Journal of the American Medical Informatics Association Volume xx Number x Month 2007

Research Paper

The Evaluation of a Temporal Reasoning System in Processing Aq:1 Clinical Discharge Summaries

LI ZHOU, PHD, BMED, SIMON PARSONS, PHD, GEORGE HRIPCSAK, MD, MS

Abstract Context: TimeText is a temporal reasoning system designed to represent, extract, and reason about temporal information in clinical text.

Objective: To measure the accuracy of the TimeText for processing clinical discharge summaries.

Design: Six physicians with biomedical informatics training served as domain experts. Twenty discharge summaries were randomly selected for the evaluation. For each of the first 14 reports, 5 to 8 clinically important medical events were chosen. The temporal reasoning system generated temporal relations about the endpoints (start or finish) of pairs of medical events. Two experts (subjects) manually generated temporal relations for these medical events. The system and expert-generated results were assessed by four other experts (raters). All of the twenty discharge summaries were used to assess the system's accuracy in answering time-oriented clinical questions. For each report, five to ten clinically plausible temporal questions about events were generated. Two experts generated answers to the questions to serve as the gold standard. We wrote queries to retrieve answers from system's output.

Measurements: Correctness of generated temporal relations, recall of clinically important relations, and accuracy in answering temporal questions.

Results: The raters determined that 96.9% of subjects' 295 generated temporal relations were correct and that 96.5% of the system's 995 generated temporal relations were correct. The system captured 79.2% of 307 temporal relations determined to be clinically important by the subjects and raters. The system answered 83.7% of the temporal questions correctly.

Conclusion: The system encoded the majority of information identified by experts, and was able to answer simple temporal questions.

J Am Med Inform Assoc. 2007;xx:xxx. DOI 10.1197/jamia.M2467.

Introduction

Temporal information is an essential component of medical records.^{1–3} Effective use of temporal information can help health care providers and researchers study and understand medical phenomena such as the progress of a disease, the patient's clinical course, and the clinician's reasoning. Many medical information systems use temporal information to

answer time-oriented clinical queries.^{4,5} to predict future consequences based on the current status of a patient,⁶ to explain the possible causes of a given clinical situation,⁷ and to recognize temporal patterns and create an abstract view of the data.^{8–10} However, most previous studies have focused on temporal information stored in structured clinical databases.

Medical text, such as progress notes, discharge summaries and radiology reports, contain important clinical findings^{11,12} (e.g., evolution of a disease and its corresponding treatment at the different stages). Medical natural language processing (NLP) systems¹¹ have been developed for the extracting, structuring and encoding clinical information from the text. Automatically discovering temporal relations among medical events stated in the text will dynamically link the extracted clinical information, which in turn will facilitate subsequent processing, such as conducting information retrieval and text summarization, inferring other relations (e.g., causal and explanatory relations), and detecting clinical practice patterns. In addition, having time attached to medical events will make extracted clinical information much more understandable to users. Despite the recent developments in biomedical NLP, temporal information in medical text has not been widely exploited for the support of temporal reasoning tasks.¹

l

Affiliations of authors: Department of Biomedical Informatics (LZ, GH), Columbia University, New York, NY; Clinical Informatics Research and Development (LZ), Partners HealthCare, Boston, MA; Department of Computer and Information Science (SP), Brooklyn College, Brooklyn, NY.

This work was funded by National Library of Medicine (NLM) "Discovering and applying knowledge in clinical databases" (R01 LM006910).

The authors thank Carol Friedman for the use of MedLEE (NLM support R01 LM007659 and R01 LM008635). The authors also thank John Chelico, Amy Chused, Peter Hung, Xin Liu, Daniel Stein, and Ying Tao for conducting the system evaluation.

Correspondence and reprints Li Zhou, PhD, BMed, Clinical Informatics Research and Development, Partners HealthCare, 93 Worcester Street, 2nd Floor, Wellesley, MA 02481; e-mail: <lzhou2@ partners.org>.

Received for review: 04/03/07; accepted for publication: 09/20/07.

A few studies^{13,14} presented methods on modeling and processing temporal information in medical narrative reports. They applied natural language processing and medical knowledge to obtain a representation of time for the narrated medical events and to order these events chronologically. However, these systems' performance for such tasks was not clear. Recent research^{15,16} in this area embraces probabilistic and machine learning approaches.

