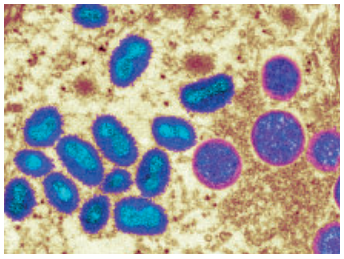
research

Covid-19 vaccination during pregnancy, and neonatal outcomes p 271



2022 Human monkeypox outbreak in London p 272

Reducing sitting time in office workers p 274

ORIGINAL RESEARCH Population based retrospective cohort study

Risk of preterm birth, small for gestational age at birth, and stillbirth after covid-19 vaccination during pregnancy

Fell DB, Dimanlig-Cruz S, Regan AK, et al

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Study question Is covid-19 vaccination during pregnancy associated with risk of preterm birth, small for gestational age at birth, and stillbirth?

Methods Provincial databases in Ontario, Canada, were used to identify all liveborn and stillborn infants of gestational age ≥20 weeks or birth weight ≥500 g (birth registry), linked to data on covid-19 vaccination data (vaccine registry) for births between 1 May and 31 December 2021. The exposure measure was covid-19 vaccination during pregnancy (ie, vaccine administered between the estimated date of conception up to one day before birth). The main outcome measures were preterm birth before 37 weeks, small for gestational age at birth (<10th centile), and stillbirth (fetal death at ≥20 weeks).

Study answer and limitations Among 85 162 births, more than 43 099 (50.6%) occurred in individuals who received one dose or more of a covid-19 vaccine (99.7% received an mRNA vaccine) during pregnancy. Vaccination during pregnancy was not associated with any increased risk of overall preterm birth (6.5% among vaccinated *v* 6.9% among unvaccinated; adjusted hazard ratio 1.02, 95% confidence interval 0.96 to 1.08), spontaneous preterm birth (3.7% *v* 4.4%; 0.96, 0.90 to 1.03), or very preterm birth (0.59% *v* 0.89%; 0.80, 0.67 to 0.95). No increase was found in risk of small for gestational age at birth (9.1% *v* 9.2%; 0.98, 0.93 to 1.03) or stillbirth (0.25% *v* 0.44%; 0.65, 0.51 to 0.84). The study was restricted to assessment of mRNA vaccine products, as use of other covid-19 vaccine types in the pregnant population in Canada has been limited. It was not possible to evaluate booster doses because pregnant Ontario residents were not eligible until December 2021, and most of these pregnancies were still ongoing.

Association between covid-19 vaccination during pregnancy and study outcomes

Outcomes	No vaccine (n=42 063)	≥1 vaccine dose* (n=43 099)
Preterm birth <37 weeks	n=41 879	n=42 992
No with outcome (rate/100 live births)	2907 (6.9)	2812 (6.5)
Adjusted hazard ratio (95% confidence interval)	1.00	1.02 (0.96 to 1.08)
Small for gestational age at birth†	n=40 280	n=41 333
No with outcome (rate/100 singleton live births)	3722 (9.2)	3743 (9.1)
Adjusted hazard ratio (95% confidence interval)	1.00	0.98 (0.93 to 1.03)
Stillbirth	n=42 063	n=43 099
No with outcome (rate/100 live births and stillbirths)	184 (0.44)	107 (0.25)
Adjusted hazard ratio (95% confidence interval)	1.00	0.65 (0.51 to 0.84)

*Vaccination treated as time varying exposure within outcome specific risk windows. Hazard ratios adjusted using stabilised inverse probability of treatment weights, trimmed at 0.01st and 99.99th centiles. Maternal age (continuous variable) added to adjusted models as it remained imbalanced between the two groups after weighting.
†885 records excluded from analysis (34 with gestational age below or above values in reference standard for small for gestational age at birth, 851 with missing information on infant sex and/or birth weight).

