



# EFI Bulletin

## Bulletin of Epidemiology Foundation of India

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Dear Colleagues,

It is a matter of immense pleasure and pride that the EFI Bulletin is entering in the 1<sup>st</sup> year of its publication. The Bulletin will be a quarterly publication of the Epidemiology Foundation of India and addresses important issues pertaining to Epidemiology and Evidence Based Medicine.

The Bulletin will reach out to a large number of scientists, administrators, policy makers, nutritionists, dieticians, doctors and people's representatives who are interested in the application of science of Epidemiology and its application. The contributors will include distinguished scientists from fields of Epidemiology with the vast knowledge and experience.

EFI was founded in the year 2019. The EFI is a non-profitable, non-commercial, non-governmental voluntary organization dedicated to improving the practice of Epidemiology that will dedicate its resources in a focused manner by undertaking scientific programs which will have a high impact in advancing practice of Epidemiology.

Opinions expressed from readers will be published in every issue of the Bulletin. Kindly feel free to express your opinion. It will help us in shaping our future issues and address your concerns in a objective way.

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## SELECTED ABSTRACTS IN EVIDENCED BASED EPIDEMIOLOGY

### ABSTRACT 1

**Title:** Hypertension prevalence as a function of different guidelines, India

**Reference:** Dubey M, Rastogi S, Awasthi A. Hypertension prevalence as a function of different guidelines, India. *WHO Bulletin*, Volume 97, Number 12, December 2019, 799-809

**Objective:** To determine the effect of different hypertension management guidelines and of basing diagnosis on a single reading of blood pressure on the hypertension prevalence in the Indian population.

**Methods:** We performed a secondary analysis of data acquired as part of the Fourth national family health survey, 2015 to 2016, over all districts in India. We calculated the proportion of the population within three different age groups (18 to 34, 35 to 49 and 18 to 49 years of age) with raised blood pressure according to six different guidelines, and how prevalence changed if diagnoses were based on a single blood pressure measurement.

**Findings:** We observed that the Government of India and the American College of Cardiology/American Heart Association guidelines consistently yielded the lowest and highest prevalence of raised blood pressure; in the combined age group, we calculated the proportion of the population categorized as having raised blood pressure as 7.5% (95% confidence interval (CI): 7.4 to 7.7) and 40.1% (95% CI: 39.7 to 40.7), respectively. When basing diagnosis on a single reading of blood pressure only, a total of 56 million individuals would be erroneously categorized as hypertensive following the Government of India guidelines. We also showed that prevalence of hypertension in India varies with guidelines adhered to; in the combined age group, the national hypertension prevalence was three times higher when following the American College of Cardiology/American Heart Association compared with the Government of India guidelines.

**Conclusion:** To optimize current clinical practice, health-care providers need to follow universally agreed, evidence-based methods of diagnosing hypertension.

### ABSTRACT 2

**Title:** Correlation between non-communicable disease mortality in people aged 30–69 years and those aged 70–89 years

**Reference:** Byass P. Correlation between noncommunicable disease mortality in people aged 30–69 years and those aged 70–89 years. *WHO Bulletin*, Volume 97, Number 9, September 2019 :589-596

**Objective:** To investigate whether the key metric for monitoring progress towards sustainable development goal target 3.4 that is measuring premature noncommunicable disease mortality (deaths among people aged 30–69 years), is ageist.

**Methods:** To examine the relationship between premature noncommunicable disease mortality and noncommunicable disease mortality in older people, a database of mortality rates for cardiovascular disease, cancer, chronic obstructive pulmonary disease and diabetes in people aged 30 to 69 years and 70 to 89 years was compiled using estimates from the Global Burden of Disease Study 2017. The data covered 195 countries, six time-points and both sexes, giving 2340 instances. The World Health Organization's (WHO's) life-table method for the premature noncommunicable disease mortality metric was applied to the data.

**Findings:** There was a strong correlation between noncommunicable disease mortality patterns in the premature and older age groups, which suggests that measuring premature noncommunicable disease mortality is informative about such mortality in later life. Neither time nor geographical location had a substantial effect on this correlation. However, there were female-to-male differences in age-specific probabilities of death due to noncommunicable disease,

implying that noncommunicable disease mortality should be assessed using a sex-disaggregated approach.

**Conclusion:** As the established WHO metric for premature noncommunicable disease mortality was predictive of noncommunicable disease mortality in older people, the metric should not be construed as ageist. Focusing resources on measuring premature noncommunicable disease mortality will be appropriate, particularly in settings without universal civil death registration. This approach should not prejudice the provision of health services throughout the life-course.

### ABSTRACT 3

#### Title: Educational note: types of causes

**Reference:** Neil Pearce, Jan P. Vandenbroucke. *Educational note: types of causes*. *International Journal of Epidemiology*, 2019, 1–10

We explore the different types of causes that are commonly investigated by epidemiologists. We first distinguish between causes which are events (including actions) and causes which are states. Second, we distinguish between modifiable and non-modifiable states. This yields three types of causes: fixed states (non-modifiable), dynamic states (modifiable) and events (including actions). Different causes may have different characteristics: the methods available to study them, the types of possible biases, and therefore the types of evidence needed to infer causality, may differ according to the specific cause-effect relationship under study. Nevertheless, there are also substantial commonalities.

This paper is intended to improve understanding of the different types of causes, and the different types of causality, that underpin epidemiological practice.

