

OHDSI Covid-19: Alpha-blocker for Palliating Inflammatory injury Severity (APIS) Study

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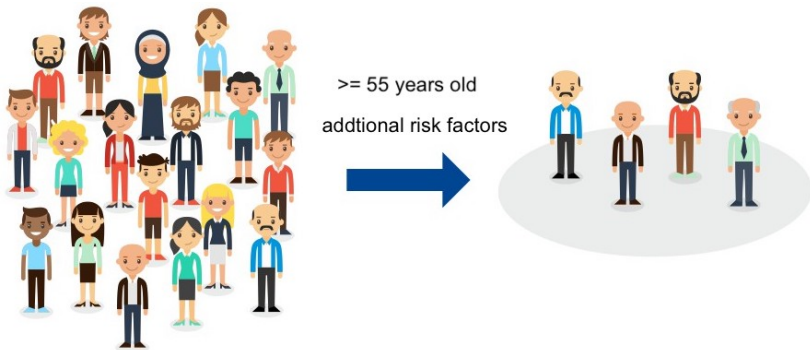
JOHNS HOPKINS
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Biostatistics

Observational healthcare data: promise & reality

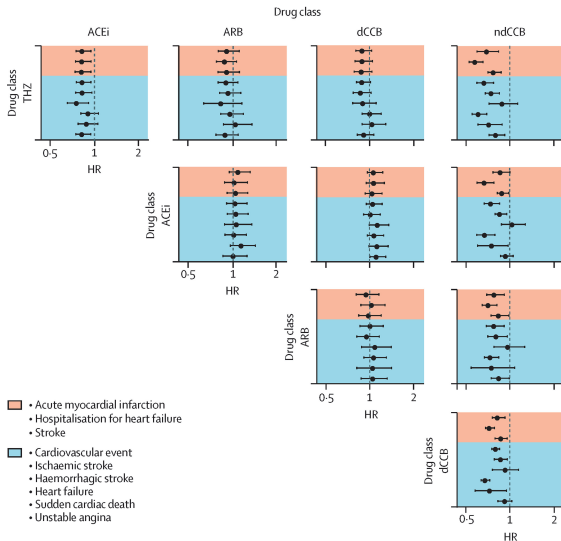
Clinical trials — gold standard but with inherent limitations:

- Limited sample size & follow-up time
- Not inclusive of all the potential treatment recipients



Observational healthcare data: promise & reality

Healthcare analytics provides opportunities for real-world evidences,



OHDSI's LEGEND study finds **most popular** hypertension treatment **isn't most effective**.

Study involves 4.9 million patient data from 9 databases.

Observational healthcare data: **promise & reality**

Healthcare analytics provides opportunities for real-world evidences, *but* has suffered from **untested reliability** and **publication bias**.

ORIGINAL CONTRIBUTION

JAMA

Exposure to Oral Bisphosphonates and Risk of Esophageal Cancer

Chris R. Cardwell, PhD
Christian C. Abnet, PhD
Marie M. Cantwell, PhD
Liam J. Murray, MD

Context Use of oral bisphosphonates has increased c and elsewhere. Esophagitis is a known adverse effect-cent reports suggest a link between bisphosphonate u this has not been robustly investigated.

Objective To investigate the association between b

“in UK General Practice Research Database, the use of oral bisphosphonates was **not significantly associated** with incident esophageal ... cancer”

“within [General Practice Research Database], we found a **significantly increased** risk of esophageal cancer... for oral bisphosphonates [users]”

BMJ

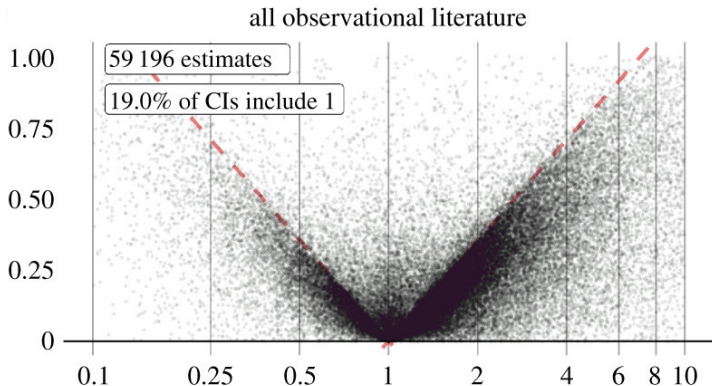
RESEARCH

Oral bisphosphonates and risk of cancer of oesophagus, stomach, and colorectum: case-control analysis within a UK primary care cohort

