

SUMMER 2007

Introducing the New Clin-eguide

Wolters Kluwer Health has just announced the introduction of Clin-eguide™, a new online clinical decision support tool designed to give health care providers access to the most accurate, evidence-based, expert-authored clinical and drug information available today. Clin-eguide™ makes it easier for doctors, nurses, and pharmacists to make better decisions in less time. The New Clin-eguide includes our existing EBM guidelines and represents newly integrated content across WKH divisions including Facts & Comparisons™, Ovid, and Lippincott Williams & Wilkins. We hope you will take a moment to write to us at the following link to learn more about this unique, single solution for clinical decision support:

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Hot Topics

Coming soon: Wolters Kluwer Health's order set authoring tool

The release of Wolters Kluwer Health's order set authoring tool is fast approaching! This tool enables hospitals to establish evidence-based standards of care regarding patient orders, including lab tests, diagnostic tests, medications, consults, and nursing care.

Along with the tool, Wolters Kluwer Health delivers complete order sets for a wide variety of conditions that account for the majority of hospital admissions and quality initiatives. Embedded within each WKH order set are concise narratives and links to specific sections within **Clin-eguide EBM Guidelines**. Using the tool, hospital personnel may customize the WKH order sets to make them consistent with their own institutional guidelines and they may create entirely new order sets.

Is your institution migrating from paper-based, physician-specific order sets to facility-wide order sets? Our tool can help your clinicians resolve questions about current medical evidence and work toward consensus. Are you preparing to go live with CPOE and developing order sets as part of the project? We may already be working in partnership with your CPOE vendor. Are you already using CPOE and need better control over the process of managing a large library of order sets? Our tool allows you to notify the appropriate personnel when an order set is due for reassessment, to manage the review process electronically, to maintain an audit trail, and much more.

Wolters Kluwer Health's order set authoring tool will be available in early 2008. Interested in learning more about this great new product? Please write to us today at:

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A meta-analysis on rosiglitazone: the risk of MI may be increased

While rosiglitazone is widely used to lower blood glucose levels in patients with type 2 diabetes mellitus, its effect on cardiovascular morbidity and mortality has not previously been determined. A recent meta-analysis shows significantly increased risk of myocardial infarction (MI).¹

Steven Nissen and Kathy Wolski at the Cleveland Clinic performed a meta-analysis using the data on rosiglitazone from the Food and Drug Administration, a clinical-trials registry maintained by the drug manufacturer (GlaxoSmithKline), and a search of the literature. The authors pointed out that the original approval of rosiglitazone was based on the ability of the drug to reduce blood glucose and glycated hemoglobin levels, but not on the prevention of the complications of diabetes including cardiovascular morbidity and mortality.

A total of 116 phase-2, -3, and -4 trials were screened and 42 of these were included in the analysis by meeting the criteria of having a randomized comparator group, a similar duration of treatment in all groups, >24 weeks of drug exposure, and report of MI and cardiovascular morbidity. 15,560 patients in the rosiglitazone group and 12,283 patients in the comparator groups were analyzed.



Key findings of the meta-analysis were:

- Statistically significantly higher odds of MI appeared in the rosiglitazone group.
 - 86 MI occurred in the rosiglitazone group compared with 72 in the control group.
 - The odds ratio was 1.43 (95% CI, 1.03-1.98).
- A trend towards higher cardiovascular mortality appeared in the rosiglitazone group.
 - 39 deaths occurred in the rosiglitazone group compared with 22 in the control group.
 - The odds ratio was 1.64 (95% CI, 0.98-2.74).

While the mechanism for the apparent increase in MI is uncertain, the authors suggest that rosiglitazone's adverse effect on serum lipids, increased risk of congestive heart failure, and modest reduction in the hemoglobin level, may contribute to provoking MI.

