

# Oscillocochinum (*Anas barbariae hepatis et cordis extractum* 200CK HPUS)

An Evidence-Based Systematic Review by the Natural Standard Research Collaboration

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## Clinical Bottom Line

### Brief Background

- Oscillocochinum® (*Anas barbariae hepatis et cordis extractum* 200CK HPUS) is a patented homeopathic preparation manufactured by a French-based company (Boiron Laboratories) that is marketed and widely used for the treatment and prevention of influenza symptoms. The product is made from the heart and liver of wild duck and undergoes several dilutions (one part in 100; 200 times in a row [i.e., 200C]), after which there are reportedly little to no original duck-liver or heart molecules in the final product. According to secondary sources, wildfowl houses are a major reservoir of human influenza virus.
- In available clinical trials, Oscillocochinum has been shown to reduce the severity and shorten the duration of influenza symptoms within a few days.<sup>1,2</sup> However, despite modest positive findings for the treatment of influenza, additional studies are warranted to evaluate this product's prophylactic effectiveness.
- In 2009 and 2010, the U.S. Food and Drug Administration (FDA) and the U.S. Federal Trade Commission (FTC) issued warning letters stating that the manufacturer's website may contain information suggesting that Oscillocochinum may "diagnose, mitigate, prevent, treat

(including to treat the symptoms of) or cure the H1N1 Flu Virus in people," which had not been approved or authorized by the FDA.

- More research is required to determine the efficacy and safety of Oscillocochinum, especially in young children and pregnant and lactating women.

## Scientific Evidence for Common/Studied Uses

Influenza (prevention)	C
Influenza (treatment)	C

### Historical or Theoretical Uses That Lack Sufficient Evidence

There is insufficient available evidence regarding the safety or efficacy of Oscillocochinum for prevention or treatment of influenza.

### Expert Opinion and Historic/Folkloric Precedent

Oscillocochinum is marketed as a remedy for influenza-like symptoms, including "feeling run down," headache, body aches, chills, and fever. There is some evidence that suggests that Oscillocochinum may shorten the duration of the flu<sup>1,2</sup>; however, the product has not been found to prevent the flu. Many experts suggest that, despite its popularity, there is little evidence that the effects of Oscillocochinum are superior to placebo. These experts claim that it is difficult to determine from available clinical research if symptoms resolved through use of Oscillocochinum or because of the passage of time.

### Brief Safety Summary

**Likely safe**—When used in manufacturer-recommended doses for a short time (3 days).

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**Possibly safe**—When used in those performing tasks or jobs that require alertness (e.g., truck drivers, those who operate heavy machinery); however, according to secondary sources, Oscillocochinum does not cause drowsiness.

**Possibly unsafe**—When used in patients who have symptoms that persist for more than 7 days or worsen, according to secondary sources; when used in patients younger than 2 years of age (safety information in this age group is lacking); when used in pregnant or lactating women (safety information for this population is lacking); or when used in children, the elderly, patients with chronic disease, or those who cannot be vaccinated, according to secondary sources.

**Likely unsafe**—When used in patients with known allergy/hypersensitivity to Oscillocochinum or any component of the formulation.

*Note:* In 2009 and 2010, the U.S. Food and Drug Administration (FDA) and the U.S. Federal Trade Commission (FTC) issued warning letters stating that the manufacturer's website may contain information suggesting that Oscillocochinum may "diagnose, mitigate, prevent, treat (including to treat the symptoms of) or cure the H1N1 Flu Virus in people," which had not been approved or authorized by the FDA.

## Dosing/Toxicology

### General

Doses may be based on those most commonly used in available trials or on historical practice. However, with natural products, it is often not clear what the optimal doses are to balance efficacy and safety. Preparation of products may vary from manufacturer to manufacturer, and from batch to batch within one manufacturer. Because it is often not clear what the active component(s) of a product are, standardization may not be possible, and the clinical effects of different brands may not be comparable.