Jane Green, clinical epidemiologist,* Gabriela Canner, statistician,† Gillian Reeves, statistical epidemiologist,‡ Joanna Wilson, epidemiologist,‡ Lesley Wise, manager, Pharmacoepidemiology Research and Intelligence Unit,‡ Valerie Benal, professor of cancer epidemiology

Observational healthcare data: **promise** & reality

Healthcare analytics provides opportunities for real-world evidences, *but* has suffered from **untested reliability** and **publication bias**.



OHDSI's approach to observational healthcare research

Reproducible, consistent, and comprehensive

via standardized data model (OMOP) & analytic tools (HADES)

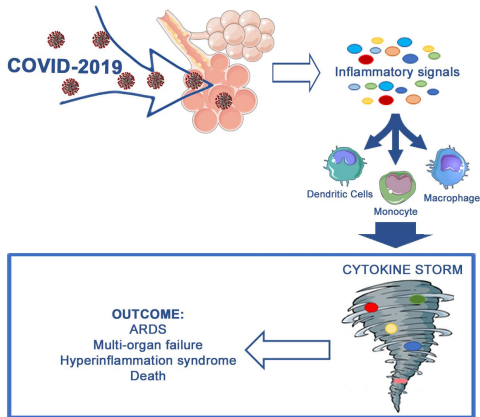
Objective and data-driven

via large-scale propensity score model

State-of-the-art statistical techniques

via propensity score matching & empirical calibration

Alpha-blocker to protect against severe Covid symptoms



Hyper-inflammation seems to account for many of severe Covid cases.

Hypothesis:

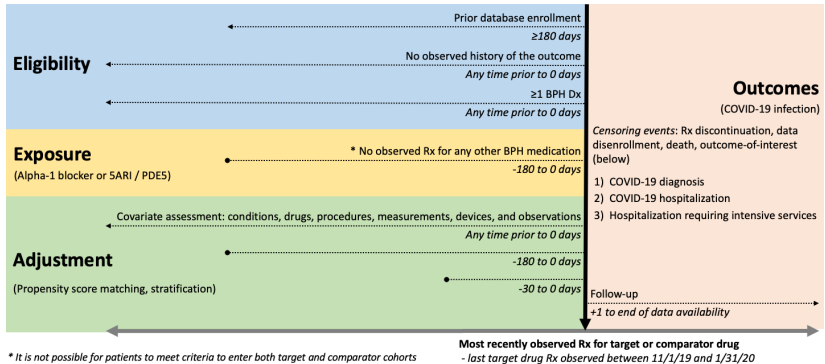
Blocking alpha-1 adrenergic receptor signaling may reduce inflammatory injury.

APIS study: risk of severe Covid symptoms among BPH patients

Alpha-blocker for Palliating Inflammatory injury Severity study

Among BPH patients, compare incidences of

Covid diagnosis / + Hospitalization / + Intensive services
between those on alpha-blocker and on 5ARI / PDE5.



Reproducibility is in completeness and explicitness

Example cohort definition in the study protocol:

[COVID ID133] Persons with a COVID-19 diagnosis or a SARS-CoV-2 positive test with no required prior observation

Initial Event Cohort

People having any of the following:

- a measurement of SARS-CoV-2 positive test measurement pre-coordinated:
 - occurrence start is after 2019-12-01
- a measurement of SARS-CoV-2 test measurement:
 - occurrence start is after 2019-12-01
 - value as concept is any of: Detected, Detected, Positive, Positive, Present, Present
- an observation of SARS-CoV-2 test measurement:
 - occurrence start is after 2019-12-01
 - value as concept is any of: Detected, Detected, Positive, Positive, Present, Present
- a condition occurrence of COVID-19 conditions:
 - occurrence start is after 2019-12-01

with continuous observation of at least 0 days prior and 0 days after event index date, and limit initial events to: **earliest event per person.**

Limit qualifying cohort to: **earliest event per person.**

Date Offset Exit Criteria

This cohort definition end date will be the index event's start date plus 1 days

Cohort Collapse Strategy:

Collapse cohort by era with a gap size of 90 days.



