

CaseMed-Pregnancy Resource Newsletter

March 2008

MEDICAL STUDIES

Foetal chondrodysplasia: intrauterine diagnosis

Adesiyun AG, Eka A, Samaila MO

Ann Afr Med, 2007; 6(3): 128-9

The authors present a case of short-limbed chondrodysplasia diagnosed in a 22-week fetus of a 28 year old. She was 4(+0) with two children alive. She had similar occurrences in her last two pregnancies. The index pregnancy and the last two eventful pregnancies were preceded with ingestion of trado-herbal drug to treat subfertility.

Withdrawal of 17 alpha-hydroxyprogesterone: a possible trigger for preterm labor?

Bernstein PS

Am J Obstet Gynecol, 2008; 198(2): 244; author reply 244-5

No abstract available.

Non-steroidal anti-inflammatory drugs are not fully safe for fetus: comments on the article Treating common ear problems in pregnancy: what is safe? by Vlastarakos et al.

Burdan F

Eur Arch Otorhinolaryngol 2008 Feb 7 [Epub ahead of print]

No abstract available.

Antifungal drugs and the risk of selected birth defects

Carter TC, Druschel CM, Romitti PA, et al

Am J Obstet Gynecol, 2008; 198(2): 191.e1-7

This study examined whether first-trimester antifungal drug use was associated with the risk of selected birth defects. The subjects were participants in the case-control study, the National Birth Defects Prevention Study. Based on maternal interviews, first-trimester antifungal drug use was compared between 7,047 cases with isolated defects and 4,774 nonmalformed controls using unconditional logistic regression. Carter and colleagues conclude that first-trimester antifungal drug exposure was not strongly associated with the risk of most birth defects, however, further studies should examine the preliminary results of an association with hypoplastic left heart syndrome.

Data resources for investigating drug exposure during pregnancy and associated outcomes: the General Practice Research Database (GPRD) as an alternative to pregnancy registries

Charlton RA, Cunnington MC, de Vries CS, et al

Drug Saf, 2008; 31(1): 39-51

Pregnancy registries are the most commonly used data resource for the post-marketing surveillance of drug teratogenicity. However, the limited sample size and potential selection bias in these registries led Charlton and colleagues to investigate the potential of the UK General Practice Research Database (GPRD) as an alternative data source for monitoring drug safety during pregnancy. In addition, a literature review identified further observational data sources that monitor pregnancy outcomes for future evaluation. Initial feasibility studies focused on the ability of the GPRD to capture pregnancy outcomes for a range of drug class exposures, all of which are currently under investigation in pregnancy registries, during pregnancy. The authors conclude that data from the GPRD meet established criteria for evaluating outcomes of pregnancy. For prevalent conditions, it has the potential to replace or work alongside standard pregnancy registries and the alternative data sources identified. Further studies are now needed to assess its ability to replicate known teratogenic associations.

Cholecystitis during pregnancy. A case report and brief review of the literature
Chloptsios C, Karanasiou V, Ilias G, et al
Clin Exp Obstet Gynecol, 2007; 34(4): 250-1

Chloptsios and colleagues present a case of a 33-year-old obese pregnant woman with fever, moderately elevated bile acids, and leukocytosis in the 28th week of pregnancy. As the need for surgery in these cases is controversial, the patient was treated conservatively. In this particular case cholecystitis responded very well to treatment with amoxicillin, with no detrimental effects for mother and child. A healthy child was born at term.

Prenatal drug exposure and teratological risk: One-year experience of an Italian Teratology Information Service
De Santis M, Cesari E, Ligato MS
Med Sci Monit, 2008 Feb; 14 (2): PH1-8

This study presents data on the most common pharmaceutical products responsible for teratogenic risk in the one-year experience of a teratology information service in Italy. The majority of the calls concerned drug exposure. Increased risk was present in only 5% of the pregnant women calling during pregnancy. Selective serotonin reuptake inhibitors (SSRIs) are the first category that is actually considered of increased risk to the fetus. The second category is represented by antiepileptic drugs. The results of this study confirm there is a high teratological risk perception among both women and physicians. The drugs estimated to present increased risk are medications used for chronic neurological diseases, mainly mood disorders and epilepsy. The authors conclude that preconceptional counseling for these women could be an effective strategy to prevent such exposure and to improve maternal and fetal outcome.