### ABSTRACT 4

#### Title: Dietary n-3 polyunsaturated fatty acids, fish intake and healthy ageing

**Reference:** Esther García-Esquinas, Rosario Ortolá, Jose Ramón Banegas, Esther López-García, Fernando Rodríguez-Artalejo, *Dietary n-3 polyunsaturated fatty acids, fish intake and healthy ageing*, *International Journal of Epidemiology*, dyz196, <https://doi.org/10.1093/ije/dyz196>

**Background:** Seafood consumption and dietary intake of n-3 polyunsaturated fatty acids (PUFA) protect from cardiovascular disease, muscle wasting and mortality; however, their role in delaying unhealthy ageing is uncertain.

**Methods:** A prospective cohort study with 1592 community-dwelling individuals aged  $\geq 60$  years recruited in 2008–2010, and followed through 2015. Intake of seafood and n-3 PUFA [eicosapentanoic acid (EPA) and docosahexanoic acid (DHA)] was estimated using a validated diet history and food composition tables. Unhealthy ageing was assessed across the domains of physical and cognitive function, mental health, morbidity, self-rated health and vitality.

**Results:** Higher blue fish consumption was negatively associated with unhealthy ageing in 2015 [multivariate  $\beta$  (95% confidence interval) per interquartile range (IQR) increase of fish:  $-0.49$  ( $-0.90$ ;  $-0.08$ )] and, specifically, was associated with lower accumulation of functional impairments [ $-1.00$  ( $-1.71$ ;  $-0.28$ )] and morbidities [ $-0.30$  ( $-0.73$ ;  $0.13$ )]. Individuals with high intakes of EPA ( $\geq 0.47$  g/day) and DHA ( $\geq 0.89$  g/day) presented the highest reductions in age-related deficits accumulation:  $-1.61$  ( $-3.01$ ;  $-0.22$ ) and  $-1.34$  ( $-2.76$ ;  $0.08$ ), respectively. Intake of EPA and DHA were negatively associated with the accumulation of functional deficits [results per IQR increase:  $-0.79$  ( $-1.64$ ;  $-0.06$ ) and  $-0.84$  ( $-1.67$ ;  $-0.01$ ), respectively] and morbidities [ $-0.60$  ( $-1.10$ ;  $-1.11$ ) and  $-0.60$  ( $-1.09$ ;  $-0.11$ )]. No associations were observed between n-3 PUFA and self-rated or mental health, or between white fish and unhealthy ageing.

**Conclusions:** In this cohort of Spanish individuals with elevated intake of fish and a high adherence to the Mediterranean diet,

consumption of blue fish and n-3 PUFA had a prospective protective association with deficits accumulation.

## ABSTRACT 5

**Title:** Are cities good for health? A study of the impacts of planned urbanization in China

**Reference:** Bo Hou, James Nazroo, James Banks, Alan Marshall. *Are cities good for health? A study of the impacts of planned urbanization in China. Int J Epidemiol, Volume 48, Issue 4, August 2019, Pages 1083–1090*

**Background:** Urbanization in developing countries is usually accompanied by migration to cities, making it a challenge to unpack the independent relationships between migration, urbanization and health, particularly in the presence of health-selective migration. Since 1978, unprecedented planned urbanization has taken place in China and further increases to the urban population are expected. This paper explored the impacts of urbanization in China through a comparative study of in situ urbanized population.

**Methods:** Using the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative dataset for people aged 45 years or older, we compared self-assessed general health, depressive symptoms and waist circumference among three groups: (i) in situ urbanized-rural residents; (ii) rural residents; and (iii) urban residents. Using a model informed by the literature on the social determinants of health in later life, we investigated the patterning and drivers of differences in health outcomes between these three groups, in order to explore the impact of urbanization independent of the impact of migration.

**Results:** There are consistent advantages in health and less depression among urbanized-rural residents compared with the rural group; and this group has even better health outcomes than the urban group after adjusting for early life differences. However, this relationship is reversed for waist circumference. Socioeconomic circumstances

and factors related to a planned urbanization partly explain these effects.

**Conclusions:** Urbanization in China has, on average, had an independent and positive effect on health and well-being. Planned urbanization could benefit people's health in developing countries. It is likely that improved infrastructure is a key driver.

## ABSTRACT 6

**Title:** Use of standardised patients to assess gender differences in quality of tuberculosis care in urban India: a two-city, cross-sectional study

**Reference:** Benjamin Daniels, Ada Kwan, Srinath Satyanarayana, Ramnath Subbaraman, Ranendra K Das, Veena Das, Jishnu Das, Madhukar Pai. *Use of standardised patients to assess gender differences in quality of tuberculosis care in urban India: a two-city, cross-sectional study. Lancet Glob Health 2019; 7: e633–43*

**Background:** In India, men are more likely than women to have active tuberculosis but are less likely to be diagnosed and notified to national tuberculosis programmes. We used data from standardised patient visits to assess whether these gender differences occur because of provider practice.

**Methods:** We sent standardised patients (people recruited from local populations and trained to portray a scripted medical condition to health-care providers) to present four tuberculosis case scenarios to private health-care providers in the cities of Mumbai and Patna. Sampling and weighting allowed for city representative interpretation. Because standardised patients were assigned to providers by a field team blinded to this study, we did balance and placebo regression tests to confirm standardised patients were assigned by gender as good as randomly. Then, by use of linear and logistic regression, we assessed correct case management, our primary outcome, and other dimensions of care by standardised patient gender.

