Sero-Survey in Karnataka State

Summary, Design, and Statistical Methodology

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Plan of the Talk

- **Part I**
  - Survey Design and Implementation
  - Probability Model and Statistical Methodology
  - Summary of Findings.

- **Part II**
  - Nuances of the methodology
  - C-optimal Design
  - Worst Case Design

Goal: To Estimate

- (IgG-Antibody)--the proportion of people who already have had SARS-CoV2 infection;
- (Active Infection)--the proportion of people current active infection;
- (COVID-19 Burden)--the prevalence of COVID-19 in the general population of Karnataka state.

Survey: Units and Implementation

Geographical Spread

- Each of the 29 districts (other than Bengaluru-Urban) was a unit.
- Each zone of BBMP is considered as a unit;
- There will be total of 38 units. (30 districts+ 8 zones)

Within Unit

- Locations around District Hospital, Primary/Community Health Care centres were surveyed.
- Counsellors from ICTC and Health Care workers: conducted the survey.
- Survey used existing public health infrastructure.

Design of Sample at Each Unit

	Risk Subgroups	Samples*	Tests done
Low Risk	Pregnant women presenting for ANC clinic	72	RTPCR and IgG
	Persons attending the outpatient department in the hospitals/ attendees	72	
Moderate Risk	Bus conductors/Auto drivers	28	RAT, RTPCR** and IgG
	Vendors at the vegetable markets	28	
	Healthcare workers	30	
	Individuals in containment zones	28	
	Markets, Malls, Retail stores, Bus stops, Railway stations	30	
High Risk	Elderly (over 60)	72	
	Persons with co-morbid condition	72	
		432	

*-Divided uniformly across Health Facilities; **-only if RAT was negative.

Sampling Design

Participant in each group

- Chosen via systematic sampling and Consent was sought.
  Excluded:
  --if under 18 years of age
  --COVID-19 positive patient
  --Unable to provide informed consent or Not willing to provide sample for test.

Samples

- Blood was drawn for Antibody test, post centrifugal processing sent to designated IgG Lab.
- Rapid Antigen Test done on spot for Moderate and High Risk group participant.
- Swab was sent to designated Reverse transcription polymerase chain reaction labs.

290 Health facilities across the state.

Data from Survey

Collection and Compilation

- Surveyor Entered on an specially designed Survey app: participant details.
  (Each participant identified by a Unique S.R.F. id)
- IgG lab sent data to State government.
- RTPCR labs entered directly onto ICMR portal; were downloaded by State government.

Analysis

- Preparation of one line list for participants (with IgG, RAT, RTPCR results).
- Different Test patterns
- Joint Estimation of IgG and Active Infection

Model

Table of States and Nominal Test Responses M(s,j)

State of Individual		RAT	RTPCR	IgG
		$j = 1$	$j = 2$	$j = 3$
$s = 1$	Active infection but no IgG antibodies	1	1	0
$s = 2$	IgG antibodies present but no evidence of active infection	0	0	1
$s = 3$	Simultaneous presence of active infection and IgG antibodies	1	1	1
$s = 4$	Neither active infection nor IgG antibodies	0	0	0

Sensitivity and Specificity

Sensitivity: probability of a positive test given that the patient has the disease.

Specificity: probability of a negative test given that the patient is well.

$\sigma(m, j)$	RAT	RTPCR	IgG
	$j = 1$	$j = 2$	$j = 3$
Specificities $(m = 0)$	0.975	0.97	0.977
Sensitivities $(m = 1)$	0.5	0.95	0.921

Model Needs

- Test pattern taken by individual (E.g. No RAT at low Risk)
- Adjust for Sensitivity and Specificity of each test(s)
- Design effect - Bias in Sample.

Our First Crude Estimates

Model- Maximum Likelihood Estimate

- The likelihood at a strata, say D-district is then given by

$$L(p; t(D), y(D)) := \prod_{n:n\in D} \left(\sum_{s=1}^{4} p_s q(y(n)|s, t(n)) \right).$$

- The mapping $p \mapsto \log L(p; t(D), y(D))$ is concave
- Numerical, iterative, gradient descent procedure is used to arrive at the maximum likelihood estimate for p in this stratum,

$$\hat{p}(D) = (\hat{p}_1(D), \hat{p}_2(D), \hat{p}_3(D), \hat{p}_4(D)).$$

- IgG-Antibody-Estimate $\hat{p}_2(D) + \hat{p}_3(D)$,
- Active prevalence-Estimate $\hat{p}_1(D) + \hat{p}_3(D)$,
- Total prevalence[past and active infection]-Estimate - $\hat{\wp}(D) := \hat{p}_1(D) + \hat{p}_2(D) + \hat{p}_3(D)$.