The authors point out limitations of this study:

- The trials used in this study were not originally intended to explore cardiovascular outcomes.
- The cardiovascular outcomes were not centrally adjudicated in most trials.
- Many trials were small and short-term, resulting in few adverse cardiovascular events or deaths, resulting in wide confidence intervals for the odds ratios.
- The lack of availability of source data did not allow the time-to-event analysis.
- A meta-analysis is less convincing than a large prospective trial designed to assess the outcome of interest.

In conclusion, the authors write:

“Despite these limitations, patients and providers should consider the potential for serious adverse cardiovascular effects of treatment with rosiglitazone for type 2 diabetes.”

For more information, please see:

1. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death. *New England Journal of Medicine* 2007;356(24):2457-71
2. Psaty BM, Furberg CD. Rosiglitazone and cardiovascular risk. *New England Journal of Medicine* 2007;356(24):2522-4

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Reduced mortality in women taking aspirin

Long-term regular low-to-moderate doses of aspirin have been associated with reduced all-cause mortality in the latest analysis from the Nurses Health Study¹.

Chan et al¹ conducted a nested case-control study involving 79,439 women without known cardiovascular disease or cancer. They compared those that used regular aspirin in varying doses with those that did not. Over 24 years, low-to-moderate dose aspirin (1-14 325mg tablets per week) was associated with a significant reduction in all-cause mortality (RR 0.75; 95% CI, 0.71-0.81). The strongest association was seen with death due to cardiovascular disease (RR 0.62; 95% CI, 0.55-0.71). Benefit was evident within the first 5 years and was greatest in older women and women with more cardiac risk factors.

The study also assessed the effects of aspirin use on cancer deaths and found a modest reduction in death from all cancers (RR 0.88; 95% CI, 0.81-0.96). This effect was not significant until after 10 years of aspirin use.

In conclusion, low-to-moderate dose aspirin therapy is associated with reduced all-cause and cardiac mortality and a modest decline in deaths from all cancers in women without established cardiovascular disease. The authors note that the observational nature of the study means that current clinical recommendations remain unchanged. However, the length of follow-up and large number of events makes this a significant contribution to the body of evidence regarding aspirin use.

For more information please see:

1. Chan AT, Manson JE, Feskanich D et al. Long-term aspirin use and mortality in women. Archives of Internal Medicine 2007;167(6):562-72



Chlamydia infection in pregnancy: Azithromycin added to new recommended regimen

Chlamydia trachomatis genital infection is the most frequently reported infectious disease in the United States. Infection of neonates results from perinatal exposure to a mother's infected cervix and may affect the mucous membranes of the eye, oropharynx, urogenital tract and rectum. The most common manifestation is ocular conjunctivitis occurring 5-12 days after birth; however, a subacute afebrile pneumonia can also occur 1-3 months after birth exposure. Screening and treating pregnant women for *C. trachomatis* prevents transmission to neonates during birth.

In 2002 the recommended CDC¹ regimen for treatment of chlamydia in pregnancy was erythromycin or amoxicillin. Azithromycin was at the end of the list of alternative regimens. In the new 2006 CDC² Sexually Transmitted Disease Treatment Guidelines azithromycin is listed as the first of 2 recommended regimens, amoxicillin being the second. However this recommendation was qualified by the statement "...clinical experiences and studies suggest that azithromycin is safe and effective."

Two studies, included in the latest Clin-eGuide chlamydia guideline, support the safe and effective use of azithromycin in pregnancy. Rahangdale et al³ conducted a retrospective cohort study of 277 pregnant women with genital chlamydia infections treated with either azithromycin, amoxicillin or erythromycin. 81% had a test of cure 7 or more days after diagnosis and before delivery.

Treatment efficacy was:

- Azithromycin: 97% (95% CI, 92.9-99.2)
- Amoxicillin: 95% (95% CI, 76.2-99.9)
- Erythromycin: 64% (95% CI, 44.1-81.4)
- Azithromycin and amoxicillin were significantly more effective than erythromycin.