What this study adds This study adds to growing evidence that covid-19 vaccination during pregnancy is not associated with higher risks of adverse birth outcomes.

Funding, competing interests, and data sharing Funded by the Public Health Agency of Canada, through the Vaccine Surveillance Reference Group and the COVID-19 Immunity Task Force. No competing interests declared. Although the dataset is held securely, the analytical doc may be available on request.

The changing face of monkeypox

ORIGINAL RESEARCH Descriptive case series

FAST TRACK

Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak

Patel A, Bilinska J, Tam JCH, et al

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Study question What are the clinical presentations of monkeypox infection in humans in the 2022 outbreak?

Methods The study reviewed the clinical features of 197 participants with polymerase chain reaction confirmed monkeypox infection at a regional high consequences infectious disease centre and affiliated sexual health services in south London between May and July 2022.

Study answer and limitations The median age of participants was 38 years. All 197 participants were men, and 196 identified as gay, bisexual, or other men who have sex with men. All presented with mucocutaneous lesions, most commonly on the genitals (111 participants, 56.3%) or in the perianal area (82, 41.6%). 170 (86.3%) participants reported systemic illness, with the most common symptoms being fever (122, 61.9%), lymphadenopathy (114, 57.9%), and myalgia (62, 31.5%). Rectal pain (71, 36.0%) and penile oedema (31, 15.7%) were frequent presentations and the most common reason for hospital admission. Participants also presented with solitary lesions and biphasic appearances of lesions, and a variable temporal association was found between mucocutaneous and systemic features. Other atypical features included tonsillar lesions, maculopapular rash, and abscesses. See full paper on bmj.com for images of the novel presentations. Limitations of this study are the retrospective design, observational nature, potential variability of clinical record keeping, and data limited to a single centre.

What this study adds The clinical features and variable temporal progression of monkeypox infection observed in humans during the 2022 London outbreak suggest a change from the classic disease description. Common symptoms are currently not included in public health messaging, including rectal pain and penile oedema. Data characterising clinical presentations, progress, and management of these cases are urgently needed to help guide management and the response to the outbreak.

Funding, competing interests, and data sharing No funding received. No competing interests declared. Anonymised data are available on reasonable request.

COMMENTARY What should patients and clinicians look out for?

More than 50 years ago the then US Surgeon General allegedly stated that we could "close the book on infectious diseases, declare the war against pestilence won and shift national resources to such chronic problems as cancer and heart disease."[1]

Instead, we continue to reel from the emergence of viral threats, including HIV and AIDS, Ebola virus disease, covid-19, and now an international outbreak of monkeypox. But not monkeypox as we know it, as Patel and colleagues report in a series of 197 patients from the UK.[2]

The striking new distribution of clinical features and presentations reported in their paper differs from previously characterised outbreaks in the Democratic Republic of Congo[3] and Nigeria.[4] These changes may well lead to delayed diagnoses and avoidable onward transmission. Four out of five patients in the series sought care within the national network of genitourinary medicine clinics, established more than a century ago. A large proportion of these clinics' workload is to encourage men who have sex with men to access regular testing for sexually transmitted diseases; vaccines, including for hepatitis B and human papillomavirus; and drug prophylaxis for HIV in accordance with risk.

The striking new distribution of clinical features and presentations differs from previously characterised outbreaks

These clinics have emerged as the mainstay of outpatient risk assessment and testing for monkeypox, with disease in the remaining patients being diagnosed in hospital or through emergency departments. However, not all men who have sex with men will identify as being at risk, or will disclose this behavioural information to healthcare providers, or indeed recognise personal risk of exposure.[5]

Key features

So, what are the key features of monkeypox that every clinician should be aware of? Patel and colleagues report a strikingly high frequency of penile, perianal, and rectal symptoms, with or without initial skin lesions, and also penile oedema, rectal pain, and pain on defecation. Unlike in classic descriptions of monkeypox, the lesion count is often low at presentation, and atypical single lesions can mimic abscesses and other deep tissue phenomena. Sore throat, sometimes with tonsillar abscesses, occurs in a minority of patients, and is often severe.

