1. Versioned OHDSI docker library
2. Argos Project

Seng Chan You
Mission, Vision, and Values of OHDSI

• Our Mission
To improve health by empowering a community to collaboratively generate the evidence that promotes better health decisions and better care.

• Our Vision
A world in which observational research produces a comprehensive understanding of health and disease.
Mission, Vision, and Values of OHDSI

• Innovation: Observational research is a field which will benefit greatly from disruptive thinking. We actively seek and encourage fresh methodological approaches in our work.

• Reproducibility: Accurate, reproducible, and well-calibrated evidence is necessary for health improvement.

• Community: Everyone is welcome to actively participate in OHDSI, whether you are a patient, a health professional, a researcher, or someone who simply believes in our cause.

• Collaboration: We work collectively to prioritize and address the real world needs of our community’s participants.

• Openness: We strive to make all our community’s proceeds open and publicly accessible, including the methods, tools and the evidence that we generate.

• Beneficence: We seek to protect the rights of individuals and organizations within our community at all times.
OHDSI: Open Innovation based on the open community

GLOBAL COMMUNITY

REPRODUCIBILITY

SCALABILITY

BENEFICIENCE

STANDARDS

OPENNESS

DATA

COLLABORATION
Dear all,

The new network study is launched to evaluate the efficacy and safety of febuxostat in gout compared to allopurinol.

**Comparative Effectiveness Study of Febuxostat versus Allopurinol in Gout**

**Objective:** The goal of this protocol is conducting comparative effectiveness research to establish evidence for benefits and harms of febuxostat and allopurinol. The primary endpoint is the risk of sudden cardiac death. The secondary endpoints include acute myocardial infarction, stroke, heart failure, gout flare and drug hypersensitivity (TEN, SJS, and DRESS).

**Rationale:** Febuxostat is widely used urate-lowering agent because it is more effective than allopurinol to lower serum urate in patients with gout. Furthermore, febuxostat can be used without dosage adjustment in chronic kidney disease. The Cardiovascular Safety of Febuxostat and Allopurinol in Patients with Gout and Cardiovascular Morbidities (CARES) group was a prospective multicenter, double-blind randomized clinical trial, which assessed the cardiovascular risk of febuxostat compared with allopurinol in patients with gout and a history of CVD. This study concluded that febuxostat was associated with significantly higher overall and cardiovascular mortality compared to allopurinol, mostly driven by sudden cardiac death. Still, there is scarce evidence for risk of sudden cardiac death between febuxostat and allopurinol in real-world practice.

The whole protocol is released at github

[GitHub](https://github.com/OHDSI/StudyProtocolSandbox)

This repository is for developing study packages for OHDSI studies. Once completed, they can be moved to the StudyProtocols repository. - OHDSI/StudyProtocolSandbox
The whole protocol is released at github

GitHub

**OHDSI/StudyProtocolSandbox**

This repository is for developing study packages for OHDSI studies. Once completed, they can be moved to the StudyProtocols repository. - OHDSI/StudyProtocolSandbox

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You can download our code from the URL supplied. Good luck downloading the only postdoc who can get it to run, though #overlyhonestmethods

오전 8:52 - 2013년 1월 8일

https://twitter.com/ianholmes/status/288689712636493824
Reproducibility in OHDSI research

2 MONTHS LATER

George_Argyriou

Hi Chan,

I have difficulties installing the package in my local machine.

I've tried to install using two different ways:

1. With `install_github("chandryou/FebuxostatVsAllopurinolCVD")` I get:

   Error in read.dcf(path) :

   Found continuation line starting ’ DatabaseConnecto …’ at begin of record.

