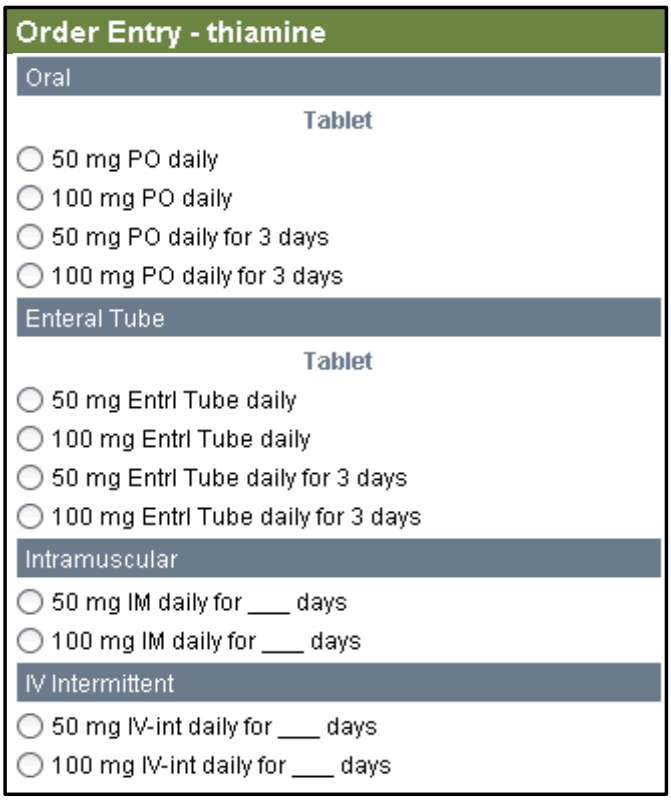
Appendix 1 (as supplied by the authors): Detailed description of intervention methods

This Appendix outlines the procedures undertaken to implement changes to the computerized provider order entry system (CPOE; Centricity, GE Healthcare) at University Health Network (Toronto, Ontario Canada), and provides additional details concerning the order sets included in the CPOE pre- and post-intervention. At UHN, the CPOE is integrated within the electronic health record and is the primary means for order entry on inpatients. Order sets are frequently used to promote treatment of complex conditions and to increase the efficiency of order entry and reduce errors.

Pre-intervention assessment of thiamine prescribing practices

Institutional thiamine prescribing practices were evaluated through a retrospective observational study using data collected from computerized pharmacy information systems from January 2010 to December 2011. The results of this review were published February 3, 2015.[1]

The UHN CPOE thiamine order set in use during the preintervention period is shown in Figure 1. In addition, the UHN had a written protocol promoting parenteral thiamine prescribing (thiamine 100 mg IV QD) to patients undergoing treatment for alcohol withdrawal (not shown). The written protocol was not referenced or accesssible via the CPOE.



Supplemental Figure S1. Pre-intervention thiamine order set.

Planning / recommendation development

In response to findings from our review of institutional thiamine prescribing practices, study authors proposed comprehensive changes to the institutional CPOE to promote administration of higher doses of parenteral thiamine to inpatients with suspected deficiency. The proposal included the following recommendations for "therapeutic substitution", referencing available clinical practice guidelines, and published evidence. The following proposal was submitted to the UHN Pharmacy and Therapeutics Committee in March 2013.

> Effective treatment of Wernicke's encephalopathy (WE) and prevention in at risk patients requires rapid realization and maintenance of very high serum thiamine levels. University Health Network treatment guidelines should be updated to emphasize this goal. In line with this, we suggest that current online orders for thiamine 100 mg IV should be changed, reflecting the observation that doses of thiamine between 100 mg and 250 mg per day may not restore vitamin status,[2] improve clinical

signs[3] or prevent death[4] in patients with WE. Additionally, to prevent under-treatment, the option for oral thiamine should be removed from the formulary. Daily multivitamins remain a suitable option for dietary supplementation of thiamine in at risk patients without concomitant neurologic dysfunction.

Class I evidence supporting specific doses and schedules for administration of intravenous thiamine is not available.[5] There is, however, ample evidence from controlled trials, case series and epidemiologic series to support higher doses of thiamine. A single randomized control trial looking at the role of thiamine prophylaxis in at risk patients in the Emergency Department found that those who received doses in excess of 200 mg performed better than cohorts receiving 5 mg in cognitive testing.[6]

Current consensus guidelines suggest that patients with suspected WE should be treated with thiamine 500 mg IV TID for 3 days, and continued at 250 mg QD x 3-5 days depending on response. Thiamine 250mg IV QD x 3 days should be used in patients with nutritional deficiency at risk of developing WE during hospital stay (i.e., patients with history of alcohol abuse, requiring IV administration of glucose, or presenting with signs and symptoms of sepsis).[7]

The following treatment algorithms are endorsed:

Patient with suspected WE (presentation with nutritional deficiency AND confusion, ophthalmoplegia OR gait disturbance):

- Thiamine 500mg IV TID x 3 days. If clinical response, continue thiamine 250mg IV QD x 3-5 days.
- Thereafter, multivitamin PO QD.

Patient at risk of developing WE (poor nutritional status, AND subject to metabolic stress or planned administration of carbohydrates):

- Thiamine 250mg IV QD x 3 days.
- Thereafter, multivitamin PO QD.