### Standardization

There is no well-known standardization for Oscillocochinum.

### Dosing

For adults (age  $\geq$  18):

- **Form**—The product is ingested orally from a tube.
- **General**—According to secondary sources, age, health, and other conditions may alter the effects of Oscillocochinum. Oscillocochinum purportedly works best when taken immediately upon the onset of flu symptoms.
- **Cold/flu symptoms**—According to the manufacturer, the entire contents of one tube should be dissolved in the mouth every 6 hours, up to three times daily until symp-

toms resolve. The contents of the tube, taken sublingually three times daily for 3 days, has been used.<sup>1</sup> In other clinical research, five doses were taken (the first sublingual dose in the doctor's office, and then the four remaining doses on the following mornings and evenings).<sup>2</sup>

For children (age <18):

- **Form**—Pellets that can be dissolved or via a tube.
- **General**—According to secondary sources, when administered to children, pellets may be dropped into 4–6 ounces of water, stirred, and then given by teaspoonful or sipped; further details are lacking. There is a lack of safety information regarding the use of Oscillocochinum in children less than 2 years old.
- **Cold/flu symptoms (children 2 years and older)**—According to the manufacturer, the entire contents of one tube should be dissolved in the mouth every 6 hours, up to three times daily until symptoms resolve.

### Toxicology

There is insufficient available evidence on the toxicology of this product.

## Adverse Effects/Precautions/Contraindications

### Allergy

Avoid in patients with known allergy/hypersensitivity to Oscillocochinum or to any component of the formulation.

### Adverse Effects/Post-Market Surveillance

**General**—According to secondary sources, Oscillocochinum is generally well-tolerated when used in recommended doses for a short time (3 days). If symptoms persist for more than 7 days or worsen, the manufacturer recommends consulting with a health care provider. According to secondary sources, Oscillocochinum does not cause drowsiness and is safe for use in individuals performing tasks or jobs that require alertness (e.g., truck drivers, people who operate heavy machinery). In clinical research, the most frequent reported adverse effects with Oscillocochinum included myalgia, low-grade fever, rhinorrhea, headache, skin rash, itching, and earache.<sup>1,3</sup>

**Dermatologic**—In clinical research, skin rash and itching were associated with Oscillocochinum use.<sup>3</sup>

**Immune system effects**—In theory, Oscillocochinum may interact with the immune system.

**Musculoskeletal**—In clinical research, myalgia was associated with Oscillocochinum use.<sup>1,3</sup>

**Neurologic**—In clinical research, headache was associated with Oscillocochinum use.<sup>1,3</sup>

**Other**—In clinical research, low-grade fever, rhinorrhea, and earache were associated with Oscillococcinum use.<sup>1,3</sup>

#### *Precautions/Warnings/Contraindications*

- Use cautiously in patients who have symptoms that persist for more than 7 days or worsen, according to secondary sources.
- Use cautiously in patients younger than 2 years old; safety information in this age group is lacking.
- Use cautiously in pregnant or lactating women; safety information for this population is lacking.
- Use cautiously in children, elderly, patients with chronic disease, or those who cannot be vaccinated, according to secondary sources.
- Use cautiously in immunocompromised people, those taking immunomodulators or antivirals, as the mechanism of action and therefore potential interactions are not well-understood.
- Avoid in patients with known allergy/hypersensitivity to Oscillococcinum or any component of the formulation.

*Note:* In 2009 and 2010, the U.S. Food and Drug Administration (FDA) and the U.S. Federal Trade Commission (FTC) issued warning letters stating that the manufacturer's website may contain information suggesting that Oscillococcinum may “diagnose, mitigate, prevent, treat (including to treat the symptoms of) or cure the H1N1 Flu Virus in people,” which had not been approved or authorized by the FDA.