2. With `install.packages("https://github.com/chandryou/FebuxostatVsAllopurinolCVD.git")` I get:

   Warning in install.packages :

   package ‘https://github.com/chandryou/FebuxostatVsAllopurinolCVD.git’ is not available (for R version 3.5.1)

Can you help?
Reproducibility

4.2 But, Does it Build?

It is not unreasonable to believe that build numbers could be dependent on the skills of our team of undergraduate and graduate student research assistants. It may well be that, given more time and better background, more systems would build successfully. In our experiments we instructed the students to spend no more than 30 minutes on building the systems. In many cases this involved installing additional libraries and compilers, editing makefiles, etc. The students were also instructed to be liberal in their evaluations, and, if in doubt, mark systems as buildable.

The types of build errors encountered can be found in Table 2.

Table 2: Build error summary.

<table>
<thead>
<tr>
<th>error</th>
<th>count</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>incomplete documentation</td>
<td>10</td>
<td>7.9%</td>
</tr>
<tr>
<td>none</td>
<td>1</td>
<td>0.8%</td>
</tr>
<tr>
<td>distribution is missing files</td>
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<td>16.7%</td>
</tr>
<tr>
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<td>14</td>
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<tr>
<td>missing third party package</td>
<td>22</td>
<td>17.5%</td>
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<td>other errors</td>
<td>22</td>
<td>17.5%</td>
</tr>
<tr>
<td>prerequisite failed to build</td>
<td>23</td>
<td>18.3%</td>
</tr>
<tr>
<td>runtime error</td>
<td>12</td>
<td>9.5%</td>
</tr>
<tr>
<td>internal compiler error</td>
<td>1</td>
<td>0.8%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>126</strong></td>
<td></td>
</tr>
</tbody>
</table>

Collberg et al., Measuring Reproducibility in Computer Systems Research

(1) A growing number of researchers (opensourceforneuroscience.org) & journals are committed to openly publishing code that generated results in computational neuroscience studies. This is great! However: Is code alone enough for reproducibility?

#brainTC

Fig 1: Even when code was available, over half of published projects failed to build or run without significant effort in fixing or debugging (In computer systems research, figure adapted from Collberg et al. 2014)

https://twitter.com/Felix11H/status/971819728040808448
Broadsea

Broadsea – The OHDSI Open Source Standard Software Stack Packaged as Docker Container Images for Cross-Platform Installation

Lee D. Evans\textsuperscript{1}, Marc A. Suchard, MD, PhD\textsuperscript{2}, Jon D. Duke, MD, MS\textsuperscript{3}
\textsuperscript{1}LTS Computing LLC, West Chester, PA; \textsuperscript{2}Department of Biomathematics, David Geffen School of Medicine, University of California, Los Angeles, CA; \textsuperscript{3}Center for Biomedical Informatics, Regenstrief Institute, Indianapolis, IN;

Abstract

We packaged the OHDSI open source standard software stack into Docker containers with the aim of simplifying cross-platform OHDSI software installation on a range of Operating Systems, DBMSs and infrastructure. We believe this simpler software deployment option will help encourage OHDSI Community members to download and install the full OHDSI software stack for research on their own CDM databases and more easily participate in OHDSI Network studies.

The software container image build process and the OHDSI container images are collectively known as Broadsea. The OHDSI Broadsea Docker containers may be configured to connect to an OMOP Common Data Model Version 5 database.

OHDSI symposium, 2016
LTS Broadsea API

LTS Broadsea API – OHDSI methods as a service

Lee D. Evans
1LTS Computing LLC, West Chester, PA

Abstract

The LTS Broadsea API provides access to OHDSI methods as a service in the cloud. For example, run Achilles on any OMOP CDM dataset in any OHDSI supported database within Amazon AWS and Google Cloud by making a simple secure web service call referencing the database connection details. The Broadsea API is currently under development.

Introduction

Many organizations are taking advantage of managed database services like AWS RDS, Redshift, Google BigQuery and Hadoop to host their observational databases and convert them into the OMOP Common Data Model.

However, running the OHDSI methods on that data is not so simple. It requires additional skilled resources to deploy, administer and upgrade the required web servers, R servers, Proxy servers and middleware (tomcat, rstudio, docker, etc).