In order to process temporal information in clinical narrative data, researchers in biomedical informatics face many challenges.¹ Evaluating temporal NLP systems is critical to progress. In this paper, we present our evaluation of a comprehensive temporal reasoning system called TimeText in processing discharge summaries. In the background section, we will introduce the TimeText system and briefly describe our previous evaluation of the components of the system. This study is an overall evaluation of the entire system. We assess the system's performance on ordering medical events and answering queries of interest, using experts as judges. We discuss its strengths and weakness as well as providing insights in building such systems.

Background

The TimeText System

87 We developed a systematic temporal reasoning methodol-88 ogy and a corresponding system, called TimeText, for han-89 dling temporal information in electronic clinical reports, 90 with the aim of improving biomedical information applica-91 tions such as information retrieval, medical errors detection, 92 and syndromic surveillance. TimeText is an end-to-end 93 system that mainly consists of four components.¹⁷ Figure 1 F1 94 shows an overview of the system. It formalizes temporal 95 assertions stated in clinical discharge summaries in the form 96 of a Temporal Constraint Structure (TCS).¹⁸ A temporal 97 information recognition and normalization program, named 98 TCS tagger, was developed to implements the TCS. TimeText 99 uses the MedLEE^{19,20} natural language processor to parse the 100 non-temporal information (i.e., medical events). MedLEE is 101 a comprehensive NLP system developed at Columbia Uni-102 versity Medical Center that reads textual clinical reports and 103 generates structured information. TimeText also includes a 104 knowledge-based subsystem²¹ which uses medical and 105 linguistic knowledge for handling implicit temporal in-106 formation and resolving issues such as granularity and 107 uncertainty. After extracting and structuring temporal 108 information and medical events, a computational mecha-109 nism called a Simple Temporal Constraint Satisfaction Prob-110 lem (STP) was adopted for further reasoning about temporal 111 relationships in clinical reports.²² TimeText models tempo-112

ral assertions about medical events in a discharge summary as an STP and produces the derived temporal information. The system-generated information can be used to answer questions about the time of events and the temporal relation between pairs of events. Examples included, "When was the operation conducted?" and "Did the infection occur before or after this operation?" The TimeText system architecture and detailed description of each component have been published.17

The TimeText system mainly consists of four components, including 1) a Temporal Constraint Structure (TCS)¹⁸ for representing various temporal expressions and the TCS tagger; 2) an integration component with an existing medical NLP system (MedLEE)^{19,20} for processing clinical information; 3) a knowledge-based subsystem²¹ which uses medical and linguistic knowledge for handling implicit and uncertain temporal information; and 4) a formal temporal model²² based on simple temporal constraint satisfaction problem for reasoning about related information in clinical reports.

Review of Previous Formative Evaluations of the TimeText Components

We conducted evaluations testing the suitability and feasibility of models and methodologies for the major components of TimeText while the system was in development. Evaluation of the Temporal Constraint Structure (TCS)¹⁸ showed that 1961 out of 2022 (97%) temporal expressions identified in 100 discharge summaries were effectively modeled using the TCS. Note that medical dosing and some temporal adjectives and adverbs (e.g., "occasional" and "chronic") were not counted. The natural language processor MedLEE^{19,20} has been used by investigators at Columbia University Medical Center since 1995. It has been applied to most types of medical text, including radiology reports, discharge summaries, pathology reports and visit notes, and achieved great accuracy across this wide range of medical text.19,23,24 We have tested and demonstrated that most of the temporal assertions found in electronic discharge summaries can be modeled as a simple temporal constraint satisfaction problem (STP),²² including a description of fifteen special issues on encoding and how we dealt with them.

In our previous work, we addressed fundamental issues encountered at different linguistic layers and modeling processes, conducted system architecture design, and carried out some formative evaluations which shaped the course of subsequent integration of the components. In this paper, we evaluate the overall functionality and performance of the system after all the components were put



2

63

64

65

66

67

68

69

70

71

72

73

74

75

76

77

78

79

80

81

82

83

84

85

86

122

123

Journal of the American Medical Informatics Association Volume xx Number x Month 2007

together and a comprehensive temporal reasoning system
for clinical reports was developed. In particular, we assess
the accuracy of the system on ordering medical events and
on answering temporal questions. We also discuss critical
issues encountered during the evaluation.

