education

FROM THE JOURNALS Edited highlights of weekly research reviews on https://bit.ly/2PLtil8

Benralizumab for the prevention of COPD exacerbations

Exacerbations of chronic obstructive pulmonary disease (COPD) in people with moderate to severe COPD with high eosinophil counts were not reduced by benralizumab in either the GALATHEA or TERRANOVA randomised controlled trials. The trials were funded by AstraZeneca.

The rationale for these studies, which included thousands of participants, was debatable as earlier studies had shown no reduction in COPD exacerbations with benralizumab. However, in the subgroup of people with raised eosinophil counts there was a "numerical, albeit non-significant, improvement." The drug, which has supporting evidence for asthma, really needs shelving for COPD.

N Engl J Med doi:10.1056/NEJMoa1905248

Roxadustat rocks anaemia world

Chinese researchers tested whether roxadustat increases haemoglobin in patients with chronic kidney disease in two double blind randomised controlled trials. Posed as an alternative to epoeitin, roxadustat is an oral drug designed to inhibit hypoxia-inducible factor (HIF) prolyl hydroxylase. Both trials showed improvements in anaemia, one in patients receiving dialysis, and one in patients with chronic kidney disease not on dialysis. I expect regulators and patients will be pleased with this, but it is also our duty to expect evidence that roxadustat improves patients' symptoms without increasing the risk of death or cardiovascular disease. There was also an unexplained higher rate of hyperkalaemia in those receiving roduxastat.

N Engl J Med doi:10.1056/NEJMoa1813599
N Engl J Med doi:10.1056/NEJMoa1901713

Uveitis treatment

An international randomised controlled trial of methotrexate versus mycophenolate has been inconclusive in showing which is more effective in controlling uveitis inflammation. Rathinam and colleagues randomly allocated 216 people at nine eye centres across the globe and assessed them at six months for "treatment success." This endpoint was defined as control of inflammation in both eyes, ≤7.5 mg prednisone daily, and ≤2 drops of prednisolone acetate 1%, and no treatment failure due to safety or intolerability.

I like this endpoint because it encompasses all the factors that make up treatment success, certainly from the clinician's perspective. Being off steroids is critical in inflammatory conditions due to the serious adverse effects. It would have been good to know whether methotrexate or mycophenolate is better, so I commend this study for answering a key question, even if the answer was that mycophenolate was no better.

JAMA doi:10.1001/jama.2019.12618

Surgical options for heavy menstrual bleeding

The HEALTH trial randomly allocated 660 women aged <50 years with heavy menstrual bleeding to either endometrial ablation or laparoscopic supracervical hysterectomy. Hysterectomy may sound like a radical approach to heavy menstrual bleeding, but participants were required to have been referred to a gynaecologist for surgical treatment of the condition so, by definition, it was severe enough to warrant treatment and the women had to have no desire for (further) children.

The co-primary endpoint was patient satisfaction and menorrhagia-specific quality of life at 15 months. On this basis laparoscopic supracervical hysterectomy was superior to ablation, with 97% of women satisfied versus 87% of women in the ablation group, and 69% with the best menorrhagia quality of life score versus 54%. Complication rates were similar in both groups, but ablation was quicker to perform and had shorter recovery. Infection rates were similar, but voiding dysfunction was slightly more common in the laparoscopic supracervical hysterectomy group. The only caveat would be that it was open-label with no objective endpoints to assess its efficacy. That said, double-blind trials of surgical procedures are no mean feat.

Lancet doi:10.1016/S0140-6736(19)31790-8

Alleviating peanut allergy

A randomised controlled trial has shown the efficacy of oral immunotherapy in desensitising people with peanut allergy. The study randomly allocated 120 adults and children to three arms: two years build-up oral immunotherapy followed by withdrawal, two years build-up followed by continuation at a lower dose, or placebo (oat powder) throughout, with use of nose clips in an attempt to blind to smell.

But what counts as efficacy for an allergy therapy? Ideally one would want a safe "cure" without the need for further treatment, but oral immunotherapy isn't a golden bullet. This study's primary endpoint was passing a double blind, placebo controlled food challenge with peanut protein at 2 years, and at 2 years and 3 months. I would say this study length is a reasonable balance between long enough to claim the response is "sustained" and short enough to be a practical study with minimal dropout.

This study found 21 of the 60 people in the build-up and withdraw arm passed both challenges, compared with only one of 25 of those in the placebo group. However, the build-up and continue arm were much less likely to become desensitised after passing the initial food challenge.

Lancet doi:10.1016/S0140-6736(19)31793-3

Alex Nowbar is a clinical research fellow at Imperial College London

GUIDELINES

Diagnosis and management of hypertension in pregnancy: summary of updated NICE guidance

CPD READING
0.5 HOURS

Katie Webster,[1] Sarah Fishburn,[1] Mike Maresh,[1] Sarah C Findlay, Lucy C Chappell,[2] on behalf of the Guideline Committee

[1]National Guideline Alliance, Royal College of Obstetricians and Gynaecologists, London
[2]King's College London
Correspondence to: L C Chappell lucy.chappell@kcl.ac.uk

Hypertension in pregnancy is a common condition, affecting about 10% of pregnant women. This includes women with chronic hypertension—which may be diagnosed before pregnancy or in the early stages of pregnancy (<20 weeks' gestation)—and women with hypertension related to pregnancy (gestational hypertension and pre-eclampsia) (box). If not identified and treated, hypertension can lead to adverse events for both the woman and her baby, including increased risk of maternal stroke, lower birth weight, and increased risk of the baby requiring neonatal intensive care.