[Management of type 2 diabetes mellitus during pregnancy]
de Valk HW, Eekhoff EM
Ned Tijdschr Geneesk, 2008 Jan 19;152(3):121-4

This article describes three cases of women with type 2 diabetes mellitus during pregnancy. The authors conclude that insulin therapy should be initiated before conception in women with preconceptional type 2 diabetes mellitus that requires glucose-lowering therapy. Women with a history of gestational diabetes should be counseled and tested before conception to detect silent type 2 diabetes mellitus. Specialist team care is also considered mandatory given the high-risk nature of type 2 diabetes mellitus and pregnancy.

Prescription drug use among fathers and mothers before and during pregnancy. A population-based cohort study of 106,000 pregnancies in Norway 2004-2006

Engeland A, Bramness JG, Daltveit AK, et al

Br J Clin Pharmacol, 2008; Feb 20 [Epub ahead of print]

In this registry-based study, Engeland and colleagues examined more than 100,000 Norwegian pregnancies and described the drug prescription pattern of both fathers and mothers around conception and during pregnancy (mothers). Results showed that among mothers, 83% were prescribed drugs during the period 3 months prior to estimated conception until 3 months after giving birth. The mothers who received drugs were prescribed on average 3.3 different Anatomical Therapeutic Chemical (ATC) codes (range 1-38). During pregnancy, 57% were prescribed drugs. In the first trimester, 33% of mothers were dispensed drugs, while the figure was 29% for mothers in the last trimester. Among fathers, 25% used prescribed drugs during the 3 months prior to conception; with on average 1.9 different ATC codes (range 1-22). The authors conclude large proportions of both fathers and mothers were dispensed drugs prior to conception or during pregnancy. While there is a high awareness of the issues involved in maternal drug use in pregnancy, possible teratogenic effects of drug use in fathers shortly before conception should be further explored.

Maternal use of selective serotonin re-uptake inhibitors and persistent pulmonary hypertension of the newborn

Källén B, Olausson PO

Pharmacoepidemiol Drug Saf, 2008; Mar 4 [Epub ahead of print]

In this study, the researchers used data from the Swedish Medical Birth Register for the years 1997-2005 to evaluate the previously published association between maternal use of selective serotonin re-uptake inhibitors (SSRI) and persistent pulmonary hypertension in the neonate (PPHN). Källén and Olausson conclude that the mechanism behind the association between SSRI and PPHN is unclear but an increased risk for respiratory problems after maternal use of SSRI is well known, and PPHN could be a rare part of this association.

Treating the mother - protecting the unborn: The safety of hypoglycemic drugs in pregnancy

Klieger C, Pollex E, Koren G

J Matern Fetal Neonatal Med, 2008; 21(3):191-6

This review provides a brief overview of the safety of antidiabetics in pregnancy. Specifically, concerns over teratogenicity due to the possible placental transfer of antidiabetics as well as maternal and neonatal outcomes are addressed. Several new insulin analogs are currently available for the treatment of diabetes. Due to the improved glycemic control demonstrated in non pregnant patients, these analogs may also prove to be beneficial in pregnancy. Insulin lispro is the only insulin analog that has been systematically studied in pregnancy. Results of these studies show a lack of transfer across the placenta and no adverse fetal and neonatal outcomes. The use of oral hypoglycemic agents in pregnancy is also generating interest. To date, there has been only one randomized controlled trial investigating the use of glyburide which found it to be safe and effective in the management of gestational diabetes mellitus. Klieger and colleagues conclude that the lack of randomized controlled trials for antidiabetics in pregnancy highlights the need for more comprehensive investigation regarding their safety and efficacy.

Recommendations for thyroxin therapy during pregnancy

Kyriazopoulou V, Michalaki M, Georgopoulos N, et al

Expert Opin Pharmacother, 2008; 9(3): 421-7

Over recent years there has been an expansion of knowledge regarding thyroid disease in pregnancy and subsequently controversies concerning the management of thyroid disease in pregnancy. This review focuses on maternal overt and subclinical hypothyroidism in pregnancy, suggesting guidelines for appropriate treatment for this disease due to its frequency, especially the subclinical manifestation, and the controversy that exists. It also reviews the complications in mother and fetus when hypothyroidism is untreated. On the other hand, with respect to other differing opinions, some recommendations should be given by the authors about supplying thyroxin to pregnant women with thyroid disease other than hypothyroidism.