131 Methods

130

132 The evaluation of the TimeText temporal reasoning system 133 in processing clinical discharge summaries consists of two 134 parts: a verification of its output temporal constraints and an 135 assessment of its performance in answering clinical queries. 136 We randomly selected 20 discharge summaries from a 137 clinical data repository at Columbia University Medical 138 Center, which contains 300,000 reports from 1989. Six phy-139 sicians who have biomedical informatics training served as 140 evaluation domain experts and helped with the evaluation. 141 Four of them are biomedical informatics postdoctoral fel-142 lows and another two are biomedical informatics PhD 143 candidates. None of them participated in the design or 144 development of the TimeText system.

Part I: Verification of Output

146 Due to time limitations, only the first fourteen discharge 147 summaries were used to assess the accuracy and coverage of 148 the system-generated temporal relations between pairs of 149 medical events (see Figure 2; Note that readers may also 150 refer to Figure 4, which presents a summative illustration for 151 both evaluation methods and results). From each discharge 152 summary, five to eight clinically significant events were 153 selected by one author (LZ, a biomedical informatics PhD 154 candidate with a medical degree), based on the following 155 criteria: the events included 1) reference events (e.g., admis-156 sion and discharge) for the purposes of assessing the sys-157 tem's capability of detecting situations such as whether an 158 event occurred before, during, or after hospitalization, be-159 cause this function might be helpful for detecting medical 160 errors; and 2) encounter-based patient-specific medical 161

events for the purposes of assessing whether the system can capture these events as well as related temporal references and whether the system can infer correct temporal relationships. The latter included different types of medical events such as the patient's chief complains and symptoms (e.g., chest pain), important examinations and procedures (e.g., cholecystectomy), major medications (e.g., Lasix), and leading diagnoses (e.g., esophageal cancer), which were largely critical to the patient's hospital encounter. In total, 92 medical events were used for evaluation. Appendix 1, available as a JAMIA online-only data supplement at www. jamia.org, shows a simple example in the questionnaire, including a discharge summary, selected medical events, the orderings of these events generated by the system and physicians, querying questions, and the corresponding answers, which will be described in Part II. Appendix 2, available as a JAMIA online-only data supplement at www. jamia.org, shows all of the 92 selected medical events.

We model the time over which an event occurs as an interval.²² Each interval has a start point and a finish time point and the start is never after the finish. The TimeText temporal reasoning system generated temporal relations between endpoints of paired medical events. All of the six physicians participated in this part. We asked two physicians (one is a postdoctoral fellow who completed an internship in Internal Medicine and another is a PhD student who was an astronaut physician) to serve as subjects to manually generate temporal relations for endpoints of these medical events; one encoded nine reports and another encoded five reports. Before the manual encoding, training was provided to the two subjects, including encoding instructions and a concrete example. The subjects did not attempt to exhaustively list all the temporal relations about each medical event, which would have been prohibitively time-consuming, but instead listed clinically important ones in regard to each specific patient case.



125

126

127

128

129

130

131

132

133

134

135

136

137

138

139

140

141

142

143

144

145

146

147

148

149

150

151

152

153

154

155

156

157

158

159

ZHOU ET AL., Temporal Reasoning in Clinical Discharge Summaries



In order to compare the performance on ordering medical events between the system and the subjects, both the system and subject-generated results were presented, blindly, to four other physicians (raters). A pair of raters reviewed the results generated by one subject and the system. They 208 assessed the accuracy of these relations. They further iden-209 tified other clinically important temporal relations that the 210 subjects missed. Based on subject-generated results, after 211 incorrect relations were removed and missing relations were 212 added, a new set of relations were then generated. This new 213 set served as a reference to assess the system's ability to 214 identify clinically important temporal relations. Because 215 inferring complex temporal relations was difficult even for 216 our domain experts (subjects and raters), disagreement 217 between the system and the experts was studied in more 218 detail by the investigators to ascertain which was correct. 219

We calculated the correctness of generated temporal rela-220 tions, as well as recall of the system for generating clinically 221 important relations. We further studied spurious temporal 222 relations (relations that were not really there) and misinter-223 preted temporal relations. We analyzed the sources of 224 disagreement between the system and the subjects. 225

