



Global Solutions from the World's Largest Data-Focused CRO

Evolution of Next Gen Clinical Trials and Potential Trial Site Identification using Real World Evidence (RWE)

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Agenda

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- Site Selection – Importance and Challenges
- What is RWE?
- Sources of RWE
- Applications of RWE
- RWE Scenario in India
- Case Study - Potential Trial Site Identification using Heat Maps
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 - ✓ Use of Heat Maps in Clinical Trials
 - ✓ Number of On-going Diabetes Trials
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 - ✓ Potential Trial Site Identification



Clinical Trial Challenges

There are 8 biggest challenges faced by clinical trial professionals:

- Complexity of trials / Identifying the potential trial site (21%)
- Regulations (15%)
- Spiraling costs (15%)
- Patient access (12%)
- Staff Roles & Responsibilities (9%)
- Technology (9%)
- Governance and oversight (9%)
- New drugs (5%)



Site Selection - Importance

Site selection, an often underrated and poorly understood discipline, has become a critical factor in the time taken and cost incurred in bringing new drugs to market.

- Proper Site selection
 - Highly critical to the success of any clinical trial.
 - Proactive planning and identification of the appropriate site will cut down on the financial and monitoring resources required by a trial.
 - Can also help establish the credibility/acceptability of the data generated.
 - Reports suggest that 11% of sites selected for a study are in fact never activated, the main reason being due to contracting issues.



Site Selection - Challenges

- Lack of information about the protocol.
- Competition for trial sites, investigators and patients.
- Competition for patients in certain therapeutic areas.
- Decrease in the total number of active investigators.
- Up to 30% of the clinical product development lifecycle resides in patient recruitment.
- Patient recruitment difficulties accounts for up to 45% of study delays.
- Up to 80% of site fail to meet enrolment timelines.
- Up to 50% of research trial sites enrol one or no patients.



What is RWE?



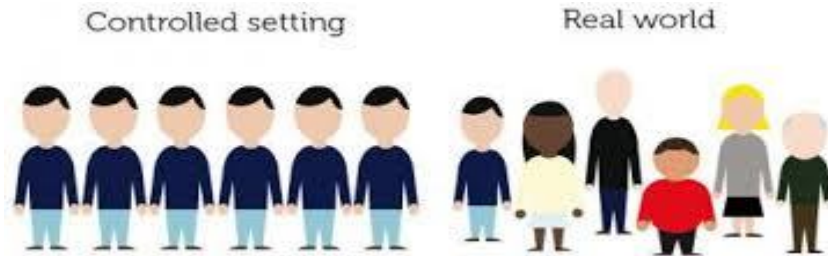
Real World
Analytics



Real World Evidence(RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of Real World Data(RWD).

- RWE and RWD are playing an increasing role in **health care** decisions.
- FDA uses RWD and RWE to monitor **Post-market safety** and **adverse events** and to make regulatory decisions.
- The health care community is using these data to **support coverage decisions** and to develop guidelines and decision support tools for use in clinical practice.
- Medical product developers are using RWD and RWE to support **clinical trial designs** (e.g., large simple trials, pragmatic clinical trials) and observational studies to **generate innovative, new treatment approaches**.
- The 21st Century Cures Act, passed in 2016, place additional focus on the use of these types of data to **support regulatory decision making**.

What is RWE?...



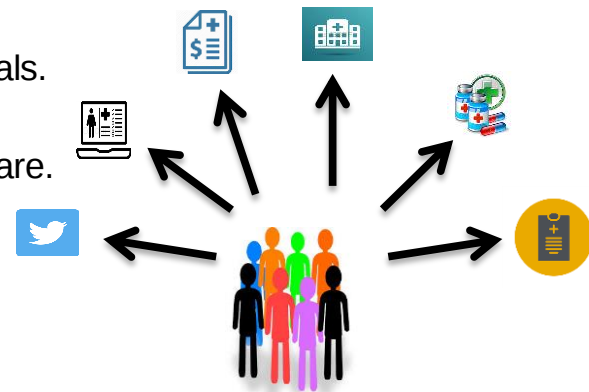
Traditional Evidence have been derived as randomized clinical trials, where patients recruited are typically highly homogenous and data collected is closely controlled and monitored.