The aim of the Broadsea API is to provide simple, immediate access to the OHDSI methods as a cloud service via a simple REST API service that can be called from any web application/service.

OHDSI symposium, 2017
Docker, What is it? and What for?
What is Docker?

- Docker is an open platform for developers and sysadmins to build, ship, and run distributed applications. Consisting of Docker Engine, a portable, lightweight runtime and packaging tool, and Docker Hub, a cloud service for sharing applications and automating workflows, Docker enables apps to be quickly assembled from components and eliminates the friction between development, QA, and production environments.

Ok, seriously, what *is* Docker?

- Docker is a **very lightweight abstraction** using recent Linux kernel features which lets us to run code in **cheap** (to launch) and **easy** (to build) units: containers
- We can share containers across OSs, across time.
Virtual Machine vs Docker

**Virtual machines**
Virtual machine runs one complete OS on top of another OS

**Containers**
A Docker container is like a virtual machine that shares guest OSs, which makes them very lightweight

https://matsen.github.io/2018/04/19/docker.html
Docker and Reproducibility

• Capturing the computational environment
  – A substantial challenge in reproducing analysis is installing and configuring the web of dependencies of specific versions of various analytic tools.
  – Popular VM applications include VirtualBox and VMWare. One challenge of working with VMs is that the files that contain the environment are not small, typically one gigabyte or more, which can be awkward to share.

From http://ropensci.github.io/reproducibility-guide/sections/introduction/
Docker Advantage for Reproducibility

• Small footprint
• Easier deployment
• Easier sharing and publication
• Open source platform
• Standard scripting of image setup with Dockerfile
• Rocker images as baseline

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- Standard scripting of image setup with Dockerfile
- Rocker images as baseline

From http://ropensci.github.io/reproducibility-guide/sections/introduction/
Versioned docker library for Rstudio: ROCKER project

https://github.com/rocker-org/rocker-versioned/tree/master/rstudio
Versioned docker library for OHDSI Tools

https://github.com/ABMI/ohdsi-docker
How to build docker image for individual research

• Make a Dockerfile for the individual research based on versioned OHDSI docker image

```bash
FROM chandryou/cohortmethod:3.0.2
RUN R -e "devtools::install_github('chandryou/FebuxostatVsAllopurinolCVD')"
```

https://github.com/chandryou/FebuxostatVsAllopurinolCVD/blob/master/docker/Dockerfile
Run Docker

3. Alternatively, you can pull docker image for FebuxostatVsAllopurinolCVD. In the 'shell', use following code to pull docker image for FebuxostatVsAllopurinolCVD

```bash
$docker run --name plp -e USER=user -e PASSWORD=password1 -d -p 8787:8787 chandryou/febuxostatvsallopurinolcvd
```

Then in the 'browser' activate Rstudio with following address

http://localhost:8787

The ID and PW are user and password1 as set above.

https://github.com/chandryou/FebuxostatVsAllopurinolCVD/
Run entangled system of PLP package (R + Python + Deep learning) in Docker
Suggestion for better reproducibility in OHDSI

• Build and maintain versioned Docker image library for OHDSI tools
  – I hope this versioned docker image library to be merged with BroadSea project

• Release docker image for each OHDSI research
ARGOS

- A Rigorous Global Observation System for burden of diseases
- Monitoring system of disease burden across OHDSI community
  - Temporal trends in
    - Incidence
    - Mortality
    - Cost
    - DALY (Disability-Adjusted Life Year)

https://github.com/ABMI/Argos
Measuring the Global Burden of Disease

• To improve population health, it is crucial to estimate the burden of disease and understand how it changes over time.