Definitions for hypertensive disorders of pregnancy

- *Chronic hypertension*—Hypertension that is present at the booking visit or before 20 weeks' gestation, or if the woman is already taking antihypertensive medication when starting maternity care. It can be primary or secondary in aetiology
- *Gestational hypertension*—New hypertension presenting after 20 weeks of pregnancy without significant proteinuria
- *Pre-eclampsia*—New onset hypertension (>140 mm Hg systolic or >90 mm Hg diastolic) after 20 weeks of pregnancy and the coexistence of one or both of the following new-onset conditions:
  - Proteinuria (urine protein:creatinine ratio ≥30 mg/mmol, or albumin:creatinine ratio ≥8 mg/mmol, or ≥1 g/L [2+] on dipstick testing)
  - Other maternal organ dysfunction, including features such as renal or liver involvement, neurological or haematological complications, or uteroplacental dysfunction (such as fetal growth restriction, abnormal umbilical artery Doppler waveform analysis, or stillbirth)

WHAT YOU NEED TO KNOW

- Hypertension affects about 10% of pregnant women, including those with pre-existing hypertension, chronic hypertension that is first diagnosed during pregnancy, and hypertension related to pregnancy (gestational hypertension and pre-eclampsia)
- Target blood pressure during the antenatal period should be 135/85 mm Hg for women with hypertension during pregnancy
- Hypertension during pregnancy is associated with an increased risk of hypertension and cardiovascular disorders in later life. Women should be offered appropriate lifestyle and dietary advice to minimise this risk

General practitioners and specialists other than obstetricians play a vital role in the identification of hypertension during pregnancy, first line management, and appropriate referral to specialist care. Women with pre-existing (chronic) hypertension may require pre-pregnancy counselling from their primary or secondary care team, modifications to their usual treatment, and referral to specialist care. Women are likely to have shared care between specialists and non-specialists throughout their pregnancy, meaning that GPs need to be aware of current blood pressure targets, suitable medication, and thresholds for urgent referral to specialist care. Furthermore, hypertensive disorders of pregnancy are known to predispose women to ongoing hypertension and associated cardiovascular morbidity in later life. The primary care team plays a crucial role in risk reduction and surveillance for these conditions. It is therefore vital that all healthcare professionals have an understanding of the optimal management of hypertension during pregnancy and the postpartum period.

This article summarises the updated recommendations from the National Institute for Health and Care Excellence (NICE) on the diagnosis and management of hypertension in pregnancy.[1]

VOISIN / PHANIE / SPL

Recommendations

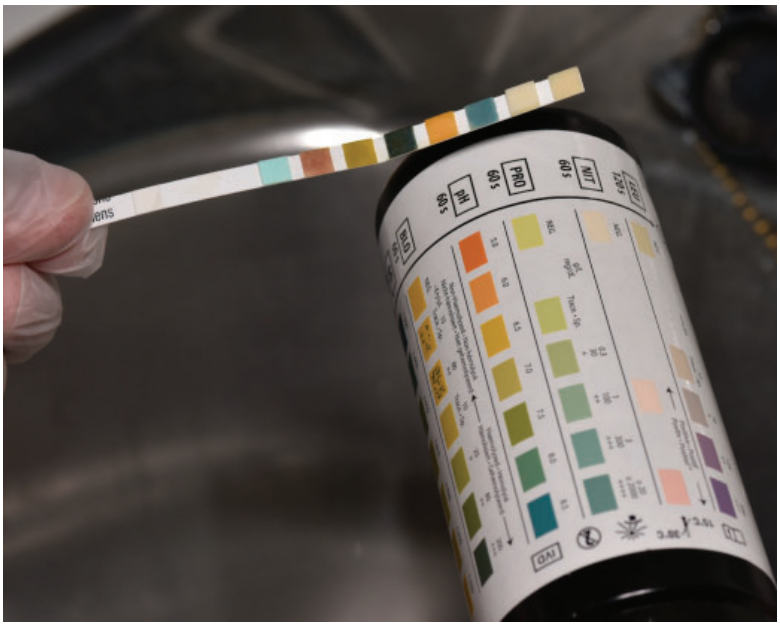
NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the guideline committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

Treatment of chronic hypertension

For women with chronic hypertension, recommended diet and lifestyle advice have been brought in line with that given to non-pregnant individuals. However, the choice of anti-hypertensive drugs is different during pregnancy, because of the need to consider the effects of the drug on the fetus. No specific medication was recommended in the previous version of the guideline, but labetalol, nifedipine, and methyldopa are now specified as suitable options to discuss with women for use in pregnancy. New evidence was identified to provide guidance on blood pressure targets during pregnancy, and the target has now been amended to 135/85 mm Hg (reduced from the previous guidance of 150/100 mm Hg), also reflecting evidence informing the management of hypertension in adults.

In addition to the new recommendations, NICE diagnostic guidance DG23 has been published since the previous guideline, and provides guidance on the use of placental growth factor (PlGF)-based testing.[2] This offers an additional diagnostic test to rule out pre-eclampsia in women with suspected pre-eclampsia (including those at increased risk of developing it, such as women with chronic hypertension or gestational hypertension), and so a link has been included in the updated guideline.

The recommendations are summarised in the full article on bmj.com.



DR P. MARAZZI / SPL

Management of gestational hypertension

Management of gestational hypertension requires regular monitoring, to ensure that blood pressure control is maintained and that there is not progression to pre-eclampsia. The evidence for the type and frequency of monitoring was reviewed as part of this update, and the recommendations amended. The blood pressure target has been reduced to 135/85 mm Hg (in line with that for chronic hypertension), and the drug choices aligned to those used in chronic hypertension to simplify management for clinicians.

The recommendations are summarised in the infographic.