Reproducibility is in completeness and explicitness

Example cohort definition in the study protocol:

1. COVID-19 conditions

Concept Id	Concept Name	Domain	Vocabulary	Excluded	Descendants	Mapped
439676	Coronavirus infection	Condition	SNOMED	NO	YES	NO
4100065	Disease due to Coronaviridae	Condition	SNOMED	NO	YES	NO
37311060	Suspected disease caused by 2019-nCoV	Observation	SNOMED	NO	YES	NO
37311061	Disease caused by 2019-nCoV	Condition	SNOMED	NO	YES	NO

2. SARS-CoV-2 positive test measurement pre-coordinated

Concept Id	Concept Name	Domain	Vocabulary	Excluded	Descendants	Mapped
37310282	2019 novel coronavirus detected	Measurement	SNOMED	NO	YES	NO

3. SARS-CoV-2 test measurement

Concept Id	Concept Name	Domain	Vocabulary	Excluded	Descendants	Mapped
756055	Measurement of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)	Measurement	OMOP Extension	NO	YES	NO
37310281	2019 novel coronavirus not detected	Measurement	SNOMED	YES	YES	NO

ATLAS: API for exposure & cohort definitions + study package

The screenshot displays the ATLAS web interface for defining a cohort. The browser address bar shows the URL: `atlas-cohd19.ohdsi.org/#!/cohorts/definition/972`. The page title is "ATLAS".

Left Navigation Menu:

- Home
- Data Sources
- Search
- Concept Sets
- Cohort Definitions**
- Characterizations
- Cohort Pathways
- Incidence Rates
- Profiles
- Estimation
- Prediction
- Jobs
- Configuration
- Feedback

Bottom Left Footer:

Atsachs 2.0
open source software
provided by
OHDSI
join the journey

Main Content Area:

Cohort #972

[COVID ID133 V1] Persons with a COVID-19 diagnosis or a SARS-CoV-2 positive test with no required prior observation

Definition | Concept Sets | Generation | Reporting | Export | Messages 1

enter a cohort definition description here

Cohort Entry Events

Events having any of the following criteria:

- Event 1:** a measurement of SARS-CoV-2 positive test measurement. Occurrence start is: After | 2019-12-01. Buttons: + Add attribute..., Delete Criteria.
- Event 2:** a measurement of SARS-CoV-2 test measurement. Occurrence start is: After | 2019-12-01. Value as Concept is: Detected, Detected, Positive, Positive, Present, Present. Buttons: + Add attribute..., Delete Criteria, Add, Import.
- Event 3:** an observation of SARS-CoV-2 test measurement. Occurrence start is: After | 2019-12-01. With Value as Concept is: Detected, Detected, Positive, Positive, Present, Present. Buttons: + Add attribute..., Delete Criteria, Add, Import.
- Event 4:** a condition occurrence of COVID-19 conditions. Occurrence start is: After | 2019-12-01. Buttons: + Add attribute..., Delete Criteria.

with continuous observation of at least 0 days before and 0 days after event index date

Limit initial events to: earliest event per person.

Restrict initial events

ATLAS: API for exposure & cohort definitions + study package

The screenshot displays the ATLAS web application interface. The top navigation bar includes 'Home', 'Data Sources', 'Search', 'Concept Sets', 'Cohort Definitions', 'Characterizations', 'Cohort Pathways', 'Incidence Rates', 'Profiles', 'Estimation', 'Prediction', 'Jobs', 'Configuration', and 'Feedback'. The main content area is titled 'Population Level Effect Estimation - Comparative Cohort Analysis #51' and features a search bar with the query '[Aki] Covid susceptibility among users of alpha-1 blocker and 5-alpha inhibitor'. Below the search bar are tabs for 'Specification' and 'Utilities'. A text input field is provided for a description (1000 characters max). The 'VIEW:' section includes tabs for 'Full Specification', 'Comparisons', 'Analysis Settings', and 'Evaluation Settings'. The 'Comparative Cohort Settings' section shows a table of comparisons with columns for 'Remove', 'Target', 'Comparator', 'Outcomes', 'ND Outcomes', and 'Copy'. The 'Effect Estimation Analysis Settings' section shows a table of analysis settings with columns for 'Remove', 'Description', 'Time At Risk Start', 'Time At Risk End', 'Minimum Time At Risk', 'Adjustment Strategy', 'Outcome Model', and 'Copy'. The bottom left corner features the 'Atacbs 2.0 open source software provided by OHDSI join the journey' logo.