226 Part II: Performance in Answering Time-oriented 227 **Clinical Ouestions**

228 We assessed the ability of TimeText to answer time-oriented 229 F3-4 clinical questions (Figure 3 and Figure 4). All twenty dis-

charge summaries were used in this part. For each report, 187 one author (LZ) created five to ten clinically plausible 188 temporal queries about medical events in the reports. Simi-189 190 lar to evaluation Part I, these queries related to the patient's predominant clinical findings. In particular, the queries 191 might ask when an event occurred (absolute date/time); 192 193 how long did an event last (duration); or whether an event occurred during hospitalization. Appendix 3, available as a 194 JAMIA online-only data supplement at www.jamia.org, lists 195 all the time-oriented querying questions for evaluation Part 196 197 II. Two physicians, who also were subjects in Part I, served 198 as experts to generate answers to the queries. For disagreement, we asked the experts to modify responses on the basis 199 of the others' opinions. The modified responses were col-200 lated and returned to the experts for further modification. 201 The process was repeated until a consensus was achieved or 202 203 there were no further changes. The responses that were agreed upon then served as the reference standard. The 204 authors wrote simple queries to retrieve answers from the 205 system-generated temporal relations of medical events. 206 They compared the answers generated by the system to the 207reference standard. 208 209

To assess the system performance, we calculated the accuracy (the proportion of correct responses) and ascertained the causes of the errors. We also calculated inter-rater disagreement to assess our experts' reliability on temporal queries.

Results

Part I: Verification of Output

Physician Performance and Reference Standard Table 1 and Table 2 show the performance of the subjects in T1-2 219 generating temporal relations between endpoints of pairs of medical events. Figure 4 illustrates the results graphically. Two physicians (subjects) encoded 295 temporal relations about the 92 selected clinically important events. Four other physicians (raters) examined these relations, found 4 spurious relations, corrected 5 misinterpreted relations, and added 16 missing temporal relations that they considered clinically significant. In summary, 307 (295-4-5+5+16) clinically important temporal relations about 92 medical events were identified and they served as a reference stan-



216

217

210

211

236

237

238

239

240

241

242

243

244

245

246

247

Journal of the American Medical Informatics Association Volume xx Number x Month 2007

<i>Table 1</i> Temporal	l Re	lations	Generated	by	the
Subjects versus the	e Sya	stem			

249

250

261

262

263

264

265

266

267

268

269

270

296

297

298

299

300

301

302

303

	Subjects	System
Total generated relations	295	995
Correct relations	286	960
Incorrect relations (inferred incorrectly)	5	30
Spurious relations (no evidence in report)	4	5
Correct relations in common with the	286	243
reference standard of clinically		
important relations		

dard to assess the system's recall. Of the 614 endpoints referenced in these relations (two per relation), 84.7% were start points of medical events and 15.3% were finish points. Raters determined that 96.9% (286 out of 295; 95% CI: 94.3-98.4) of subjects' relations were correct (Table 2). The subjects captured 93.2% (286 of 307; 95% CI: 89.8-95.5) of the clinically important temporal relations, but because subjects helped to determine the reference standard, this result is likely an overestimate.

Error Analysis on Physician Performance

271 We analyzed the incorrect relations generated by subjects. 272 There were several types. Some errors were obvious. For 273 example, one patient was admitted for sickle cell crisis. The 274 finish of the event should be after admission, but the 275 annotator wrote "before." In another case, it was stated in 276 the report that "he underwent a V-Q scan on 8/23" and that 277 the admission was on 8/24, so that V-Q scan occurred before 278 admission. However, the subject encoded that the V-Q scan 279 occurred after admission. In another case, "The patient 280 cleared of nausea and vomiting" was after using "Thor-281 azine," while the subject encoded it the other way around. 282 The subjects also made spurious temporal assertions. For 283 example, based on the statement "he experienced pancreati-284 tis secondary to the IV Pentamidine," the subject inferred 285 that "the finish of the IV Pentamidine was after the finish of 286 pancreatitis." There was no evidence in the report to support 287 this assertion. 288

289 The subjects also missed 16 temporal relations which the 290 evaluators considered important. For example, in a report, 291 the patient had a resection of petrous apex meningioma. His 292 postoperative course was complicated by hemiparesis. The 293 temporal relation between the operation (resection of pet-294 rous apex meningioma) and its complication (hemiparesis) 295 was missed.