Assessment of proteinuria in hypertensive disorders of pregnancy

Proteinuria is one of the key features of pre-eclampsia and should be assessed at each antenatal visit alongside blood pressure monitoring (see related NICE guidance on antenatal care for uncomplicated pregnancies[4]). The updated recommendations stress that proteinuria measurements should always be interpreted alongside a full clinical review—to highlight that women may develop pre-eclampsia in the absence of proteinuria, and that there may be value in repeating a measurement if there is doubt over the diagnosis of pre-eclampsia.

Previous NICE guidelines recommended that proteinuria was assessed using a 24-hour urine collection or a spot urinary protein:creatinine ratio. The updated guideline assessed the evidence for the accuracy of protein:creatinine ratio and of the alternative test albumin:creatinine ratio and found both to have high specificity and sensitivity, meaning they can be used instead of 24-hour urine collection, which is no longer recommended.

The recommendations are summarised on bmj.com.

Pre-eclampsia

Pre-eclampsia can be associated with severe complications for a woman and her baby, so appropriate risk assessment and management is critical. The updated guidance uses the same blood pressure target and treatment choices as for chronic and gestational hypertension, simplifying management for the clinician, but no longer recommends that all women with pre-eclampsia be admitted to hospital as evidence for this approach was lacking. Instead, the guideline provides more information on the features which may indicate more severe disease requiring admission and provides information on new risk prediction models that may help identify women at risk of severe complications.

Recommendations for management of pre-eclampsia are described in the infographic. Guidance on the indications and optimum timing for birth in women with pre-eclampsia has also been updated (see bmj.com for details).

thebmj Visual summary

Managing hypertension in pregnancy

Visual summary of NICE guidelines

GPs and specialists other than obstetricians play a vital role in the identification of hypertension during pregnancy, first-line management and referral to specialist care. This graphic summarises the updated recommendations from the National Institute for Health and Care Excellence (NICE) on the diagnosis and management of hypertension in pregnancy. Management guidance is now the same for women with chronic and gestational hypertension. Choice of antihypertensive medication is the same for women with all types of hypertension in pregnancy.

	HYPERTENSION PATHWAY		PRE-ECLAMPSIA PATHWAY	
	HYPERTENSION	SEVERE HYPERTENSION	HYPERTENSION	SEVERE HYPERTENSION
Blood pressure	140/90 to 159/109 mmHg	160/110 mmHg or more	140/90 to 159/109 mmHg	160/110 mmHg or more
Admission to hospital	Do not admit routinely	Admit	Admit if clinical concern (see below)	Admit
Initial management	Offer pharmacological treatment for all patients with blood pressure above 140/90 mmHg			
	First choice: **Labetalol** (LAB)	Second choice: **Nifedipine** (NIF)	Third choice: **Methyldopa** (MET)	Aim for blood pressure of 135/85 mmHg or less

MONITORING				
Blood pressure	Once or twice a week	Every 15–30 minutes	At least every 48 hours More frequently if admitted	Every 15-30 minutes
Proteinuria	Once or twice a week	Daily	Only repeat if clinically indicated	
Blood tests Full blood count Liver function Renal function	At presentation Then once a week Offer PlGF-based testing once, if pre-eclampsia is suspected		twice a week	3 times a week

FETAL ASSESSMENT				
Heart auscultation	At every antenatal appointment		At every antenatal appointment	
Ultrasound	At diagnosis Then every 2 to 4 weeks, if clinically indicated	At diagnosis Then every 2 weeks	At diagnosis Then every 2 weeks	
Cardiotocography	If clinically indicated	At diagnosis Then if clinically indicated	At diagnosis Then if clinically indicated	

If dipstick is positive quantify proteinuria

Re-test with new sample

Uncertainty about diagnosis

Protein:creatinine ratio
Use 30 mg/mmol as a diagnostic threshold

or

Albumin: creatinine ratio
Use 8 mg/mmol as a diagnostic threshold

Interpret findings in the context of a full clinical review, including:

Symptoms and signs of pre-eclampsia, such as:
- Severe headache
- Problems with vision
- Severe pain just below the ribs
- Vomiting
- Sudden swelling of the face, hands or feet

Other investigation results, such as:
- Evidence of haemolysis
- Worsening of renal function
- Abnormal liver function
- Falling platelet count

No proteinuria, no clinical features of pre-eclampsia

Pre-eclampsia diagnosed

Continue monitoring

<37 weeks

≥37 weeks

Do not offer planned early birth to women whose blood pressure is lower than 160/110 mmHg, unless there are other medical indications

Agree the maternal and fetal indications for birth and its timing between the woman and the senior obstetrician

Offer full clinical assessment at each antenatal appointment

Consider using maternal risk prediction models

- fullPIERS: Any time during pregnancy
- PREP-S: Up to 34 weeks of pregnancy

Admit to hospital if there are concerns for woman or baby, such as:
- Sustained systolic blood pressure ≥160 mmHg
- Concerning maternal haematological or biochemical investigations
- Signs of impending pulmonary oedema
- Signs of impending eclampsia
- Suspected fetal compromise
- Any other clinical signs that cause concern

Signs of severe pre-eclampsia

Involve a senior obstetrician in any birth timing decisions for women with pre-eclampsia

- 37 weeks or earlier: Consider planned early birth in women with severe pre-eclampsia
- After 37 weeks: Initiate birth within 24-48 hours

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See more visual summaries http://www.bmj.com/infographics

Table 1 | Prevalence of hypertensive disorder in a future pregnancy in women with hypertension in previous or current pregnancy

Prevalence of hypertension in future pregnancy	Type of hypertension in previous or current pregnancy		
	Any hypertension	Pre-eclampsia	Gestational hypertension
Any hypertension	~21% (1 in 5 women)	~20% (1 in 5 women)	~22% (1 in 5 women)
Pre-eclampsia	~14% (1 in 7 women)	Up to ~16% (1 in 6 women). If birth was at 28-34 weeks*, ~33% (1 in 3 women). If birth was at 34-37 weeks, ~23% (1 in 4 women)	~7% (1 in 14 women)
Gestational hypertension	~9% (1 in 11 women)	~6-12% (up to 1 in 8 women)	~11-15% (up to 1 in 7 women)
Chronic hypertension	Not applicable	~2% (up to 1 in 50 women)	~3% (up to 1 in 34 women)

*No evidence identified for women who gave birth at <28 weeks, but the GC agreed that the risk was likely to be at least as high as that for women who gave birth between 28 and 34 weeks.

