Using machine learning to optimize quality of care delivery for patients with cancer

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Stanford University
Outline

- Goals of care / advance care planning
- Machine learning survival models
- Quality initiatives to increase and improve advance care planning
- Patient perspective
Patients with life-threatening cancer can have varying goals of care (e.g. maximize aggressiveness, live independently at home, attend a life event, transition to hospice).

People often wish to die at home / enrolled in hospice.

Interview study with families of 1146 patients with Medicare who died of lung or colorectal cancer (response rate 74%)

- 57% died in their preferred location, 51% rated quality of end of life care as “excellent” (best of 5 levels)
- Higher care rating for death in hospice, lower for death in hospital and if ICU in last 30d.
- If died in hospital, only 25% reported dying in preferred place.

McNiff, The Oncologist 26(7) 533.
Wright, JAMA 2016 315(3):284
Goals of care

- Advance care planning (ACP) helps people understand and share their goals and values
- May include filling out advance health care directive: preferences for care if unable to make decisions for oneself
- Guidelines recommend ACP conversation with all patients with metastatic cancer [ASCO, etc.]; CMS now tracking this
• Patients and physicians agree ACP is important, but often avoid ACP conversations which can be emotionally difficult [Jimenez JPSM 2018;56(3)]

• ACP can be infrequent. Of patients with cancer who died in nursing home, only 9% had documented advance directive [De Gendt JPSM 2013;45(2)].
• About 1/3 of patients with incurable cancer stated they expected the treatment to cure the cancer [Weeks NEJM 2012; 367(17)]
• Physicians cite prognostic uncertainty as a barrier to ACP conversations [Manali Patel et al., Am J Hosp Palliat Med 2018;35(3)]
Advance care planning

• Low rates of early ACP despite guidelines suggest that other interventions required
• Train non-physicians/APPs to help with ACP
  • Lay health worker
  • Care coach
  • Nurse navigator
  • Etc.
Palo Alto VA study [M. Patel, JAMA Oncology 2018;4(10)]
• Lay health worker received palliative care training, assisted pts with establishing care preferences, fill out AD, encourage to discuss with providers
• 213 pts w/ stage 3-4 or recurrent cancer randomized to intervention or usual care. 6 months follow-up.
• More goals of care documentation (92% vs. 18%)
• Higher satisfaction with provider
• 56% of patients deceased
  • Intervention group more hospice (77% vs. 48%), less ER, less hospitalization, lower costs

Stanford study
• Parikh et al, ASCO Quality Care Symposium 2021. Coaches Activating Reaching and Engaging Patients (CAREPlan): A randomized controlled trial combining two evidence-based interventions to improve goals of care documentation
Advance Care Planning form prompts (based on Serious Illness Care Program)

1. What is your understanding of where you are with your illness?
2. How much information about what is likely ahead with your illness would you like to have?
3. I want to share my understanding of where things are with your illness [prognosis].
4. If your health situation worsens, what's most important to you?
5. What are your biggest fears and worries about the future?
6. What gives you strength as you think about the future with your illness?
7. What abilities are so critical to your life that you cannot imagine living without them?
8. If you become sicker, how much are you willing to go through for the possibility of gaining more time?
9. How much does your healthcare proxy or family know about these priorities and wishes?
10. Given what you've told me and what we know about your illness, I recommend we do the following things.
Patient identification

- Would be helpful to identify high-risk patients for prioritization by providers and care coaches
- Providers struggle with predicting survival time
  - Stanford survey study: Doctors’ C-index 0.55-0.86
- Non-providers do not have expertise to estimate. Time-consuming to apply rules to entire clinic schedules
- Could an automated survival prediction model help?
- Need to test impact carefully. Automation bias etc.
Survival models

- University of Pennsylvania [Manz JAMA Onc 2020 6(11):1723]
  - Predict 180-day mortality in outpatients with cancer
  - 559 structured EMR features (no note text)
  - Trained with ~26,000 patients, tested prospectively on ~25,000
  - AUC 0.89, good calibration
University of Pennsylvania randomized study [Manz JAMA Onc 2020;6(12)]

- 78 oncology clinicians, 14,607 patients included in stepped wedge randomized study
  - Intervention included weekly emails with 6 upcoming clinic patients with highest mortality risk, text messages reminding to have Serious Illness Conversation
- Serious Illness Conversation rate 4.6% intervention group vs. 1.3% control group, p<0.001
Our use case