Neurodevelopmental outcomes of extremely low birth weight infants exposed prenatally to dexamethasone versus betamethasone

***Lee BH, Stoll BJ, McDonald SA, et al
Pediatrics, 2008; 121(2): 289-96***

The objective of this study was to compare the development of adverse neurodevelopmental outcomes at corrected ages of 18 to 22 months for extremely low birth weight infants exposed prenatally to dexamethasone, betamethasone, or no steroid. Results showed that prenatal betamethasone exposure was associated with increased likelihood of unimpaired neurodevelopmental status and reduced risk of hearing impairment at corrected ages of 18 to 22 months among extremely low birth weight infants, compared with prenatal dexamethasone exposure or no prenatal steroid exposure. The researchers conclude that pending a randomized, clinical trial, it may be in the best interests of infants to receive betamethasone, rather than dexamethasone, when possible.

Review article: the use of anti-TNF therapy in inflammatory bowel disease during pregnancy and conception

***O'Donnell S, O' Morain C
Aliment Pharmacol Ther 2008 Feb 14 [Epub ahead of print]***

The aim of this study was to review available data regarding the safety of biological therapies during pregnancy, primarily in woman with inflammatory bowel disease (IBD). Based on available data, results showed that biological therapies appear to be safe in pregnancy. Most studies looking at the effects of any one medication on pregnancy in IBD are confounded by the fact that most patients are on multiple medications and have varying levels of disease activity. O'Donnell and O'Morain conclude that discontinuing therapy in the third trimester should be considered and large registries with longer follow up periods will be necessary before firm conclusions about the safety of Anti-TNF-alpha therapies during conception and pregnancy can be drawn.

Cancer in pregnancy: Gaps, challenges and solutions

***Pereg D, Koren G, Lishner M
Cancer Treat Rev, 2008; Feb 19 [Epub ahead of print]***

Cancer is the second leading cause of death during the reproductive years complicating between 0.02% and 0.1% of pregnancies. This article reviews the available data regarding the different aspects of the diagnosis and treatment of cancer during pregnancy as well as the effect of pregnancy on cancer prognosis. In pregnant patients diagnosed with cancer during the first trimester, treatment with multi-drug anti-cancer chemotherapy or radiotherapy (with fetal exposure >0.1-0.2Gy) is associated with an increased risk of congenital malformations and therefore should follow a strong recommendation for pregnancy termination. The risk for

malformation diminishes as pregnancy advances and when cancer is diagnosed during the second or third trimesters there is usually no clear indication for abortion. Treatment postponement, until achieving fetal maturity, while closely monitoring tumor growth may be considered in selected cases. According to the available experience it seems that non-obstetrical surgery may be performed during pregnancy without an increased risk for adverse outcomes. In most types of cancer, pregnancy has no effect on maternal prognosis when compared to non-pregnant patients matched by age, cancer stage and treatment.

Update on the Use of Antihypertensive Drugs in Pregnancy

Podymow T, August P

Hypertension, 2008; Feb 7 [Epub ahead of print]

No abstract available.

Acetaminophen use during pregnancy: effects on risk for congenital abnormalities

Rebordosa C, Kogevinas M, Horváth-Puhó E, et al

Am J Obstet Gynecol, 2008; 198(2): 178.e1-7

The objective of this study was to evaluate whether acetaminophen use among pregnant women was associated with an increased prevalence of congenital abnormalities. Results showed that children exposed to acetaminophen during the first trimester of pregnancy did not have an increased prevalence of congenital abnormalities compared with nonexposed children. No association was found between congenital abnormalities and duration of use during the first trimester. The authors conclude that acetaminophen is not associated with an increased prevalence of congenital abnormalities overall or with any specific group of major abnormalities

[Graves disease in pregnancy a risk for the child. Maternal TSH receptor antibodies can cause fetal and neonatal thyrotoxicosis]

Roos M, Sjöberg O, Axelsson O, et al

Lakartidningen, 2008; 105(3): 120-4

No abstract available.

Quantifying antiretroviral risk in pregnancy

Rossouw T

S Afr Med J, 2007; 97(11): 1014, 1016

No abstract available.