Table 2 | Relative risk* of future cardiovascular morbidity in women with hypertension in previous or current pregnancy

Risk of future cardiovascular disease	Type of hypertension in current or previous pregnancy			
	Any hypertension	Pre-eclampsia	Gestational hypertension	Chronic hypertension
Major adverse cardiovascular event	Risk increased (up to ~2 times)	Risk increased (~1.5-3 times)	Risk increased (~1.5-3 times)	Risk increased (~1.7 times)
Cardiovascular mortality	Risk increased (up to ~2 times)	Risk increased (~2 times)	No data	No data
Stroke	Risk increased (up to ~1.5 times)	Risk increased (~2-3 times)	Risk may be increased	Risk increased (~1.8 times)
Hypertension	Risk increased (~2-4 times)	Risk increased (~2-5 times)	Risk increased (~2-4 times)	Not applicable

*Risks are overall estimates—summarised from risk ratios, odds ratios, and hazard ratios—compared with the background risk in women who did not have hypertensive disorders during pregnancy. Absolute risks will vary considerably depending on follow-up time (from 1 to 40 years postpartum).

Postnatal care for women with hypertension during pregnancy

Many women with hypertension during pregnancy will require antihypertensive treatment in the postnatal period, although the duration of treatment required will vary. Selection of an appropriate antihypertensive depends on the efficacy, safety, and tolerability of the different medications. To improve adherence, preparations with once daily use that are compatible with breastfeeding are recommended. The recommendations were updated (see bmj.com for details), based on the NICE guideline for the management of hypertension in adults,[3] adapted to support breastfeeding in women who may choose to breastfeed and to minimise the chance of women choosing not to breastfeed because of their medication.

Long term consequences of hypertension during pregnancy

The occurrence of hypertension during one pregnancy is known to predispose women to hypertension in the future—with an increased likelihood of recurrence of hypertensive disorders of pregnancy in future pregnancies and of long term hypertension in later life.

Precisely quantifying the likelihood of recurrence during pregnancy is challenging, but the updated guidance provides some estimates of how likely hypertensive disorders are to recur (table 1). Advise women with hypertensive disorders of pregnancy that the overall risk of recurrence in future pregnancies is approximately 1 in 5.

In addition, hypertensive disorders during pregnancy are known to be associated with an increased likelihood of hypertension, and associated cardiovascular morbidity, in later life. The updated guideline provides estimates of this increase in likelihood for women with hypertensive disorders during pregnancy, to enable them to modify their lifestyle accordingly (see table 2 and bmj.com for further details).

Competing interests: See bmj.com.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.l5119

WHAT'S NEW IN THIS GUIDANCE?

- Initiation of antihypertensive medication is now recommended for women with a blood pressure measurement of 140/90 mm Hg
- Target blood pressure for those taking antihypertensive medication is now 135/85 mm Hg
- Categories of hypertension have now been simplified to "hypertension" and "severe hypertension" (rather than mild, moderate, and severe)
- 24 hour urine collection is no longer recommended for routine quantification of proteinuria during pregnancy
- Hospital admission is no longer recommended for every woman with pre-eclampsia—risk assessment should be carried out on an individual basis to determine place of care
- Pharmacological therapy for hypertension in the postnatal period now reflects stepped treatment recommended for adults, adapted for women who are breastfeeding
- Estimates for the likelihood of recurrent hypertensive disorders in future pregnancies and of long term cardiovascular disease are provided

GUIDELINES INTO PRACTICE

- Do you refer women with chronic hypertension to a specialist in hypertensive disorders of pregnancy for pre-pregnancy advice?
- Do you stop ACE inhibitors or angiotensin II receptor blockers within two days of notification of pregnancy?
- Do you provide information for postnatal women after pregnancy hypertension on long term cardiovascular risk and interventions to reduce that risk?

HOW WOMEN WITH LIVED EXPERIENCE WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Committee members involved in this guideline update included lay members who contributed to the formulation of the recommendations summarised here.

PRACTICE POINTER

Promoting physical activity to patients

Christine Haseler,[1] Ranulf Crooke,[2] Tobias Haseler[3]

[1]Hucclecote Surgery, Gloucester
[2]Hilary Cottage Surgery, Fairford
[3]The Bloomsbury Surgery, London
Correspondence to: C Haseler christine.haseler@nhs.net

CPD READING
0.5 HOURS

The health benefits of physical activity are proved and wide ranging, exceeding that of any drug. The Academy of Medical Royal Colleges has described physical activity as a "miracle cure."[1] Meanwhile, inactivity contributes to as many deaths in the UK as smoking[2] and is the fourth leading risk factor for mortality worldwide.[3] More than 25% of adults in the UK are inactive, doing less than 30 minutes of physical activity a week.[2] Clinicians are uniquely placed to help their patients to become more physically active, and even a brief discussion within a consultation can lead to change.