Model-Confidence Interval

- The confidence interval estimations come from the Fisher information matrix associated with this model and a design effect of 3.
- For protocol and logistical reasons, the test patterns differ across the participants.
- So the Fisher information matrices for the different test patterns are averaged in proportion to the observed test patterns. This can be interpreted as a hybrid observation/Fisher information matrix.
- The inverse of this matrix provides an estimate of the covariance of $\hat{p}(D)$.

Karnataka

- The Karnataka estimates are obtained after weighting for district populations:
$$\hat{p} = \sum_{D} w(D)\hat{p}(D),$$
where $w(D)$ is the fraction of Karnataka population that lives in district D.

- Assuming independence across districts, the covariance is
$$\sum_{D} w(D)^2 \text{cov}(\hat{p}(D)).$$

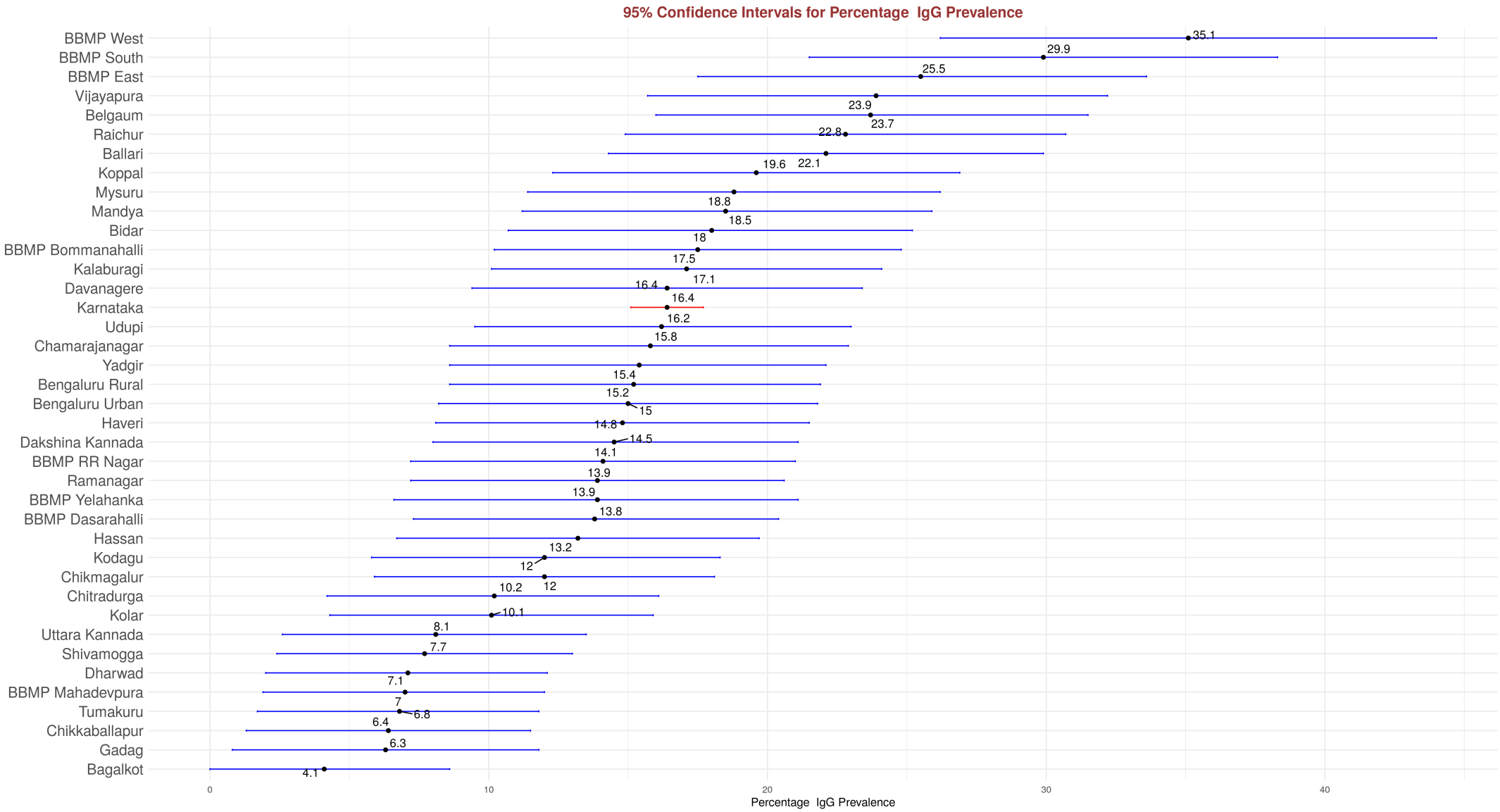
Karnataka Numbers

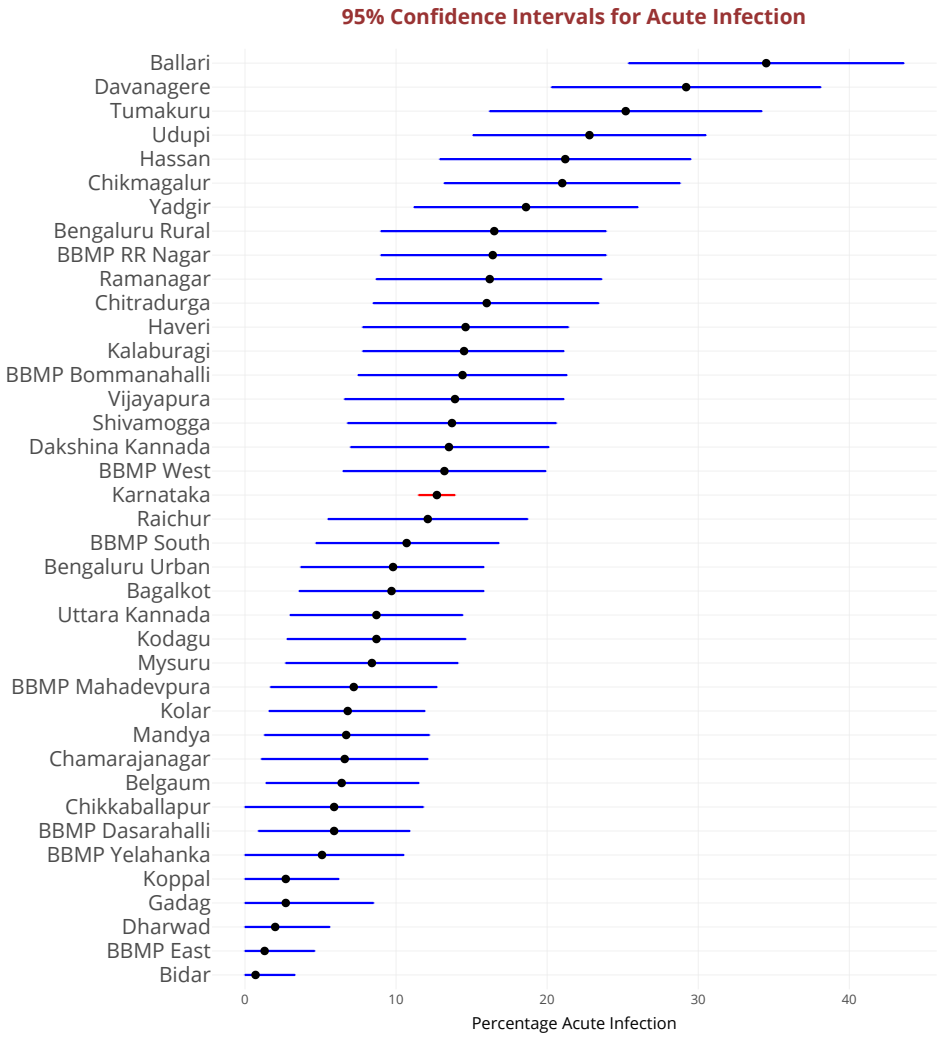
Seroprevalence of IgG and Active infection in Karnataka state.

