Accomplishments: Major Activities, Specific Objectives, Significant Results, Major Findings

--Major Goal/Specific Aim #1: Implement the nationally-vetted TBI management guidelines across a vast network of prehospital EMS systems (urban, suburban, and rural) throughout the State of Arizona.

--Objective A: Train Master Trainers all over the state to supply the necessary educational cadre to implement statewide through our "train-the-trainer" implementation plan:

--We have now trained and certified a total 434 EPIC/EPIC4Kids Master Trainers statewide. This is many more Master Trainers than we expected to have and has been a key in getting us to the level of implementation that we have obtained.

--Objective B: Implement the TBI Guidelines by training agencies throughout the state with the goal of having approximately 80% of the EMS response covered by EPIC-certified agencies.

--Metrics related to training/implementation so far:

--EMS Agencies: A total of 103 agencies have been trained and certified so far statewide (35 agencies added since last year). The 15 largest EMS agencies in the state (in terms of TBI incidence) are all EPIC-certified. As of 12/2013, 85.7% of patients meeting inclusion criteria statewide were cared for by EPIC-certified agencies (thus, we have exceeded our goal of 80%).

--EMS Providers: 8709 paramedics/EMTs have been trained and certified so far. Thus, we have trained 87% to 92% of the estimated 9500-10,000 active providers in Arizona, exceeding our 80% target.

--Major Goal/Specific Aim #2: Collection of prehospital and trauma center data on severe TBI patients cared for by participating EMS agencies.

--We have continued to access and link EMS data to the patients in the Arizona State Trauma Registry (ASTR) for all participating agencies back through 2007.

--This has gone very well. Among the EPIC-certified agencies, there were 19,740 patients who met EPIC inclusion criteria from 1/1/2007-6/30/2013 and for which we have access to the EMS data. The linkage rate for EMS to ASTR data is well over 90%. This is an important finding since linking *comprehensive, detailed* EMS and Trauma Center data from 10s of thousands of cases has never been attempted before.

--Since our sample size/power calculations are based upon the *intubated* patient subset, here we present both the intubated cohort and the overall EPIC case numbers predicted in our approved research plan as well as an estimate of the cases we will have at the interim and final analyses. These numbers look very positive:

--*Intubated* cases:

	Predicted N in sample size calculations in NIH Proposal	Estimated actual (or actual*) @ Yr. 3 Annual Report
--Total Enrollments-Phase 1 & 3:	2931	3,525 (120% of original predicted cases)
--Phase 1 (pre-implementation):	1709	2,389* (140%)
--Phase 3 (post-implementation):	1222	1,136 (93%)
--Interim analysis (P1 & 3 cases):	2429 (Year 4—2/28/15)	3,021 (124%)
--Interim analysis (P3 cases):	720 (Year 4—2/28/15)	632 (88%)

--*All* EPIC cases (intubated and non-intubated):

	Predicted N in sample size calculations in NIH Proposal	Estimated actual (or actual*) @ Yr. 3 Annual Report
--Total Enrollments-Phase 1 & 3:	24,885	26,573 (107% of original predicted cases)
--Phase 1 (pre-implementation):	14,085	17,507* (124%)
--Phase 3 (post-implementation):	10,800	9,066 (84%)
--Interim analysis (P1 & 3 cases):	20,257 (Year 4—2/28/15)	22,777 (112%)
--Interim analysis (P3 cases):	6172 (Year 4—2/28/15)	5,270 (85%)

--Major Goal/Specific Aim #3: Evaluate the impact of prehospital guideline implementation on patient outcomes.

--The key objective for year 3 related to Aim #3 was to verify that the EPIC Certified agencies are able and willing to continue to provide the data to ensure the ability to evaluate the patients cared for in Phase 3 (post-implementation). All previous participating agencies are continuing to make their data available (and 35 new agencies made their data available this year).

--Significant results, major findings, key outcomes, and other achievements

--While the first interim analysis will not occur until year 4 of the project (next year), we have analyzed various aspects of the epidemiology and EMS management of TBI in the growing EPIC Database. We have presented multiple abstracts at national and international meetings and are writing these up these manuscripts for publication in major journals. Here is a brief summary of our significant and new (even surprising) findings that are starting to emerge from our work:

--Society for Academic Emergency Medicine: "The Synergistic Effect of Prehospital Hypotension and Hypoxia in Major Traumatic Brain Injury: Profound Impact on Mortality." Conclusions: In this statewide, multi-system analysis, prehospital hypoxia and hypotension were associated with increased mortality. However, the *combination* of hypoxia and hypotension *together* had a dramatic synergistically-negative effect on mortality (>4 times a merely additive effect). This finding adds impetus to the focus on aggressive prevention and treatment of hypoxia and hypotension in the National EMS TBI Guidelines.

--International Brain Injury Association: "Association Between Lowest Prehospital Systolic Blood Pressure and Mortality in Major Traumatic Brain Injury: Is There a 'Hypotension Threshold'?" Conclusions: In major TBI, we found a *linear* relationship between lowest prehospital SBP and severity-adjusted probability of mortality across an exceptionally wide range. This suggests that: 1) the concept that 90mmHg represents a unique or important "cut-point" may not be true and 2) for the injured brain, clinically meaningful "hypotension" may not be as low as current guidelines suggest. The fact that the adjusted odds of death increase as much for a 10-point drop in SBP from to 100mmHg as for 100 to 90, suggests that the optimal treatment threshold may be higher than 90mmHg.

--International Brain Injury Association: "Mortality as a Function of Prehospital Systolic Blood Pressure in Major Traumatic Brain Injury: What is the Optimum Pressure for Survival?" Conclusions: In this multi-system analysis of major TBI patients, an SBP between 130 and 150 mmHg was associated with the highest probability of survival. This was true even after controlling for injury severity and several other key confounders. In the risk-adjusted logistic regression model, the optimal SBP value, associated with the lowest probability of death, was 144 mmHg. The U-shaped curve that results when SBP is plotted against probability of survival in this study suggests that the optimal range of SBP may be relatively narrow and that it may be significantly higher than previously thought.

--International Brain Injury Association: "The Association Between Prehospital Glasgow Coma Scale and Trauma Center Outcomes in Victims of Moderate and Severe TBI: A Statewide Trauma System Analysis." Conclusions: In this statewide analysis, prehospital GCS showed a strong association with survival and other hospital outcomes, with lower prehospital GCS associated with lower survival, greater hospital/ICU length of stay, higher hospital charges, and greater proportion of survivors discharged to rehab/skilled care facilities. While initial prehospital GCS was strongly associated with outcomes, it is notable that two-thirds of all patients who had final trauma center diagnosis of moderate or severe TBI had an initial GCS of 13-15 in the field. Furthermore, 17.3% of patients in the "mild" GCS category were discharged to rehab/skilled care facilities. Thus, while prehospital GCS is useful for risk stratification, it cannot be used alone as a determinant of whether patients have significant TBI.

--National Association of EMS Physicians: "The Influence of Prehospital Hypotension and Hypoxia on Outcomes in Patients with Major Traumatic Brain Injury." Conclusions: In this multi-system analysis, prehospital hypotension/hypoxia had a profound impact on mortality, even after controlling for injury severity, age, and prehospital intubation. Hypotensive/hypoxic patients also had much higher hospital LOS, ICU LOS, and inpatient charges and were much more likely to be discharged to long-term care. Implementation of the EMS TBI Treatment Guidelines targeting these issues is likely to have a major impact on outcomes.