This article offers a practical guide to help clinicians discuss physical activity within a consultation, including how to address concerns patients may have about becoming more active and how to help them overcome barriers to change.[6]

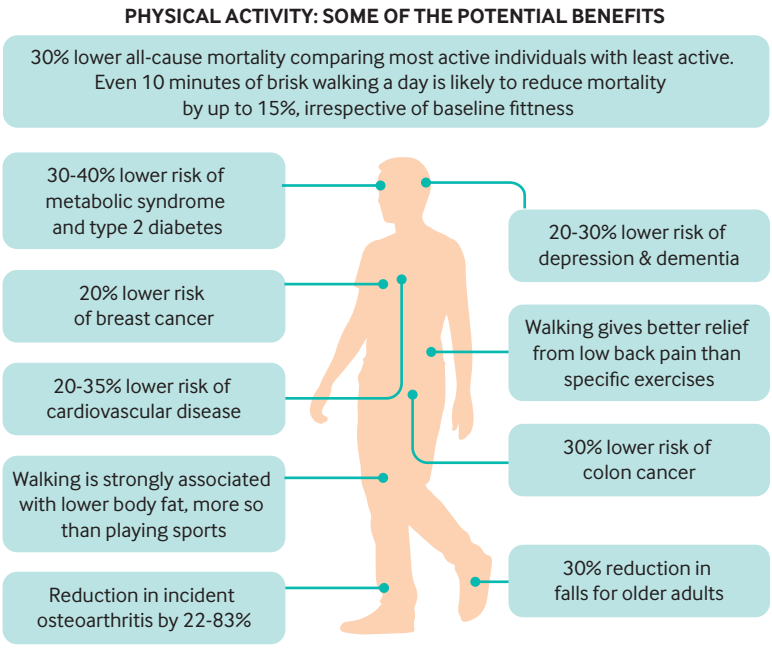

Fig 1 | The health benefits of walking and achievement of recommended levels of physical activity, adapted from Public Health England '10 minutes brisk walking each day in mid-life for health benefits and towards achieving physical activity recommendations'[4] and UK Department of Health 'Start Active Stay active'[5]

WHAT YOU NEED TO KNOW

- Benefits to health start at just 30 minutes of physical activity a week, but more than a quarter of UK adults fail to achieve this
- Physical activity can reduce all cause mortality more effectively than medication
- Risk of harm from moderate physical activity is small, while the adverse effects of inactivity and sedentary time are clear

WHAT DO WE MEAN BY "PHYSICAL ACTIVITY"?

Although exercise and physical activity are sometimes used interchangeably, they have distinct meanings. In practice, although exercise may be a more familiar term to people, it can also be off putting to some: you don't need to be *doing exercise* to be active. Physical activity, defined by the World Health Organization, is "any body movement performed by skeletal muscles that expends energy," whereas exercise is "physical activity with the primary purpose of improving or maintaining physical fitness or performance."[7] Moderate intensity physical activity "requires a moderate amount of effort and noticeably accelerates the heart rate,"[5] leads to faster breathing and feeling warmer,[15] and requires 3 to 6 times the metabolic rate of being at rest.[5 7]

Health benefits of being physically active

Strong evidence shows that individuals who are more active have lower rates of all cause mortality, cardiovascular disease, metabolic disease, colon and breast cancer, and depression, with additional benefits to bone health from weight bearing and resistance activities (fig 1).[1-8] Any level of increased physical activity is beneficial.[9] People doing just 15 minutes of moderate intensity physical activity a day have a three year greater life expectancy than those who are inactive, one large cohort study found.[10] A recent systematic review and meta-analysis found that all intensities of physical activity, including light intensity, are associated with a substantially reduced risk of death in a dose-response manner.[9]

Guidelines from the UK and World Health Organization recommend that adults undertake 150 minutes of moderate intensity physical activity per week in bouts of at least 10 minutes' duration, with muscle strengthening activities on at least two days. In the UK 33% of men and 45% of women do not achieve this level of physical activity.[2] There is evidence of further benefit from spreading this across the week, with 30 minutes of physical activity on at least five days.[7]
Even in sufficiently active individuals, daily sedentary time is an independent risk factor for all cause mortality, cardiovascular disease, and diabetes.[11]