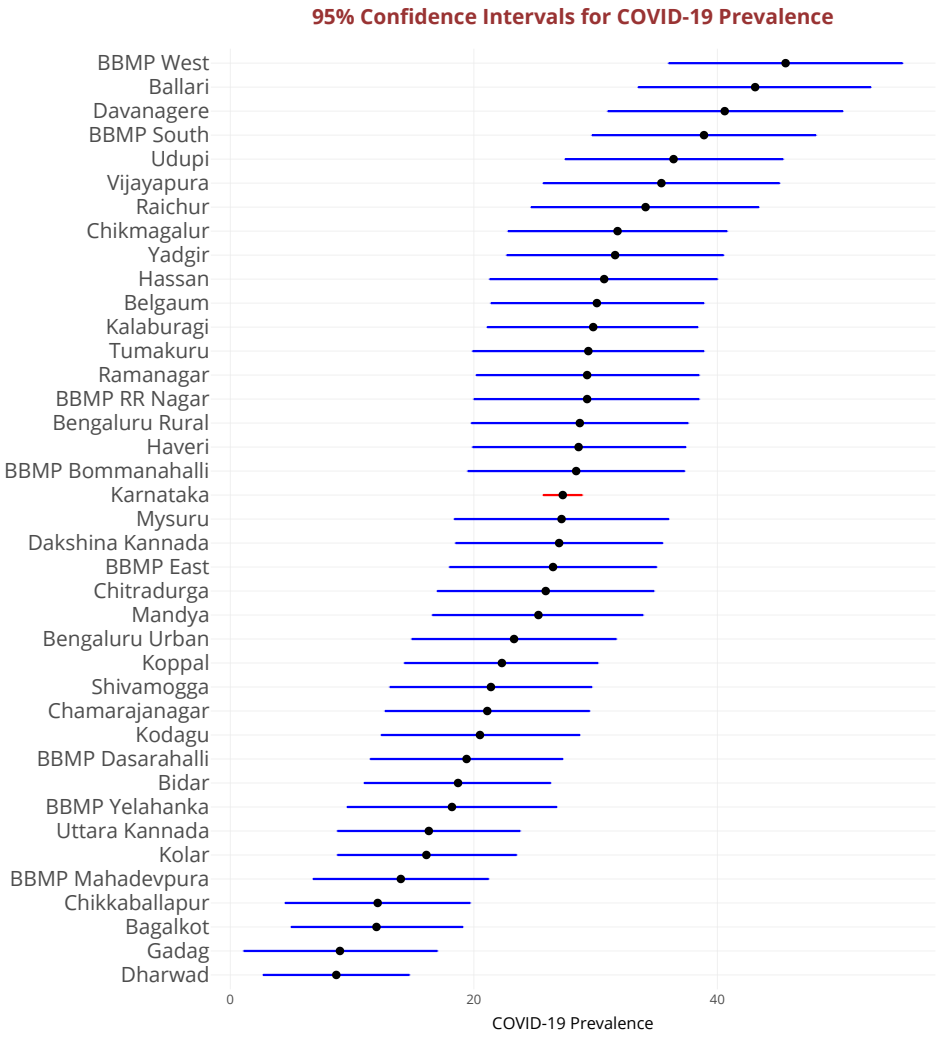
Type	Samples	%-IgG against SARS-CoV2	%-Active Infection of COVID-19	%-Prevalence of COVID-19
Crude	15939	2565/15939= 16.1	2363/14132=16.7	4582/15939=28.7
Adjusted	15939	15.4	12.2	26.1
Weighted Adjusted	15624	16.4 (15.1--17.7)	12.7 (11.5--13.9)	27.3 (25.7--28.9)

Both IgG and Active infection in Karnataka state.

$$16.4 + 12.7 - 27.3 = 1.8$$


95% Confidence Intervals for Percentage IgG Prevalence
BBMP West
BBMP South
BBMP East
Vijayapura
Belgaum
Raichur
Ballari
Koppal
Mysuru
Mandya
Bidar
BBMP Bommanahalli
Kalaburagi
Davanagere
Karnataka
Udupi
Chamarajanagar
Yadgir
Bengaluru Rural
Bengaluru Urban
Haveri
Dakshina Kannada
BBMP RR Nagar
Ramanagar
BBMP Yelahanka
BBMP Dasarahalli
Hassan
Kodagu
Chikmagalur
Chitradurga
Kolar
Uttara Kannada
Shivamogga
Dharwad
BBMP Mahadevpura
Tumakuru
Chikkaballapur
Gadag
Bagalkot
35.1
29.9
25.5
23.9
23.7
22.8
19.6
22.1
18.8
18.5
18
17.5
17.1
16.4
16.4
16.2
15.8
15.4
15.2
15
14.8
14.5
14.1
13.9
13.9
13.8
13.2
12
12
10.2
10.1
8.1
7.7
7.1
7
6.8
6.4
6.3
4.1
0
10
20
30
40
Percentage IgG Prevalence


95% Confidence Intervals for Acute Infection
Ballari
Davanagere
Tumakuru
Udupi
Hassan
Chikmagalur
Yadgir
Bengaluru Rural
BBMP RR Nagar
Ramanagar
Chitradurga
Haveri
Kalaburagi
BBMP Bommanahalli
Vijayapura
Shivamogga
Dakshina Kannada
BBMP West
Karnataka
Raichur
BBMP South
Bengaluru Urban
Bagalkot
Uttara Kannada
Kodagu
Mysuru
BBMP Mahadevpura
Kolar
Mandya
Chamarajanagar
Belgaum
Chikkaballapur
BBMP Dasarahalli
BBMP Yelahanka
Koppal
Gadag
Dharwad
BBMP East
Bidar
0
10
20
30
40
Percentage Acute Infection