- Run automatically
- Restrict to patients with metastatic cancer
- High performance needed to prevent provider disengagement
  - High quality follow-up data to train
  - Include note text
Regularized discrete-time survival model trained with data of ~15,000 Stanford patients with metastatic cancer

>4000 predictor variables:

- **Demographics**: Age, sex
- **Note text**: >3000 phrases, automatically picked from 100,000 phrases
- **Radiology impressions**
- **Vital signs**
- **Laboratory values**
- **Diagnosis codes** (ICD-9)
- **Procedure codes** (CPT)
- **Medications**


Variable selection for diagnosis codes, medications, procedure codes, laboratory values, and note terms for computational efficiency

- L1 penalized logistic regression (lasso) in the Glmnet Python package
- For each variable category, a logistic regression model was trained to predict survival greater to or less than 12 months for the visits in the training set
- **Time weighting**
  - Each variable can have multiple values over time. More recent values more relevant.
  - Each value weighted inversely to time elapsed since the measurement, with a half-life of 30 days.
  - If we wish to predict survival from today’s date, and the patient’s pulse was 100 today, 50 thirty days ago, and 75 sixty days ago, the pulse feature would be calculated as:

\[
\frac{100 \cdot 1.0 + 50 \cdot 0.5 + 75 \cdot 0.25}{1.0 + 0.5 + 0.25} = 82.1
\]
Text features (from notes and radiology reports)
  - Term frequency approach
  - Example note: “testing testing one two three”
  - Feature names: [“testing”, “one”, “two”, “three”]
  - Feature vector: [0.4, 0.2, 0.2, 0.2]
  - More complicated than this because all 1-2 word phrases are features so actual feature names vector would be [“testing”, “one”, “two”, “three”, “testing one”, “one two”, “two three”]
**Nnet-survival**: Discrete-time survival model

- Follow-up time divided into $n$ intervals, don’t have to be equally spaced
- $h_j$: conditional hazard probability (probability of death in interval $j$, given that the patient has survived at least to the beginning of interval $j$)
- To get a patient’s chances of surviving from time 0 to the end of interval $j$, multiply their $(1-h_j)$ for all the intervals from 1 to $j$.

http://github.com/MGensheimer/nnet-survival

Accurate death/follow-up outcome data critical. Use Epic/EMR data alone→biased outcomes due to informative censoring!

4077 pts diagnosed with initially metastatic cancer from 2008-2013

Gensheimer et al. JCO CCI 2022
Training data
- ~14,600 patients, ~400,000 visits, ~100,000 inpatient stays
- Patients contributed multiple rows to training data, starting from first visit after metastatic diagnosis and continuing every 6 months until death/last follow-up
- Most had gold-standard death/follow-up data from cancer registry
- Median age 64 (IQR 53-72)
- 51% female
- Most common primary cancer sites: gastrointestinal, thorax, genitourinary
- 61% deceased, median survival 21 months from first visit after metastatic diagnosis
Gensheimer, Chang, et al. Automated Survival Prediction in Metastatic Cancer Patients Using High-Dimensional Electronic Medical Record Data, JNCI 2019
Selected model coefficients

<table>
<thead>
<tr>
<th>Term</th>
<th>Coefficient*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms/appearance</td>
<td></td>
</tr>
<tr>
<td>Cachectic</td>
<td>0.020</td>
</tr>
<tr>
<td>Fatigued</td>
<td>0.0059</td>
</tr>
<tr>
<td>Ascites</td>
<td>0.0085</td>
</tr>
<tr>
<td>Completely asymptomatic</td>
<td>-0.0054</td>
</tr>
<tr>
<td>Anxious</td>
<td>-0.0031</td>
</tr>
<tr>
<td>Feel well</td>
<td>-0.0073</td>
</tr>
<tr>
<td>Cancer location/response</td>
<td></td>
</tr>
<tr>
<td>Disease progression</td>
<td>0.012</td>
</tr>
<tr>
<td>Leptomeningeal</td>
<td>0.0067</td>
</tr>
<tr>
<td>Mixed response</td>
<td>0.014</td>
</tr>
<tr>
<td>Innumerable pulmonary</td>
<td>0.0046</td>
</tr>
<tr>
<td>Minimal progression</td>
<td>-0.0012</td>
</tr>
<tr>
<td>Oligometastatic</td>
<td>-0.0066</td>
</tr>
<tr>
<td>Systemic therapy agents</td>
<td></td>
</tr>
<tr>
<td>Nivolumab</td>
<td>-0.00065</td>
</tr>
<tr>
<td>Liposomal doxorubicin†</td>
<td>0.011</td>
</tr>
<tr>
<td>Anastrozole†</td>
<td>-0.00051</td>
</tr>
<tr>
<td>Leuprolide†</td>
<td>-0.0037</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>-0.0034</td>
</tr>
</tbody>
</table>

