

## NEWSLETTER

Supporting the Derbyshire Health Community

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### JAPC Update

The Joint Area Prescribing Committee (JAPC) is a countywide group covering Derbyshire County PCT and Derby City PCT. It provides recommendations on drugs and medicines management issues.

RED drugs are those where prescribing responsibility lies with a hospital consultant or a specialist. AMBER drugs are those that are initiated within a hospital/specialist setting but are suitable for shared care with a GP under a shared care agreement. GREEN drugs are regarded as suitable for primary care prescribing.

BROWN drugs are those that JAPC does not recommend for use, except in exceptional circumstances, due to lack of data on safety, effectiveness, and/or cost-effectiveness.

The most recent updates are in the table below; the full list is available at

<http://www.derbyshirecountypct.nhs.uk/guidelines/default.asp>

The guidelines, formulary chapters, newsletters, etc can now be found via this link.

Drug	Date considered	Decision
Alitretinoin	November 2008	RED
Amantadine	November 2008	BROWN
Promixin	November 2008	BROWN
Quetiapine MR	November 2008	GREEN (only on consultant recommendation)
Rivaroxaban	November 2008	RED
Rosiglitazone	November 2008	BROWN
Duloxetine	October 2008	GREEN (third line for diabetic neuropathy) (already approved as third line antidepressant)
Anagrelide	October 2008	RED
Hyaluronic acid injection	September 2008	BROWN
Leuprorelin injection	September 2008	BROWN
Aripiprazole injection	August 2008	RED

### Self-monitoring of blood glucose

Further to the article in the June 08 issue, JAPC recently accepted recommendations from the Derbyshire Diabetes Strategy Group for appropriate SMBG which are in line with NICE Guidance:

- SMBG should not be *routinely* available to people with type 2 diabetes who do not use insulin (adjustments of oral hypoglycaemic medication can be done based on HbA1c results).

**Remember SMBG in this group of patients may not be desirable and may do harm. Patients should be considered for review. Contact your local PCT medicines management pharmacist or technician for advice and support on the best way to do this.**

- SMBG is only useful when a patient can use the results they measure, either to adjust treatment or as feedback of the results of changes made.

For example, SMBG should be available in the following situations:

- for people with type 1 diabetes;
- for people with type 2 diabetes using insulin;
- for people with type 2 diabetes not using insulin who
  - are having symptoms of hypoglycaemia;
  - are making *major* lifestyle changes likely to impact upon glycaemic control;
  - need to ensure safety during activities such as driving whilst on drugs potentially causing hypoglycaemia;
- for women who are pregnant;
- for people with diabetes when they have intercurrent illness such as when admitted into hospital (BGM may be performed by health care professionals in this situation);
- for people in whom there is a concern about a possible diagnosis of type 1 diabetes at diagnosis, or in whom it is suspected insulin therapy may be required (e.g. steroid-induced diabetes); glycaemic control should be measured by other means such as by HbA1c measurement every 3 months (2-6 months).

### **Safety of formoterol in asthma**

Further to the article on salmeterol in asthma in the September 08 issue, a Cochrane review<sup>1</sup> of serious adverse events with formoterol for chronic asthma has been published. The review includes 22 studies (8,032 participants) comparing regular formoterol to placebo and salbutamol. Non-fatal serious adverse event data could be obtained for all participants from published studies comparing formoterol and placebo but only 80% of those comparing formoterol with salbutamol or terbutaline.

Three deaths occurred on regular formoterol and none on placebo; this difference was not statistically significant. It was not possible to assess disease specific mortality in view of the small number of deaths. Non-fatal serious adverse events were significantly increased when regular formoterol was compared with placebo (Odds Ratio 1.57 [95% CI: 1.05 to 2.37]). One extra serious adverse event occurred over 16 weeks for every 179 people treated with regular formoterol [95% CI: 75 to 2022]. The increase was larger in children than in adults, but the impact of age was not statistically significant. Data submitted to the FDA indicates that the increase in asthma-related serious adverse events remained significant in patients taking regular formoterol who were also on inhaled corticosteroids. No significant increase in fatal or non-fatal serious adverse events was found when regular formoterol was compared with regular salbutamol or terbutaline.