A biphasic timing of clinical features can also complicate diagnosis—patients in this study often had skin lesions at different phases of development. Systemic symptoms also differed from those of earlier outbreaks, with expected prodromal symptoms often absent and instead emerging with or after skin signs and other symptoms. The 10th of patients admitted to hospital for supportive treatment largely required pain relief and symptom control for penile swelling and rectal pain, some experiencing substantial secondary bacterial infection.

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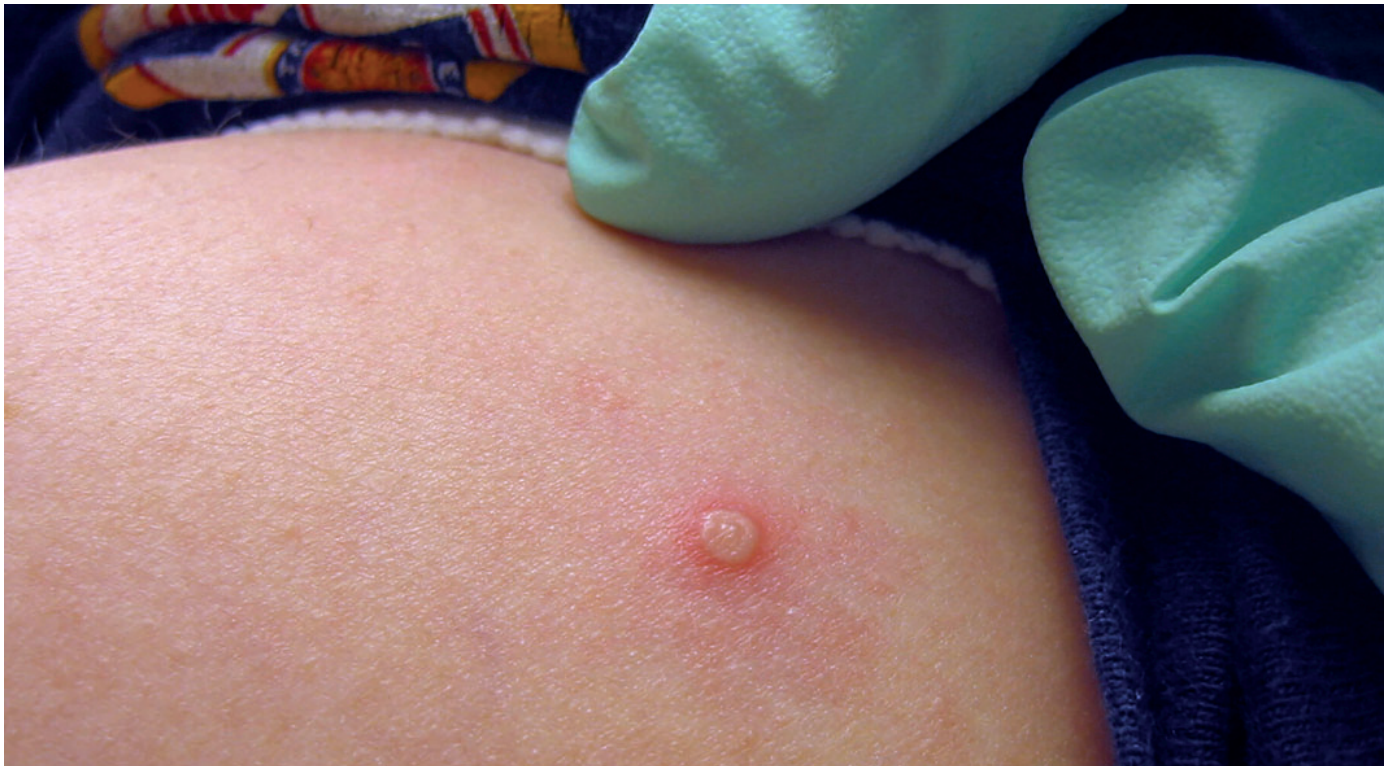

The UK Health Security Agency has updated its case definition as the outbreak has evolved,[6] and a responsive approach will continue to be essential. Widespread awareness among clinicians of these emerging presentations will be even more important in the many jurisdictions globally where specialised genitourinary medicine services are not widely available.