Sources of RWE?

RWE is derived from data associated with outcomes from the care of heterogeneous patients as experienced in real world practice settings. Data relevant to RWE comes in multiple types and forms. For Example:

- **Claims Data** - derived from insurance reimbursements.
- **Clinical Trials Data** - derived from the outcomes of randomized clinical trials.
- **Clinical Setting Data** - derived from patient medical records and patient care.
- **Pharmacy Data** - derived from prescription orders and fulfilments.
- **Patient-powered Data** - derived directly from the patient experience.



Sources of RWE?...

Claims

- Medical Claims
- Prescription Drug Claims
- State Medicaid
- Insurance Companies
- All Payer Claims Databases
- FDA Sentinel
- Insurance Company Analytics Subsidiaries



Clinical Setting

- Electronic Health Record Data
- Lab Tests
- Clinical Labs
- Specimen/Tissue Pathology Data
- Providers
- Private Genetic Test Companies
- Genomic Databases
- Professional Society Clinical Registries



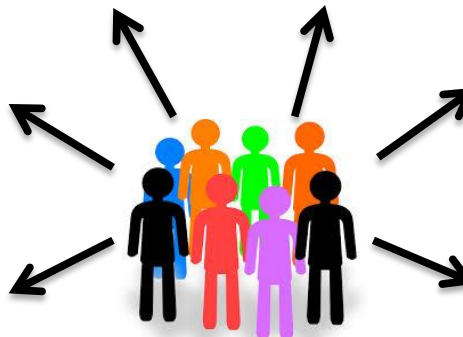
Pharmacies

- Point of Sale Data
- Prescription Fill Data
- Pharmacies
- Prescription Benefit Managers



Patient Powered

- Patient Powered Outcomes
- Social Media
- Patient Centered Outcomes
- Patients
- Patient Communities/Social Networks
- Patient Powered Networks
- Patient Advocacy Orgs



Clinical Trials

- Clinical Trial Data
- NIH
- FDA
- Pharma and Device Companies
- Third Party Analysts
- Patient Advocacy Orgs



Applications of RWE



- Improve healthcare quality.
- Augment RCT data on the efficacy and safety of new drugs and medical devices.
- Improve the labelling and approved indications of products.
- Provides valuable information after regulatory approval about the rate at which products prove their value to patients, providers, and payers.
- Enable a more precise identification of safety risks and risk/benefit trade-offs.
- Allow identification of heterogeneous responses.
- Value derived when products are delivered in diverse practice settings.
- Sources for RWD can be utilized to identify and recruit patients for RCTs.

RWE Scenario in India



There are 2 major components of Healthcare delivery system in India:

- 1.Public** - The public healthcare system(Government) comprises partial secondary and tertiary care institutions in major cities and focuses on offering basic healthcare facilities in rural areas.
- 2.Private** - The private sector offers majority of secondary, tertiary and quaternary institutions of care with a major concentration in metros, tier I and tier II cities.

Healthcare market of India

Worth US\$ 100 billion

Anticipated to rise to US\$ 280 billion by 2020 at a composite annual growth rate of 22.9%

Overall market constitutes 65%

Rural India is set to emerge as a potential demand source as it accounts for over 70% of the population



RWE Scenario in India...

- The data released by Department of Industrial Policy and Promotion reflected that many hospital and diagnostic centres attracted Foreign Direct Investment worth US\$ 3.21 billion between April 2000 and September 2015
- It is expected that in the near future health insurance will become more popular in India.
- Various government-sponsored insurance schemes have been initiated at state levels and also central level (e.g. PMSSY - **Pradhan Mantri Swasthya Suraksha Yojana**).
- The use of EMRs is gradually rising in India



RWE Scenario in India...