Study of drotaverine on first stage of labour and pregnancy outcome

Roy A, Patra KK, Mukhopadhyay S, et al

J Indian Med Assoc, 2007; 105(8): 450,452

This prospective randomized study of 200 women with spontaneous onset of labour was carried out in 100 women who were given 40 mg of drotaverine hydrochloride intravenously at > or = 3 cm dilatation of the cervix, the other 100 were taken as control. The researchers examined the effects of drotaverine on the progress and outcome of labour. Results revealed that drotaverine is highly effective in reducing the duration of active phase of labour by hastening cervical dilatation, more effective when given in more dilated cervix than with less dilatation and more effective in multigravida than in primigravida. There was no interference with uterine contractility and no increase in operative delivery. Also, it reduces the incidence of traumatic

postpartum haemorrhage by reducing the incidence of cervical tear. Roy and colleagues conclude that drotaverine is a safe drug for the mother as well as for the baby.

Hemorrhoids in pregnancy

***Staroselsky A, Nava-Ocampo AA, Koren G, et al
Can Fam Physician, 2008; 54(2):189-90***

This article discusses the safe treatment of hemorrhoids during the third trimester of pregnancy. According to the authors, most forms of the condition can be treated by increasing fibre content in the diet, administering stool softeners, increasing liquid intake, and training in toilet habits. Although none of the topical antihemorrhoidal agents commonly used have been assessed for safety in pregnancy, it is unlikely that the constituent parts (anesthetic, corticosteroids, and anti-inflammatory agents) will harm the third-trimester infant

Management of a first seizure. Special problems: adults and elderly

***Stephen LJ, Brodie MJ
Epilepsia, 2008; 49 (Suppl 1): 45-9***

This article discusses the management of first seizures in a variety of instances. The authors discuss the particular problems that can occur in patients with a single episode of provoked status epilepticus, a first tonic-clonic seizure during pregnancy and, particularly, an unprovoked event in older and learning disabled people.

Successful full-term pregnancies with assisted reproduction supported with prednisolone, acetylsalicylic acid and high progesterone doses in a lupus patient

***Trakakis E, Loghis C, Laggas D, et al
Clin Exp Obstet Gynecol, 2007; 34(4): 212-4***

Trakakis and colleagues present two rare cases of successful full-term pregnancies in a young woman suffering from lupus erythematosus for two years, who had subfertility problems and two missed abortions, before and after the diagnosis of lupus, with assisted reproduction. She received 10 mg of prednisolone daily from ovulation induction (with recombinant FSH--50 IU) until delivery, together with acetylsalicylic acid from ovulation induction until the 37th week of gestation and finally progesterone in high doses from the last insemination until the 12th week of gestation.

[Use of SSRIs during pregnancy and possible consequences for the development of the child]

***van der Veere CN, Bos AF
Ned Tijdschr Geneesk, 2007; 151(52): 2873-4***

According to the authors, approximately 2% of Dutch pregnant women are using a selective serotonin reuptake inhibitor (SSRI) which can cross the placenta easily. The consequences of prenatal exposure to SSRIs for the developing child remain to be determined. In the postnatal period, increased incidence of respiratory distress, feeding and digestive disturbances, irritability and convulsions, and admission to a neonatal intensive care unit have been described. While long-term effects of SSRIs have not yet been examined in humans, animal studies have shown permanent changes in specific parts of the brain and altered behaviour in adulthood after perinatal exposure. The authors conclude that research into motor and cognitive development at school age and adolescence in children prenatally exposed to SSRIs is urgently needed

Seizure control in antiepileptic drug-treated pregnancy
Vajda FJ, Hitchcock A, Graham J, et al
Epilepsia, 2008; 49(1): 172-6

This brief report covers an analysis of 7 years outcome data from the Australian Register of Antiepileptic Drugs in Pregnancy. In studying the control of antiepileptic drug-treated epileptic seizures during pregnancy, it was found that pregnancy had little influence on antiepileptic drug-treated epileptic seizure disorders. Seizures during pregnancy occurred in 49.7% of 841 antiepileptic drug (AED) treated pregnancies in women with epilepsy. Epilepsies that were active in the year before pregnancy tended to increase the risk of intrapartum and postpartum seizures. The risk of seizures during pregnancy was 50-70% less if the prepregnancy year was seizure free, and decreased relatively little more with longer periods of prepregnancy seizure control. Once there had been one year's freedom from seizures there seemed relatively little further advantage in deferring pregnancy to avoid seizures returning while pregnant.

