Clinical Trials Update

Financial Vouchers Led to Higher Smoking Abstinence During Pregnancy
A financial voucher of £400, equivalent to about US $400, was a highly effective incentive for pregnant participants in a recent clinical trial to stop smoking. But most of the participants took up smoking again within 6 months after they delivered.

The 941 participants were recruited from 7 stop-smoking services in England, Northern Ireland, and Scotland. The patients, who reported smoking at least 1 cigarette in the last week at their first maternity visit, were randomly assigned to an intervention or control group. Both groups were offered the usual stop-smoking support, including counseling and free nicotine-replacement therapy. The intervention group also received up to US $450 in shopping vouchers if they set a quit date and remained smoke-free throughout pregnancy. The trial results were reported in The BMJ.

By late pregnancy, 26.8% of the intervention group had stopped smoking vs 12.3% of the control group. There was no significant difference in birth weights among infants delivered in the 2 groups or in severity of preterm birth. Six months after giving birth, however, only 5.7% of the intervention group and 4.4% of the control group were smoke-free. An ongoing trial is continuing financial incentives 12 months postpartum to evaluate whether longer-term smoking abstinence rates can be improved.

Two recent trials conducted in the US also showed that financial incentives improved smoking-cessation results among pregnant and newly postpartum patients, the authors noted.

Intranasal COVID-19 Vaccine Disappointing in First-in-Human Trial
The first-in-human study of intranasal COVID-19 vaccination with an adenovirus-vector vaccine did not induce a consistent mucosal antibody response or a strong systemic response.

The first part of the phase 1 trial included 30 healthy adults who had never received a SARS-CoV-2 vaccine. The intranasal (IN) vaccination tested in the trial used the existing formulation of the ChAdOx1 nCoV-19 intramuscular (IM) vaccine developed by University of Oxford/AstraZeneca. Participants received either a low dose, mid dose, or high dose of the IN vaccine. The volunteers were then randomly assigned to receive 1 dose or 2 doses. The 2-dose group received their second IN vaccination 28 days later.

A second phase of the study investigated IN vaccination as a booster. Twelve participants received a single high-dose IN vaccination after receiving 2 IM doses of either ChAdOx1 nCoV-19 or BNT162b2 (Pfizer/BioNTech) at least 12 weeks previously.

The IN vaccine had an acceptable safety and tolerability profile, but immune responses were weak and inconsistent, according to results reported in eBioMedicine. Antigen-specific mucosal antibody responses were detected in only a minority of participants, rarely exceeding levels seen after SARS-CoV-2 infection. Systemic responses to intranasal vaccination were typically weaker than after IM vaccination. IN vaccination also did not have a clear boosting effect among previously vaccinated participants. Seven out of 42 participants developed symptomatic SARS-CoV-2 infection.

The IN vaccination evaluated in the current study does not merit further clinical development, but results from other trials of IN vaccination are eagerly awaited, according to the authors. “Development of safe, immunogenic and protective ‘platform technologies’ for needle-free vaccination remains a priority both for the response to COVID-19 and more widely,” they wrote.

Colonoscopy Did Not Reduce Cancer Deaths in Trial
Colonoscopy screening reduced the risk of colorectal cancer by 18% in a trial but did not significantly reduce cancer-related deaths during 10 years of follow-up. The results, published in the New England Journal of Medicine, were “both surprising and disappointing” and similar to reductions in colorectal cancer and deaths found in previous randomized trials of sigmoidoscopy, which is considered to be a less effective screening tool than colonoscopy, according to an accompanying editorial.

The 84 585 healthy people aged 55 to 64 years who were enrolled in the trial were randomly assigned to receive an invitation to undergo a single screening colonoscopy (the invited group) or to receive no invitation or screening (the usual-care group). The analysis included participants from Norway, Poland, and Sweden who had not previously undergone screening for colorectal cancer.

During an average follow-up of 10 years, 259 cases of colorectal cancer were diagnosed in the invited group compared with 622 cases in the usual-care group. In the intention-to-screen analyses, the risk of colorectal cancer at 10 years was 0.98% in the invited group and 1.20% in the usual-care group, a risk reduction of 18%. The risk of death from colorectal cancer was a nonsignificant 0.28% in the invited group and 0.31% in the usual-care group. The risk of death from any cause was 11% in both groups.

If all participants eligible for screening had undergone a colonoscopy—only 42% of the invited group did—the investigators estimated that screened individuals would have a 31% lower risk of colorectal cancer.
and a 50% decreased rate of death based on a per-protocol analysis with adjustments for potential confounders. But they also acknowledged that trials of sigmoidoscopy showed similar effects, suggesting that “colonoscopy screening might not be substantially better in reducing the risk of colorectal cancer than sigmoidoscopy.”

The editorialists offered several explanations for why colonoscopy was not superior to sigmoidoscopy: up to 87% of participants actually underwent sigmoidoscopy in previous trials. Also, additional follow-up may reveal greater benefits of colonoscopy. The investigators plan to repeat their analysis at 15 years.

**Shorter Duration of Antibiotics Noninferior for Lyme Disease**

A shorter course of oral doxycycline is effective in treating erythema migrans, the most frequent manifestation of early Lyme borreliosis, and can reduce harmful antibiotic use, trialists recently reported.

The trial, conducted in Slovenia, randomly assigned 300 adults with solitary erythema to receive oral doxycycline, 100 mg twice a day for 7 or 14 days. Doxycycline for 10 days is the primary treatment recommendation for erythema migrans, the investigators noted.

In the 7-day group, 3% of patients had persistent erythema 2 months after treatment compared with 2% of the 14-day group. No patients in either group developed objective signs of persistent or progressive infection. Adverse events caused 1% of patients in each group to discontinue treatment.

Although 7 days of oral doxycycline is effective for treating Lyme disease in adult European patients, the authors called for a similar study to be conducted in the US, where symptoms of Lyme disease are more frequent and more severe. The findings were reported in *The Lancet Infectious Diseases*. – Anita Slomski

**Note:** Source references are available through embedded hyperlinks in the article text online.