- Health Management Information System HMIS (Government sponsored project) in some of the states of India, which have come up in the past decade.
- The Tata Memorial Centre for the research, education, prevention, and treatment in cancer, has recently started using E-medical records
- The concept of patient - centered outcome researches has yet to catch up in India.
- Very few established registries exist such as the National Cancer Registry, The Indian Transplant Registry, etc.,



Case Study

Potential Trial Site Identification using Heat Maps



What is Heat Map?

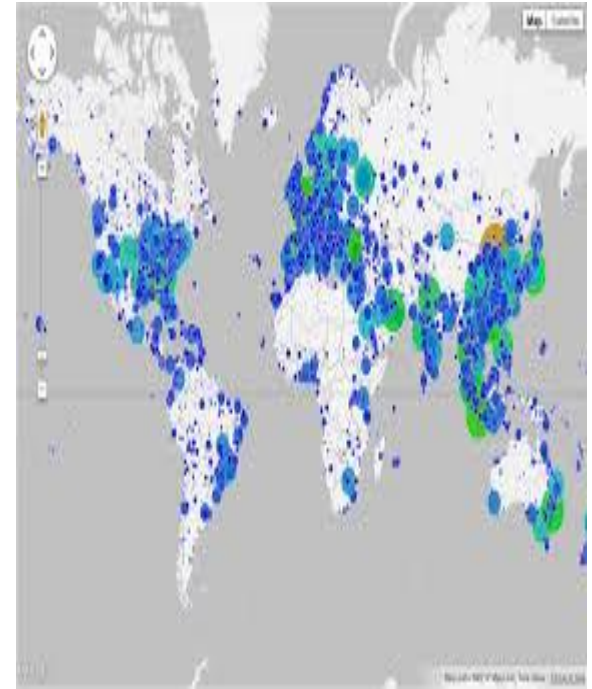
- Heat map is a representation of information/data with the help of colors.
- Heat maps help in data visualization of simple or complex information.
- Heat maps are used across a variety of industries in order to visualize complex data very quickly. In a world where the amount of data is increasing exponentially every year, heat maps have become a powerful tool to summarize complicated data. They can be utilized to enhance our understanding of financial trends, gene expression, sports odds, crime rates, weather patterns, and even election results.