*A positive coefficient indicates shorter survival.
Comparison to physician predictions

Machine learning model outperformed physicians and traditional simple model (ECOG PS alone) for prediction of 1 year survival

Model adds to physician predictions

- Physician predicts 0-6 month survival
  - ML model prediction:
    - Shorter (n=92)
    - Same (n=88)
    - Longer (n=134)
  - p<0.0001

- Physician predicts 6.1-12 month survival
  - ML model prediction:
    - Shorter (n=77)
    - Same (n=67)
    - Longer (n=81)
  - p<0.0001

- Physician predicts 12.1-24 month survival
  - ML model prediction:
    - Shorter (n=35)
    - Same (n=50)
  - p=0.008

- Physician predicts >24 month survival
  - ML model prediction:
    - Shorter (n=92)
    - Same (n=88)
    - Longer (n=134)
Prospective use

- Daily data feed from Epic
- ~6 months of work with hospital IT on data selection, data quality, harmonization with retrospective database
- Weekly simple data quality validation
Prospective validation: comparison to actual survival (Epic data, n=1,229)

Number at risk

<table>
<thead>
<tr>
<th>Follow-up (months)</th>
<th>Number at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12 mo.</td>
<td>145</td>
</tr>
<tr>
<td>12.1-24 mo.</td>
<td>214</td>
</tr>
<tr>
<td>&gt;24 mo.</td>
<td>870</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Follow-up (months)</th>
<th>Predicted survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12 mo.</td>
<td>1.00</td>
</tr>
<tr>
<td>12.1-24 mo.</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt;24 mo.</td>
<td>1.00</td>
</tr>
</tbody>
</table>

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Quality improvement pilot study

- Pilot implementation of care coaches + weekly automated emails in two medical oncology clinics that had prior Serious Illness Care Program training: genitourinary and thoracic
- Patients each week with metastatic cancer automatically identified using Epic staging module and ICD-10 codes
- Care coach contacted patients with <2 year predicted survival to have ACP discussion not including prognosis. ACP form filled out, note forwarded to provider, and optionally advance directive completed
- Providers asked to discuss prognosis with these patients
Weekly email to each provider and care coaches

This list shows patients with metastatic cancer who will be seen by Kavitha Ramchandran in the next week. Life expectancy was predicted by a computer model using data in Stanford Epic. Please consider having advance care planning conversations with these patients, if appropriate. To document the conversation in Epic, click on Adv Care Plan, then ACP Form. Paste the form contents into your note using this SmartPhrase: :ADVANCECAREPLANNINGSMRTFORM . For help structuring the conversation, read the Serious Illness Conversation Guide.

High priority: <2 year predicted survival, and no prognosis documentation in last year. Care Coach has contacted or will contact these patients to start ACP conversation. Please consider discussing prognosis with patient and doing ACP form prognosis section.

<table>
<thead>
<tr>
<th>Appt. time</th>
<th>Appt. type</th>
<th>MRN</th>
<th>Name</th>
<th>Predicted survival (months)</th>
<th>ACP form updated</th>
<th>ACP form prognosis section updated</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021-1015</td>
<td>RETURN PATIE</td>
<td></td>
<td></td>
<td>6-12</td>
<td>not done</td>
<td>not done</td>
</tr>
<tr>
<td>2021-1015</td>
<td>RETURN PATIE</td>
<td></td>
<td></td>
<td>6-12</td>
<td>not done</td>
<td>not done</td>
</tr>
</tbody>
</table>

Lower priority for conversation:

<table>
<thead>
<tr>
<th>Appt. time</th>
<th>Appt. type</th>
<th>MRN</th>
<th>Name</th>
<th>Predicted survival (months)</th>
<th>ACP form updated</th>
<th>ACP form prognosis section updated</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021-1015</td>
<td>TREATMENT 15</td>
<td></td>
<td></td>
<td>12-24</td>
<td>2021-1015</td>
<td>2021-1015</td>
</tr>
<tr>
<td>2021-1015</td>
<td>TREATMENT 15</td>
<td></td>
<td></td>
<td>&gt;24</td>
<td>not done</td>
<td>not done</td>
</tr>
<tr>
<td>2021-1015</td>
<td>TREATMENT 15</td>
<td></td>
<td></td>
<td>6-12</td>
<td>2021-1015</td>
<td>2021-1015</td>
</tr>
</tbody>
</table>
Quality improvement pilot study