• For obtaining comprehensive and consistent information for global burden of disease, the World Bank and the WHO launched the Global burden of Disease (GBD) study in 1991.
The result from GBD 2016

Figure 1. Age-Specific Global Contributions of Cancer Types to Total Cancer Incidence, Both Sexes, 2016

Figure 2. Age-Specific Global Contributions of Cancer Types to Total Cancer Mortality, Both Sexes, 2016

- Lip and oral cavity cancer
- Nasopharynx cancer
- Other pharynx cancer
- Esophageal cancer
- Stomach cancer
- Colon and rectum cancer
- Liver cancer
- Gallbladder and biliary tract cancer
- Pancreatic cancer
- Larynx cancer
- Tracheal, bronchus, and lung cancer
- Malignant skin melanoma

- Squamous cell carcinoma
- Basal cell carcinoma
- Breast cancer
- Cervical cancer
- Uterine cancer
- Ovarian cancer
- Prostate cancer
- Testicular cancer
- Kidney cancer
- Bladder cancer
- Brain and nervous system cancer
- Thyroid cancer
- Mesothelioma
- Hodgkin lymphoma
- Non-Hodgkin lymphoma
- Multiple myeloma
- Acute lymphoid leukemia
- Chronic lymphoid leukemia
- Acute myeloid leukemia
- Chronic myeloid leukemia
- Other leukemia
- Other neoplasms

JAMA Oncology 4, no. 11 (November 1, 2018)
The result from GBD 2016
Comparison between GBD 2006 and GBD 2016

Figure 7. Cancers Ranked by Absolute Years of Life Lost (YLLs) Between 2006 and 2016

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cancer 2006</th>
<th>Cancer 2016</th>
<th>Rank</th>
<th>Change in Absolute YLLs, % (UI)</th>
<th>Change in Age-Standardized YLL Rate, % (UI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tracheal, bronchus, and lung cancer</td>
<td>Tracheal, bronchus, and lung cancer</td>
<td>1</td>
<td>13.5 (9.9 to 16.8)</td>
<td>-11.9 (-14.6 to -9.3)</td>
</tr>
<tr>
<td>2</td>
<td>Liver cancer</td>
<td>Liver cancer</td>
<td>2</td>
<td>15.1 (11.2 to 19.6)</td>
<td>-8.4 (-11.5 to -4.9)</td>
</tr>
<tr>
<td>3</td>
<td>Stomach cancer</td>
<td>Stomach cancer</td>
<td>3</td>
<td>-4.0 (-6.5 to -1.5)</td>