Use of Heat Maps in Clinical Trials

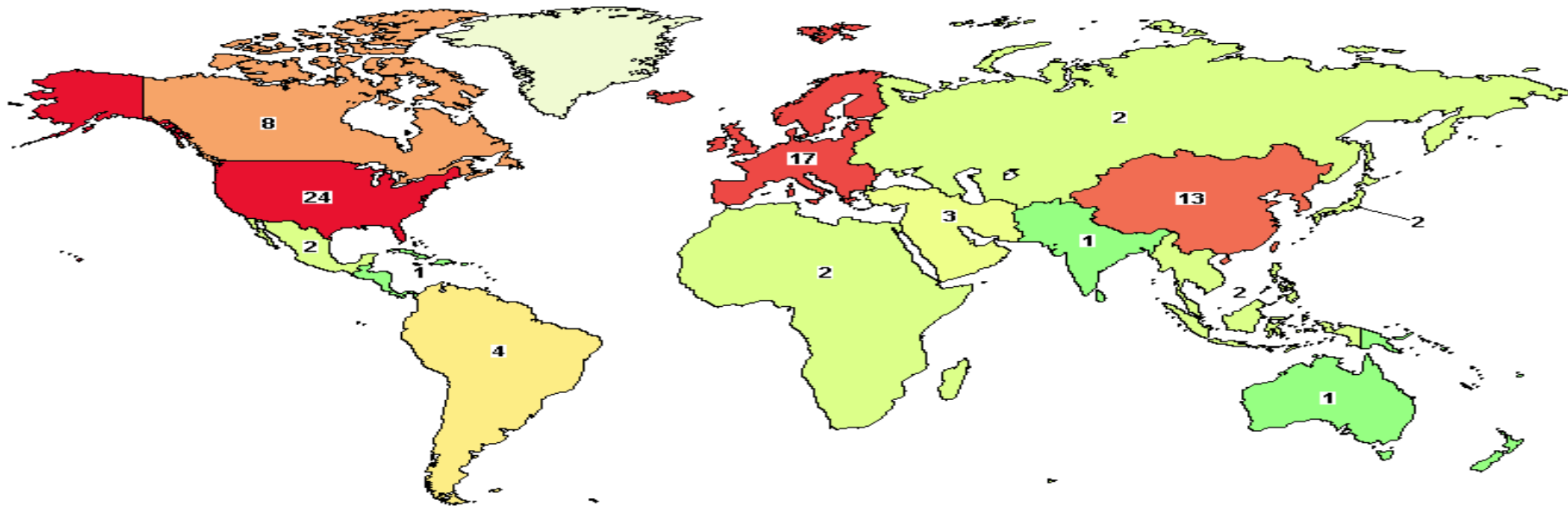
Heat Maps helps

- to visualize correlation of patients or symptoms.
- to visualize high density clinical chemistry data.
- in clinical trial site selection and patient identification.



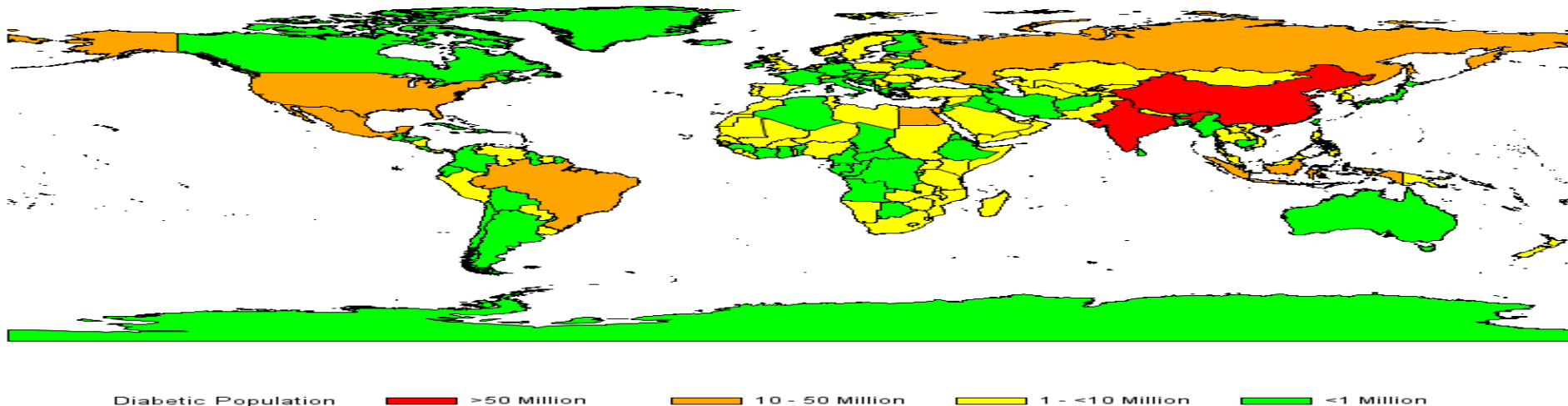
Number of Ongoing Diabetes Trials

This geographical heat map represents number of diabetic trials per each country for which recruitment is ongoing at the moment.



Diabetic Patient Population

Historical data suggests that India, China, USA, Brazil and Mexico are the countries with highest population of Diabetic patients.



