Site Visits at Risk?
Your Plan B.
Mitigate Coronavirus side-effects with RBQM

Cyntegrity | Monday, March 9, 2020
Chinese ‘patients are simply not going’ to clinical trial sites, IQVIA warns

AbbVie, GSK, Sanofi and more limit employee travel as coronavirus threatens business

Coronavirus: Dutch hospital closed after treating IC patient

Craig Lipset, former head of Clinical Innovation at Pfizer
COVID-19

What if you can no longer visit your sites?
AT RISK

- Patient safety
- Study quality
- Study timelines
ASSESS THE RISK

- Continue monitoring remotely
- Get daily updates
REduce the impact

- Centralized Monitoring
- 7 ‘Crisis Management’ KRIs
What if you can no longer visit your sites?

Mitigate, before it’s too late

- Preventive risk mitigation action
- Early detection of issue
- Late in a trial, near DB closure
- Issue noticed post EMA/FDA submission

REDUCE THE IMPACT
- Centralized Monitoring
- 7 Crisis Management KRI

Impact recovery (Costs)

$1M

$100K

$10

$1

MyRBQM® Portal powered by Cyntegrity
Scenario 1: Patient in hospital, monitor blocked
- The hospital has been put under quarantine
- You run a study in that clinic/hospital and your patients are in the clinic
- Your monitors cannot enter the hospital
- Hospital staff cannot see the monitor in person

Scenario 2: Outpatients and monitor blocked
- The hospital has been put under quarantine
- You run a study in a clinic/hospital and your patients are outpatients
- Your monitors and your patients cannot access the hospital
- Hospital staff cannot see the monitor in person
- Your patients cannot access treatment

Scenario 3: Patients cannot meet physicians in person
- Your patients have been put under quarantine
- You run a study in a private practice or your patients are outpatients
- Your patients cannot meet their physician in person
- Your patients cannot access treatment
KRI Set to Monitor Impact COVID-19

1. Under / Over-Enrollment
2. Patient Adherence to Medications
3. AEs / SAEs level too low or too high compared to the previous period
4. % of missing values in the important data items is too high
5. High level of dropouts / informed consent withdrawn
6. Abnormal patterns in lab values for any trends indicating an additional burden to the patients
7. Large gap between data generation and data entry
BETTER ACT NOW

- MyRBQM® Crisis-kit
- Within 3 weeks you’re ready to go
WE ACT FAST

- Data connectors in place
- Daily data analysis
RISK-FREE IMPLEMENTATION

- Existing infrastructure
- Based on read-only
The hospital has been put under quarantine
• You run a study in that clinic / hospital and your patients are in the clinic
• Your monitors cannot enter the hospital
• Hospital staff cannot see the monitor in person

Scenario 1: Patient in hospital, monitor blocked

KRI for this scenario

1. Check the number of adverse events / serious adverse events
   • numbers going up is an indicator that the infection may influence the safety of the patients
   • numbers going down is an indicator that the site staff may be overwhelmed with other tasks and cannot take care of the documentation

Mitigation actions
• check with sites remotely on the reason for the change in adverse events
• consider terminating patients’ participation in the study prematurely
• consider stopping or slowing down enrollment for a limited time
Scenario 1: Patient in hospital, monitor blocked

- The hospital has been put under quarantine
- You run a study in that clinic/hospital and your patients are in the clinic
- Your monitors cannot enter the hospital
- Hospital staff cannot see the monitor in person

KRI for this scenario

2. Check the number of missing values in the important data items
   - Numbers remain stable, no concerns
   - Numbers going up, staff may have too much work and more important objectives
   - Numbers going down, situation seems to be under control

Mitigation actions

- Check with sites remotely on the reason for the missing data (data entry problems or data not generated)
- Consider hiring hospital external staff to enter the data remotely, if available, with access to the electronic patient record
- Consider a protocol amendment to reduce the overall number of visits and data items to be generated and captured
Scenario 1: Patient in hospital, monitor blocked

- The hospital has been put under quarantine
- You run a study in that clinic/hospital and your patients are in the clinic
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<table>
<thead>
<tr>
<th>KRI for this scenario</th>
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<tbody>
<tr>
<td>3. Check the number of dropouts/informed consent withdrawn</td>
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<td>- numbers going up is an indicator that the infection/hospital situation is an extra burden to the patients</td>
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<tr>
<td>- numbers going down or remaining stable probably means not to worry</td>
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</table>