The authors concluded “In comparison with placebo, we have found an increased risk of serious adverse events with regular formoterol, and this does not appear to be abolished in patients taking inhaled corticosteroids. The effect on serious adverse events of regular formoterol in children was greater than the effect in adults, but the difference between age-groups was not significant.”

So there seems to be a similar risk with both salmeterol and formoterol.

Recommendations for minimising risk with LABAs in asthma:

- It is important to follow current guidelines and emphasise the use of inhaled corticosteroid (ICS) as the first-line treatment for patients with mild to moderate asthma symptoms. LABAs should not be used as initial therapy for any asthmatic patient.
- Make sure individuals are receiving an adequate dose of ICS. Escalate the dose of ICS to the levels recommended in the British Asthma Guideline (800mcg/day beclometasone equivalent in adults and 400mcg/day in children aged 12 and under) before considering a LABA. Do not jump to step 3 too early. If satisfactory control is not obtained at these doses then a LABA should be added.
- Do not move to step 3 without assessing inhaler technique and compliance. Encourage the use of spacer devices.
- If at step 3, review regularly as recommended by the British Asthma Guideline, and consider stepping down back to step 2, i.e. stop the LABA.
- It is important to carefully monitor patients on LABAs to identify those who do not respond or whose condition deteriorates in response to LABA therapy. Health professionals should be prepared to provide an alternative medication for patients in whom LABA therapy fails.
- Remember that the step 3 recommendation for children aged under 5 in the British Asthma Guideline is not a LABA.

1. Cates CJ et al. Cochrane Database of Systematic Reviews 2008, Issue 4

## **The GISSI-HF trial (Lancet 2008; 372: 1223-30)**

Heart failure is common and leads to substantial morbidity and mortality. Beneficial treatments include inhibitors of the renin-angiotensin-aldosterone system and beta-blockers. The GISSI-HF trial tested the hypothesis that n-3 polyunsaturated fatty acids (PUFA) could improve morbidity and mortality of patients with symptomatic heart failure of any cause and with any level of left ventricular ejection fraction (LVEF).

### **Method**

- This was a randomised, double-blind, placebo-controlled, multicentre study undertaken in Italy.
- Eligible patients were men and women aged 18 years or older, with clinical evidence of heart failure of any cause that was classified according to the European Society of Cardiology (ESC) guidelines as New York Heart Association (NYHA) class II-IV, provided that they had had their LVEF measured within 3 months before enrolment. When LVEF was greater than 40%, the patient had to have been admitted at least once to hospital for heart failure in the preceding year to meet the inclusion criteria.
- Eligible patients were randomised to receive one capsule per day of 1g n-3 PUFA or to matching placebo. Allocation to treatment groups was by a concealed, computerised telephone randomisation system.
- All treatments of proven efficacy for chronic heart failure (e.g. ACEIs, beta-blockers, diuretics, digoxin, spironolactone) were positively recommended.
- The study was designed with two co-primary endpoints: time to death, and time to death or admission to hospital for cardiovascular reasons. Secondary outcomes included cardiovascular mortality, cardiovascular mortality or admission for any reason, sudden cardiac death, admission for any reason, admission for cardiovascular reasons, admission for heart failure, myocardial infarction, and stroke.
- The effect of study drugs on the combined outcome of all-cause mortality or hospital admission for cardiovascular reasons was assessed in subgroups of patients defined according to age (above vs below the median value); left ventricular function (LVEF >40% vs ≤40%); cause of heart failure (ischaemic vs non-ischaemic); functional capacity (NYHA class II vs III or IV); presence of diabetes (yes vs no); and baseline total cholesterol concentrations (above vs below the median value).
- All the analyses were done in the intention-to-treat population, with the exception of a per-protocol analysis on the two co-primary endpoints that were undertaken in 4994 patients without major protocol violations who had taken the trial treatment for at least 80% of the time of observation.

