioning

In the decades that followed the observation in a single spontaneously breathing patient, the use of awake prone positioning remained limited. The covid-19 pandemic urgently resurfaced questions about the utility of prone positioning, given the surges in patients with hypoxaemia, the limited treatment options, and the constrained supply of ventilators. A series of small observational reports replicated the prepandemic observations, suggesting that awake prone positioning might improve oxygenation.<sup>8</sup> Despite the lack of high quality evidence, awake prone positioning was eagerly adopted for patients with covid-19 related hypoxaemia worldwide.<sup>9</sup>

With the inclusion of 17 randomised trials involving 2931 patients, Weatherald and colleagues captured several studies that were published after another recent systematic review and meta-analysis.<sup>10</sup> The results of both meta-analyses are similar, showing that awake prone positioning in patients with covid-19 related hypoxaemia reduces the need for endotracheal intubation. Prone positioning had no significant effect on mortality, although these results were inconclusive (relative risk 0.90, 95% confidence interval 0.76 to 1.07) and do not rule out the possibility that a mortality effect could emerge in future studies.

### Reassuring safety data

In clinical trials with selected populations and increased monitoring, awake prone positioning was found to be safe, with infrequent dislodgement of vascular catheters (2.5%) and skin breakdown or ulcers (0.7%).<sup>1</sup> It is worth noting that participants and clinicians could not be masked and this could bias decisions about intubation. Whether due to bias or physiological effects, high quality evidence now shows that awake prone positioning can safely reduce endotracheal intubation in patients with covid-19 related hypoxaemia without increasing the risk of mortality.

The reduction in intubation was driven mainly by trials that achieved longer duration of prone positioning (median  $\geq 5$

hours per day), targeted patients with more severe hypoxaemia, and focused on patients requiring high flow oxygen or non-invasive ventilation. It is not possible to distinguish which of these features is more important based on the current trial evidence. The cut-points used to define these subgroups were chosen based on post hoc observations in those two large studies and should be interpreted cautiously as they may not have specific physiological significance. Nevertheless, prone positioning in patients receiving mechanical ventilation for ARDS is also most beneficial in those with more severe hypoxaemia and longer duration of prone positioning,<sup>4</sup> strengthening the plausibility of these findings.

### Difficult for patients

Overall, patients with covid-19 related hypoxaemia find it difficult to tolerate awake prone positioning—the patients in Weatherald and colleagues' analyses spent a median of just 2.8 hours (interquartile range 2.2–5) daily prone despite careful patient selection and many trials targeting at least six hours of prone positioning daily. Trials used numerous potentially resource intensive strategies to help improve adherence, including frequent reminders to patients and clinical staff<sup>11–13</sup> and 24 hour availability of an intensivist.<sup>11</sup> Since the benefits of prone positioning in patients with covid-19 may be confined to those needing more advanced respiratory support and with more severe hypoxaemia, it may be wise to focus efforts on these subgroups.

Several unanswered questions remain, including the ideal daily duration of treatment, the level of hypoxaemia that should prompt prone positioning, and how best to improve patient comfort and encourage adherence. These questions may never be answered definitively in patients with covid-19 as, fortunately, far fewer are experiencing hypoxaemic respiratory failure or critical illness.<sup>14</sup> The pandemic should, however, renew interest and encourage further evaluation of awake prone positioning—an intervention that may benefit a wide range of patients with hypoxaemia.

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## ORIGINAL RESEARCH Two independent, pragmatic, randomised controlled trials

### Eczema Care Online behavioural interventions to support self-care for children and young people

Santer M, Muller I, Becque T, et al

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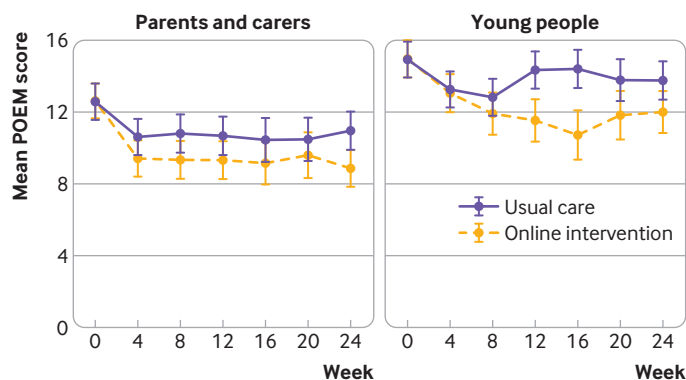
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**Study question** Can self-management behavioural interventions delivered online for parents and carers of children with eczema and young people with eczema improve outcomes?

**Methods** Two independent randomised controlled trials were performed: one for parents and carers of children (0-12 years) with eczema and the other for young people (13-25 years) with eczema, with recruitment through 98 general practices in England. Participants were randomly assigned to receive usual eczema care alone or to receive usual care plus an online behavioural intervention for eczema (Eczema Care Online). The primary outcome was eczema severity measured using the Patient-Oriented Eczema Measure (POEM score, range 0-28, with 28 representing very severe eczema) every four weeks for 24 weeks.

**Study answer and limitations** 340 parents or carers of children (169 usual care; 171 intervention) and 337 young people (169 usual care; 168 intervention) were randomly assigned. All randomly assigned participants were included in the analyses. At 24 weeks, follow-up rates were 91.5% (311/340) for parents or carers and 90.2% (304/337) for young people. After controlling for baseline eczema severity and confounders, compared with usual care over 24 weeks, eczema severity improved in the intervention groups: mean difference -1.5 (95% confidence interval -2.5 to -0.6;  $P=0.002$ ) for parents or carers and -1.9 (-3.0 to -0.8;  $P<0.001$ ) for young people. No harms were identified in either group. Although improvements over 24 weeks were less than the target of 2.5 points on the POEM, effects were sustained to 52 weeks. The number needed to treat to achieve a 2.5 difference in POEM score at 24 weeks was 6 in both trials.

**What this study adds** Online behavioural interventions supporting eczema self-management offered in addition to usual care led to sustained benefits in eczema severity in children and young people. This small but statistically significant improvement is particularly valuable given the low cost and high scalability of the interventions and absence of identifiable harms.



Mean Patient-Oriented Eczema Measure (POEM) scores for eczema severity to 24 weeks in parent and carer trial and young people trial



PAUL WHITEHILL/SPL

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Trial registration ISRCTN registry ISRCTN79282252.

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