System Performance

Table 1, Table 2, and Figure 4 show the performance of the system in generating temporal relations between medical events. The system generated 995 temporal relations about these 92 medical events. The raters determined that 5 relations were spurious and 30 were incorrect, so that 96.5%

(960 out of 995; 95% CI: 95.2–97.5) were correct. Compared to the reference standard of clinically important relations, the system missed 64 temporal relations and achieved a recall of 79.2% (243 of 307; 95% CI: 74.3-83.3). The system captured 85.8% of start points but only 42.6% of finish points that were in the reference standard of clinically important relations

Error Analysis on System Performance

We examined the missed temporal assertions. The majority were due to finish points of medical events that were not constrained. The major reason for the errors was misplaced contents in the original reports. For example, physicians sometimes wrote the patient's current problems or current treatments in the "history of present illness" section. In one report, there was no hospital course section at all and medical events occurring during hospitalization were stated in the "history of the present illness" section.

Performance Comparison of the Physicians and the System

Of the five incorrect relations that were generated by subjects, the system generated three correctly. For example, in a report, Cefuroxime was given after the patient developed papular rash. The system successfully ordered these two events. However, the subject encoded that the start of rash was after Cefuroxime. In addition, of the 21 relations that were missed by subjects, the system captured eight.

Part II: Performance in Answering Time-oriented **Clinical Ouestions**

Inter-rater Agreement and Reference Standard Overall, in 20 discharge summaries, 147 temporal questions about medical events were generated. Eighteen questions related to specific dates or times (for example, when did this patient have a skin graft?). Eight questions related to durations (for example, how long did diarrhea last?). Others were yes/no questions (did pancreatitis occur after pentamidine; did the patient vomit before using Thorazine; did the patient stop vomiting after using Thorazine?). The experts disagreed on 17 answers (raw inter-rater agreement: 88.4%). Four of these questions were related to durations and others were yes/no questions. A reference standard was established after the experts achieved an agreement upon their responses.

System Performance on Answering Temporal Queries The answers generated by the system were compared to the reference standard. For yes/no and dates/times questions, an exact match was required. For questions related to durations, range estimation was allowed. For example, the answers were considered to match if the physician's answer was "3 days" while the system estimated "2-4 days." However, the system's answer was considered incorrect if the range did not cover the exact duration. In addition, if the

Table 2 • Performance Comparison of the Subjects and the System 304

	Subjects		System		
Metric	Derivation	Value (95% CI)	Derivation	Value (95% CI)	
Correctness of relations	286/295	0.969 (0.943–0.984)	960/995	0.965 (0.952-0.975)	
Recall of clinically important relations	286/307	0.932* (0.898-0.955)	243/307	0.792 (0.743–0.833	

310 *Subjects helped define the reference standard of clinically important relations. ZHOU ET AL., Temporal Reasoning in Clinical Discharge Summaries

system only captured part of the temporal information, its
answer was judged incorrect. For example, a patient developed a rash one week before admission, but the system only
captured "before admission."

315 Compared with the reference standard, the temporal reason-316 ing system incorrectly answered 16 questions. In addition, 317 the system could not answer 8 questions since the medical 318 events were not extracted by MedLEE. For example, terms 319 like "rheumatological consultation," "GI button (gastroin-320 testinal button)," and "declared" in "the patient was de-321 clared" were not extracted by MedLEE. Therefore, the 322 overall accuracy of the system in answering temporal que-323 ries was 83.7% (123 out of 147; CI: 76.9-88.8). 324

We further ascertained the causes of the errors. Among 16 325 incorrect answers, four answers provided incomplete infor-326 mation. For example, for the statement, "well until one week 327 ago when she developed papular rash on the neck," the 328 system did not link one week ago to rash, but only inferred 329 "before admission." The system is not designed to handle 330 age information at this stage, so that for sentences like "the 331 patient was diagnosed with cystic fibrosis at age four," the 332 system only inferred "the diagnosis of cystic fibrosis was 333 made before admission" but not the exact year when the 334 diagnosis was made. The system misinterpreted some ex-335 pressions. For example, the system misinterpreted "on 1/2" 336 in "the patient was put on 1/2 maintenance IV fluids" as a 337 date. Misplaced contents (e.g., the statements about hospital 338 course were misplaced in the section of "history of present 339 illness") caused the systems use inappropriate rules in the 340 knowledge-based subsystem. For example, as noted above, 341 one report had no hospital course section. All the informa-342 tion was in the history of illness, physical examination and 343 laboratory test sections. Therefore, questions like "did the 344 patient use heparin during hospitalization" could not be 345 answered properly. 346