Treating common problems of the nose and throat in pregnancy: what is safe?
Vlastarakos PV, Manolopoulos L, Ferekidis E, et al
Eur Arch Otorhinolaryngol 2008 Feb 12 [Epub ahead of print]

The purpose of this paper was to discuss the appropriate management of rhinologic and laryngeal conditions that may be encountered during pregnancy. After conducting their research, the authors surmised that the following drugs are considered relatively safe: beta-lactam antibiotics (with dose adjustment), macrolides (although the use of erythromycin and clarithromycin carries a certain risk), clindamycin, metronidazole (better avoided in the first trimester), amphotericin-B (especially in immunocompromised situations during the second and third trimester) and acyclovir. First-line antituberculous agents isoniazid, ethambutol, pyrazinamide, and ciprofloxacin in drug-resistant tuberculosis can be also used. Non-selective NSAIDs (until the 32nd week), nasal decongestants (with caution and up to 7 days), intranasal corticosteroids, with budesonide as the treatment of choice, second generation antihistamines (cetirizine in the third trimester, or loratadine in the second and third trimester), H2 receptor antagonists (except nizatidine) and proton pump inhibitors (except omeprazole) can be used to relieve patients from the related symptoms. In cases of emergencies, epinephrine, prednisone, prednisolone, methylprednisolone, dimetindene and nebulised b(2) agonists can be used with extreme caution. By contrast, selective COX-2 inhibitors and BCG vaccination are contraindicated in pregnancy. When prescribing to a pregnant woman, the safety of the materno-foetal unit is considered paramount. Although medications are potentially hazardous, misconceptions and suboptimal treatment of the mother might be more harmful to the unborn child. Knowledge update is necessary to avoid unjustified hesitations and provide appropriate counseling and treatment for pregnant women.

Neonatal hearing assessment in very low birth weight infants exposed to antenatal steroids
Waters TP, Silva N, Denney JM, et al
J Perinatal, 2008; 28(1): 67-70

The purpose of this study was to evaluate neonatal hearing assessment by the otoacoustic emission (OAE) test in very low birth weight (VLBW) infants exposed to antenatal steroids. The authors conclude that in the population they studied, antenatal steroids were not associated with a positive or negative effect on hearing assessment of VLBW infants.

Patterns of pregnancy exposure to prescription FDA C, D and X drugs in a Canadian population

***Wen SW, Yang T, Krewski D, et al
J Perinatol, 2008; Feb 21 [Epub ahead of print]***

The objective of this study was to examine prescription Food and Drug Administration (FDA) C, D and X drugs in general obstetric population. Wen and colleagues conclude that about one in every five women uses FDA C, D and X drugs at least once during pregnancy, and the most common prescription drugs in pregnancy are anti-asthmatic, antibiotics, nonsteroid anti-inflammation drugs, antianxiety or antidepressants and oral contraceptives.

Clinical inquiries. What is the most effective and safe malaria prophylaxis during pregnancy?

***Wiltz SA, Crawford P, Nichols W, et al
J Fam Pract, 2008; 57(1): 51-3***

No abstract available.

Trastuzumab in pregnancy associated with poor fetal outcomes

***Witzel ID, Müller V, Harps E, et al
Ann Oncol, 2008; 19(1): 191-2***

No abstract available.

LAY PRESS NEWS

The herceptin baby

***Bletchly R
People, 2008; February 24***

This article discusses the case of a woman who became pregnant while taking the cancer drug herceptin. Teresa Woodhead, a 36-year-old store manager underwent a double mastectomy, followed by chemotherapy and radiotherapy which often leaves women infertile. Three months into her herceptin therapy, she found she was pregnant. There is very little information regarding the effects of herceptin on pregnancies. In fact, Teresa is one of only 3 women in the world to become pregnant while taking herceptin. After a short, straightforward labour, Teresa delivered a healthy baby girl on February 11, 2008.