#### *Pregnancy and Lactation*

- Not recommended because of lack of sufficient data.
- The manufacturer recommends that pregnant or breastfeeding women consult their physicians before using Oscillococcinum; however, according to secondary sources, this product is not expected to cause harmful effects to the expectant mother or fetus.
- Information on Oscillococcinum's effects on lactation is currently lacking in the National Institute of Health's Drugs and Lactation Database (LactMed at <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>)

## Interactions

#### *Oscillococcinum/Drug Interactions*

According to secondary sources, Oscillococcinum may be used safely with other over-the-counter or prescription medications.

**Antivirals**—In theory, Oscillococcinum may interact with antivirals.

**Immunomodulators**—In theory, Oscillococcinum may interact with immunomodulators.

#### *Oscillococcinum/Herb/Supplement Interactions*

According to secondary sources, Oscillococcinum may be used safely with other over-the-counter or prescription medications.

**Antivirals**—In theory, Oscillococcinum may interact with antivirals.

**Immunomodulators**—In theory, Oscillococcinum may interact with immunomodulators.

#### *Oscillococcinum/Food Interactions*

There is insufficient available evidence.

#### *Oscillococcinum/Laboratory Interactions*

There is insufficient available evidence.

#### *Oscillococcinum/Nutrient Depletion*

There is insufficient available evidence.

## Mechanism of Action

#### *Pharmacology*

**Constituents**—Oscillococcinum is a patented homeopathic preparation made from the heart and liver of wild duck (specifically the Muscovy duck), purportedly containing nucleic and other phosphoric compounds. The preparation undergoes several dilutions (one part in 100; 200 times in a row [i.e., 200C]), after which there are reportedly little to no original duck liver or heart molecules in the final product.

**Antiviral effects**—There are some positive findings suggesting that Oscillococcinum may reduce the duration of influenza.<sup>4,5</sup> According to the homeopathic law of similars

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*There are some positive findings suggesting that Oscillococcinum may reduce the duration of influenza.*

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(also known as “like cures like”), since the nucleic and other phosphoric compounds from the heart and liver of wild duck contained in Oscillococcinum may be structurally similar to viruses, it has been suggested that this may explain their proposed antiviral effects. It is also commonly believed that wildfowl houses are a major reservoir of human influenza virus. However, since the preparation undergoes several dilutions, there are reportedly little to no original duck liver or heart molecules in the final Oscillococcinum product. Therefore, at this time, scientific information regarding the specific mechanism of action of Oscillococcinum remains lacking.

**Review of the Evidence**

<b>Condition treated</b>	<b>Study type</b>	<b>First author, year</b>	<b>N</b>	<b>Statistically significant results?</b>	<b>Quality of study: 0-2 = poor 3-4 = good 5 = excellent</b>	<b>Magnitude of benefit (How strong is the effect?)</b>	<b>Absolute risk reduction</b>	<b># of Patients needed to treat for one outcome</b>	<b>Comments</b>
Influenza (prevention)	Systematic review	Guo, 2007	14 studies; 1 Oscillocoxinum® prevention study	NA	NA	NA	NA	NA	No significant difference found in influenza symptoms
Influenza (prevention)	Systematic review	Vickers, 2006	7 studies	NA	NA	NA	NA	NA	Updated article to be published in 2009 was withdrawn from Cochrane Library, as the authors were unable to update it <sup>9</sup>
Influenza (prevention)	Systematic review	van der Wouden, 2005	9 studies; 1 Oscillocoxinum study	NA	NA	NA	NA	NA	Lack of evidence to support the use of Oscillocoxinum for the prevention of influenza
Influenza (prevention)	Systematic review	Ernst, 2002	17 studies; 1 Oscillocoxinum study	NA	NA	NA	NA	NA	Lack of evidence to support the use of homeopathy; 1 Oscillocoxinum trial for the prevention & treatment of influenza reported positive results
Influenza (prevention)	Systematic review	Linde, 2001	18 studies; 1 Oscillocoxinum study	NA	NA	NA	NA	NA	Overall, lack of positive results indicating homeopathy is effective for any condition; promising evidence was found for Oscillocoxinum for influenza-like symptoms
Influenza (prevention)	Randomized controlled trial	Attena, 1995	1573 subjects	No (P-value not available)	3	NA	NA	NA	Oscillocoxinum had no preventive effects
Influenza (treatment)	Systematic review	Guo, 2007	14 studies; 4 Oscillocoxinum treatment studies	NA	NA	NA	NA	NA	No significant difference found in influenza symptoms
Influenza (treatment)	Systematic review	Vickers, 2006	7 studies	NA	NA	NA	NA	NA	Updated article to be published in 2009 was withdrawn from Cochrane Library, as the authors were unable to update it <sup>9</sup>
Influenza (treatment)	Systematic review	Ernst, 2002	17 studies; 1 Oscillocoxinum study	NA	NA	NA	NA	NA	Lack of evidence to support the use of homeopathy; 1 Oscillocoxinum trial for the prevention and treatment of influenza reported positive results