<td>-24.7 (-26.7 to -22.8)</td>
</tr>
<tr>
<td>4</td>
<td>Colon and rectum cancer</td>
<td>Colon and rectum cancer</td>
<td>4</td>
<td>17.0 (11.1 to 21.7)</td>
<td>-8.9 (-13.4 to -5.3)</td>
</tr>
<tr>
<td>5</td>
<td>Breast cancer</td>
<td>Breast cancer</td>
<td>5</td>
<td>13.8 (5.6 to 21.9)</td>
<td>-9.5 (-15.9 to -3.5)</td>
</tr>
<tr>
<td>6</td>
<td>Leukemia</td>
<td>Leukemia</td>
<td>6</td>
<td>-2.4 (-6.6 to 1.9)</td>
<td>-15.2 (-18.7 to -11.6)</td>
</tr>
<tr>
<td>7</td>
<td>Esophageal cancer</td>
<td>Esophageal cancer</td>
<td>7</td>
<td>0.7 (-2.3 to 4.2)</td>
<td>-22.0 (-24.3 to -19.3)</td>
</tr>
<tr>
<td>8</td>
<td>Cervical cancer</td>
<td>Pancreatic cancer</td>
<td>8</td>
<td>26.7 (22.6 to 30.4)</td>
<td>-2.2 (-5.2 to 0.7)</td>
</tr>
<tr>
<td>9</td>
<td>Brain and nervous system cancer</td>
<td>Brain and nervous system cancer</td>
<td>9</td>
<td>13.5 (9.1 to 20.5)</td>
<td>-3.9 (-7.6 to 2.1)</td>
</tr>
<tr>
<td>10</td>
<td>Pancreatic cancer</td>
<td>Cervical cancer</td>
<td>10</td>
<td>4.9 (-1.4 to 13.1)</td>
<td>-15.8 (-20.9 to -9.3)</td>
</tr>
<tr>
<td>11</td>
<td>Non-Hodgkin lymphoma</td>
<td>Non-Hodgkin lymphoma</td>
<td>11</td>
<td>22.3 (15.5 to 26.8)</td>
<td>1.2 (-4.4 to 4.8)</td>
</tr>
<tr>
<td>12</td>
<td>Other leukemia</td>
<td>Prostate cancer</td>
<td>12</td>
<td>26.5 (19.3 to 32.2)</td>
<td>-4.1 (-9.4 to 0.4)</td>
</tr>
<tr>
<td>13</td>
<td>Prostate cancer</td>
<td>Lip and oral cavity cancer</td>
<td>13</td>
<td>26.2 (20.6 to 31.4)</td>
<td>-0.4 (-4.6 to 3.7)</td>
</tr>
<tr>
<td>14</td>
<td>Lip and oral cavity cancer</td>
<td>Ovarian cancer</td>
<td>14</td>
<td>20.8 (13.8 to 27.0)</td>
<td>-5.1 (-10.4 to -0.2)</td>
</tr>
<tr>
<td>15</td>
<td>Ovarian cancer</td>
<td>Other leukemia</td>
<td>15</td>
<td>-15.1 (-20.1 to -9.6)</td>
<td>-25.5 (-29.7 to -20.9)</td>
</tr>
<tr>
<td>16</td>
<td>Gallbladder and biliary tract cancer</td>
<td>Gallbladder and biliary tract cancer</td>
<td>16</td>
<td>14.7 (9.6 to 19.7)</td>
<td>-11.3 (-15.1 to -7.5)</td>
</tr>
</tbody>
</table>