### **Results**

- 3494 were assigned to receive n-3 PUFA and 3481 to placebo. The median duration of follow-up was 3.9 years.
- The mean age of participants was 67 years and 22% were women. Mean LVEF was 33% (with only 9% having an LVEF > 40%) and 63% had NYHA class II. The cause of heart failure was ischaemic in 50% of participants and 28% of participants had diabetes mellitus.
- At study admission 94% were being treated with ACEIs or ARBs, 65% with beta-blockers, and 39% with spironolactone.
- None of the unadjusted hazard ratios were statistically significant. For time to all-cause death the adjusted HR was 0.91 (95.5% CI 0.833 to 0.998); p=0.041. For the other co-primary endpoint of time to all-cause death or admission to hospital for CV reasons the adjusted HR was 0.92 (99% CI 0.849 to 0.999); p=0.009. This p-value is on the boundary of significance at the 99% level.
- In absolute terms, the risk reduction for all-cause mortality was 1.8% (0.3% to 3.9%) and for mortality or hospital admission was 2.3% (0.0% to 4.6%) i.e. 56 patients (333 to 27) need to be treated to avoid one death or 44 patients (infinity to 22) to avoid one event like death or hospital admission for nearly 4 years.
- The paper states “the risk of all-cause death or admission to hospital for cardiovascular reasons was affected by n-3 PUFA in all predefined subgroups in much the same way, with no evidence of heterogeneity of treatment effect (table 4).” However, in table 4 most of the HRs are not statistically significant.
- By the end of the study, 1004 (29%) or patients in the n-3 PUFA group and 1029 (30%) in the placebo group were no longer taking study drug for various reasons (p=0.45). The rate of patients who had permanently discontinued taking the study drug because of adverse reactions was much the same in the n-3 PUFA and in the placebo groups (102 [3%] vs 104 [3%], p=0.87), with gastrointestinal disturbance being the most frequent cause in both groups.
- In the per-protocol analysis undertaken on 4994 fully compliant patients, who were defined as those who had taken experimental treatments for at least 80% of the time of observation and without major protocol violations, the rate of all-cause death was 26% (658 of 2512) in the n-3 PUFA group and 29% (725 of 2482) in the placebo group (adjusted HR 0.86 [95.5% CI 0.77-0.95], p=0.004).

## Discussion/implications

- The authors conclude “we have shown that n-3 PUFA treatment is effective and safe in a large population of patients with heart failure of any cause, who are receiving standard clinical care provided in hospitals and ambulatory facilities in Italy”. Should n-3 PUFA now be added to the list of standard treatments for people with heart failure?
- The results for the co-primary endpoints are of marginal statistical significance, with the upper limit of the confidence intervals very close to one.
- The NPCi blog on the study<sup>1</sup> reaches a sensible conclusion “on the basis of this one study, it is not possible to recommend the routine use of PUFA supplements in patients with heart failure. Further studies are required in a population more typical of a UK population”.
- Should patients with heart failure be advised to supplement their diets with PUFA supplements? The NPC go on to say<sup>1</sup> “as omega-3 PUFA appears to be well tolerated, there would seem no reason why patients should not take a PUFA supplement if they want to do so, especially if patients are unable to obtain the required amount of PUFA from their diet (e.g. from eating oily fish)”.

This study has been discussed at JAPC and the recommendation is that **PUFA supplements should not be routinely offered to people with heart failure.**

1. [www.npci.org.uk/blog/?p=196](http://www.npci.org.uk/blog/?p=196)

## Risks of HRT

Further to the article on the benefits and risks of HRT use in last month’s newsletter, the new BNF (56) contains a table of the key risks of HRT. It might be useful in discussions with appropriate women.

HRT RISK TABLE							
Risk	Age range (years)	Background incidence per 1000 women in Europe not using HRT		Additional cases per 1000 women using oestrogen only HRT (estimated)		Additional cases per 1000 women using combined (oestrogen-progestogen) HRT (estimated)	
		Over 5 years	Over 10 years	For 5 Years use	For 10 Years use	For 5 Years use	For 10 Years use
Breast cancer <sup>1</sup>	50 - 59	10	20	2	6	6	24
	60 - 69	15	30	3	9	9	36
Endometrial cancer <sup>2,3</sup>	50 - 59	2	4	4	32		
	60 - 69	3	6	6	48		
Ovarian cancer	50 - 59	2	4	<1	1	<1	1
	60 - 69	3	6	<1	2	<1	2
Venous thromboembolism <sup>4,5</sup>	50 - 59	5		2		7	
	60 - 69	8		2		10	
Stroke <sup>6</sup>	50 - 59	4		1		1	
	60 - 69	9		3		3	
Coronary heart disease <sup>7,8</sup>	70 - 79	29 - 44				15	