There was no difference in complications for women or infants exposed to azithromycin compared with those treated with other regimens.

The 2nd study was conducted through the Teratogen Information Service at The Hospital for Sick Children in Toronto, Canada⁴. Pregnancy outcome was evaluated for 123 women exposed to azithromycin and matched to 2 control groups. **There were no statistically significant differences among the three groups in the rates of major malformations:**

- 3.4% (exposed to azithromycin)
- 2.3% (exposure to non teratogenic antibiotics)
- 3.4% (exposed to other non teratogenic agents)



The study concluded gestational exposure to azithromycin is not associated with an increase in the rate of major malformations above the baseline rate of 1-3%. This data adds to previous research showing that azithromycin is safe in pregnancy.

The authors' take-home point:

Azithromycin is recommended as one of the drugs of choice for treatment of Chlamydia in pregnancy.

For more information, please see:

1. Sexually transmitted diseases treatment guidelines 2002. Centers for Disease Control and Prevention. Morbidity & Mortality Weekly Report. Recommendations & Reports 2002;51(RR-6):1-78.
2. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2006. Centers for Disease Control and Prevention. Morbidity & Mortality Weekly Report. Recommendations & Reports 2006;55(RR-11):1-94
3. Rahangdale L, Guerry S, Bauer HM, et al. An observational cohort study of *Chlamydia trachomatis* treatment in pregnancy. Sexually Transmitted Diseases 2006;33(2):106-10
4. Sarkar M, Woodland CC, Koren G, et al. Pregnancy outcome following gestational exposure to azithromycin. BMC Pregnancy Childbirth 2006;6:18

Minimizing the risk of Alzheimer's disease

As the US population ages, diseases that are more prevalent in the elderly will have a greater impact on public health. One of these is Alzheimer's disease. Presently affecting over 5 million Americans¹, incidence is predicted to triple in the next 50 years or so².

Although no cure for Alzheimer's has been found, there is interest in risk factors. The hope is that, by influencing those that are modifiable, incidence will be reduced or onset delayed.

The recent update to the Clin-eGuide guideline for Alzheimer's disease includes new evidence on risk factors. A longitudinal study by Weili Xu et al is the first prospective study to support the association between impaired glucose regulation and increased risk for dementia and Alzheimer's disease³. The study, appearing in *Diabetes*, followed a community-based cohort of 1173 individuals, aged 75 or older. None of the group had dementia or diabetes at the start of the study, as determined by MMSE assessment and blood glucose levels. Borderline diabetes was found in 47 individuals during the baseline measurements. Follow-up measurements occurred three times over nine years. Borderline diabetes was defined as random blood glucose level ≥ 140 mg/dL but < 200 mg/dL (≥ 7.8 mmol/liter but < 11.0 mmol/liter).

At the study's end, the individuals with borderline diabetes had a higher incidence of dementia, HR=1.61 (95% CI, 1.02-2.58), and Alzheimer's disease, HR=1.68 (95% CI, 1.03-2.86). After controlling for other factors, borderline diabetes was shown to be associated with an approximately 70% increase in the risk of developing dementia and Alzheimer's disease. The authors point out that from a public health perspective this may reinforce the importance of taking steps to detect borderline diabetes early on. Lifestyle changes to improve early stage diabetes may then in turn prevent or slow the onset of dementia and Alzheimer's disease.

For more information, please see:

1. Alzheimer's Association. Alzheimer's disease. March, 2007 Available at: <http://www.alz.org/documents/FSADFacts.pdf> [Accessed on July 2, 2007]
2. Hebert LE, Scherr PA, Bienias JL, et al. Alzheimer disease in the US population: prevalence estimates using the 2000 census. *Archives of Neurology* 2003; 60:1119-22
3. Xu W, Qiu C, Winblad B and Fratiglioni L. The effect of borderline diabetes on the risk of dementia and Alzheimer's disease. *Diabetes* 2007; 56:211-16

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