ATLAS

Home

Data Sources

Search

Concept Sets

Cohort Definitions

Characterizations

Cohort Pathways

Incidence Rates

Profiles

Estimation

Prediction

Jobs

Configuration

Feedback

Atacbs 2.0
open source software
provided by
OHDSI
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Population Level Effect Estimation - Comparative Cohort Analysis #51

[Aki] Covid susceptibility among users of alpha-1 blocker and 5-alpha inhibitor

Specification Utilities

enter a description here (1000 characters max)

VIEW: Full Specification Comparisons Analysis Settings Evaluation Settings

Comparative Cohort Settings

Comparisons + Add Comparison

Show 10 entries Filter:

Remove	Target	Comparator	Outcomes	ND Outcomes	Copy
	[Aki] Prevalent male mono-users of alpha-1 blocker at corona era onset	[Aki] Prevalent male mono-users of 5-alpha inhibitor at corona onset	[COVID ID133 V1] Persons with a COVID-19 diagnosis or a SARS-CoV-2 positive test with no required prior observation (2+ more outcomes)	[Aki] Negative controls for Covid susceptibility among BPJ patients - explicit exclusion	

Showing 1 to 1 of 1 entries Previous 1 Next

Effect Estimation Analysis Settings + Add Analysis Settings

Analysis Settings

Show 10 entries Filter:

Remove	Description	Time At Risk Start	Time At Risk End	Minimum Time At Risk	Adjustment Strategy	Outcome Model	Copy
	Without PS stratification / age-gender-month in outcome model	0d from cohort start date	0d from cohort end date	0d	None	cox	

OHDSI study R package: deployed locally by data-holders


ohdsi-studies / Covid19SusceptibilityAlphaBlockers

Unwatch 2 Star 0 Fork 0

Code Issues Pull requests 1 Actions Projects Wiki Security Insights Settings

master 5 branches 0 tags

Go to file Add file Code

	aki-nishimura Combine three outcome risk info into one table	cbddad8 17 days ago	100 commits
Documents	Update protocol		3 months ago
R	Replace OT results with IIT ones for Optum		2 months ago
extras	Combine three outcome risk info into one table		17 days ago
inst	Change shinyName of target and comparator		last month
man	Update with Roxygen re-run		2 months ago
.Rbuildignore	give better name		5 months ago
.Rprofile	put files in the correct place		5 months ago
.gitignore	profile the likelihood function		5 months ago
Covid19SusceptibilityAlphaBlockers....	give better name		5 months ago
DESCRIPTION	Update with Roxygen re-run		2 months ago
HydraConfig.json	Finish replacing package name throughout repo		5 months ago
NAMESPACE	Update with Roxygen re-run		2 months ago
README.md	add link to protocol		5 months ago
study_package_readme.md	Give more informative name to study package readme		5 months ago

README.md

OHDSI COVID-19 Studyathon: Alpha-1 blocker for Palliating Inflammatory injury Severity (APIS) study

About

No description, website, or topics provided.

Readme

Releases

No releases published
[Create a new release](#)

Packages

No packages published
[Publish your first package](#)

Contributors 2

 aki-nishimura Aki Nishimura

 msuchard Marc Suchard

Languages

R 94.4% TeX 4.9%
Other 0.7%

OHDSI study R package: deployed locally by data-holders

Requirements

- A database in [Common Data Model version 5](#) in one of these platforms: SQL Server, Oracle, PostgreSQL, IBM Netezza, Apache Impala, Amazon RedShift, or Microsoft APS.
- R version 3.5.0 or newer
- On Windows: [RTools](#)
- [Java](#)
- 25 GB of free disk space

See [this video](#) for instructions on how to set up the R environment on Windows.

How to run

1. You will build a library `Covid19SusceptibilityAlphaBlockers` from the folder of the same name, which also contain installation instruction.