Implementation of changes to CPOE

The above recommendation was reviewed by the UHN Pharmacy and Therapeutics Committee, and underwent subsequent revisions and re-review before approval on June 3, 2013. The order instructions were revised and implemented within the CPOE November 20, 2013. The post-intervention thiamine order set is shown in Figure 2. Concurrent with this change, oral thiamine was removed from the default order sets and oral thiamine tablets were discontinued from the hospital formularly. Providers retained the ability to manually enter orders for enteral thiamine, following standard "non-formulary" requests.

Changes to the CPOE were communicated to UHN providers via the Medical Staff Bulletin (Volume 42, #36), which was published on the institutional intranet and electronically disseminated November 28, 2013. The Medical Staff Bulletin included the following statements:

Current practices of prescribing oral thiamine and intravenous thiamine doses of 100 mg daily are not optimal to prevent or treat Wernicke's encephalopathy, which can progress to Korsakoff's syndrome, a chronic and irreversible form of dementia, or death.

The following changes are being implemented:

1. Removal of oral thiamine tablets from the UHN Formulary. NOTE: oral thiamine is still available in the UHN Formulary as part of multiple vitamin products, not to be used for patients with suspected thiamine deficiency (e.g., Centrum Forte® tablets and Replavite® tablets for renal dialysis patients)
2. Changes to EPR Thiamine Order Set, to read:

   Patient with suspected Wernicke's encephalopathy (presentation with nutritional deficiency AND one of confusion, ophthalmoplegia OR gait disturbance)

   - 500 mg IV-int q8h for three days followed by 250 mg IV-int daily for ___ days (generally 3 to 5 days)

   OR

   - 500 mg IM q8h until IV access obtained, then 500 mg IV-int q8h to complete three days therapy followed by 250 mg IM or IV-int daily for ___ days (generally 3 to 5 days)

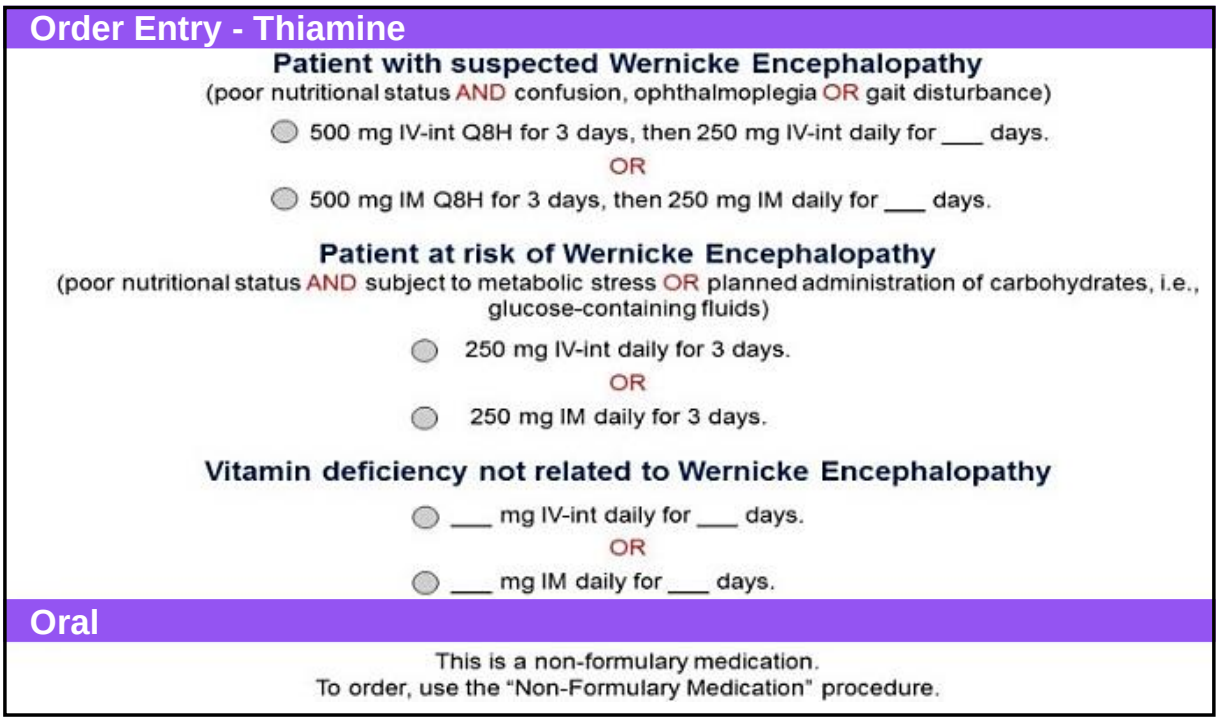
   Patient at risk of developing Wernicke's encephalopathy (poor nutritional status AND subject to metabolic stress or planned administration of carbohydrates; i.e., glucose-containing fluids)

   - 250 mg IV-int daily for 3 days

   OR

   - 250 mg IM daily for 3 days

Readers were directed to publications including general information on the diagnosis and treatment of Wernicke's encephalopathy,[7] and comparable clinical practice guidelines.[8,9]



Supplemental Figure S2. Post-intervention thiamine order set.

Appendix to: Day GS, Ladak S, del Campo CM. Improving thiamine prescribing at an academic hospital network using the computerized provider order entry system: a cohort study. *CMAJ Open* 2020. DOI:10.9778/cmajo.20200029.

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Appendix to: Day GS, Ladak S, del Campo CM. Improving thiamine prescribing at an academic hospital network using the computerized provider order entry system: a cohort study. *CMAJ Open* 2020. DOI:10.9778/cmajo.20200029.