**Findings:** Between Nov 21, 2014, and Aug 21, 2015, 2602 clinical interactions at 1203 private facilities were completed by 24

standardised patients (16 men, eight women). We found standardised patients were assigned to providers as good as randomly. We found no differences in correct management by patient gender (odds ratio 1·05; 95% CI 0·76–1·45;  $p=0·77$ ) and no differences across gender within any case scenario, setting, provider gender, or provider qualification.

**Interpretation:** Systematic differences in quality of care are unlikely to be a cause of the observed under-representation of men in tuberculosis notifications in the private sector in urban India.

## ABSTRACT 7

**Title:** Global prevalence of diabetes in active tuberculosis: a systematic review and meta-analysis of data from 2·3 million patients with tuberculosis

**Reference:** Jean Jacques Noubiap, Jobert Richie Nansseu, Ulrich Flore Nyaga, Jan René Nkeck, Francky Teddy Endomba, Arnaud D Kaze, Valirie N Agbor, Jean Joel Bigna. Global prevalence of diabetes in active tuberculosis: a systematic review and meta-analysis of data from 2·3 million patients with tuberculosis. *Lancet Glob Health* 2019; 7: e448–60

**Background:** Although diabetes and poor glycaemic control significantly increase the risk of tuberculosis and adversely affect tuberculosis treatment outcomes, the global burden of diabetes in the context of tuberculosis remains unknown. We did a systematic review and meta-analysis to estimate the prevalence of diabetes among patients with tuberculosis at global, regional, and country levels.

**Methods:** We searched PubMed, Excerpta Medica Database, Web of Science, and Global Index Medicus to identify studies published between Jan 1, 1986, and June 15, 2017, on the prevalence of diabetes in patients with active tuberculosis, with no language restrictions. Criteria to diagnose tuberculosis and diabetes concurred with WHO guidelines. Methodological quality of eligible studies was assessed, and random-effect models meta-analysis served to obtain the pooled

prevalence estimate of diabetes among patients with active tuberculosis, globally. Heterogeneity ( $I^2$ ) was assessed via the  $\chi^2$  test on Cochran's Q statistic. This study is registered with PROSPERO, number CRD42016049901.

**Findings:** We screened 7565 records of which 200 studies (2 291 571 people with active tuberculosis) were included in meta-analyses. The pooled prevalence of diabetes was 15·3% (95% prediction interval 2·5–36·1;  $I^2$  99·8%), varying from 0·1% in Latvia to 45·2% in Marshall Islands. Subgroup and metaregression analyses for identifying sources of heterogeneity showed that four International Diabetes Federation (IDF) regions (North America and Caribbean [19·7%], western Pacific [19·4%], southeast Asia [19·0%], Middle East and North Africa [17·5%]) had significantly higher prevalence estimates than the three others (Africa [8·0%], South and Central America [7·7%], and Europe [7·5%];  $p <0·0001$ ). Additionally, the prevalence increased with age, in men, and in countries with low tuberculosis burden. The prevalence of diabetes was decreased in countries that had low incomes and low Human Development Index scores. The form of tuberculosis infection and presence of HIV seemed not to affect the prevalence of diabetes among patients with active tuberculosis.

**Interpretation:** This study suggests a high burden of diabetes among patients with active tuberculosis, with disparities according to age, sex, regions, level of country income, and development. Cost-effective strategies to curb the burden of diabetes among patients with active tuberculosis are needed.

## ABSTRACT 8

**Title:** HIV and Viral Hepatitis among Imprisoned Key Populations

**Reference:** Andrea L Wirtz, Ping T Yeh, Natalie L Flath, Chris Beyrer, Kate Dolan. HIV and Viral Hepatitis among imprisoned key populations. *Epidemiol Rev*, Volume 40, Issue 1, 2018, Pages 12–26

**Background:** Prisons and other closed facilities create opportunities for transmission of human immunodeficiency virus (HIV) and viral hepatitis during detention and after release. We conducted a systematic review and meta-analysis of peer-reviewed publications (2005–2015) to describe the prevalence of HIV, hepatitis C virus, and hepatitis B virus among key populations in prisons worldwide and to compare estimates of infection with those of other prison populations.

Most data were reported for people who inject drugs (PWID;  $n = 72$ ) and for men who have sex with men (MSM;  $n = 21$ ); few data were reported on sex workers (SW;  $n = 6$ ), or transgender women ( $n = 2$ ). Publications were identified from 29 countries, predominantly middle- and high-income countries. Globally, PWID had 6 times the prevalence of HIV (pooled prevalence ratio (PPR) = 6.0, 95% CI: 3.8, 9.4), 8 times the prevalence of hepatitis C virus (PPR = 8.1, 95% CI: 6.4, 10.4), and 2 times the prevalence of hepatitis B virus (PPR = 2.0, 95% CI: 1.5, 2.7) compared with non-injecting prisoner populations. Among these articles, only those from Iran, Scotland, Spain, and Italy included the availability of methadone therapy; 2 articles included information on access to needle exchange programs by PWID detainees. HIV prevalence was more than 2 times higher among SW (PPR = 2.6, 95% CI: 2.2, 3.1) and 5 times higher among MSM (PPR = 5.3, 95% CI: 3.5, 7.9) compared with other prisoners. None of these articles reported HIV prevention coverage among SW or transgender women; 1 described HIV and sexually transmitted infection screening for MSM in prison.

Prevention programs specific to key populations are important, particularly for populations that are criminalized and/or may cycle in and out of prison.

## ABSTRACT 9

**Title:** Low birth weight and childhood health: the role of maternal education

**Reference:** Melissa L Martinson, Kate H Choi. Low birth weight and childhood health: the role of maternal education. *Annals of Epidemiology*, November 2019, Volume 39: 39-45.