Creating Heat Map using SAS

/*GMAP to produce Geographical Heat Maps. Alternatively
SGMAP procedure can be used to produce Heat Maps*/

```
proc gmap data=diabetes map=maps.world;
```

```
id id;
```

```
choro count ;
```

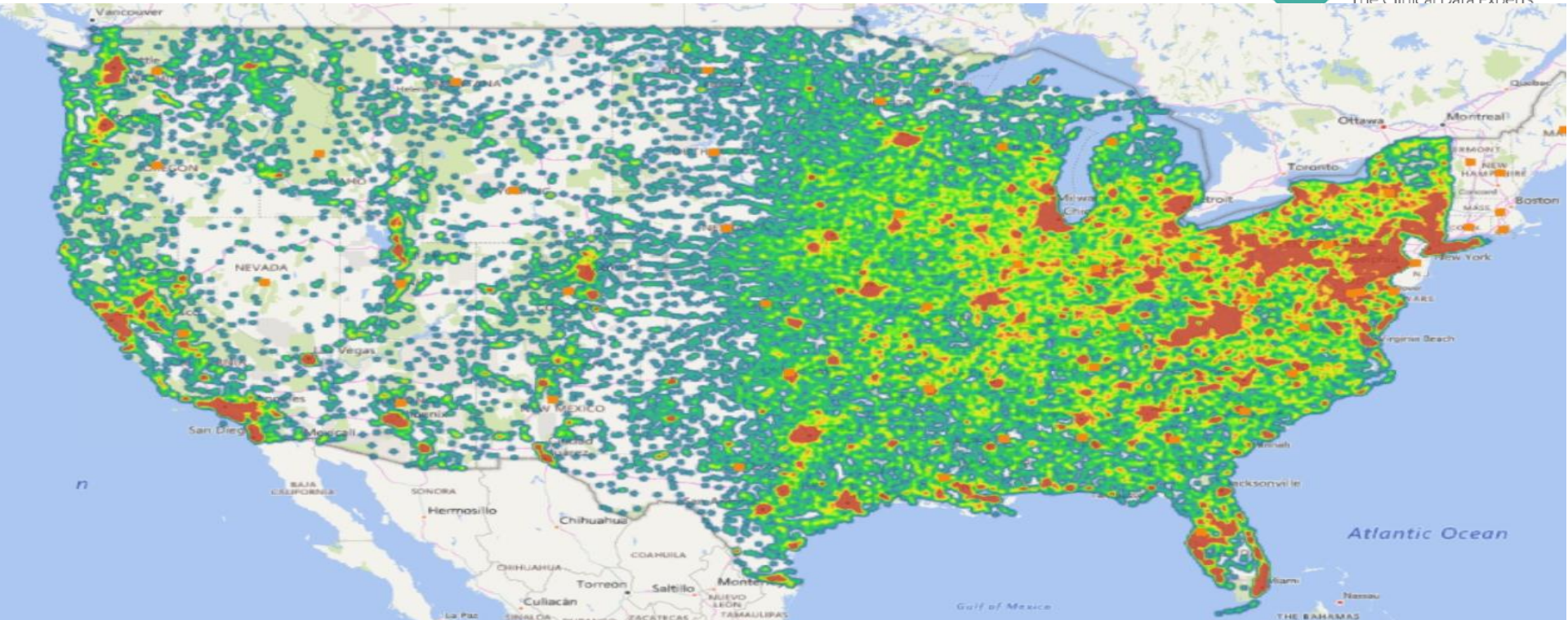
```
label count="Diabetic Population in millions";
```

```
run;
```

```
quit;
```

- DIABETES dataset is source data which contains diabetic population count per Country. Source of this data is "clinicaltrial.gov"
- MAPS.WORLD dataset contains longitude and latitude information to draw world map.
- ID statement links information of DIABETES and MAPS.WORLD dataset using country identifiers
- CHORO statement is used to create Heat Maps. COUNT variable in DIABETES dataset contains population count and determines color patterns
- Label statement is used to assign label for legends