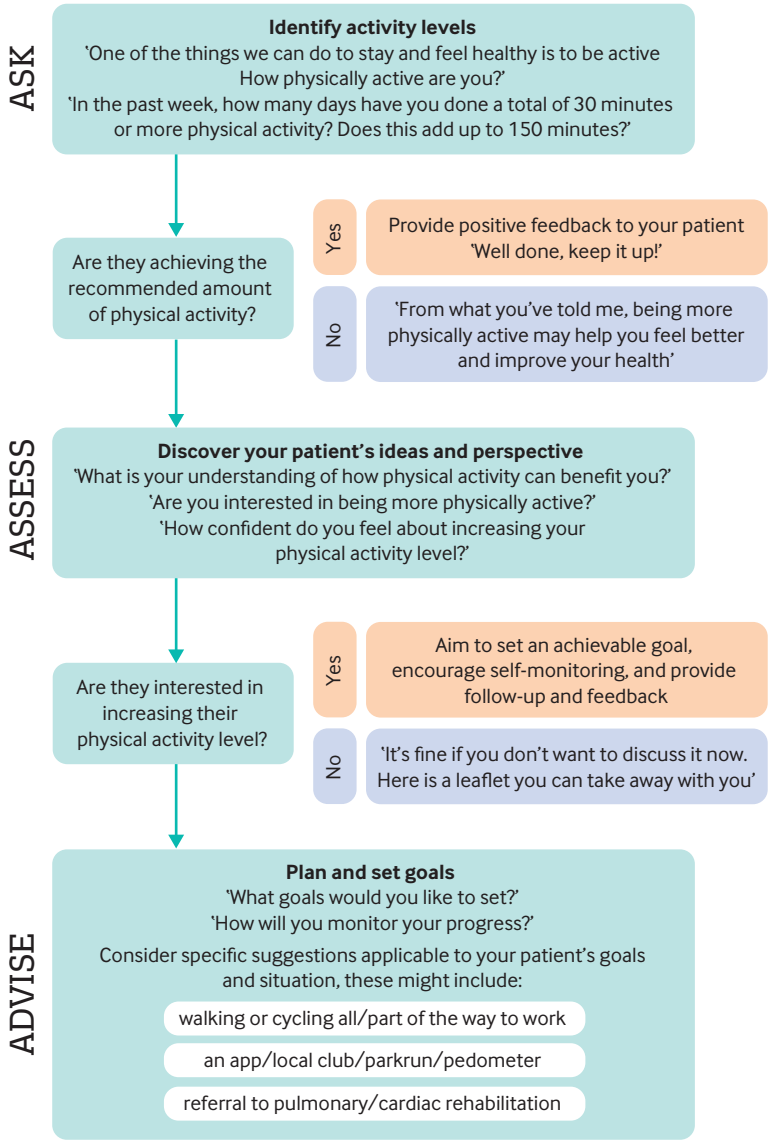

Fig 2 | The 'Ask-Assess-Advise' structure for discussing physical activity behaviour change in the consultation. Adapted with permission from NHS Health Scotland's Physical activity screening and brief intervention script and NICE guidance: Physical activity; brief advice for adults in primary care (PH44)[13 15]

Examples of moderate intensity physical activity[1-7]

- Brisk walking or cycling
- Household chores such as cleaning or gardening, stair climbing, home improvement works
- Manual work
- Games and sports such as dancing, swimming, or team sports; individual sports such as tennis, martial arts, skateboarding
- Jogging, running
- Exercise machine run/row/cycle at home or in the gym
- Outdoor activities
- Charity or event participation
- Sexual activity.

Examples of moderate intensity physical activity for people with low exercise capacity, such as frail individuals[5 7]

Same relative intensity but lower absolute intensity:

- Sitting exercises
- Community activity groups, such as strength and balance classes, Tai Chi, and dance classes
- Walking, cycling, or moving at normal or lower than normal pace.

How does physical activity improve health?

Regular physical activity produces beneficial changes in body composition such as reduced visceral adiposity. It improves metabolic dysfunction and has anti-inflammatory effects that result in reduced measures of systemic inflammation.[12 13] These changes are protective in chronic conditions, as visceral adiposity is linked to impaired glucose and lipid metabolism, and low grade systemic inflammation is associated with metabolic syndrome, cognitive dysfunction, and depression.[13]

Beneficial adaptations from regular physical activity are found in the sympathetic nervous system and the hypothalamic-pituitary axis, leading to increased resilience to physical and psychological stress. Chronic conditions where dysregulation of these systems is observed, such as autoimmune, metabolic, and cardiovascular diseases, and stress related health problems, such as depression, are reduced.[13] Increased neuroplasticity and growth factor expression in the brain may further improve both mood and cognition.[13]

Discussing physical activity in the consultation

When to ask about activity

Any contact with a patient is an opportunity for a discussion about physical activity, and even a brief discussion can help someone to become more active. In one randomised controlled trial of 255 patients, a 3-5 minute discussion in a routine health appointment, with a brief booster call after two weeks, increased physical activity levels 4-6 weeks later by 37 minutes per week, 30 minutes more than controls.[14] Opportunities for discussion can be found in new patient appointments, NHS health checks, or chronic disease reviews, and can be prompted by waiting room questionnaires, promotional posters, and videos.[15]

Screening for inactivity

One approach to discussing physical activity in a consultation is to use "ask-assess-advise," outlined in fig 2. This is a simple framework for discussing activity adapted from National Institute for Health and Care Excellence (NICE) guidance and NHS Health Scotland's physical activity screening and brief intervention scripts.[13 15] "Ask-assess-advise" begins with a validated single question: In the past week, on how many days have you done a total of 30 minutes or more of physical activity, which was enough to raise your breathing rate? This may include sport, exercise, and brisk walking or cycling for recreation or to get to and from places, but should not include housework or physical activity that may be part of your job.[16 17] The question is followed by an assessment of the patient's ideas about becoming more active, followed by goal setting and making a plan.

Becoming more physically active

Inactivity may be due to several factors, such as lack of awareness, uncertainty about the benefits of physical activity, difficulty in self motivation, or other personal barriers.[18-21] Encouraging people who are inactive to simply move more is a good start,[2 7] and for many people, incorporating walking or cycling into day-to-day life can be the easiest change to make.[5 7] There is benefit from limiting sedentary time to 20 minutes.[11] Those who are sufficiently active but have long periods of sedentary time may be encouraged to take regular breaks from sitting. Motivational interviewing techniques can be particularly useful in helping people to identify and overcome barriers.[22] See examples of activities listed above for patients to consider.

Get to know what local physical activity promotion services are available to direct or refer people. Services that offer advice and counselling to promote physical activity can be more effective than those for smoking cessation.[23] Remote or web based interventions can be as effective as face-to-face discussions.[24]

Social prescribing initiatives are another way to help support people who want to get active. These can increase use of local services and encourage increased physical activity levels.[25] Activities that include a supportive network or a "social contract," such as a club or local parkrun, can help, as can smartphone apps or a pedometer.[15]

Risks of physical activity

Physical activity is safe and beneficial for almost everyone.[5 26] A safeguard against doing too much physical activity too soon is to "start slow and build up," beginning with approximately 10 minutes' activity and gradually building up by about 10% per day. Physical activity recommendations are valid for people with disabilities and chronic conditions, taking into account the individual's capacity or limitations.[7]

An exercise prescription, a specific set of exercises aimed to improve fitness, is distinct from physical activity advice and has defined contraindications. These include increased cardiovascular demand in unstable angina, severe aortic stenosis, or uncontrolled severe hypertension.[27] In pregnancy, impact activities causing trauma, prolonged supine lying, high altitude, or underwater activities are not advised.[28] Activity moderation and psychological support are required for exercise addiction, characterised by obligatory and excessive exercise.[29]

GETTY IMAGES

Physical activity in people with long term conditions

Availability of exercise interventions for people with long term conditions vary locally. For those interested in thinking more about how to get more active, resources such as Moving Medicine provide condition specific, evidence based advice.