**Purpose:** Low birth weight (LBW) is associated with myriad health and developmental problems in childhood and later in life. Less well-documented is the variation in the relationship between LBW status and subsequent child health by socioeconomic status—such as education levels and income. This article examines whether differences exist in the relationship between LBW and subsequent child health by maternal education.

**Methods:** We used data from the 1998–2017 National Health Interview Survey to estimate multivariate logistic regression models to determine whether the association between LBW and subsequent child health as measured by general health status, developmental disability, and asthma diagnosis differed by maternal education, net of differences in children's sociodemographic factors, family background, and medical access.

**Results:** The negative association between LBW and subsequent health was typically weaker for children of mothers with less than high school education than it was for children of mothers with higher levels of education.

**Conclusions:** The findings on the enduring impact of LBW status on child health for all children, especially those born to mothers with higher levels of education, suggest that all children born LBW should be provided appropriate medical and support services to reduce the lifelong repercussions of poor health at birth.

## ABSTRACT 10

**Title:** Trade openness and the obesity epidemic: a cross-national study of 175 countries during 1975–2016

**Reference:** Ruopeng An, Chenghua Guan, Junyi Liu, Nan Chen, Caitlin Clarke. Trade openness and the obesity epidemic: a cross-national study of 175 countries during 1975–2016. *Annals of Epidemiology*, September 2019, Volume 37: 31-36

**Purpose:** This study assessed the longitudinal relationship between trade openness and obesity rate across 175 countries during 1975–2016.

**Methods:** Two-way (country and year) fixed-effects regressions were performed to examine the openness index (i.e., sum of export and import over gross domestic product) in relation to country obesity rate, using data from World Health Organization and World Bank.

**Results:** The openness index was found to be positively associated with country obesity prevalence—a 10% increase in the openness index was associated with an increase in obesity rate by 0.80% (95% confidence interval, 0.67%–0.94%). Across continents, the positive relationship between the openness index and obesity prevalence was strongest among Asian countries, followed by countries in North America and Africa. Across income levels, the positive relationship between the openness index and obesity prevalence was strongest among lower middle-income countries, followed by upper middle-income countries and low-income countries. In contrast, no relationship between the two was identified among high-income countries.

**Conclusions:** Trade openness was positively associated with country obesity prevalence, and its influence concentrated among developing nations. Policy makers should closely monitor the evolution in obesity rate during trade liberalization and nutrition transition to minimize its negative impact on weight-related population health.

## ABSTRACT 11

**Title:** Acute Air Pollution Exposure and the Risk of Violent Behavior in the United States

**Reference:** Berman, Jesse D.; Burkhardt, Jesse; Bayham, Jude et al. *Acute Air Pollution Exposure and the Risk of Violent Behavior in the United States. Epidemiology. November 2019* 30(6):799-806

**Background:** Violence is a leading cause of death and an important public health threat,

particularly among adolescents and young adults. However, the environmental causes of violent behavior are not well understood. Emerging evidence suggests exposure to air pollution may be associated with aggressive or impulsive reactions in people.

**Methods:** We applied a two-stage hierarchical time-series model to estimate change in risk of violent and nonviolent criminal behavior associated with short-term air pollution in U.S. counties (2000–2013). We used daily monitoring data for ozone and fine particulate matter (PM 2.5) from the Environmental Protection Agency and daily crime counts from the Federal Bureau of Investigation. We evaluated the exposure–response relation and assessed differences in risk by community characteristics of poverty, urbanicity, race, and age.

**Results:** Our analysis spans 301 counties in 34 states, representing 86.1 million people and 721,674 days. Each 10  $\mu\text{g}/\text{m}^3$  change in daily PM 2.5 was associated with a 1.17% (95% confidence interval [CI] = 0.90, 1.43) and a 10 ppb change in ozone with a 0.59% (95% CI = 0.41, 0.78) relative risk increase (RRI) for violent crime. However, we observed no risk increase for nonviolent property crime due to PM 2.5 (RRI: 0.11%; 95% CI = -0.09, 0.31) or ozone (RRI: -0.05%; 95% CI = -0.22, 0.12). Our results were robust across all community types, except rural regions. Exposure–response curves indicated increased violent crime risk at concentrations below regulatory standards.

**Conclusions:** Our results suggest that short-term changes in ambient air pollution may be associated with a greater risk of violent behavior, regardless of community type.

## ABSTRACT 12

**Title:** Treatment correlates of successful outcomes in pulmonary multidrug-resistant tuberculosis: an individual patient data meta-analysis.

**Reference:** Ahmad N, Ahuja SD, Akkerman OW, Alffenaar JC, Anderson LF, Baghaei P et al. *Treatment correlates of successful*

*outcomes in pulmonary multidrug-resistant tuberculosis: an individual patient data meta-analysis.* Lancet. 2018 Sep 8;392 (10150):821-834.

**Background:** Treatment outcomes for multidrug-resistant tuberculosis remain poor. We aimed to estimate the association of treatment success and death with the use of individual drugs, and the optimal number and duration of treatment with those drugs in patients with multidrug-resistant tuberculosis.