95% Confidence Intervals for COVID-19 Prevalence
BBMP West
Ballari
Davanagere
BBMP South
Udupi
Vijayapura
Raichur
Chikmagalur
Yadgir
Hassan
Belgaum
Kalaburagi
Tumakuru
Ramanagar
BBMP RR Nagar
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Mandya
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Koppal
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Chamarajanagar
Kodagu
BBMP Dasarahalli
Bidar
BBMP Yelahanka
Uttara Kannada
Kolar
BBMP Mahadevpura
Chikkaballapur
Bagalkot
Gadag
Dharwad
0
20
40
COVID-19 Prevalence

Epidemiological Metrics

Estimated Infection (EI)

$$\text{EI} = \text{COVID-19 prevalence} \times \text{Population}$$

Case to Infection Ratio (CIR)

$$\text{CIR} = \frac{\text{EI}}{\text{Reported Cases up to 2nd September}}$$

Past Infection (PI)

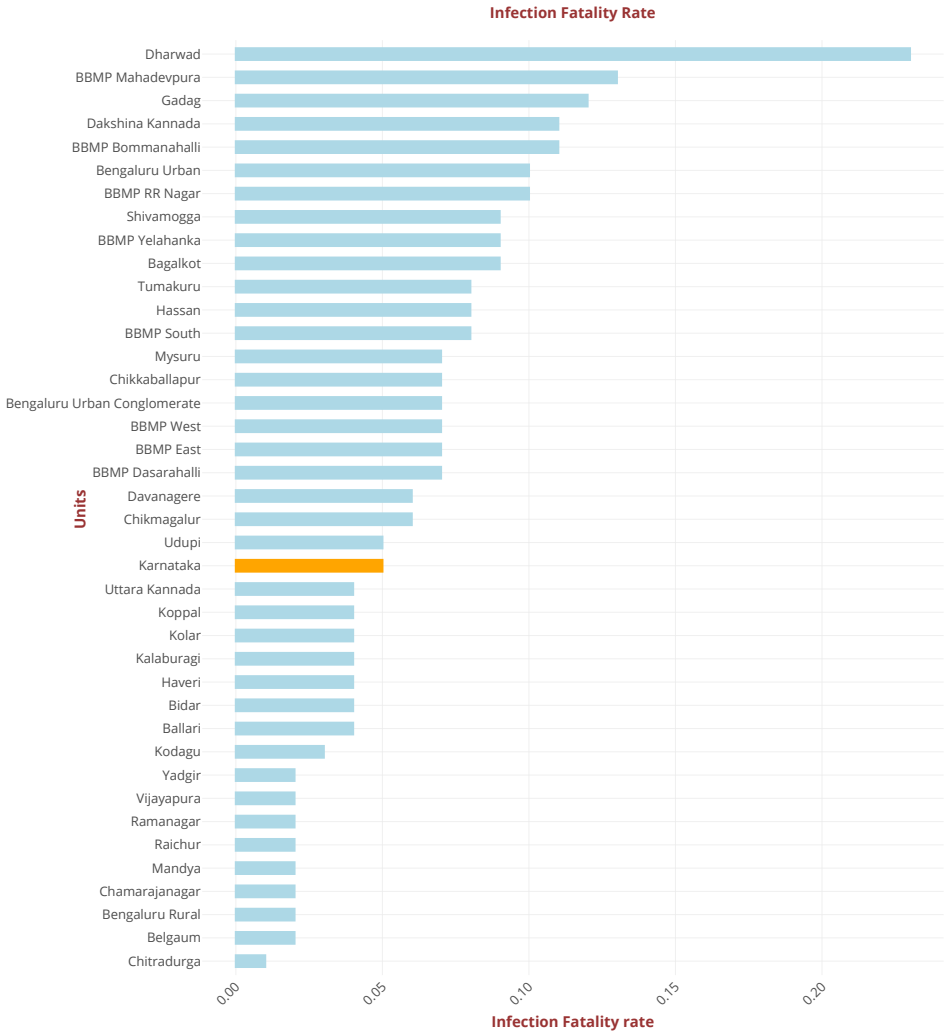
$$\text{PI} = \text{IgG Prevalence} \times \text{Population}$$

Infection Fatality Rate (IFR)

$$\text{IFR} = \frac{\text{Fatalities Reported up to 2nd September}}{\text{Fatalities Reported up to 2nd September} + \text{PI}}$$

Karnataka Estimated Numbers

Cases up to 16/09	Estimated total prevalence as on 16/09	CIR	IFR	Active case per day 02-16	Estimated Active Infection
484954	19321334	1:40	0.05%	98028.5	8988313