Osteoarthritis

Physical activity is a core treatment for osteoarthritis.[30] Osteoarthritis has been unhelpfully referred to as "wear and tear," with descriptions such as "bone on bone," leading to people fearing that physical activity will make it worse. It can instead be described as a "flare and repair" process. The pain from osteoarthritis is multifactorial,[31] mainly from synovial inflammation trying to repair a joint, but also from capsule, muscle, ligament stiffness, and bony pain.

Explain that physical activity improves muscle control and tone, which support the joint while it heals. Physical activity also improves range of movement and stiffness, improving function and optimising recovery.

Chronic obstructive pulmonary disease and cardiovascular disease

People with chronic obstructive pulmonary disease or cardiac disease who increase physical activity by completing structured rehabilitation programmes have reduced hospital admissions, greater quality of life, and increased exercise capacity. The benefits in severe disease are just as pronounced as in mild to moderate disease.[32 33]

Advising patients that exercise can be as effective as medication in some chronic diseases can be powerful: a 2013 meta-analysis found that exercise interventions (which were variable between all the studies, including structured rehabilitation and home or community exercise programmes) are often similar to medications in terms of their mortality benefits in the secondary prevention of coronary heart disease, rehabilitation after stroke, treatment of heart failure, and prevention of diabetes.[34]

Frailty

In older people, decline in muscle power and speed, cardiorespiratory function, and standing balance contribute to frailty. Objective measures of strength and balance, such as grip strength, chair rise, and standing balance, are predictors of all-cause mortality.[35] Conversely, preserved muscle strength is associated with reduced cardiovascular mortality, fewer hospital admissions, improved mental health, and a lower risk of falls and fall related injuries.[8 36] There is evidence that improving fitness (strength, stamina, suppleness, and skill) improves cognitive ability and reduces the risk of dementia.[36]

Competing interests: None declared.

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EDUCATION INTO PRACTICE

- How do you describe to your patients what constitutes physical activity?
- How do you explain the benefits of physical activity to your patients?
- What one thing can your practice do that will lead to increased physical activity in your patients?
- How might you develop a system to follow up on activity advice within resource constraints? Consider what systems within your workplace might allow telephone or face-to-face reviews, or how you might use available technologies such as SMS.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

We contacted patients through social media, our patient participation groups, and surveys handed out in our practices. Their responses and ideas have been incorporated throughout the article. The sections on benefits of physical activity and discussing physical activity in the consultation were developed reflecting patients' enthusiasm for information and guidance on how to become more active.

CASE REVIEW

A mass on the shin

A 55 year old white woman presented with a mass on her shin. It had been present for six months and had an exophytic growth pattern. She reported a history of psoriasis for the past 13 years, for which she had received ciclosporin, a T-lymphocyte immunosuppressant, intermittently for the first 12 years (3 mg/kg for six months each year), and secukinumab, a human monoclonal antibody against interleukin 17A (IL-17A) (300 mg every four weeks), for the past 12 months. She did not report increased sun exposure or use of a tanning bed.

Physical examination revealed a 5×4 cm growth, sparsely scattered with micro-haemorrhages and crusts (figure). Popliteal and inguinal lymph nodes were not palpable. She had slightly erythematous thin plaques without desquamation on her legs and trunk, suggesting psoriasis that was being treated.

Excisional biopsy of the lesion revealed moderately differentiated invasive cutaneous squamous cell carcinoma. Histology showed anaplastic cells, considerable atypia, eosinophilic nucleoli, areas of keratinisation, and scattered mitoses with thickness <6 mm.

A 5×4 cm growth sparsely scattered with micro-haemorrhages and crusts on the shin

1 What are the differential diagnoses of lesions like this?
2 How would you manage this condition?
3 What is the prognosis of primary cutaneous squamous cell carcinoma?

Submitted by Stamatis Gregoriou, Anastasia I Petra, and George Kontochristopoulos
Patient consent obtained.

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If you would like to write a Case Review or Spot Diagnosis for Endgames, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

answers

CASE REVIEW

A mass on the shin

1 What are the differential diagnoses of lesions like this?

Benign differentials include mycobacterial skin infection, soft tissue infection, and pyogenic granuloma. Malignant differentials include invasive cutaneous squamous cell carcinoma, nodular basal cell carcinoma, Merkel cell carcinoma, and melanoma.

Cutaneous squamous cell carcinomas are observed more frequently in patients with severe psoriasis than in patients with mild psoriasis, especially when they are managed with immunosuppressive therapy. Sex, age, and geographic location of the individual, as well as severity of psoriasis, affect risk.

2 How would you manage this condition?

According to the European Dermatology Forum, the European Association of Dermato-Oncology, and the European Organisation of Research and Treatment of Cancer, cutaneous squamous cell carcinomas with histological thickness of ≤6 mm should be surgically excised. For patients with psoriasis and recent malignancy, treat with topical therapy, acitretin, and (where treatment is ineffective) methotrexate after excision of the carcinoma. Advise patients to protect their skin from the sun.

3 What is the prognosis of primary cutaneous squamous cell carcinoma?

The overall five year survival for patients with a successfully treated primary cutaneous squamous cell carcinoma is greater than 90%, but local recurrences or regional lymph node metastasis with increased risk for subsequent distant metastases may develop if the initial treatment fails.

LEARNING POINT

- Include skin cancer in the differentials for any new lesions in patients with psoriasis who are receiving long term immunosuppressive therapy.