Note: If you encounter errors in devtools pulling the study packages, you may find it easier to download the repo zip locally and uploading it through your RStudio console. Instructions to upload packages are provided in [The Book of OHDSI](#).

2. When completed, the output will exist as a .ZIP file in the `export` directory in the `output` folder location. This file contains the results to submit to the study lead. To do so, please use the function below. You must supply the directory location to where you have saved the `<study key name>.dat` file to the `privateKeyFileName` argument. You must contact the [study coordinator](#) to receive the required private key.

```
keyFileName <- "<directory location of where you saved the study key name.dat>"
userName <- "study-data-site-covid19"
OhdsiSharing::sftpUploadFile(privateKeyFileName = keyFileName,
                             userName = userName,
                             remoteFolder = "Covid19Apis",
                             fileName = "<directory location of outputFolder/export>")
```

If you are unable to utilize the `OhdsiSharing` package, you may utilize a SFTP client of your choosing (e.g. FileZilla) and upload through that tool. If you have questions, contact the [study coordinator](#).

Suggested PostgreSQL cache settings

Multiple outcomes / databases / analyses — all at once

Question:

- Which outcome? (diagnosis, hospitalization, intensive service)
- Which database? (SIDIAP, VA, CUIMC, OpenClaims, Optum)
- Which analytical methods to use? (stratified, matched)

Answer: Do them all, report them all.

	Patients		Time (years)		Diagnosis		Hospital		Intensive		MDRR (Diagnosis)
	T	C	T	C	T	C	T	C	T	C	
Stratified analysis											
SIDIAP	11,793	1,318	4,162	471	334	51	132	20	0	0	1.61
VA	360,802	54,723	189,564	29,642	1,854	236	636	96	111	12	1.20
CUIMC	2,414	582	338	84	27	<5	16	<5	0	0	4.53
OpenClaims	1,995,594	366,734	817,994	160,225	4,809	767	2,621	407	0	0	1.11
Optum DOD	241,842	39,032	56,438	9,613	193	47	131	35	18	6	1.69
Optum EHR	15,275	2,136	1,031	149	50	7	32	5	<5	0	3.10
Matched analysis											
SIDIAP	8,994	1,315	3,211	471	275	51	115	20	0	0	1.59
VA	312,522	54,642	165,688	29,600	1,485	236	495	96	92	12	1.21
CUIMC	1,873	520	261	74	18	<5	11	<5	0	0	6.58
OpenClaims	1,873,014	365,534	774,635	159,742	4,351	764	2,361	407	0	0	1.11
Optum DOD	218,032	38,988	51,451	9,602	175	47	118	35	18	6	1.69
Optum EHR	12,303	2,114	848	148	33	7	19	5	<5	0	3.50

Emulating randomization via large-scale propensity score model

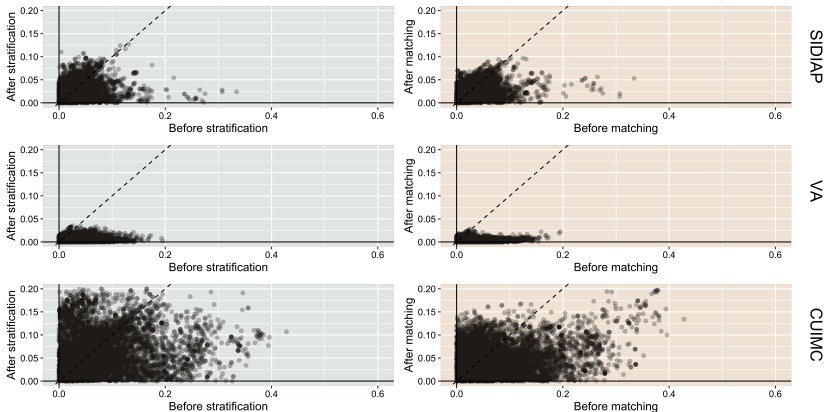
Alpha-blocker and 5ARI/PDE5 cohort are **not** directly comparable.