Patel and colleagues' study confirms the importance of testing people with monkeypox for sexually transmitted infections (STIs).[7] Alternative causes of penile and rectal symptoms were common—an STI was also diagnosed in more than three in 10 patients. Interestingly, half of men testing negative for monkeypox virus were found to have an STI accounting for their symptoms, most frequently herpes simplex, syphilis, or gonorrhoea.

Prevention in the form of targeted vaccination to break transmission chains offers hope for the control of the UK's current outbreak if challenges in supply and distribution of smallpox vaccines can be overcome. Smallpox vaccines provide cross protection against monkeypox. The new study corroborates other evidence that infections are occurring predominantly among higher risk men who have sex with men.[9] This pattern enables vaccine prioritisation, which may need flexibility if and when new at risk groups emerge.[10] Vaccination must be delivered sensitively to avoid the kind of stigmatising public health messaging used early in the HIV epidemic. Creative approaches will be needed to ensure equitable distribution to people at risk who have poorer access to services or health literacy, both in the UK and globally.[11]

The distribution of cases, clinical characteristics, and patterns of accessing care seen in this study confirms a central role for genitourinary medicine clinics in the response to monkeypox, including contact tracing. Investment is urgently required. Wider sexual health services are being limited as resources are reoriented to the monkeypox response, causing major concern for public health leaders in the UK.[12]

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Effectiveness of an intervention for reducing sitting time and improving health in office workers

Edwardson CL, Biddle SJH, Clemes SA, et al

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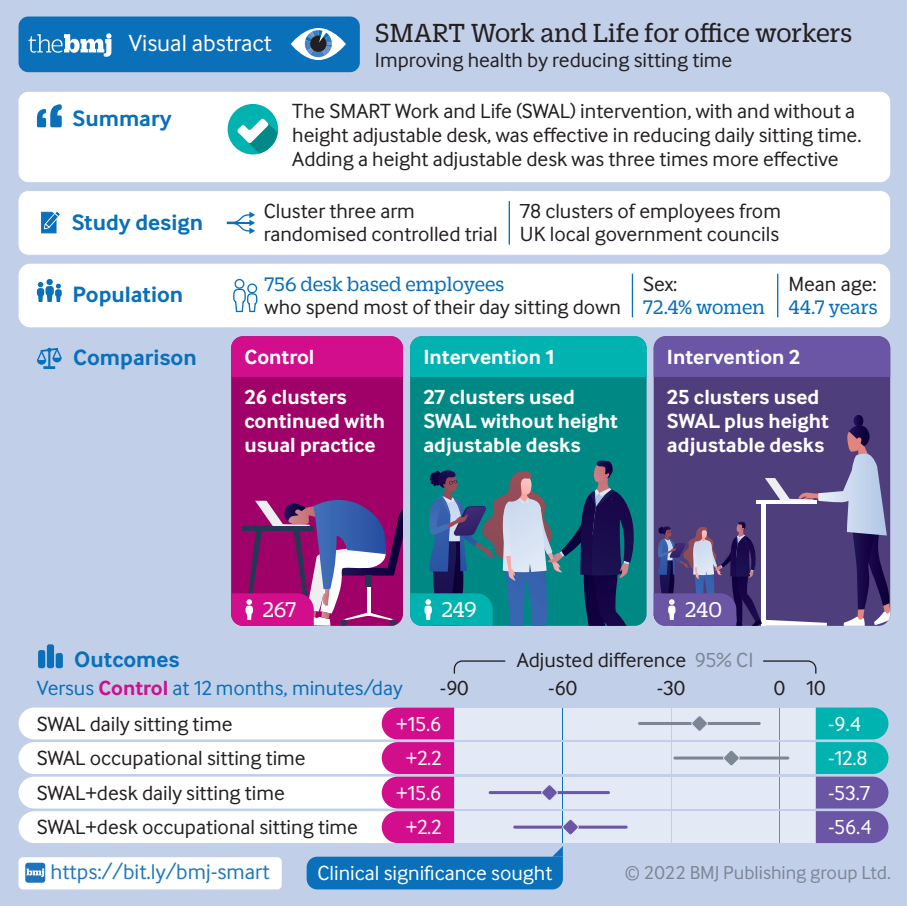
Study question How effective is an intervention delivered with and without a height adjustable desk at reducing daily sitting time at 12 months compared with usual practice?