- Compared outcomes to two other clinics that had prior Serious Illness Care Program training (cutaneous and sarcoma)
- Eligible visits for analysis met all of these criteria:
  - Patient has cancer with distant metastases
  - Age $\geq 18$
  - Scheduled for outpatient follow-up appointment (in-person or virtual) with a provider in one of the four clinics from April 15, 2020 to February 5, 2021
  - Sufficient data in EMR to run ML model (at least one note, laboratory result, and procedure code)
  - No prior prognosis in ACP form
  - No prior visit in the same week
- Primary outcome: Advance Care Planning form edits by care coaches and providers
Quality improvement pilot study

- April 2020
  - genitourinary + thoracic: Usual care
  
- June 2020
  - Care coaches + weekly automated emails
  - cutaneous + sarcoma: Usual care

- Feb. 2021
### Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intervention clinics (n=910)</th>
<th>Control clinics (n=341)</th>
<th>Total (n=1,251)</th>
<th>P-value for intervention vs. control*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer type/clinic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoracic</td>
<td>504 (55%)</td>
<td>-</td>
<td>504 (40%)</td>
<td></td>
</tr>
<tr>
<td>Urologic</td>
<td>406 (45%)</td>
<td>-</td>
<td>406 (32%)</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>-</td>
<td>198 (58%)</td>
<td>198 (16%)</td>
<td></td>
</tr>
<tr>
<td>Cutaneous</td>
<td>-</td>
<td>143 (42%)</td>
<td>143 (11%)</td>
<td></td>
</tr>
<tr>
<td>Age (IQR)</td>
<td>69 (59,76)</td>
<td>62 (52,73)</td>
<td>67 (57,75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>332 (36%)</td>
<td>166 (49%)</td>
<td>498 (40%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>578 (64%)</td>
<td>175 (51%)</td>
<td>753 (60%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>285 (31%)</td>
<td>44 (13%)</td>
<td>329 (26%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Black</td>
<td>26 (3%)</td>
<td>9 (3%)</td>
<td>35 (3%)</td>
<td></td>
</tr>
<tr>
<td>Other/multiple</td>
<td>139 (15%)</td>
<td>60 (18%)</td>
<td>199 (16%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>10 (1%)</td>
<td>2 (1%)</td>
<td>12 (1%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>450 (49%)</td>
<td>226 (66%)</td>
<td>676 (54%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>98 (11%)</td>
<td>42 (12%)</td>
<td>140 (11%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Not Hispanic</td>
<td>801 (88%)</td>
<td>296 (87%)</td>
<td>1,097 (88%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>11 (1%)</td>
<td>3 (1%)</td>
<td>14 (1%)</td>
<td></td>
</tr>
<tr>
<td>Computer-predicted survival &lt;24 months</td>
<td></td>
<td></td>
<td></td>
<td>0.053</td>
</tr>
<tr>
<td>at first visit</td>
<td>271 (30%)</td>
<td>82 (24%)</td>
<td>353 (28%)</td>
<td></td>
</tr>
</tbody>
</table>

* Wilcoxon rank sum test used for age; chi-squared test used for other variables.
Outcomes

Any advance care planning documentation

- ACP at this visit
- Prior ACP
- Neither

Visit month

Num. visits

Control clinics

Intervention clinics

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Outcomes

Prognosis documentation

![Graph showing outcomes over time with different categories and months.](image)

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Outcomes

- For patients with prognosis documentation (n=204), median time from first email to first prognosis documentation was 65 days (IQR 23-152)

- Care coaches edited ACP forms for 276/1,251 patients
- Providers edited ACP forms for 229 patients
- For high-priority patients highlighted in emails (<2 year predicted survival and no prognosis documentation prior to visit), positive correlation between care coach edits and provider edits (odds ratio 2.4, 95% CI 1.6-3.6, p<0.0001).
- For patients whose ACP form was edited by both care coaches and providers (n=98), median days from first care coach edit to first provider edit was 2 (IQR -24 to 42).
Outcomes

- Analysis of end of life care in 176 deceased patients
- Presence of at least one provider ACP form edit (present in 59/176 deceased patients) was negatively correlated with number of National Quality Forum quality measures met (coefficient -0.72, p=0.04)
- Presence of at least one care coach edit (present in 67/176 patients) was not significantly correlated with number of quality measures met (coefficient -0.16, p=0.63)
Pilot study conclusions