Copper may inhibit the transmission of HIV

ScienceDaily, 2008; February 26

Researchers from the U.S. and abroad have developed an inexpensive copper-based filter that may prevent HIV from being passed through breast milk and blood. Worldwide statistics of HIV transmission through breast milk and blood transfusions are at a disastrous high, especially in developing countries. In 2001 breast-feeding was attributed to up to 50% of the 700,000 mother-to-child transmission cases reported. The World Health Organization has estimated that blood transfusions are responsible for 80,000 to 160,000 HIV infections each year, while the Center for Disease Control reports that transfusions are the cause of 5 to 10% of HIV infections in developing countries. In previous studies copper has shown potent antibacterial and antiviral activity. In this study viral levels of HIV-1 in cultures were noted both before and after exposure to copper oxide powder, copper oxide fibers and copper-based filters. Researcher's determined HIV-1 inhibition occurred following dose-dependant exposure to both copper oxide and copper

fibers. Following filtration with copper powder or copper fibers viral deactivation of all isolates was observed. "This inexpensive methodology may significantly reduce HIV-1 transmission from mother-to-child and/or through blood donations if proven to be effective in breast milk or plasma and safe for use," say the researchers. "The successful application of this technology may impact HIV-1 transmission, especially in developing countries where HIV-1 is rampant."

Is codeine a risk when breast-feeding?

Pulse, 2008; February 27

This article answers the following question: We are all aware that a significant proportion of the population is unable to metabolize codeine. Is it true that some women are such effective metabolizers that if they are given codeine when breast-feeding their baby is at risk of opiate toxicity? According to Dr. William Campbell, the majority of individuals metabolize codeine to morphine via cytochrome P450 (CYP) isozymes. There is considerable variation in this metabolism and higher plasma levels of the morphine metabolite may be attained in women, partly because of their physiology (lower body weight, organ size, body fat and lower glomerular filtration rate compared with men) as well as differences in metabolism. Since drugs like morphine within the plasma may be transferred to an infant by breast-feeding, caution should be exercised when prescribing to a feeding mother. The short-term use of paracetamol, NSAIDs and aspirin are deemed safe. The consumption of opioids for longer than a few days may lead to problems. Since the infant's organs, especially the kidneys, are not as well developed as the adult's, they may not excrete morphine as readily when opioids are consumed, resulting in accumulation. Increasing drowsiness would be one warning sign of opioid toxicity. There have been isolated cases of infant death reported in the literature, as a result of breast-feeding in a mother consuming co-codamol. Although this is rare it should be borne in mind when prescribing co-codamol for more than a few days to a mother who is currently breast-feeding.

Cancer drug may harm the developing fetus

Reuters Health E-Line, 2008; March 7

The majority of women who become pregnant while taking the cancer drug Gleevec, usually for a type of blood cancer called chronic myeloid leukemia, will probably have a successful outcome. However, there is a substantial risk of serious fetal malformations, according to a study reported this week. Some research has suggested that Gleevec, known generically as imatinib, may cross the placenta and damage the developing cells. The drug's label reflects this potential risk and warns women to avoid pregnancy while using the drug. Imatinib has been in use for nearly 10 years, yet data regarding its effects on pregnancy is limited, Dr. Seonaid M. Pye and colleagues note. This lack of information has made it difficult to counsel women who conceive while taking the drug. To better understand the drug's impact on pregnancy outcomes, Pye, from Imperial College, London, and associates reviewed the records of 180 pregnant imatinib users who were reported to drugmaker Novartis, the Hammersmith Hospital in London, or M. D. Anderson Cancer Center in Houston. Pregnancy outcome data were available for 125 women. Sixty-three women - roughly half - delivered normal infants and 35 women (28 percent) elected to terminate their pregnancy, including 3 cases prompted by the identification of a fetal abnormality. Another 18 pregnancies ended in miscarriage. The remainder of the births - 9 in total - involved the delivery of an infant with abnormalities, including 1 case of stillbirth. The abnormalities included exomphalos (umbilical hernia), renal agenesis (underdeveloped kidney), and hemivertebrae (underdeveloped spine) and, in the stillborn infant, meningocoele (cerebral hernia). The fact that some of the abnormalities had previously been reported in animal studies of imatinib suggests that they were, in fact, caused by exposure to the drug. "Our study suggests that a concern about conceiving a child while taking imatinib is justified and that patients should be advised to avoid

conception while on treatment," Pye said in a statement. "In those patients who do become pregnant, balancing the risk of the fetus from taking therapy to the risk of the mother from interrupting therapy will be an individual decision," the study leader added.