Review of the Evidence (continued)

Condition treated	Study type	First author, year	N	Statistically significant results?	Quality of study: 0-2 = poor 3-4 = good 5 = excellent	Magnitude of benefit (How strong is the effect?)	Absolute risk reduction	# of Patients needed to treat for one outcome	Comments
Influenza (treatment)	Systematic review	Linde, 2001	18 studies; 1 Oscillococinum study	NA	NA	NA	NA	NA	Overall, lack of positive results indicating homeopathy is effective for any condition; promising evidence was found for Oscillococinum for influenza-like symptoms
Influenza (treatment)	Randomized controlled trial	Papp, 1998	334 subjects	Yes	5	Medium	10% (clearly improved)	10	Decline of symptoms after 48 hours was significant with Oscillococinum; symptoms were resolved faster with Oscillococinum compared to placebo
Influenza (treatment)	Randomized controlled trial	Ferley, 1989	478 subjects	Yes	4	Medium	7%	14	Greater recovery rate with Oscillococinum compared to placebo

**Immune system effects**—In theory, Oscillococinum may have immunomodulating effects.

**Pharmacodynamics/kinetics**—There is insufficient available evidence.

History

Oscillococinum was reportedly introduced in the 1920s. It is a popular homeopathic medicine, particularly in France, for the treatment and prevention of influenza. A French physician, Joseph Roy, created the term “oscillococinum” in 1925 while on military duty during the Spanish flu epidemic, during which he examined the blood of flu victims and found oscillating bacteria. Currently, Oscillococinum is a patented homeopathic preparation manufactured by Boiron Laboratories, a French-based company.

Historically, the French have prepared duck liver (foie gras) in large quantities in the winter. According to proponents of homeopathic medicine, this tradition may have been a subconscious response for the desire for an antiviral substance to protect against influenza virus during the winter.

Review of the Evidence: Discussion

Influenza (Prevention)

**Summary**—Oscillococinum was introduced in the 1920s and is currently a popular homeopathic medicine, particularly in France, for the treatment and prevention of influenza. It is a patented, commercially available product. There are some positive findings suggesting that Oscillococinum may reduce the duration of influenza<sup>4,5</sup> but, despite positive findings, the effect size tends to be small. Additionally, there is a lack of evidence to support its use for prevention of influenza. Additional research is needed before a firm conclusion can be made.

**Systematic reviews**—Guo et al. conducted a systematic review to evaluate complementary medicines used for the prevention and treatment of influenza-like symptoms.<sup>6</sup> MEDLINE,<sup>®</sup> Embase, the Cochrane Library, CINAHL, and AMED were searched, from inception to June 2006. Trials were included if they were randomized and placebo-controlled or controlled against an antiviral agent; treatment trials included subjects who were clinically diagnosed with influenza or influenza-like illness; and prevention trials included healthy individuals.