**Methods:** In this individual patient data meta-analysis, we searched MEDLINE, Embase, and the Cochrane Library to identify potentially eligible observational and experimental studies published between Jan 1, 2009, and April 30, 2016. We also searched reference lists from all systematic reviews of treatment of multidrug-resistant tuberculosis published since 2009. To be eligible, studies had to report original results, with end of treatment outcomes (treatment completion [success], failure, or relapse) in cohorts of at least 25 adults (aged  $>18$  years). We used anonymised individual patient data from eligible studies, provided by study investigators, regarding clinical characteristics, treatment, and outcomes. Using propensity score-matched generalised mixed effects logistic, or linear regression, we calculated adjusted odds ratios and adjusted risk differences for success or death during treatment, for specific drugs currently used to treat multidrug-resistant tuberculosis, as well as the number of drugs used and treatment duration.

**Findings:** Of 12 030 patients from 25 countries in 50 studies, 7346 (61%) had treatment success, 1017 (8%) had failure or relapse, and 1729 (14%) died. Compared with failure or relapse, treatment success was positively associated with the use of linezolid (adjusted risk difference 0.15, 95% CI 0.11 to 0.18), levofloxacin (0.15, 0.13 to 0.18), carbapenems (0.14, 0.06 to 0.21), moxifloxacin (0.11, 0.08 to 0.14), bedaquiline (0.10, 0.05 to 0.14), and clofazimine (0.06, 0.01 to 0.10). There was a significant association between reduced mortality and use of linezolid (-0.20, -0.23 to -0.16), levofloxacin (-0.06, -0.09 to -0.04), moxifloxacin (-0.07, -0.10 to -0.04), or

bedaquiline (-0.14, -0.19 to -0.10). Compared with regimens without any injectable drug, amikacin provided modest benefits, but kanamycin and capreomycin were associated with worse outcomes. The remaining drugs were associated with slight or no improvements in outcomes. Treatment outcomes were significantly worse for most drugs if they were used despite in-vitro resistance. The optimal number of effective drugs seemed to be five in the initial phase, and four in the continuation phase. In these adjusted analyses, heterogeneity, based on a simulated  $I^2$  method, was high for approximately half the estimates for specific drugs, although relatively low for number of drugs and durations analyses.

**Interpretation:** Although inferences are limited by the observational nature of these data, treatment outcomes were significantly better with use of linezolid, later generation fluoroquinolones, bedaquiline, clofazimine, and carbapenems for treatment of multidrug-resistant tuberculosis. These findings emphasise the need for trials to ascertain the optimal combination and duration of these drugs for treatment of this condition.

## ABSTRACT 13

**Title:** *Intermittent preventive treatment for malaria in infants.*

**Reference:** Esu EB, Oringanje C, Meremikwu MM. *Intermittent preventive treatment for malaria in infants.* Cochrane Database Syst Rev. 2019 Dec 2;12:CD011525.

**Background:** Intermittent preventive treatment could help prevent malaria in infants (IPTi) living in areas of moderate to high malaria transmission in sub-Saharan Africa. The World Health Organization (WHO) policy recommended IPTi in 2010, but its adoption in countries has been limited.

**Objectives:** To evaluate the effects of intermittent preventive treatment (IPT) with antimalarial drugs to prevent malaria in infants living in malaria-endemic areas.

**Search Methods:** We searched the following sources up to 3 December 2018: the Cochrane

Infectious Diseases Group Specialized Register, CENTRAL (the Cochrane Library), MEDLINE (PubMed), Embase (OVID), LILACS (Bireme), and reference lists of articles. We also searched the metaRegister of Controlled Trials (mRCT) and the WHO International Clinical Trials Registry Platform (ICTRP) portal for ongoing trials up to 3 December 2018.

**Selection Criteria:** We included randomized controlled trials (RCTs) that compared IPT to placebo or no intervention in infants (defined as young children aged between 1 to 12 months) in malaria-endemic areas.

**Data Collection And Analysis:** The primary outcome was clinical malaria (fever plus asexual parasitaemia). Two review authors independently assessed trials for inclusion, evaluated the risk of bias, and extracted data. We summarized dichotomous outcomes and count data using risk ratios (RR) and rate ratios respectively, and presented all measures with 95% confidence intervals (CIs). We extracted protective efficacy values and their 95% CIs; when an included trial did not report this data, we calculated these values from the RR or rate ratio with its 95% CI. Where appropriate, we combined data in meta-analyses and assessed the certainty of the evidence using the GRADE approach.

**Main Results:** We included 12 trials that enrolled 19,098 infants; all were conducted in sub-Saharan Africa. Three trials were cluster-RCTs. IPTi with sulfadoxine-pyrimethamine (SP) was evaluated in 10 trials from 1999 to 2013 (n = 15,256). Trials evaluating ACTs included dihydroartemisinin-piperaquine (1 trial, 147 participants; year 2013), amodiaquine-artesunate (1 study, 684 participants; year 2008), and SP-artesunate (1 trial, 676 participants; year 2008). The earlier studies evaluated IPTi with SP, and were conducted in Tanzania (in 1999 and 2006), Mozambique (2004), Ghana (2004 to 2005), Gabon (2005), Kenya (2008), and Mali (2009). One trial evaluated IPTi with amodiaquine in Tanzania (2000). Later studies included three conducted in Kenya (2008), Tanzania (2008), and Uganda (2013), evaluating IPTi in multiple trial arms that included artemisinin-based