To get the right answer, complex queries are necessary for some questions. Manual checking was used to assist in finding the answers. For example, a term, "Bactrim," appeared several times in a report. If we want to know "was the patient treated with Bactrim during hospitalization," a manual summarization of retrieved temporal information about all the occurrences of "Bactrim" is needed.

Discussion

354

355

We found that the TimeText system generated many tem-356 poral relations, that most of them were correct (97%), and 357 that it generated most of the temporal relations deemed 358 clinically important by subjects and raters (79%). The human 359 subjects achieved a similar level of correctness. They cap-360 tured a higher proportion of the clinically important rela-361 tions, but they helped to create the reference standard. When 362 the relations were placed in a database and queried, the 363 system answered 84% of 147 time-oriented questions cor-364 rectly. This compared to 88% correct for the experts when 365 compared to each other. 366

This study is one of the few attempts in the literature to
assess temporal reasoning systems for medical text. It is
difficult to evaluate a system that processes medical narrative data:^{23,25} 1) it involves much manual processing by
domain experts; 2) inter-rater and intra-rater agreement may
be low; and 3) obtaining a gold standard is difficult. In

addition, temporal reasoning using medical narrative data involves complex reasoning and calculations, which places an even heavier burden on the experts. 311

312

313

314

315

316

317

318

319

320

321

322

323

324

325

326

327

328

329

330

331

332

333

334

335

336

337

338

339

340

341

342

343

344

345

346

347

348

349

350

351

352

353

354

355

356

357

358

359

360

361

362

363

364

365

366

367

368

369

370

371

372

Hirschman et al.^{13,26} developed "the time program" for obtaining a representation of time for each medical event stated in a discharge summary, either in terms of a fixed time point, or in terms of another events in the narrative. They also applied a special time comparison retrieval routine which compared the temporal information for two events and returned one of four values: greater than, less than, equal, or not comparable. Only three discharge summaries were used to assess the performance of the system on retrieving clinical information. The system-generated responses showed 90% agreement with the results obtained by a physician reviewer. However, their evaluation methods were not described in detail.

A report by Rao and colleagues¹⁵ described a system, called REMIND, for inferring disease state sequences for recurrence using both clinical text and structured data. Phrase spotting was applied to information extraction from free text and a Bayesian Network was used for temporal inference. They assessed REMIND's classification accuracy (whether the patient recurred or not) and sequence accuracy (if the patient recurred, did the system correctly estimate the disease-free survival time). The purpose of this study differed from ours in that they focused on specific recurrent medical events instead of different events. Bramsen et al.¹⁶ described a supervised machine-learning approach for temporally segmenting discharge summaries and ordering these segments. They defined a temporal segment to be a fragment of text that does not exhibit abrupt changes in temporal focus. Their learning method achieved 83% F-measure in temporal segmentation, and 78.3% accuracy in inferring pairwise temporal relations. Compared with this approach, the TimeText system performs temporal analysis at a finer granularity.

The TimeText system generates the timelines from three sources: 1) the constraints encoded in the temporal constraint structures, which represent only what is stated explicitly in the report; 2) the constraints discovered using linguistic and medical domain knowledge, which include implicit information; and 3) the constraints derived from resolving the simple temporal constraint satisfaction problems, which include derived information. Compared with the system, the human subjects tended to focus on listing temporal relations for the events that occurred next to each other in a timeline. They mentioned that transitive relations can be inferred based on this information but that they might not list the inferred relations unless they were very important. As the result of using different strategies for timeline generation, TimeText generated three times more temporal relations than the annotators. Our belief is that many of these additional relations are obvious to humans, and so they do not bother to write them down. Our system infers these relations ahead of time, but they could in theory be generated by a reasoning system in the process of answering a question.

While many challenges exist specifically for the system, some difficulties are common both for the physicians and the system. We found that most of the temporal assertions