1. Tibolone increases the risk of breast cancer but to a lesser extent than with combined HRT.
2. Evidence suggests an increased risk of endometrial cancer with tibolone. After 2.7 years of use (in women of average age 68 years) 1 extra case of endometrial hyperplasia and 4 extra cases of endometrial cancer were diagnosed compared with placebo users.
3. The risk of endometrial cancer cannot be reliably estimated in those using combined HRT because the addition of progestogen for at least 10 days per 28-day cycle greatly reduces the additional risk, and addition of a daily progestogen eliminates the additional risk. The risk of endometrial cancer in women who have not used HRT increases with body mass index (BMI); the increased risk of endometrial cancer in users of oestrogen-only HRT or tibolone is more apparent in women who are not overweight.

4. Limited data does not suggest an increased risk of thromboembolism with tibolone compared to combined HRT or women not taking HRT
5. Although the level of risk of thromboembolism associated with non-oral routes of administration of HRT has not been established, it may be lower for the transdermal route.
6. Tibolone use increases the risk of stroke about 2.2 times from the first year of treatment; risk of stroke is age-dependent and therefore the absolute risk of stroke with tibolone increases with age.
7. Increased risk of coronary heart disease in women who start combined HRT more than 10 years after menopause.
8. There is insufficient data to draw a conclusion on the risk of coronary heart disease with tibolone.

### **Antibiotic prescribing for respiratory tract infections**

NICE has issued clinical guideline 69 – “Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care”. As a result, clinicians should seek to reach agreement with patients to defer from prescribing antibiotics immediately for most people who present with ear infections, sore throats, sinusitis, coughs and colds.

#### ***Guideline recommendations:***

- The guideline applies to adults and children (older than three months)
- Following clinical assessment, a **no antibiotic prescribing strategy or a delayed antibiotic prescribing strategy** (*i.e. no immediate prescribing*) should be agreed for patients with acute otitis media; acute sore throat/acute pharyngitis/acute tonsillitis; common cold; acute rhinosinusitis or acute cough/acute bronchitis.
- All patients, regardless of the antibiotic prescribing strategy, should be given advice about managing symptoms, including fever (particularly analgesics and antipyretics) and advice about the usual natural history of the illness, including the average total length of the illness (before and after seeing the doctor),
  - acute otitis media : 4 days;
  - acute sore throat/acute pharyngitis/acute tonsillitis: 1 week;
  - common cold: 1½ weeks;
  - acute rhinosinusitis: 2½ weeks;
  - acute cough/acute bronchitis: 3 weeks
- When the no antibiotic prescribing strategy is adopted, patients should be offered reassurance that antibiotics are not needed immediately, because they are likely to make little difference to symptoms and may have side effects (e.g. diarrhoea, vomiting and rash), and a clinical review if the condition worsens or becomes prolonged.
- When the delayed antibiotic prescribing strategy is adopted, patients should be offered reassurance that antibiotics are not needed immediately because they are likely to make little difference to symptoms and may have side effects, and advice about using the delayed prescription if symptoms are not starting to settle in accordance with the expected course of the illness or if a significant worsening of symptoms occurs. Advice should also be given about re-consulting if there is a significant worsening of symptoms despite using the delayed prescription.
- **Immediate prescribing of antibiotics** and/or further appropriate investigation and management should **only** be offered to patients (both adults and children) in the following situations:
  - if the patient is systemically very unwell
  - if the patient has symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital and intracranial complications)
  - if the patient is at high risk of serious complications because of pre-existing comorbidity. This includes patients with significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis, and young children who were born prematurely
  - if the patient is older than 65 years with acute cough and two or more of the following criteria, or older than 80 years with acute cough and one or more of the following: hospitalisation in the previous year, type 1 or type 2 diabetes; a history of congestive heart failure; current use of corticosteroids.
- Depending on clinical assessment of severity, also **consider an immediate prescribing strategy** for:
  - children younger than 2 years with bilateral acute otitis media;
  - children with otorrhoea who have acute otitis media;
  - patients with acute sore throat/acute pharyngitis/acute tonsillitis when three or more Centor criteria (tonsillar exudate, tender anterior cervical lymphadenopathy or lymphadenitis, history of fever and an absence of cough) are present.