A total of 14 trials were included, testing seven preparations: Oscillococinum; *Sambucus nigra*; *Echinacea purpurea*; CVT-E002 (*Panax quinquefolius*); Mucococinum; GMJN; and *Kan*

\*Casanova P, Gerard R. Results of three years of randomised, multi-centre studies on Oscillococinum/placebo [in French]. 1992;unpublished; see page 46 for citation in text.

*Jang.* Four studies evaluating Oscillocoquinum for treatment of influenza were included.<sup>1,2,7,\*</sup> Significant improvements and intergroup differences for symptoms were noted. One Oscillocoquinum trial evaluating the prevention of influenza-like symptoms was included.<sup>3</sup> No significant intergroup difference was noted. Overall, there was no evidence to support the use of complementary medicine for the treatment or prevention of influenza or influenza-like symptoms.

Vickers et al. conducted a systematic review to determine whether homeopathic Oscillocoquinum or similar medicines are more effective than placebo in the prevention and treatment of influenza and influenza-like syndromes.<sup>5</sup> The Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library, Issue 1, 2006), MEDLINE (January 1966 to February 2006), and Embase (1980 to February 2006) were searched, and the manufacturers of Oscillocoquinum were contacted.

Trials were included if they were placebo-controlled studies of Oscillocoquinum or homeopathically prepared influenza virus, influenza vaccine, or avian liver for the prevention and treatment of influenza and influenza-like syndromes. Seven studies were included<sup>1-3,7,8,\*;†</sup> (three prevention<sup>3,8;†</sup> and four treatment studies<sup>1,2,7,\*</sup>)

There was only adequate reported information in two of the studies.<sup>1,2</sup> Two studies were not published in the available scientific literature.<sup>7,\*</sup> Two other studies<sup>8;†</sup> evaluated homeopathically prepared inactivated viruses and bacteria, but did not specify the use of Oscillocoquinum. Evidence to support the use of Oscillocoquinum for the prevention of influenza was lacking (relative risk [RR], 0.64; 95% confidence interval [CI], 0.28–1.43). In the two treatment studies,<sup>1,2</sup> Oscillocoquinum reduced the length of influenza by 0.28 days (95% CI, 0.50–0.06) as well as reducing the number of days until return to work. It was also found that there was an increased chance that a patient would have considered treatment to be effective (RR, 1.08; 95% CI, 1.17–1.00). It was noted that the two studies evaluating homeopathically prepared inactivated viruses and bacteria (not Oscillocoquinum) had “suspiciously” round numbers.<sup>7,\*</sup> Most studies did not report adverse effects. One study reported migraine headache as a possible side-effect of Oscillocoquinum.

<sup>†</sup>Nolleaux MA. Clinical study of Mucococquinum 200K as a preventative treatment against flu: A double blind trial versus placebo [in Dutch]. 1990;unpublished.

### Natural Standard Evidence-Based Validated Grading Rationale™

- Grades reflect the level of available scientific evidence in support of the efficacy of a given therapy for a specific indication.
- Expert opinion and folkloric precedent are not included in this assessment, and are reflected in a separate section of each monograph (“Strength of Expert Opinion and Historic/Folkloric Precedent”).
- Evidence of harm is considered separately; the grades below apply only to evidence of benefit.

#### Level of Evidence Grade Criteria A (Strong Scientific Evidence)

Statistically significant evidence of benefit from >2 properly randomized trials (RCTs), OR evidence from one properly conducted RCT AND one properly conducted meta-analysis, OR evidence from multiple RCTs with a clear majority of the properly conducted trials showing statistically significant evidence of benefit AND with supporting evidence in basic science, animal studies, or theory.

