Supplementary Appendix

<u>Biomarker screening test results</u>: The model assumes that positive screening tests result in the performance of a CT scan and prompt treatment of positive findings; negative screening will result in hospital discharge. Possible results of biomarker or clinical screening are:

- 1. True negative, in which the test correctly concludes there is no intracranial lesion, and the patient can be discharged safely without negative (unnecessary) CT scanning.
- 2. True positive, in which the test correctly predicts the need for a CT scan, thus assuring prompt treatment.
- 3. False positive, in which the screening test results in a negative CT scan being obtained.
- False negative, in which the screening test misses a lesion, perhaps resulting in delayed treatment, increased morbidity and costs.

<u>The model</u>: Illustrated in Figure 2, the model compares four different management strategies for deciding whether to perform a CT scan on a patient presenting soon after a mild TBI:

- 1. Apply Canadian CT head rule: If the rule suggests medium to high risk, perform CT. If the rule rates the patient low risk or CT normal, discharge from hospital. No biomarker screen is involved.
- 2. Perform biomarker screen. CT scan if positive, discharge if negative. No Canadian CT Head rule screen is involved.
- Apply Canadian CT Head rule: If the rule suggests medium to high risk, perform biomarker screen. If biomarker screen is positive, perform CT scan. If negative, or if CT normal, discharge from hospital.
- 4. Perform biomarker screen. If biomarker screen positive, obtain CT scan. If biomarker screen negative, perform Ca-

nadian CT Head rule. If Canadian rule suggests medium to high risk, obtain CT scan. Otherwise discharge.

<u>Pathways and outcomes following employment of a treatment</u> strategy are illustrated in Figure 3.

- 1. In the event of a true positive result, the patient receives a timely CT scan and appropriate treatment.
- 2. A true negative result is followed by appropriate hospital discharge and uneventful recovery.
- 3. A false positive result leads to an unnecessary (negative) CT scan but no clinical harm.
- 4. For a false negative result we assume that all patients harboring lesions which require surgery will return to the hospital and undergo the procedure, but in a delayed fashion.

We assume all patients found to have surgical lesions are treated aggressively. Outcomes reflect the negative effects of delayed surgery, including increased mortality and morbidity (and increased associated costs). A proportion of patients with nonsurgical lesions will recover at home. The rest will return to the hospital and incur additional testing, observation and treatment.

<u>Utility</u>: In the context of this study, utility is a measure of quality of life. It is based on the subject's relative preference for a given health state, as determined by validated questionnaires or direct measurement. Utility is a parametric measurement (half the score = half the utility), anchored between 0 (dead) and 1 (perfect health). Equally important is quantity of life, the time for which quality is measured. In our case, the quantity equals expected longevity. Multiplying utility by years of expected life yields quality-adjusted life years (QALYs). Hence 5 QALYs equal 5 years in perfect health or 10 years with a utility of 0.5. The concept of QALYs or related estimates of utility over time are essential in cost-effectiveness (cost-utility) studies.