Evidence note

The landscape of diagnostic tests for COVID-19

Government of Nepal
Ministry of Health and Population
Policy, Planning and Monitoring Division

Background

As a part of building evidence to support the health sector response to COVID-19 pandemic, the Ministry of Health and Population (MoHP) through the knowledge café secretariat at the Policy, Planning and Monitoring Division (PPMD) organised a virtual Knowledge Café (a platform for promoting the use of evidence) on landscape of diagnostic tests for COVID-19 on 17 April 2020. The purpose of the meeting was to discuss how evidence relating to diagnostics tests of COVID-19 and approaches taken by other countries in testing COVID-19 can be useful to inform generating recommendations for defining testing strategy for COVID-19 in the Nepalese context. This evidence note is a product of knowledge café discussion and presentation, backed up by a rapid evidence synthesis.

Landscape of Diagnostic Tests

Table 1: Summary of the relevant diagnostic tests for COVID-19 detection

Tests	Company	Description	Test time	Performance	Validation	Test Consideration
SARS-CoV-2 Antibody Test (Zhihua, 2020)	Guangzhou Wondfo Biotech (Guangzhou, China)	POC lateral flow Immunoassay (detects IgG & IgM in blood serum)	15 min	Sensitivity: 86% Specificity: 99%	ICMR	Suitable for screening but early infection undetectable
SARS-CoV-2 IgG-IgM combined antibody reagent (Li et al., 2020)	Jiangsu Medomics Medical Technologies (Nanjing, China)	POC lateral flow Immunoassay; detects IgG & IgM in blood serum	15 min	Sensitivity: 88.66% Specificity: 90.63%.	N/A	Suitable for screening but early infection undetectable
Lateral flow assay (Johns Hopkins Center for Health Security, 2020)	Cellex Inc.	POC lateral flow Immunoassay detects IgM & IgG (combined)	N/A	Sensitivity: 93.8% Specificity: 95.6%	FDA EUA, CE	Suitable for screening but early infection undetectable
COVID-19 IgG/IgM Combo Rapid Test Device (Johns Hopkins Center for Health Security, 2020)	Liming Bio	Colloidal gold lateral flow Immunoassay: detect IgG & IgM separate & combined	N/A	Sensitivity: 82% IgG, 62% IgM, 93.1% combined Specificity: 100% IgG, 100% IgM, 100% combined	CE-IVD	Suitable for screening but early infection undetectable
SGTi-flex COVID-19 IgM/IgG (Sugentech, 2020)	Sugentech, Inc.	Immunochromato graphic test; detects IgM / IgG in whole blood, serum, or plasma	10 min	Sensitivity: 91% Specificity: 97.67%.	FDA, CE-IVD, Korea MFDS	Sophisticated technology not required; suitable for mass screening
The (COVID-19) IgG/IgM Rapid Test (Johns Hopkins Center for Health Security, 2020)	Aytu Biosciences/O rient Gene Biotech	Solid phase immunochromatog raphic assay detects IgM & IgG (separately) in blood or plasma samples	N/A	Sensitivity: 87.9% IgG, 92.7% IgM Specificity: 100% IgG, 100% IgM	CE, awaiting FDA approval	Suitable for screening; early infection undetectable; Used in clinical setting, China

Tests	Company	Description	Test time	Performance	Validation	Test Consideration
iFlash-SARS-CoV-2-IgG and the iFlash SARS-CoV2-IgM (Johns Hopkins Center for Health Security, 2020)	Shenzhen Yhlo Biotech Company	Immunoassay detects IgM & IgG (separately)	N/A	Sensitivity: >90% IgG, >95% IgM Specificity: >95% IgG, >95% IgM	CE/IVD	Suitable for screening but early infection undetectable
SARS-CoV-2 Rapid Test (PharmACT, 2020)	PharmACT	Immunochromatography; detects IgM & IgG in capillary blood, whole blood, or serum	20 min	Sensitivity 4-10 day: 70% IgM, N/A IgG 11-24 days: 92.30% IgM, 98.6% IgG	N/A	Suitable for screening but early infection undetectable
ELISA kit for antibody detection RT-PCR for RNA (Zhao et al., 2020)	Beijing Wantai Biological Pharmacy Enterprise Co.,Ltd	Immunoassay detecting IgM/IgG combine antibody (Ab) and IgM and IgG separately	N/A	Sensitivity Overall: 67.1% RNA (RT-PCR), 93.1% Ab, 82.7% IgM, 64.7% IgG, 99.4 % RNA + Ab Day 1-7: 66.7%RNA (RT-PCR),38.3% Ab, 28.7% IgM, 19.1% IgG, 78.7% RNA + Ab Day 8-14: 54.0% RNA (RT-PCR), 89.6% Ab, 73.3% IgM, 54.1% IgG, 97.0% RNA + Ab Day 15-39: 45.5%RNA (RT-PCR), 100% Ab, 94.3% IgM, 79.8% IgG, 100% RNA +Ab Specificity: N/A RNA (RT-PCR), 99.1% Ab, 98.6% IgM, 99% IgG, N/A RNA + Ab	N/A	Suitable for screening but early infection undetectable
Abbott Real Time SARS-CoV-2 EUA test (Abbott Molecular Inc., 2020)	Abbott Molecular Inc.	Molecular Assay (RT-PCR) to detect viral RNA in nasal swabs qualitatively	5 min	N/A	FDA EUA, CE-IVD	May not be immediately available outside USA
SAMBA II COVID-19 Test (Hohn, 2020)	Spin-out to Diagnostics for the Real World Ltd by University of Cambridge	Molecular Assay (detects traces of genetic material of the virus)	90 min	Sensitivity: 98.7% Specificity: 100%	Public Health England, Cambridge, CE-IVD	Just used in Cambridge hospitals; expands to others; may not be available immediately
CT imaging (Jiang et al., 2020)	-	Ren, et al reported that combination of RT-PCR and CT delivered higher sensitivity and offers an	-	Sensitivity: 97%	-	Requires higher level health facilities; not suitable for rapidly expanding