Characteristic	VA					
	Before stratification <i>N</i> = 360,802 (T)			After stratification <i>N</i> = 54,723 (C)		
	T (%)	C (%)	SDF	T (%)	C (%)	SDF
Medical history: General						
Chronic liver disease	2.6	1.5	0.08	2.5	2.3	0.01
Chronic obstructive lung disease	15.7	14.3	0.04	15.6	15.6	0.00
Dementia	3.9	6.0	-0.10	4.1	4.3	-0.01
Diabetes mellitus	32.8	31.0	0.04	32.5	32.8	0.00
Hyperlipidemia	48.7	48.3	0.01	48.6	48.3	0.01
Hypertensive disorder	58.6	57.0	0.03	58.4	58.1	0.01
Obesity	12.3	8.8	0.11	11.8	11.7	0.00
Renal impairment	14.2	14.5	-0.01	14.2	14.2	0.00
Medication use						
Antiinflammatory and antirheumatic products	43.6	37.2	0.13	42.7	42.8	0.00
Antineoplastic agents	4.8	4.5	0.01	4.8	4.7	0.00
Antithrombotic agents	39.6	40.1	-0.01	39.7	39.7	0.00
Drugs used in diabetes	32.3	29.7	0.06	31.9	32.1	0.00
Immunosuppressants	3.5	3.0	0.03	3.4	3.3	0.00
Race						
American Indian or Alaska Native	0.6	0.6	0.01	0.6	0.6	0.00
Asian	0.6	0.7	-0.01	0.6	0.6	0.00
Black or African American	16.1	12.2	0.11	15.5	15.4	0.00
Native Hawaiian or Other Pacific Islander	0.7	0.7	0.00	0.7	0.7	0.00
White	76.1	79.7	-0.09	76.6	76.7	0.00
Other or unknown	5.9	6.2	-0.01	6.0	6.0	0.00

Propensity score method groups patients into pairs or strata, within which their clinical characteristics are balanced.

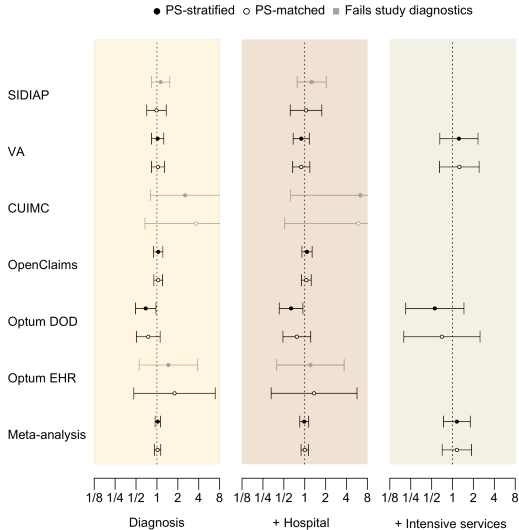
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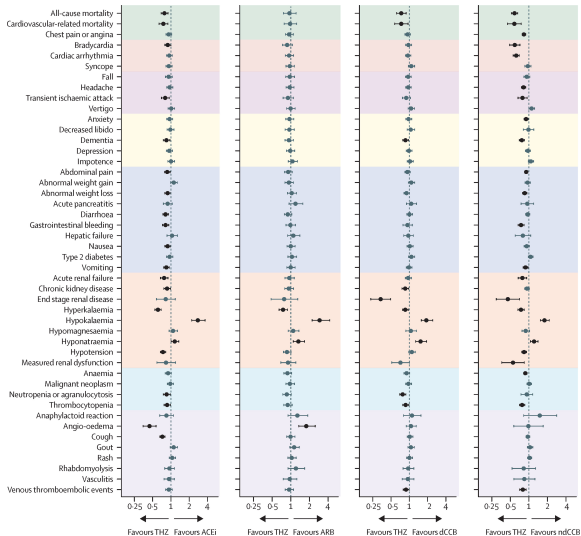
Results: does alpha-blocker alleviate Covid symptoms?



Confidence intervals consistently indicates “null effects.”

Meta-analysis hazard estimate is also close to the null.

LEGEND: example of more ambitious OHDSI studies



- 5 drug classes
 - 55 outcomes
 - 9 databases
 - 4 analyses
- ⇒ **21,780**
estimates!

End of talk, but journey continues (and you should join us)

Thank you!

Protecting Health, Saving Lives — *Millions at a Time*
(Motto of Johns Hopkins School of Public Health)