The NICE care pathway for respiratory tract infections is presented as an attachment to this newsletter.

## **Clostridium difficile infection**

A series of four Q & As on *C. difficile* have been published by the UK Medicines Information Service. These are the summaries.

### ***Which antimicrobials are implicated? (Q&A 242.1)***

- *Clostridium difficile* infection is a leading cause of iatrogenic outbreaks of diarrhoea. Patients most at risk from *Clostridium difficile* infection are the elderly, immunosuppressed and debilitated.
- Previous antimicrobial use is a major risk factor for *Clostridium difficile*-associated disease (CDAD). Antimicrobials disrupt the normal microflora of the colon and allow colonisation of the pathogen.
- Broad-spectrum antimicrobials are most strongly implicated in CDAD, particularly third generation cephalosporins, aminopenicillins and quinolones. The use of broad-spectrum antimicrobials should be avoided, especially in patients with risk factors for *Clostridium difficile* infection.
- Risk of CDAD is increased by long or repeated courses and use of multiple antimicrobials.

### ***Are probiotics useful? (QKA 243.1)***

- *Clostridium difficile* infection can occur following treatment with antibiotics that disrupt the normal microflora of the colon, allowing colonisation of the pathogen. *C. difficile* is a leading cause of iatrogenic outbreaks of diarrhoea and increases mortality and healthcare costs.
- There are local and national initiatives to reduce the incidence of *C. difficile* infection.
- *C. difficile* infection is treated with oral metronidazole or vancomycin. It has been suggested that probiotics may be useful in the management of the infection by helping to maintain or re-establish normal gut flora.
- Two systematic reviews and a meta-analysis have examined the evidence of the effectiveness of probiotics in preventing and treating *C. difficile*-associated diarrhoea.
- Assessment of efficacy is compounded by a diversity of probiotics products, lack of product standardisation and methodological flaws in the clinical trials.
- Available studies do not provide enough evidence to support the routine use of probiotics for preventing or treating *C. difficile* infection.

### ***Are acid suppressant medicines a risk factor? (Q & A 244.1)***

- Risk factors for CDAD include antibiotic use and hospitalisation. Patients most at risk are the elderly, particularly if they have underlying disease or immunosuppression.
- The use of proton pump inhibitors (PPIs) and histamine H<sub>2</sub> receptor antagonists (H<sub>2</sub>RAs), which suppress gastric acid secretion, have also been suggested to be a risk factor for the development of CDAD.
- A number of observational case-control and cohort studies have explored this association. The studies have a number of limitations, the data are conflicting and a causal link has not been established. However, the evidence suggests that if there is an association, it is probably stronger for PPIs than for H<sub>2</sub>RAs.
- For this, and other well established reasons, it is recommended that PPIs should only be used where there is a clear indication.

Q & A 245.1 includes an academic detailing aid on best practice in antimicrobial drug prescribing. If you want a copy of the full answer to any of these, please get in touch.

## **Drug Safety update**

This can be found at [www.mhra.gov.uk/drugsafetyupdate](http://www.mhra.gov.uk/drugsafetyupdate). Here are some of the key points from the October issue.

### **Ergot-derived dopamine agonists: risk of fibrotic reactions in chronic endocrine uses**

Chronic use of ergot-derived dopamine agonists is associated with a risk of fibrosis, particularly cardiac fibrosis. Cardiac valvulopathy should be excluded by echocardiography before treatment with cabergoline or bromocriptine. Patients should be monitored during treatment.