#### B (Good Scientific Evidence)

Statistically significant evidence of benefit from 1–2 properly randomized trial(s), OR evidence of benefit from ≥1 properly conducted meta-analysis OR evidence of benefit from >1 cohort/case-control/non-randomized trial AND with supporting evidence in basic science, animal studies, or theory. *This grade applies to situations in which a well designed randomized controlled trial reports negative results but stands in contrast to the positive efficacy results of multiple other less well designed trials or a well designed meta-analysis, while awaiting confirmatory evidence from an additional well designed randomized controlled trial.*

#### C (Unclear or Conflicting Scientific Evidence)

Evidence of benefit from ≥1 small RCT(s) without adequate size, power, statistical significance, or quality of design by objective criteria,\* OR conflicting evidence from multiple RCTs without a clear majority of the properly conducted trials showing evidence of benefit or ineffectiveness, OR evidence of benefit from ≥1 cohort/case-control/non-randomized trial(s) AND without supporting evidence in basic science, animal studies, or theory, OR evidence of efficacy only from basic science, animal studies, or theory.

#### D (Fair Negative Scientific Evidence)

Statistically significant negative evidence (i.e., lack of evidence of benefit) from cohort/case-control/non-randomized trials, AND evidence in basic science, animal studies, or theory suggesting a lack of benefit. *This grade also applies to situations in which >1 well designed randomized controlled trials report negative results, notwithstanding the existence of positive efficacy results reported from other less well designed trials or a meta-analysis.* (Note: if there are ≥1 negative randomized controlled trial(s) that are well designed and highly compelling, this will result in a grade of “F” notwithstanding positive results from other less well designed studies.)

#### F (Strong Negative Scientific Evidence)

Statistically significant negative evidence (i.e. lack of evidence of benefit) from ≥1 properly randomized adequately powered trial(s) of high-quality design by objective criteria.\*

\* Objective criteria are derived from validated instruments for evaluating study quality, including the 5-point scale developed by Jadad et al., in which a score below 4 is considered to indicate lesser quality methodologically (Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials* 1996;17[1]:1–12.)

This review was to be updated in 2009.<sup>9</sup> However, this review was withdrawn from the Cochrane Library, Issue 3, 2009, as the authors were unable to update it. It was indicated that a new team would conduct the update.<sup>9</sup>

van der Wouden et al. conducted a systematic review to evaluate agents for the prevention of influenza.<sup>10</sup> MEDLINE, Embase, and CENTRAL were searched, from inception to June 2004. Nine reviews, five of them addressing influenza vaccination and four addressing other agents (neuraminidase inhibitors, amantadine, rimantadine, and Oscilloccinum), were included.<sup>5</sup> The researchers concluded that there was a lack of supportive evidence for the use of Oscilloccinum for the prevention of influenza. Overall, the largest body of evidence supported the use of the influenza vaccine for the prevention of influenza.

Ernst et al. conducted a systematic review to evaluate homeopathy as a therapeutic method for various conditions.<sup>11</sup> MEDLINE, Embase, AMED, and CISCOM were searched from inception to October 2001. Terms used were homeopath, homoeopath, clinical trial, meta-analysis, systematic review, efficacy, and effectiveness. Seventeen trials met the inclusion criteria, including one Oscilloccinum study.<sup>5</sup> This trial reported a reduced length of illness by 0.28 days; however, because of a small effect size, the researchers stated that the data were “not strong enough to make a general recommendation.” Overall, this systematic review found that evidence suggesting that homeopathy is clinically different than placebo is lacking.

Linde et al. conducted a systematic review to evaluate the effects of homeopathy for various conditions.<sup>12</sup> The Cochrane Complementary Medicine Field, the Cochrane Library, MEDLINE, and bibliographies of articles and books were searched. Reviews were included if they described review methods explicitly, were published, and focused on treatment effects. Information on conditions, interventions, methods, results, and conclusions were reviewed. Eighteen of 22 potentially relevant reviews met the inclusion criteria. One review was included for Oscilloccinum.<sup>5</sup> Six articles addressed whether homeopathy is effective across conditions and interventions. Overall, there was a lack of positive results indicating that homeopathy is effective for any condition. Promising evidence was found for Oscilloccinum for influenza-like symptoms.