Infection Fatality Rate
Dharwad
BBMP Mahadevpura
Gadag
Dakshina Kannada
BBMP Bommanahalli
Bengaluru Urban
BBMP RR Nagar
Shivamogga
BBMP Yelahanka
Bagalkot
Tumakuru
Hassan
BBMP South
Mysuru
Chikkaballapur
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Davanagere
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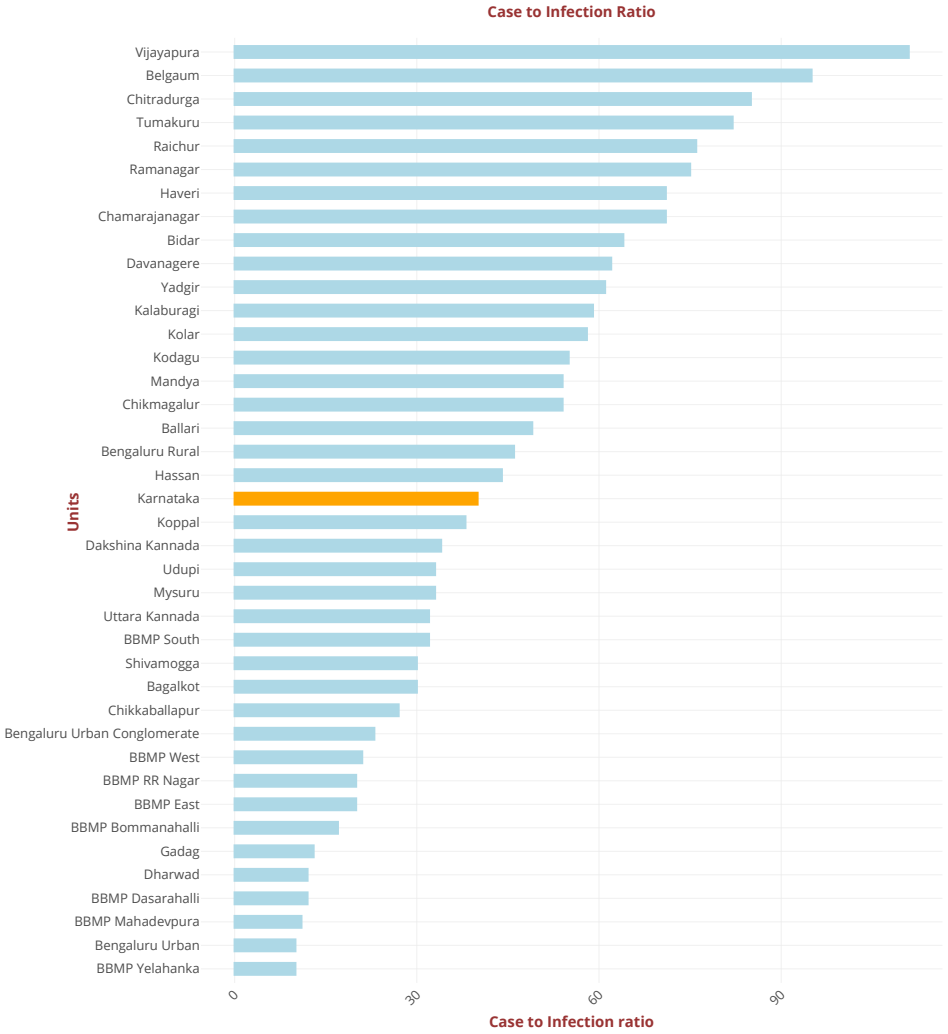
Ramanagar
Raichur
Mandya
Chamarajanagar
Bengaluru Rural
Belgaum
Chitradurga
Units
0.00
0.05
0.10
0.15
0.20
Infection Fatality rate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Belgaum
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Tumakuru
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Bidar
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BBMP RR Nagar
BBMP East
BBMP Bommanahalli
Gadag
Dharwad
BBMP Dasarahalli
BBMP Mahadevpura
Bengaluru Urban
BBMP Yelahanka
Units
0
30
60
90
Case to Infection ratio

Karnataka: 16.7 % IgG and 0.05 % IFR

High IgG and Low IFR

- The district has had surge in cases in the past
- Underreporting of COVID-19 deaths is a possibility