Mitigation actions

- check with sites remotely on the reasons for patients dropping out
- consider lowering the patient burden by reducing the number of examinations
- check for certain interactions potentially explaining the increasing number of dropouts
Scenario 1: Patient in hospital, monitor blocked

- The hospital has been put under quarantine
- You run a study in that clinic/hospital and your patients are in the clinic
- Your monitors cannot enter the hospital
- Hospital staff cannot see the monitor in person

**KRI s for this scenario**

4. Check the lab values for any trends indicating an additional burden to the patients
   - lab values are ranging within the same boundaries as prior to the quarantine is positive
   - lab values are ranging outside, i.e. significantly lower / higher than prior to the quarantine, patient may suffer from a coronavirus infection

**Mitigation actions**

- check for drug-drug interactions and potentially terminate patient participation
- consider a protocol amendment and a study drug dosage lowering for a limited time
Scenario 1: Patient in hospital, monitor blocked

- The hospital has been put under quarantine
- You run a study in that clinic/hospital and your patients are in the clinic
- Your monitors cannot enter the hospital
- Hospital staff cannot see the monitor in person

KRI for this scenario

5. Analyse the time between data generation and data entry
   - data are being entered much later than in the pre-Coronavirus period and patient safety may be compromised
   - data are entered not differently than in the pre-Coronavirus period

Mitigation actions
- ask site to at least enter the safety data and enter any other data at a later point in time
- consider remote data entry outside of the hospital if access to patient records can be granted remotely
Scenario 2: Outpatients and monitor blocked

- The hospital has been put under quarantine
- You run a study in a clinic / hospital and your patients are outpatients
- Your monitors and your patients cannot access the hospital
- Hospital staff cannot see the monitor in person
- Your patients cannot access treatment

KRI for this scenario

1. Analyse the number of adverse events / serious adverse events (and all other cases described in scenario 1 since they are all requiring the same / similar mitigation actions)

Mitigation actions

- Check with sites remotely on the reason for the change in adverse events
- Consider hiring external medical staff / study nurses that could visit the patients and document the findings
- Grant EDC access to external / new staff for data entry of safety data
- Consider setting up video consultation between the patient and the study investigator
- Worst case, consider opening another site in the same region and transfer responsibilities to such a new site
Scenario 3: Patients cannot meet physicians in person

- Your patients have been put under quarantine
- You run a study in a private practice or your patients are outpatients
- Your patients cannot meet their physician in person
- Your patients cannot access treatment

KRI for this scenario

1. Check the number of adverse events / serious adverse events
   - numbers going up is an indicator that the infection may influence the safety of the patients
   - numbers going down is an indicator that the patient worries about other things than study drug related adverse events

Mitigation actions

- check with sites remotely on the reason for the change in adverse events
- consider hiring external medical staff / study nurses that could contact the patients remotely and document the findings
- grant EDC access to external / new staff for data entry of safety data
- consider setting up video consultation between the patient and the study investigator
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2. Check the number of missing values in the important data items
   - numbers remain stable, no concerns
   - numbers going up, patient does not see the site
   - numbers going down, situation seems to be under control

Mitigation actions

- consider hiring staff that could see the patient at home and take for example a blood sample, measure blood pressure, check on AEs etc
- have the external staff enter the data into the EDC system
- consider terminating the patient participation in the study
Scenario 3: Patients cannot meet physicians in person

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KRI s for this scenario

3. Check the number of dropouts / informed consent withdrawn
   - numbers going up is an indicator that the infection is an extra burden to the patients
   - numbers going down or remaining stable probably means not to worry

Mitigation actions

- consider a protocol amendment and terminate the study participation for infected patients
- consider hiring external staff to motivate the patients to stay in the study, as far as that is possible
Scenario 3: Patients cannot meet physicians in person

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“Your Plan B.” Package

*Mitigate Coronavirus side-effects with RBQM*

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<tr>
<td>➔ Monthly fee</td>
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<td>➔ Includes: <a href="#">MyRBQM® Portal</a>, special COVID-19 KRI-set (7 KRIs), 20 seats.</td>
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<td>➔ Includes: The <a href="#">White Belt' training</a> is dedicated to the fundamental RBQM knowledge you and your team must have before developing your RBQM strategy, 20 enrollments.</td>
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