Methods The SMART Work and Life (SWAL) intervention was designed to reduce sitting time both at work and outside of work. SWAL includes organisational, environmental, group, and individual strategies and is delivered by a workplace champion. A cluster randomised controlled trial was performed to examine the effectiveness of the interventions. 756 office workers were recruited from local councils in Leicester, Liverpool, and Greater Manchester, with participants grouped into 78 clusters (office groups). Each cluster was randomised to one of three conditions: SWAL, SWAL with a height adjustable desk, and usual practice (control). Data were collected at baseline, with follow-up measurements at three and 12 months. The primary outcome was daily sitting time, assessed by a thigh worn accelerometer.

Study answer and limitations Mean age of participants was 44.7 years, 72.4% (n=547) were women, and 74.9% (n=566) were white. Daily sitting time at 12 months was significantly lower in the intervention groups (SWAL −22.2 min/day, 95% confidence interval −38.8 to −5.7 min/day, P=0.003; SWAL plus desk −63.7 min/day, −80.1 to −47.4 min/day, P<0.001) compared with the control group. The SWAL plus desk intervention was found to be more effective than SWAL at changing sitting time (−41.7 min/day, −56.3 to −27.0 min/day, P<0.001). As participants worked in local government, the results might not be generalisable to other employment sectors.

What this study adds Both SWAL and SWAL plus desk were associated with a reduction in sitting time, although the addition of a height adjustable desk was found to be threefold more effective.



Funding, competing interests, and data sharing
This project was funded by the National Institute for Health and Care Research public health research programme.

See full paper on bmj.com for competing interests. Requests for access to data should be sent to the corresponding author (ce95@le.ac.uk).

Study registration ISRCTN Registry ISRCTN11618007.

Changes in daily sitting time using data from any valid days at 12 months in participants randomised to the SMART Work and Life (SWAL) intervention with or without a desk or to usual practice (control)

Primary outcome	Mean (SD) at baseline			Mean (SD) change from baseline to follow-up			Adjusted mean difference at follow-up (95% CI); P value		
	Control	SWAL	SWAL+desk	Control	SWAL	SWAL+desk	SWAL *v* control	SWAL+desk *v* control	SWAL+desk *v* SWAL
Sitting time (min/day)*†	596.5 (84.1)	601.7 (80.9)	610.4 (78.7)	15.6 (75.0)	−9.4 (80.5)	−53.7 (79.1)	−22.2 (−38.8 to −5.7); 0.003†	−63.7 (−80.1 to −47.4); <0.001†	−41.7 (−56.3 to −27.0), <0.001

SD=standard deviation; CI=confidence interval.

*Control 26 clusters (183 participants), SWAL 27 (177), SWAL plus desk 25 (187).

†≥1 valid day at baseline and 12 months. Adjusted for respective average daily outcome at baseline, average wear time of monitor during waking hours across baseline and 12 months, and stratification factors of area (Leicester, Liverpool, Greater Manchester) and cluster size category (small <10, large ≥10).