**Evidence**—Attena et al. conducted a randomized, double-blind, placebo controlled trial to evaluate the effects of Oscilloccinum in the prevention of influenza-like syndromes in 1573 subjects.<sup>3</sup> Subjects were eligible for the study if they had a fever exceeding 37.7°C and presented with at least two of the following symptoms: chills; cough; myalgia; rhinitis; and sore throat lasting at least 48 hours. Subjects received four oral administrations: three given a week apart and the last one administered 1 month after the third dose. The primary objective, however, was not clearly stated. Treatment with Oscilloccinum revealed no preventive effects (*P*-value was not reported). The most frequent reported adverse effects with Oscilloccinum included myalgia (21.4%), low-grade fever (20.4%), rhinor-

rhea (15.3%), headache (12.2%), skin rash (8.1%), itching (6.1%), and earache (5.1%). Randomization and dropouts were not clearly described.

### *Influenza (Treatment)*

**Summary**—Oscilloccinum was introduced in the 1920s and is currently a popular homeopathic medicine, particularly in France, for the treatment and prevention of influenza. It is a patented, commercially available product. There are some positive findings suggesting that Oscilloccinum may reduce the duration of influenza,<sup>4,5</sup> but despite positive findings, the effect size tends to be small. In addition, there is a lack of evidence to support this product's use for prevention of influenza. Additional research is needed before a firm conclusion can be made.

**Systematic reviews**—Guo et al. conducted a systematic review to evaluate complementary medicines used for the prevention and treatment of influenza-like symptoms.<sup>6</sup> MEDLINE, Embase, the Cochrane Library, CINAHL, and AMED were searched, from inception to June 2006. Trials were included if they were randomized and placebo-controlled or controlled against an antiviral agent; treatment trials included subjects that were clinically diagnosed with influenza or influenza-like illness; and prevention trials included healthy individuals.

A total of 14 trials were included, testing seven preparations: Oscilloccinum; *Sambucus nigra*; *Echinacea purpurea*; CVT-E002 (*Panax quinquefolius*); Mucococcinum, GMJN; and *Kan Jang*. Four studies evaluating Oscilloccinum for treatment of influenza were included.<sup>1,2,7,\*</sup> Significant improvements and intergroup differences for symptoms were noted. One Oscilloccinum trial evaluating the prevention of influenza-like symptoms was included.<sup>3</sup> No significant intergroup difference was noted. Overall, there was no evidence to support the use of complementary medicine for the treatment or prevention of influenza or influenza-like symptoms.

Vickers et al. conducted a systematic review to determine whether homeopathic Oscilloccinum or similar medicines are more effective than placebo in the prevention and treatment of influenza and influenza-like syndromes.<sup>5</sup> CENTRAL (The Cochrane Library, Issue 1, 2006), MEDLINE (January 1966 to February 2006), and Embase (1980 to February 2006) were searched, and the manufacturers of Oscilloccinum were contacted.

Trials were included if they were placebo-controlled studies of Oscilloccinum or homeopathically prepared influenza virus, influenza vaccine, or avian liver for the prevention and treatment of influenza and influenza-like syndromes. Seven studies were included<sup>1-3,7,8,\*†</sup> (three prevention<sup>3,8,†</sup> and four treatment studies.<sup>1,2,7,\*</sup>)

There was only adequate reported information in two of the studies.<sup>1,2</sup> Two studies were not published in the available scientific literature.<sup>7,\*</sup> Two other studies<sup>8,†</sup> evaluated homeopathically prepared inactivated viruses and bacteria, but did not specify the use of Oscilloccinum. Evidence to support the use of Oscilloccinum for the prevention of influenza was lacking (*RR*, 0.64; 95% CI, 0.28–1.43). In the two treatment studies,<sup>1,2</sup> Oscilloccinum reduced the length of influenza by 0.28 days (95% CI,