combination therapy (ACT). Although the effect size varied over time and between drugs, overall IPTi impacts on the incidence of clinical malaria overall, with a 27% reduction (rate ratio 0.73, 0.65 to 0.82; 10 studies, 10,602 participants). The effect of SP appeared to attenuate over time, with trials conducted after 2009 showing little or no effect of the intervention. IPTi with SP probably resulted in fewer episodes of clinical malaria (rate ratio 0.79, 0.74 to 0.85; 8 trials, 8774 participants, moderate-certainty evidence), anaemia (rate ratio 0.82, 0.68 to 0.98; 6 trials, 7438 participants, moderate-certainty evidence), parasitaemia (rate ratio 0.66, 0.56 to 0.79; 1 trial, 1200 participants, moderate-certainty evidence), and fewer hospital admissions (rate ratio 0.85, 0.78 to 0.93; 7 trials, 7486 participants, moderate-certainty evidence). IPTi with SP probably made little or no difference to all-cause mortality (risk ratio 0.93, 0.74 to 1.15; 9 trials, 14,588 participants, moderate-certainty evidence). Since 2009, IPTi trials have evaluated ACTs and indicate impact on clinical malaria and parasitaemia. A small trial of DHAP in 2013 shows substantive effects on clinical malaria (RR 0.42, 0.33 to 0.54; 1 trial, 147 participants, moderate-certainty evidence) and parasitaemia (moderate-certainty evidence).

**Authors' Conclusions:** In areas of sub-Saharan Africa, giving antimalarial drugs known to be effective against the malaria parasite at the time to infants as IPT probably reduces the risk of clinical malaria, anaemia, and hospital admission. Evidence from SP studies over a 19-year period shows declining efficacy, which may be due to increasing drug resistance. Combinations with ACTs appear promising as suitable alternatives for IPTi. 2 December 2019 Up to date All studies incorporated from most recent search All eligible published studies found in the last search (3 Dec, 2018) were included.

## ABSTRACT 14

**Title:** Hepatitis C virus infection among people who inject drugs in Bangkok, Thailand, 2005–2010

**Reference:** Michael Martin, Suphak Vanichseni, Wanna Leelawiwat, Rapeepan

*Anekvorapong, Boonyos Raengsakulrach, Thitima Cherdtrakulkiat, Udomsak Sangkum, Philip A Mock, Manoj Leethochawalit, Sithisat Chiamwongpaet, Janet M McNicholl, Somyot Kittimunkong, Marcel E Curlin, Kachit Choopanya, for the Bangkok Tenofovir Study Group. Hepatitis C virus infection among people who inject drugs in Bangkok, Thailand, 2005–2010. WHO South-East Asia Journal of Public Health, April 2019, 8(1): 50 - 55*

**Background** Approximately 1% of adults in Thailand are infected with hepatitis C virus (HCV). New direct-acting antiviral agents achieve sustained virologic responses in >95% of HCV-infected patients and are becoming available in countries around the world. To prepare for new HCV treatment options in Thailand, this study characterized HCV infections among people who inject drugs (PWID) in Bangkok.

**Methods** The Bangkok Tenofovir Study (BTS) was a pre-exposure prophylaxis trial conducted among PWID, 2005–2013. Blood specimens were randomly selected from PWID screened for the BTS, to test for anti-HCV antibody and HCV RNA. The HVR1 region was amplified by polymerase chain reaction, using multiplex primer sets with unique identifier sequences; amplification products were pooled in sets of 25; and consensus sequencing was performed to characterize individual HCV genotypes.

**Results** The median age of 3679 participants tested for anti-HCV antibody was 31 years, 3016 (82.0%) were male and 447 (12.2%) were HIV infected. The prevalence of anti-HCV antibody was 44.3%. The adjusted odds of testing positive for anti-HCV antibody were higher in men (adjusted odds ratio [aOR] 3.2, 95% confidence interval [CI] 2.4–4.3), those aged 40 years or older (aOR 2.7, 95% CI 2.1–3.5), those who had more than a primary school education (aOR 1.7, 95% CI 1.4–2.1), and those who tested HIV positive (aOR 5.2, 95% CI 3.7–7.4). HCV RNA was detected in 644 (81.3%) of the 792 anti-HCV antibody-positive specimens, yielding an HCV RNA-positive prevalence of 36.0% (95% CI 33.8–38.2). Among a random sample of 249 of the 644 specimens, 218 could be characterized,

and the most common HCV subtypes were 1a (30.3%), 1b (12.8%), 3a (35.8%), 3b (6.9%) and 6n (8.7%).

**Conclusion** The prevalence of anti-HCV antibody among PWID was 44.3% and more than one third (36.0%) were HCV RNA positive. Genotypes 1, 3 and 6 accounted for all typable infections. As the government of Thailand considers introduction of direct-acting antiviral medications for people with hepatitis C, it will be important to ensure that the medications target these subtypes.

### ABSTRACT 15

**Title:** Phase 3 Efficacy Analysis of a Typhoid Conjugate Vaccine Trial in Nepal

**Reference:** Mila Shakya, Rachel Colin-Jones, Katherine Theiss-Nyland, Merryn Voysey, Dikshya Pant, Nicola Smith, Xinxue Liu, Susan Tonks, et al. for the TyVAC Nepal Study Team. Phase 3 Efficacy Analysis of a Typhoid Conjugate Vaccine Trial in Nepal. *N Engl J Med* 2019; 381:2209-2218

**Background:** *Salmonella Typhi* is a major cause of fever in children in low- and middle-income countries. A typhoid conjugate vaccine (TCV) that was recently prequalified by the World Health Organization was shown to be efficacious in a human challenge model, but data from efficacy trials in areas where typhoid is endemic are lacking.