## Advice for healthcare professionals:

### *Cabergoline and bromocriptine*

- Exclude cardiac valvulopathy as determined by echocardiography before treatment.
- Monitor patients for signs or symptoms of pleuropulmonary disease (e.g. dyspnoea, shortness of breath, persistent cough, or chest pain) and retroperitoneal disorders during treatment. Renal insufficiency or ureteral or abdominal vascular obstruction might occur, with pain in the loin or flank and leg oedema. Abdominal masses or tenderness could suggest retroperitoneal fibrosis.

### *Cabergoline*

- Monitor patients for signs or cardiac fibrosis during treatment
- Echocardiography should be done within 3-6 months of starting treatment and subsequently at 6-12 month intervals
- Stop treatment if echocardiography shows new or worsened valvular regurgitation, valvular restriction, or valve leaflet thickening
- Pregnancy should be excluded before administration of cabergoline
- Women who are planning pregnancy should stop taking cabergoline 1 month before they try to conceive.

## Use of antibiotics in premature labour: *latest information*

In the ORACLE Children Study – a 7-year follow-up of a large randomised, placebo-controlled trial to investigate the effects of erythromycin and co-amoxiclav in premature labour – parents reported small increases in the number of children with mild functional impairment or cerebral palsy born to mothers whose membranes were intact and who had received antibiotics. This finding requires further study. Antibiotics save lives, and pregnant women with possible or obvious infections must be considered for treatment with antibiotics.

## Advice for healthcare professionals:

- This research was conducted in a very specific group of women and so the results do not mean that antibiotics are generally unsafe for use in pregnancy. Untreated infections can be dangerous and potentially life-threatening for pregnant women and their unborn babies, and antibiotics should continue to be prescribed in line with current guidance and the product licence
- The study confirms existing practice that antibiotics should not be given routinely to women who are in premature labour with intact membranes and who have no obvious infection
- These results were unexpected and the mechanism by which this reported association occurred in women with intact membranes is unclear, particularly as no increase in functional impairment or cerebral palsy was reported in the children of mothers who received the same antibiotics but whose membranes had ruptured. Additional research is required to shed light on these findings.

## Which antidepressant in pregnancy and breast-feeding?

During the development of the CNS chapter of the primary care formulary it became apparent that advice on the use of antidepressants for women who are pregnant or breast-feeding was required.

There is a UK Drugs in Lactation Advisory Service and these are their recommendations for antidepressant use<sup>1</sup>:

- Individual maternal and infant situations must be taken into account before any drug is prescribed for the mother.
- In general, all drugs should be avoided in premature or low birth weight infants, or in those who have any underlying conditions.
- If a drug is prescribed, it should be at the lowest practical dose and for the shortest time.

Drugs		Suitability for use in lactation	Comments
Choice of class of drug should be made on clinical grounds			
Monitor for drowsiness and poor feeding			
Avoid exposure of premature infants. Caution in neonates			
<b>Tricyclics and related drugs</b>	Non-sedating agents e.g. imipramine, nortriptyline	Yes	Short term use e.g. for postnatal depression
	Sedating agents e.g. amitriptyline dothiepin	?	
	Doxepin	No	Single report of apnoea and sedation
<b>SSRIs</b>	Fluvoxamine, paroxetine, sertraline	Yes	Second-line to non-sedating tricyclic agent. Infant withdrawal symptoms seen after abrupt discontinuation of maternal sertraline.
	Fluoxetine, citalopram	No	Long half-lives. Risk of infant drug accumulation ADRs (irritability, reduced weight gain) reported for fluoxetine
<b>MAOIs</b>		No	No clinical data available
<b>Others</b>	Nefazodone	No	Single report of infant hospitalisation due to drowsiness and poor feeding in a premature infant
	Venlafaxine	?	

Drugs classified with '?' should be used with caution and only after an assessment of benefit to the mother versus risk, real or potential, to the infant. These drugs either have insufficient clinical data on their use in lactation to regard as absolutely safe or they have had minor, reversible side effects reported in a breast-fed infant.