Fitzmaurice et al., *JAMA Oncology* 4, no. 11 (November 1, 2018)
Lesson from GBD study

• Large disparities exist between countries
  – In cancer incidence
  – In mortality of cancer patients
  – In cancer associated disability

• Large disparities exist across a decade

• Differences in data collection practices and coding systems, as well as quality of data sources, remain major challenges, as do underreporting of cancers requiring advanced diagnostics in low-resource settings
Disability-Adjusted Life Loss (DALY)

• A measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.

• One of fundamental estimates for cost-effectiveness research

Objectives of ARGOS project

- Development of ARGOS package based on OHDSI tool ecosystem, which provides semi-automatic process to monitor burden of user-defined conditions in OMOP-CDM database by assessing
  - Temporal trend in incidence
  - Incidence according to age, gender, and birth year
  - Temporal trend in outcome of care
  - Disability-Adjusted Life Loss (DALY)

- In Korea
  - Conversion of HIRA DB for whole cancer patients from 2007~2017

- Under development
  - Today’s result is based on NHIS-NSC (2003-2013, 1M sample)
  - Today’s result is not fully evaluated.

https://github.com/ABMI/Argos
Validation of temporal trend in Incidence of cancers

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>Argos</td>
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<td>32.0</td>
<td>36.4</td>
<td>37.2</td>
<td>39.3</td>
<td>39.0</td>
<td>41.7</td>
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<td>37.6</td>
<td>40.7</td>
<td>43.8</td>
<td>47.0</td>
<td>51.4</td>
<td>53.4</td>
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<td>30.9</td>
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<td>37.6</td>
<td>40.4</td>
<td>42.7</td>
<td>44.3</td>
<td>44.6</td>
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<tr>
<td>Stomach</td>
<td>Argos</td>
<td>44.2</td>
<td>42.9</td>
<td>44.3</td>
<td>43.3</td>
<td>42.3</td>
<td>48.1</td>
<td>46.5</td>
<td>43.7</td>
<td>54.1</td>
</tr>
<tr>
<td></td>
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<td>49.5</td>
<td>48.8</td>
<td>54.2</td>
<td>54.1</td>
<td>54.6</td>
<td>57.5</td>
<td>60.5</td>
<td>61.6</td>
<td>63.8</td>
</tr>
<tr>
<td>Liver</td>
<td>Argos</td>
<td>34.9</td>
<td>29.9</td>
<td>32.0</td>
<td>28.4</td>
<td>26.1</td>
<td>30.1</td>
<td>28.0</td>
<td>26.3</td>
<td>29.3</td>
</tr>
<tr>
<td></td>
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<td>29.1</td>
<td>29.9</td>
<td>31.1</td>
<td>30.6</td>
<td>31.3</td>
<td>32.0</td>
<td>32.2</td>
<td>32.4</td>
<td>32.7</td>
</tr>
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<td>Breast</td>
<td>Argos</td>
<td>16.1</td>
<td>16.4</td>
<td>15.8</td>
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<td>21.7</td>
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<td>19.0</td>
<td>21.1</td>
<td>22.4</td>
<td>24.5</td>
<td>26.0</td>
<td>27.5</td>
<td>29.4</td>
<td>32.3</td>
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<td>21.5</td>
<td>26.3</td>
<td>33.0</td>
<td>43.3</td>
<td>55.3</td>
<td>65.5</td>
<td>73.7</td>
<td>82.4</td>
</tr>
</tbody>
</table>

Table. Comparison of estimated cancer incidence from Argos with the findings of relevant published report

https://github.com/ABMI/Argos
Temporal trends of incidence, incidence according to birth year: Is breast cancer really increasing in Korea?

Though overall age standardized incidence of breast cancer increases, the incidence of breast cancer decreases in women born after 1960.

https://github.com/ABMI/Argos
Temporal trends of incidence according to year:
For which age group should we promote screening for prevention of colon cancer?

After rapid increase of incidence in colon cancer, overall incidence of colon cancer decreased in Korea.

Still, the incidence of colon cancer increases in old ages.

We are neglecting these population in national screening system

https://github.com/ABMI/Argos
Temporal trend of overall cost in cancer patients

breast Cancer Total Cost during 1 year after diagnosis

liver Cancer Total Cost during 1 year after diagnosis

https://github.com/ABMI/Argos
Cost plot according to the time before and after diagnosis

colon Cancer Total Cost per month 2mt before and 11mt after diagnosis

breast Cancer Total Cost per month 2mt before and 11mt after diagnosis
Temporal trend of overall cost in lung cancer paid by patient and national insurance

### Lung Cancer Cost paid by patient during 1 year after diagnosis

- **Total Cost per Year (1000 won)**
- **Diagnosis Year**
  - 2003 - 2013

### Lung Cancer Cost paid by payer during 1 year after diagnosis

- **Total Cost per Year (1000 won)**
- **Diagnosis Year**
  - 2003 - 2013

Legend:
- Red: inpatient
- Green: outpatient
- Blue: emergency room
Assessing temporal trends in DALY based on incidence data
OHDSI: Open Innovation based on the open community

Diagram:
- Reproducibility
- Scalability
- Beneficience

Global Community
- Standards
- Openness
- Data
- Collaboration
Mission, Vision, and Values of OHDSI

• Our Mission
To improve health by empowering a community to collaboratively generate the evidence that promotes better health decisions and better care.

• Our Vision
A world in which observational research produces a comprehensive understanding of health and disease.
Mission, Vision, and Values of OHDSI

• Innovation: Observational research is a field which will benefit greatly from disruptive thinking. We actively seek and encourage fresh methodological approaches in our work.

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• Openness: We strive to make all our community’s proceeds open and publicly accessible, including the methods, tools and the evidence that we generate.

• Beneficence: We seek to protect the rights of individuals and organizations within our community at all times.
Thank You for your time