**Methods:** In this phase 3, randomized, controlled trial in Lalitpur, Nepal, in which both the participants and observers were unaware of the trial-group assignments, we randomly assigned children who were between 9 months and 16 years of age, in a 1:1 ratio, to receive either a TCV or a capsular group A meningococcal conjugate vaccine (MenA) as a control. The primary outcome was typhoid fever confirmed by blood culture. We present the prespecified analysis of the primary and main secondary outcomes (including an immunogenicity subgroup); the 2-year trial follow-up is ongoing.

**Results:** A total of 10,005 participants received the TCV and 10,014 received the MenA vaccine. Blood culture-confirmed typhoid fever occurred in 7 participants who received

TCV (79 cases per 100,000 person-years) and in 38 who received MenA vaccine (428 cases per 100,000 person-years) (vaccine efficacy, 81.6%; 95% confidence interval, 58.8 to 91.8;  $P<0.001$ ). A total of 132 serious adverse events (61 in the TCV group and 71 in the MenA vaccine group) occurred in the first 6 months, and 1 event (pyrexia) was identified as being vaccine-related; the participant remained unaware of the trial-group assignment. Similar rates of adverse events were noted in the two trial groups; fever developed in 5.0% of participants in the TCV group and 5.4% in the MenA vaccine group in the first week after vaccination. In the immunogenicity subgroup, seroconversion (a Vi IgG level that at least quadrupled 28 days after vaccination) was 99% in the TCV group (677 of 683 participants) and 2% in the MenA vaccine group (8 of 380 participants).

**Conclusions:** A single dose of TCV was immunogenic and effective in reducing *S.Typhi* bacteremia in children 9 months to 16 years of age.

## ABSTRACT 16

**Title:** *Dairy fat intake and risk of type 2 diabetes in 3 cohorts of US men and women*

**Reference:** Andres V Ardisson Korat, Yanping Li, Frank Sacks, Bernard Rosner, Walter C Willett. *Dairy fat intake and risk of type 2 diabetes in 3 cohorts of US men and women*. *Am J Clin Nutr*, Volume 110, Issue 5, November 2019, Pages 1192–1200,

**Background:** Previous studies have examined dairy products with various fat contents in relation to type 2 diabetes (T2D) risk, although data regarding dairy fat intake per se are sparse.

**Objectives:** We aimed to evaluate the association between dairy fat intake and risk of T2D in 3 prospective cohorts. We also examined associations for isocalorically replacing dairy fat with other macronutrients.

**Methods:** We prospectively followed 41,808 men in the Health Professionals Follow-Up Study (HPFS; 1986–2012), 65,929 women in

the Nurses' Health Study (NHS; 1984–2012), and 89,565 women in the NHS II (1991–2013). Diet was assessed quadrennially using validated FFQs. Fat intake from dairy products and other relevant sources was expressed as percentage of total energy. Self-reported incident T2D cases were confirmed using validated supplementary questionnaires. Time-dependent Cox proportional hazards regression was used to estimate the HR for dairy fat intake and T2D risk.

**Results:** During 4,219,457 person-years of follow-up, we documented 16,511 incident T2D cases. Dairy fat was not associated with risk of T2D when compared with calories from carbohydrates (HR for extreme quintiles: 0.98; 95% CI: 0.95, 1.02). Replacing 5% of calories from dairy fat with other sources of animal fat or carbohydrate from refined grains was associated with a 17% (HR: 1.17; 95% CI: 1.13, 1.21) and a 4% (HR: 1.04; 95% CI: 1.00, 1.08) higher risk of T2D, respectively. Conversely, a 5% calorie replacement with carbohydrate from whole grains was associated with a 7% lower risk of T2D (HR: 0.93; 95% CI: 0.88, 0.98).

**Conclusions:** Dairy fat intake was not associated with T2D risk in these cohort studies of US men and women when compared with calories from carbohydrate. Replacing dairy fat with carbohydrates from whole grains was associated with lower risk of T2D. Replacement with other animal fats or refined carbohydrates was associated with higher risk.

## ABSTRACT 17

**Title:** *The effect of time since measles vaccination and age at first dose on measles vaccine effectiveness – A systematic review*.

**Reference:** Hughes SL, Bolotin S, Khan S, Li Y, Johnson C, Friedman L, Tricco AC, Hahné SJM, Heffernan JM, Dabbagh A, Durrheim DN, Orenstein WA, Moss WJ, Jit M, Crowcroft NS. *The effect of time since measles vaccination and age at first dose on measles vaccine effectiveness - A systematic review*. *Vaccine*. 2019 Nov 12. pii: S0264-410X(19)31479-3.

**Background:** In settings where measles has been eliminated, vaccine-derived immunity may in theory wane more rapidly due to a lack of immune boosting by circulating measles virus. We aimed to assess whether measles vaccine effectiveness (VE) waned over time, and if so, whether differentially in measles-eliminated and measles-endemic settings.

**Methods:** We performed a systematic literature review of studies that reported VE and time since vaccination with measles-containing vaccine (MCV). We extracted information on case definition (clinical symptoms and/or laboratory diagnosis), method of vaccination status ascertainment (medical record or vaccine registry), as well as any biases which may have arisen from cold chain issues and a lack of an age at first dose of MCV. We then used linear regression to evaluate VE as a function of age at first dose of MCV and time since MCV.

**Results:** After screening 14,782 citations, we identified three full-text articles from measles-eliminated settings and 33 articles from measles-endemic settings. In elimination settings, two-dose VE estimates increased as age at first dose of MCV increased and decreased as time since MCV increased; however, the small number of studies available limited interpretation. In measles-endemic settings, one-dose VE increased by 1.5% (95% CI 0.5, 2.5) for every month increase in age at first dose of MCV. We found no evidence of waning VE in endemic settings.