High IgG and High IFR

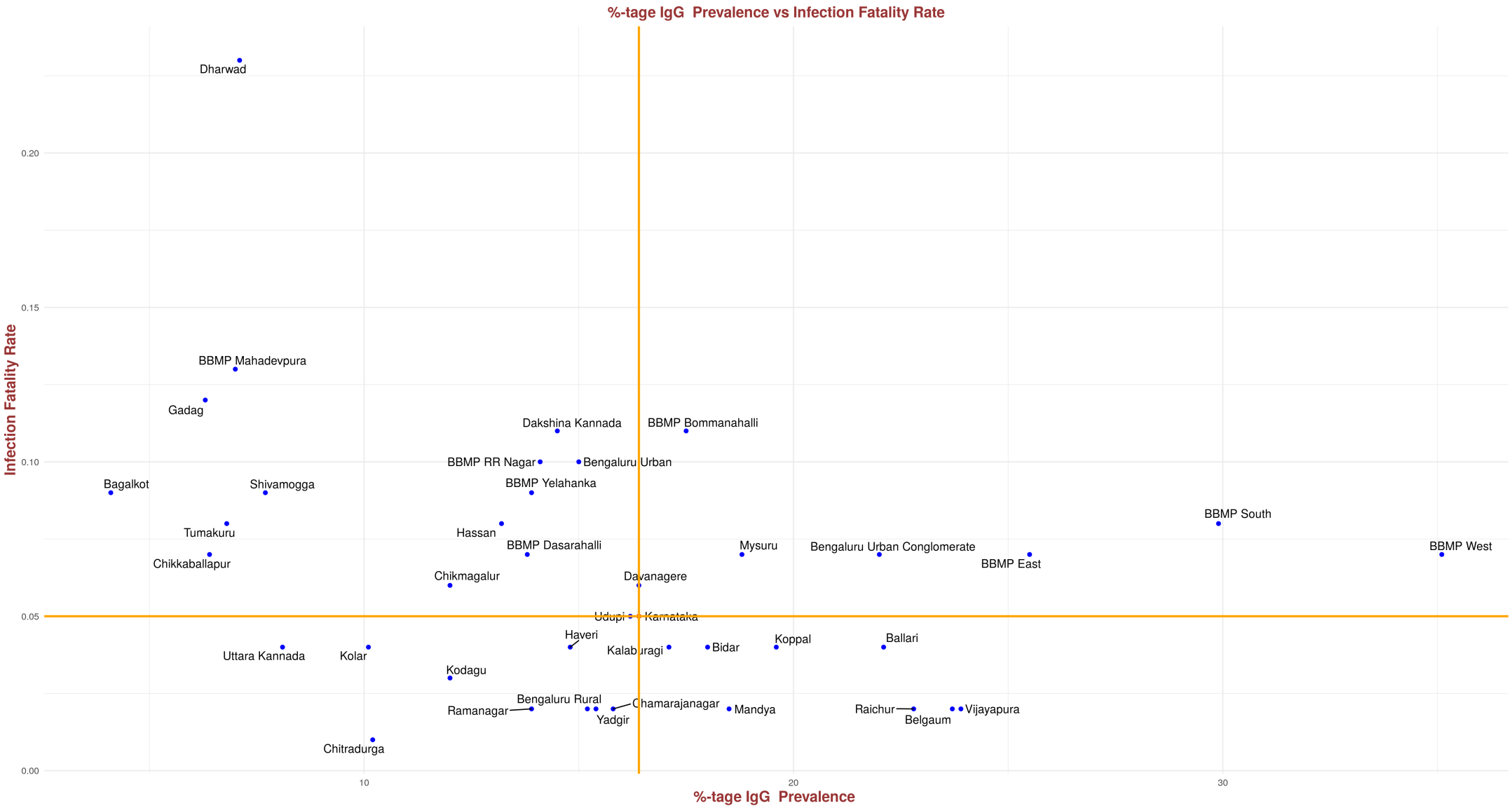
- The district has had surge in cases in the past
- The reporting of deaths in the district is relatively reliable

Low IgG and Low IFR

- District will have surge in cases in the near future
- Low IFR can mean that either there are fewer deaths or there is underreporting.

Low IgG and High IFR

- The district is yet to see surge in cases
- High proportion of deaths due to COVID-19 in the early phase of outbreak


%-tage IgG Prevalence vs Infection Fatality Rate
Infection Fatality Rate
%-tage IgG Prevalence
0.00
0.05
0.10
0.15
0.20
10
20
30
Dharwad
BBMP Mahadevpura
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Ramanagar
Mandya
Raichur
Vijayapura
Yadgir
Belgaum
Chitradurga