Clinical Knowledge Summaries<sup>2</sup> (formerly known as Prodigy) has the following section:

### Which antidepressant should I prescribe for a woman who is pregnant?

- If the woman has had a good response to a particular antidepressant in the past, consider prescribing this antidepressant, after careful consideration of the potential risks to the fetus.
- Tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs) are the antidepressants of choice in pregnancy:
  - TCAs are well established for the management of depression in pregnancy, but their use may be limited by adverse effects, safety in overdose, and the need to titrate the dose
    - amitriptyline, imipramine, and nortriptyline, are preferred
  - SSRIs are the drugs of choice for women at high risk of self harm
    - fluoxetine, citalopram, and sertraline are preferred. However, fluoxetine and citalopram are not recommended in breastfeeding, so try to establish the woman's preference for infant feeding.
- If possible avoid using paroxetine, monoamine oxidase inhibitors, venlafaxine, duloxetine, mirtazapine, and reboxetine during pregnancy.
- The use of St John's wort is not recommended for the management of depression during pregnancy.

1. [www.ukmicentral.nhs.uk/drugpreg/antidepressants.asp](http://www.ukmicentral.nhs.uk/drugpreg/antidepressants.asp)
2. [www.cks.library.nhs.uk](http://www.cks.library.nhs.uk)

# Care pathway for respiratory tract infections

At the first face-to-face contact in primary care, including walk-in centres and emergency departments, offer a clinical assessment, including:

- History (presenting symptoms, use of over-the-counter or self medication, previous medical history, relevant risk factors, relevant comorbidities)
- Examination as needed to establish diagnosis.

Address patients' or parents'/carers' concerns and expectations when agreeing the use of the three antibiotic strategies (no prescribing, delayed prescribing and immediate prescribing)

Agree a no antibiotic or delayed antibiotic prescribing strategy for patients with acute otitis media, acute sore throat/pharyngitis/acute tonsillitis, common cold, acute rhinosinusitis or acute cough/acute bronchitis.

However, also consider an immediate prescribing strategy for the following subgroups, depending on the severity of the RTI.

The patient is at risk of developing complications.

## No antibiotic prescribing

Offer patients:

- Reassurance that antibiotics are not needed immediately because they will make little difference to symptoms and may have side effects, for example, diarrhoea, vomiting and rash.
- A clinical review if the RTI worsens or becomes prolonged.

## Delayed antibiotic prescribing

Offer patients:

- Reassurance that antibiotics are not needed immediately because they will make little difference to symptoms and may have side effects, for example, diarrhoea, vomiting and rash.
- Advice about using the delayed prescription if symptoms do not settle or get significantly worse.
- Advice about re-consulting if symptoms get significantly worse despite using the delayed prescription.

The delayed prescription with instructions can either be given to the patient or collected at a later date.

## No antibiotic, delayed antibiotic or immediate antibiotic prescribing

Depending on clinical assessment of severity, also consider an immediate prescribing strategy for:

- Children younger than 2 years with bilateral acute otitis media
- Children with otorrhoea who have acute otitis media
- Patients with acute sore throat/acute tonsillitis when three or more Centor criteria<sup>1</sup> are present.

<sup>1</sup>Centor criteria are: presence of tonsillar exudate, tender anterior cervical lymphadenopathy or lymphadenitis, history of fever and an absence of cough.

## Immediate antibiotic prescribing or further investigation and/or management

Offer immediate antibiotics or further investigation/management for patients who:

- Are systemically very unwell
- Have symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital or intracranial complications)
- Are at high risk of serious complications because of pre-existing comorbidity. This includes patients with significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis, and young children who were born prematurely
- Are older than 65 years with acute cough and two or more of the following, or older than 80 years with acute cough and one or more of the following:
  - hospitalisation in previous year
  - type 1 or type 2 diabetes
  - history of congestive heart failure
  - current use of oral glucocorticoids

Offer all patients:

- Advice about the usual natural history of the illness and average total illness length:
  - acute otitis media: 4 days
  - acute sore throat/acute pharyngitis/acute tonsillitis: 1 week
  - common cold: 1½ weeks
  - acute rhinosinusitis: 2½ weeks
  - acute cough/acute bronchitis: 3 weeks
- advice about managing symptoms including fever (particularly analgesics and antipyretics), For information about fever in children younger than 5 years, refer to 'Feverish illness in children' (NICE clinical guideline 47)