- Sustained increase in ACP and prognosis documentation in the intervention clinics after the start of the intervention
- In control clinics, rates remained low through the study period, which helps rule out a secular trend of increased ACP documentation throughout the institution
- Despite providers not receiving incentives for participation, engagement was high

Possible contributors to success
- Care coaches helped jump-start ACP
- Weekly emails reduced ambiguity and conflicts about patient prioritization
- Specific roles for care coaches, providers, and support staff
Randomized study

- Stepped wedge design, ~6 month duration
- Eight disease site and outreach clinics
- All attendings started in control condition
- Every 4 weeks from Feb.-July 2021, 5-6 randomly chosen attendings switched to intervention (weekly emails, care coach) until all switched
- Analysis ongoing
Patient perceptions/education

926 respondents to national survey administered by 3rd party organization

- 86.5% said it would be important to be told when an AI program has played a small role in their diagnosis or treatment
- 58% uncomfortable receiving a diagnosis from a computer program that made the right diagnosis 98% of the time but could not explain why it made the diagnosis
The computer model predicts that patients with similar characteristics to this patient would have:
- a median survival time of 15.2 months
- a 75% chance of living more than 6 months

Here is a predicted survival curve for this patient:

Some factors that are increasing the predicted survival are (ordered from most to least important):
- Lab: low MCV
- Note text: “six months”
- Lab: high RBC
- Note text: “sclerotic change”
- Diagnosis: other malignant lymphomas
- Medication: pembrolizumab
- Lab: high PSA
- Lab: low MCH

Some factors that are decreasing the predicted survival are (ordered from most to least important):
- Note text: “progression”
- Medication: docetaxel
- Note text: “new”
- Procedure: encounter for chemotherapy
- Note text: “brain”
- Note text: “metastasis”
- Diagnosis of non-small cell lung cancer
- Lab: low MCH
Interviewed ten attendings (five medical oncology, five radiation oncology)

- Typically inform incurable: MedOnc 5, RadOnc 3
- Typically discuss prognosis: MedOnc 3, RadOnc 3
- Would show model to patients: MedOnc 4, RadOnc 4
- Would use model in clinical practice: MedOnc 5, RadOnc 5

R Hildebrand, ASTRO 2022
Use in the clinic

Themes – Physician Interviews

• Lack of patient-specific data hinders prognosis conversations
• Model would be most useful in triage and enhancing patient understanding
• Concerns over validation and explainability

“It’s not going to be enough [for a model] to spit out a number, it’s going to need to explain why,” because “patients will need a little bit more”
Interviewed fifteen patients with metastatic cancer

- Have discussed prognosis w/ physician: Yes (5), No (5), Unanswered (5)
- Want to have prognosis conversation: Yes (8), No (7)
- Want option of model being used in care: Yes (15)

R Hildebrand, ASTRO 2022
Use in the clinic

Themes – Patient Interviews

- Prognosis conversations give valuable insight and can be empowering
- Patients trust the computer model because it comes from physicians and uses a wide range of predictors
- Fear of giving up or denial of finite lifespan hinders prognosis conversations

A tool using “data from thousands and thousands of cases” can be superior to a doctor relying on their “own opinion from their own personal experiences”

“It’s very easy [for a physician] to forget something that’s a minor issue or a minor thing”

R Hildebrand, ASTRO 2022
Future directions

- Better infrastructure for model updates
- Generalizability: Multicenter models and studies
- Study physician and patient acceptance, and best uses
- Predict other outcomes most meaningful to patients
Thanks

Faculty
- Kavitha Ramchandran
- Winnie Teuteberg
- Manali Patel
- Nigam Shah
- Balasubramanian Narasimhan
- Daniel Chang
- Daniel Rubin

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- Rachel Hildebrand
- Touran Fardeen

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- Rebecca Fong

Care coach team
- Nina Alves
- Brian Rogers
- Jennifer Hansen
- Khay Asuncion
- Jan DeNofrio

Data teams
- Solomon Henry
- Douglas Wood
- Sigi Javitz

Patients and doctors who participated in qualitative study

And many others

Stanford University
Extra slides
## Goals of care

<table>
<thead>
<tr>
<th>Occurrence in last 30 days of life</th>
<th>USA</th>
<th>Canada</th>
<th>Germany</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization</td>
<td>52%</td>
<td>60%</td>
<td>45%</td>
</tr>
<tr>
<td>Chemotherapy infusion</td>
<td>11%</td>
<td>9%</td>
<td>11%</td>
</tr>
<tr>
<td>ICU stay</td>
<td>27%</td>
<td>10%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

Bekelman et al., JAMA 2016;315(3)
Training: maximum likelihood. Assume model is correct. What is the probability of the observed outcomes occurring given each patient’s predictor variable data?