0.50–0.06) as well as reducing the number of days until return to work. It was also found that there was an increased chance that a patient would have considered treatment to be effective (*RR*, 1.08; 95% *CI*, 1.17–1.00). It was noted that the two studies evaluating homeopathically prepared inactivated viruses and bacteria (not Oscillococinum) had “suspiciously” round numbers.<sup>7\*</sup>

Most studies did not report adverse effects. One study reported migraine headache as a possible side-effect of Oscillococinum.<sup>5</sup> This review was to be updated in 2009.<sup>9</sup> However, this review was withdrawn from the Cochrane Library, Issue 3, 2009, as the authors were unable to update it. It was indicated that a new team would conduct the update.<sup>9</sup>

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**Evidence**—Papp et al. conducted a randomized, double-blind, placebo controlled trial to evaluate the effects of Oscillococinum after 48 hours of treatment and to determine if symptoms were eliminated faster compared to placebo.<sup>1</sup> Patients (*N* = 334) were allocated to one of two treatment groups, Oscillococinum or placebo. Patients were instructed to take the contents of the tube sublingually, three times daily for 3 days. The primary objective was to test the effectiveness of Oscillococinum on influenza. It was considered effective if patients were symptom-free after the first 48 hours. Another objective of the study was to determine the date of elimination of symptoms.

After 48 hours, 43.7% of patients using Oscillococinum were “clearly improved” (i.e., symptom-free after 48 hours), compared to 33.5% in the placebo group (*P* = 0.0028). It was also noted that on the second day, 9.6% of patients in the Oscillococinum group had no symptoms, compared to 1.8% in

the placebo group (*P* = 0.023). Oscillococinum was generally well-tolerated, with 1 patient reporting headache with treatment. This study was well-designed and well-reported.

Ferley et al. conducted a randomized, double-blind, placebo-controlled evaluation of homeopathic preparations in the treatment of influenza-like conditions in 478 patients.<sup>2</sup> Patients were eligible if they were ≥ 12 years old, suffered from influenza-like symptoms (defined as a rectal temperature above 38°C, and at least two of the following symptoms: headache; stiffness; lumbar and articular pain; or shivers), with manifestation that occurred < 24 hours before entry.

Patients received Oscillococinum or placebo. The patients were instructed to take the first sublingual dose in the doctor’s office, and then the four remaining doses on the following mornings and evenings. Rectal temperature was recorded twice daily along with symptoms including headache, stiffness, lumbar and articular pain, shivers in conjunction with cough, coryza (general cold symptoms), and fatigue. The primary objective was recovery from symptoms. Recovery was defined as rectal temperature less than 37.5°C and complete resolution of the symptoms (headache, stiffness, lumbar and articular pain, and shivers). Within 48 hours, 17.1% of patients improved with active treatment, compared to 10.3% in the placebo group (*P* = 0.03). Dropouts were not described.

**Studies of lesser quality (not included in the Review of Evidence table)**—Cassanova et al. conducted randomized, multicenter studies on Oscillococinum compared to placebo, over three years.\* Three hundred patients complaining of influenza were included. The average age in the treatment group was 44 (38 for the placebo group). The treatment group received Oscillococinum twice daily for 3–4 days. Outcome measures included body temperature, which was recorded twice daily for 4 days, and the presence of chills and aches at day 4. It was noted in the Vickers review that there were inconsistencies between the table and text.<sup>5</sup> Further details are lacking.

Cassanova conducted a double-blind study to evaluate homeopathy for flu syndromes.<sup>7</sup> One hundred patients with influenza-like syndrome with an onset that occurred less than 48 hours before entry were included. The average age in the treatment group was 42 (41 for the placebo group). The treatment group received four doses of Oscillococinum over 2 days at 6-hour intervals. Outcome measures included patients’ global assessment of success and the presence of chills, aches, rhinitis, night cough, day cough, and fever at day 8. It was noted in the Vickers review that few experimental details were given and that this study was published in a general medical magazine and not a scientific magazine.<sup>5</sup> Further details are lacking. ■

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