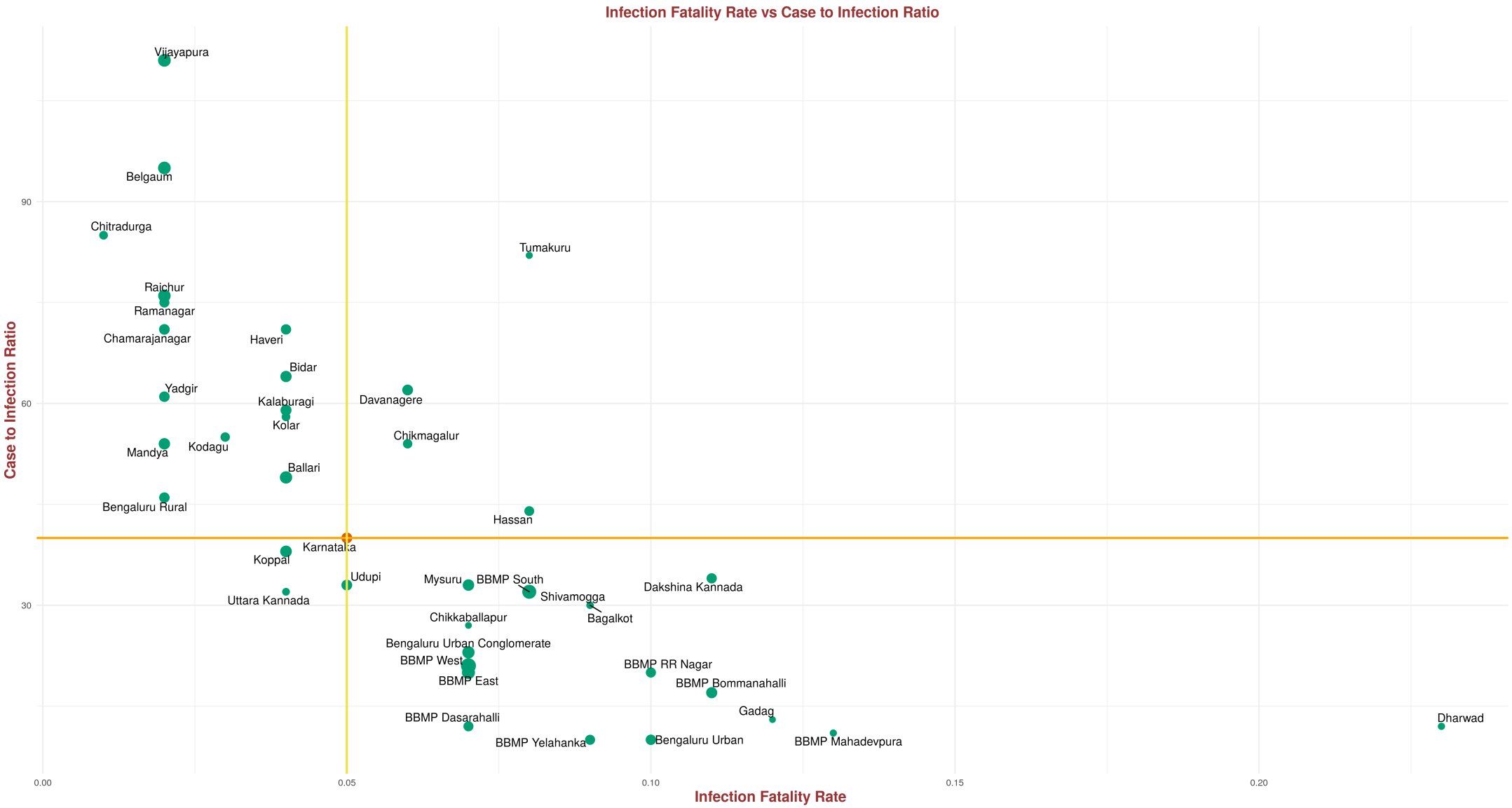
Karnataka: 16.7 % IgG, 1:40 CIR, and 0.05 % IFR

High IgG, High CIR, Low IFR

- District has gone through a surge.
- High IgG and high CIR is a clear indication that cases or areas of circulation have been missed.
- High IgG with Low IFR means that there is underreporting of deaths

High IgG, Low CIR, High IFR

- Despite going through surge in cases in the past, district seems to be detecting cases and areas of circulation
- High IgG with high IFR means that there is reliable reporting of deaths


Infection Fatality Rate vs Case to Infection Ratio
Case to Infection Ratio
Infection Fatality Rate
90
60
30
0.00
0.05
0.10
0.15
0.20
Vijayapura
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Gadag
BBMP Dasarahalli
Dharwad
BBMP Yelahanka
Bengaluru Urban
BBMP Mahadevpura

Survey Findings

- Estimates Across Risk Groups: Age, Gender, Sub-Categories
- RAT Sensitivity amongst : asymptomatic ~ 0.46 and symptomatic ~ 0.67
- Prediction of past and current infection from: Symptoms and Pre Existing Health Conditions
- District wise reports and impacting testing policy
- Prediction of past and current infection from: Symptoms and Pre Existing Health Conditions.
  E.g. Diarrhea and In-contact for past infection.

Predictions