PATIENT OUTCOME

The patient underwent a new surgical excision at healthy margins of 5 mm. A lymph node ultrasound showed no other abnormalities. She was followed up weekly for the first month and opted to continue treatment with secukinumab after being informed about the lack of long term safety data for patients with a history of malignancies using secukinumab. She also received advice to avoid radiation (sun, phototherapy), to use sunscreen, and to follow up with a dermatological clinic every six months for the next two years and then yearly for life.

CPD READING
0.5 HOURS

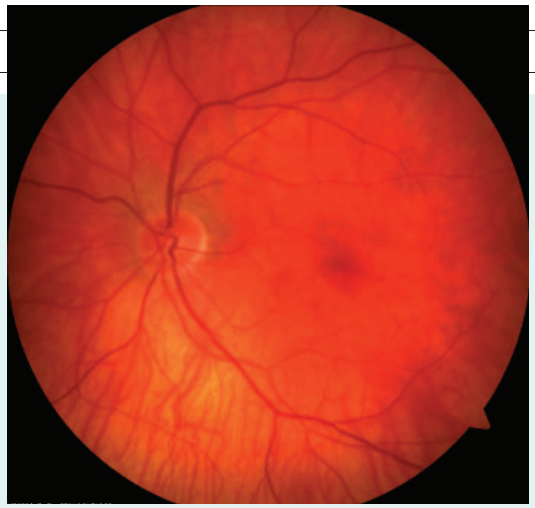
You can record CPD points for reading any article. We suggest half an hour to read and reflect on each.

LEARNING MODULE

Articles with a "learning module" logo have a linked BMJ Learning module at http://learning.bmj.com.

MINERVA

Ocular albinism



This is a picture taken during funduscopy of a hypopigmented albinotic fundus, indicative of ocular albinism (right). The hypopigmentation makes the choroidal vessels clearly visible.

The patient was a 33 year old woman with mild myopia for 20 years who presented for refractive surgery. Her corrected visual acuity was 20/20 in both eyes. The patient reported experiencing photophobia since childhood but had no history of eye disease.

Ocular albinism is a type of albinism where skin and hair pigmentation are usually unaffected. It can present with reduced pigmentation of the retina and iris, nystagmus, visual defect, and/or macular hypoplasia.

This was an incidental finding made during routine examination before refractive surgery.

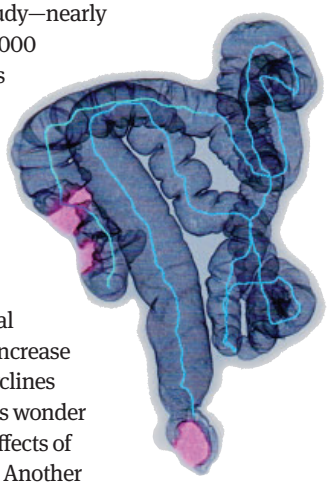
Jing Liu (jingliu030@qq.com), Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China

Patient consent obtained.

Cite this as: *BMJ* 2019;366:l5304

If you would like to write a Minerva picture case, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

Antibiotics and colorectal cancer



An enormous case-control study—nearly 30 000 cases matched to 140 000 controls—reports associations between use of antibiotics and risk of colorectal cancer (*Gut*). However, there's no consistent pattern.

Exposure to antibiotics increased risk of cancer in the proximal colon but had a small protective effect on rectal cancer. Penicillins tended to increase risk of cancer whereas tetracyclines reduced risk. The investigators wonder if the explanation lies in the effects of antibiotics on gut microbiota. Another possibility is that these are chance findings arising from multiple hypothesis testing in a large dataset.

Locked-in syndrome

The locked-in state is characterised by complete immobility and loss of speech in the absence of impairment of consciousness. Communication is possible only by eye movements or blinking. Most healthy people find it hard to imagine a worse predicament.

However, interviews with 19 people in a locked-in state as a result of motor neurone disease challenge assumptions that quality of life must be poor and feelings of hopelessness common (*Neurology*). Most patients reported that they were glad they had chosen the life sustaining techniques they currently used (invasive or non-invasive ventilation and percutaneous gastrostomy). Few expressed a wish for hastened death.

Weight loss on medication

People taking antidepressant and antipsychotic drugs often experience a small gain in weight. But that doesn't mean that it's futile for them to try to lose weight. In a retrospective analysis of 17 000 adults enrolled in a lifestyle weight loss programme, nearly a quarter were taking one or more psychiatric medications, most commonly antidepressants (*Obesity*).

The amount of weight lost by this group was hardly different from that in the group taking no regular medication. Mind you, as with most of these programmes, the average weight loss achieved over 15 months (3.4 kg) was modest.

Visualising uncertainty

In the medical literature, the commonest way of expressing uncertainty in an estimate is by the use of 95% confidence intervals.

Many doctors believe that this interval has a 95% chance of containing the true value but it actually refers to the percentage of confidence intervals that would include the true value if the study were repeated a large number of times and a confidence interval calculated on each occasion. This may be a hair-splitting point but, as pointed out in an article in *Scientific American* about visual methods of displaying doubt and imprecision, it shows what a tricky subject uncertainty is.

Blood pressure in children

The European Human Early-Life Exposome (Helix) study investigated 1300 children aged 6 to 11 to explore associations between blood pressure and at least 200 prenatal and postnatal environmental variables, including air pollution, housing, weather, natural spaces, traffic, noise, chemicals, and lifestyles. It's described as an exposome-wide association study—by analogy with genome-wide association studies.

The results seem rather analogous too. Just as most of the genetic variations found in genome-wide association studies account for only tiny differences in risk of disease, most of the environmental exposures in the Helix study accounted for only tiny differences in blood pressure (*J Am Coll Cardiol*).

Cite this as: *BMJ* 2019;366:l5510