- Patient who dies in interval \( j \) (uncensored)
  - Likelihood = \((1-h_1) \times (1-h_2) \times \ldots \times (1-h_{j-1}) \times h_j\)

- Patient who is lost to follow-up in interval \( j \) (censored)
  - Likelihood = \((1-h_1) \times (1-h_2) \times \ldots \times (1-h_{j-1})\)

Strengths of Nnet-survival:

- Easy to train with minibatch gradient descent
- Simple, trains fast
- Flexible (no proportional hazards assumption)

http://github.com/MGensheimer/nnet-survival

**Model**

**Input:** 3813x1 feature vector

**Output:** 12x1 vector with conditional survival probability for each time interval. The twelve time intervals are defined by these cut-points (in days): 0, 30, 91, 182, 365, 548, 730, 913, 1095, 1278, 1470, 1643, 1825

```
Input (3813x1 vector)

Hidden layer #1
   Fully connected
       Output: 1x1

Hidden layer #2
   Fully connected
       Output: 4x1
   ReLu activation
       Output: 4x1

Hidden layer #3
   Fully connected
       Output: 12x1 = conditional log odds of surviving each time interval
e.g. [1.09, 1.09, 0, 1.09, 1.09, 2.18, 2.18, 2.18, 2.18, 2.18, 2.18, 2.18]

   Sigmoid activation
       Output: 12x1 = conditional probability of surviving each time interval
e.g. [0.75, 0.75, 0.5, 0.75, 0.75, 0.9, 0.9, 0.9, 0.9, 0.9, 0.9, 0.9]
```
Model

Input: 3813x1 feature vector
Output: 12x1 vector with conditional survival probability for each time interval. The twelve time intervals are defined by these cut-points (in days): 0, 30, 91, 182, 365, 548, 730, 913, 1095, 1278, 1470, 1643, 1825

Lots of variables, can lead to overfitting. L2 regularization, cross-validation to pick regularization strength.
Comparison to physician predictions

Care team members completed surveys for patients receiving palliative radiotherapy, generally for metastatic cancer

Attending, resident, nurses, radiation therapists

Q1: Based on your personal experience, what would you predict is the life expectancy for this patient?
   - A. 0 – 3 months
   - B. >3– 6 months
   - C. >6– 9 months
   - D. >9– 12 months
   - E. >12 – 18 months
   - F. >18 - 24 months
   - G. >24 months

Q2: What are the top 1-3 reasons for your answer to question #1?

   PLEASE RANK FROM 1-3

   ______ Performance status
   ______ Type of cancer (Cancer Histology)
   ______ Tumor burden (amount of active cancer cells present)
   ______ Pace of disease
   ______ Co-morbidities (other existing medical conditions)
   ______ Lack of social support/follow-up
   ______ Symptoms
   ______ Don’t know
   ______ Other: ______________________________________

Q3: (For faculty only)
Which of these is the primary reason why you chose this fractionation schedule?
   - A. Life expectancy
   - B. Need for rapid response
   - C. Patient convenience
   - D. Concern of toxicity
   - E. Preference of referring doctor
   - F. Per protocol/research study

Other: ________________________________________________
Comparison to physician predictions


<table>
<thead>
<tr>
<th>Physician prediction (months)</th>
<th>ML model prediction (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;24</td>
<td>27              58              81              50</td>
</tr>
<tr>
<td>12.1-24</td>
<td>39              76              67              21</td>
</tr>
<tr>
<td>6.1-12</td>
<td>59              88              53              11</td>
</tr>
<tr>
<td>0-6</td>
<td>130             92              24              3</td>
</tr>
</tbody>
</table>

No. treatment courses

- 125
- 100
- 75
- 50
- 25
Validation: subgroups

- Detailed analysis of 685 patients who received palliative radiotherapy
- Similar performance (AUC and calibration) for all subgroups (but note that sex, race, ethnicity data in Epic are not highly accurate)
  - Sex
  - Race
  - Ethnicity
  - Primary cancer site
Prospective validation: comparison to physician predictions (n=100)