Potential Trial Site Identification



Creation of Heat Map using Excel

Subset of
Data in
Excel 2016



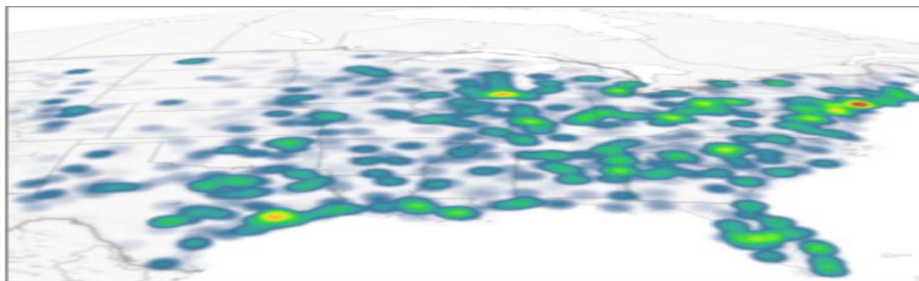
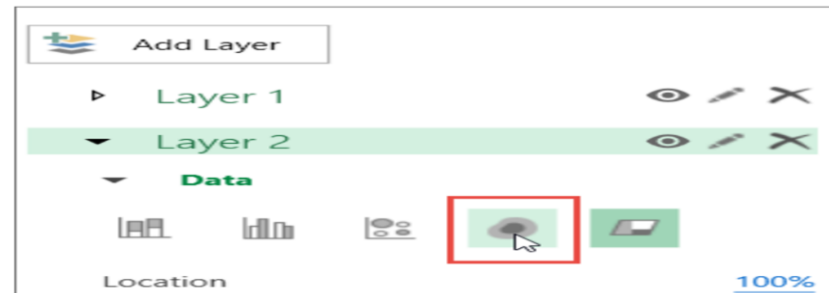
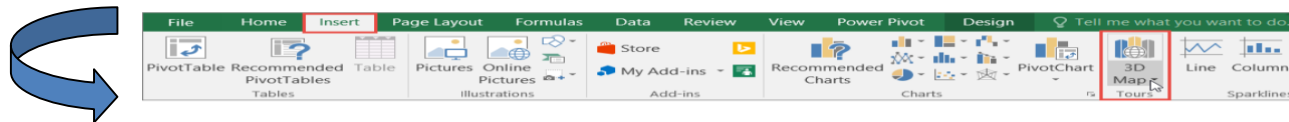
S No	State	Population
1	Alabama	4874747
2	Alaska	739795
3	Arizona	7016270
4	Arkansas	3004279
5	California	39536653
6	Colorado	5607154
7	Connecticut	3588184
8	Delaware	961939
9	District of Columbia	693972
10	Florida	20984400



1. In Excel, open a workbook that has the table or Model data (eg., US Census data) you want to explore in 3D Maps.
2. Click any cell in the table.
3. Click Insert > 3D Map (3D Maps uses Bing to geocode your data based on its geographic properties. After a few seconds, the globe will appear next to the first screen of the Layer Pane.)

Creation of Heat Map using Excel...

You'll find the **3D Map** button in the **Tours** group, on the **Insert** tab of the Excel ribbon, as shown in this picture.



References



- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5079087/>
- <https://knect365.com/clinical-trials-innovation/article/e414c9b9-8de9-4525-8fe6-fe6264d36df0/report-biggest-challenges-clinical-trials-pt-1>
- <https://support.office.com/en-us/article/get-started-with-3d-maps-6b56a50d-3c3e-4a9e-a527-eea62a387030>
- https://www.nehi.net/writable/publication_files/file/rwe_issue_brief_final.pdf
- https://www.clinipace.com/wp-content/uploads/2014/12/final_sitepatienttrends_infographic.pdf
- <https://www.census.gov/geo/reference/zctas.html>
- <https://blog.splitwise.com/2014/01/06/free-us-population-density-and-unemployment-rate-by-zip-code/>

Entering into Real World....

Thank you





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