**Conclusions:** The paucity of data from measles-eliminated settings indicates that additional studies and approaches (such as studies using proxies including laboratory correlates of protection) are needed to answer the question of whether VE in measles-eliminated settings wanes. Age at first dose of MCV was the most important factor in determining VE. More VE studies need to be conducted in elimination settings, and standards should be developed for information collected and reported in such studies.

**Title: Exercise interventions for smoking cessation**

**Reference:** Ussher MH, Faulkner GEJ, Angus K, Hartmann-Boyce J, Taylor AH. *Exercise interventions for smoking cessation. Cochrane Database Syst Rev. 2019 Oct 30;2019(10)*

**Background:** Taking regular exercise, whether cardiovascular-type exercise or resistance exercise, may help people to give up smoking, particularly by reducing cigarette withdrawal symptoms and cravings, and by helping to manage weight gain.

**Objectives:** To determine the effectiveness of exercise-based interventions alone, or combined with a smoking cessation programme, for achieving long-term smoking cessation, compared with a smoking cessation intervention alone or other non-exercise intervention.

**Search methods:** We searched the Cochrane Tobacco Addiction Group Specialized Register for studies, using the term 'exercise' or 'physical activity' in the title, abstract or keywords. The date of the most recent search was May 2019.

**Selection criteria:** We included randomised controlled trials that compared an exercise programme alone, or an exercise programme as an adjunct to a cessation programme, with a cessation programme alone or another non-exercise control group. Trials were required to recruit smokers wishing to quit or recent quitters, to assess abstinence as an outcome and have follow-up of at least six months.

**Data collection and analysis:**

We followed standard Cochrane methods. Smoking cessation was measured after at least six months, using the most rigorous definition available, on an intention-to-treat basis. We calculated risk ratios (RRs) and 95% confidence intervals (CIs) for smoking cessation for each study, where possible. We grouped eligible studies according to the type of comparison, as either smoking cessation or relapse prevention. We carried out meta-analyses where appropriate, using Mantel-Haenszel random-effects models.

**Main Results:** We identified 24 eligible trials with a total of 7279 adult participants randomised. Two studies focused on relapse prevention among smokers who had recently stopped smoking, and the remaining 22 studies were concerned with smoking cessation for smokers who wished to quit. Eleven studies were with women only and one with men only. Most studies recruited fairly inactive people. Most of the trials employed supervised, group-based cardiovascular-type exercise supplemented by a home-based exercise programme and combined with a multi-session cognitive behavioural smoking cessation programme. The comparator in most cases was a multi-session cognitive behavioural smoking cessation programme alone. Overall, we judged two studies to be at low risk of bias, 11 at high risk of bias, and 11 at unclear risk of bias. Among the 21 studies analysed, we found low-certainty evidence, limited by potential publication bias and by imprecision, comparing the effect of exercise plus smoking cessation support with smoking cessation support alone on smoking cessation outcomes (RR 1.08, 95% CI 0.96 to 1.22; I<sup>2</sup> = 0%; 6607 participants). We excluded one study from this analysis as smoking abstinence rates for the study groups were not reported. There was no evidence of subgroup differences according to the type of exercise

promoted; the subgroups considered were: cardiovascular-type exercise alone (17 studies), resistance training alone (one study), combined cardiovascular-type and resistance exercise (one study) and type of exercise not specified (two studies). The results were not significantly altered when we excluded trials with high risk of bias, or those with special populations, or those where smoking cessation intervention support was not matched between the intervention and control arms. Among the two relapse prevention studies, we found very low-certainty evidence, limited by risk of bias and imprecision, that adding exercise to relapse prevention did not improve long-term abstinence compared with relapse prevention alone (RR 0.98, 95% CI 0.65 to 1.47; I<sup>2</sup> = 0%; 453 participants).

#### AUTHORS' CONCLUSIONS:

There is no evidence that adding exercise to smoking cessation support improves abstinence compared with support alone, but the evidence is insufficient to assess whether there is a modest benefit. Estimates of treatment effect were of low or very low certainty, because of concerns about bias in the trials, imprecision and publication bias. Consequently, future trials may change these conclusions.

## UPCOMING EVENTS

### IAPSMCON 2020

**The 47th National Conference of Indian Association of Preventive & Social Medicine** from 28<sup>th</sup>– 30<sup>th</sup>January 2020 organized by Institute of Community Medicine, Madras Medical College, Chennai at Ideal Beach Resorts, Mahabalipuram, India. **IAPSMCON2020** is a four-day Scientific extravaganza themed “Universal Health Coverage – Evidence Driven Solutions”.

### IPHACON 2020

**The 64<sup>th</sup> Annual National Conference of Indian Public Health Association (IPHACON 2020)** is being organized by the Centre for Community Medicine, AIIMS, New Delhi and IPHA Delhi State Branch from 29 February to 2 March 2020. The venue of the IPHACON 2020 is the sprawling campus of the AIIMS, New Delhi. The theme of is 'Promoting Public Health Leadership for Universal Health Coverage in India'.

### WCE 2020

**The World Congress of Epidemiology (WCE)** is held every 3 years by the International Association of Epidemiology (IEA) and attracts 800 -1200 delegates involved in research and teaching of epidemiology. **Dates:** 13 -16 September 2020. **Abstract submission for WCE 2020** has now opened. Please visit web site for details: <http://wce2020.org/>