Tests	Company	Description	Test time	Performance	Validation	Test Consideration
		optimal pattern to screen COVID-19				community testing but alternative for RT-PCR
Loop-Mediated Isothermal Amplification (LAMP) test (Zhang et al., 2020)	New England Biolabs	Molecular diagnostic detecting viral RNA in respiratory specimen (swab)	30 min	Predictive values:100%	N/A	Limited sample size, may take time to be available in Market
Thirty-minute test (University of Oxford, 2020)	University of oxford and Oxford Suzhou Centre for Advanced Research (OSCAR)	Recognises SARS-CoV-2 (COVID-19) RNA and RNA fragments. Early stage patients may be identified sooner	30 min	Predictive values: 100%	N/A	Limited sample size, may take time to be available in Market
The Xpert Xpress SARS-CoV-2 test (Cepheid, 2020)	Cepheid, USA	Molecular Assay (detects viral nucleic acid in either nasopharyngeal swab and/or nasal wash/ aspirate specimens)	45 min	Sensitivity: 95% with 95% C.I. Specificity: detects Human and Bat SARS-coronavirus but no cross reactivity with others	WHO (EUL) Under process, FDA EUA	Suitable for definitive diagnosis. *Needs Bio-safety cabinet

Abbreviations: POC – Point of Care, CE-IVD - Conformité Européene-In Vitro Diagnostic Medical Device, FDA – Food and Drug Administration (USA), EUA – Emergency Use Authorization, MFDS - Ministry of Food & Drug Safety, WHO EUL – World Health Organization Emergency Use Listing Procedure

Approaches of various countries to increase COVID-19 testing

South Korea

Since reporting of the first case on 20 January 2020, though a high infection rate in the beginning, South Korea was quickly able to flatten the epidemiological curve by mid-March 2020. Achievement of South Korea has been mostly linked with the following strategies the country adopted to combat COVID-19 in the country:

- **Extensive Screening:** Screening clinics were set up at the public health centres and health institutions which diagnosed suspected cases and tested them in separate area before their entry in emergency centre. The range of screening was broadened to include all pneumonia cases. This was done to minimize the contamination of health facilities. (Republic of Korea, 2020)
- **Active case finding in high risk groups:** Mobile specimen collection teams were mobilized to make door-to-door visits. They conducted diagnostic tests targeting those showing symptoms with priority and also focussed on senior citizens and those with comorbidities. (Republic of Korea, 2020)
- **Free mass testing centres:** Since 26 February 2020, the Korean government initiated "drive-through" testing centers, in facilities like petrol station where people can get tested sitting inside their vehicle (Republic of Korea, 2020). Test results were shared via text message. Such a centre aimed to minimise the contact between suspected cases and medical workers. In such facilities, it is possible to test 10 persons in an hour. Within one month of its operation, the facility expanded to sites across the country (Duchâtel et al., 2020).
- **Use of technology:** The Korean government's Ministry of the Interior and Safety has developed an application, "self-quarantine safety protection" that is available in Android and IoS platforms. The app monitors the location of those in-home quarantines and connects them with health authorities to report symptoms (Duchâtel et al., 2020). Then mobile teams are deployed to collect samples for the diagnostic test when the quarantined individuals develop symptoms (M. S. Kim, 2020).

Germany

The first case of COVID-19 in Germany was reported 27 January 2020 (Reisinger, 2020). Number of daily recorded COVID-19 cases increased sharply from 59 on 4 May to 6813 on 2 April. Since then, daily recorded cases as decreased and reached to 1388 on 18th April (D. Kim, 2020; Reisinger, 2020). On 17 April 2020, the Robert Koch Institute for public health announced that the rate of infection - the number of people each ill person contaminates - had dropped below one for the first time, thereby leading to the conclusion that outbreak is under control (D. Kim, 2020). Overall, the German response has been a good example of how countries can combat the spread and severity of COVID-19. The core of the German response matches very well with recommendations from the World Health Organization: Prepare, test (isolate and treat) and mitigate the spread of the virus (Gostic et al., 2020).

- **Robust and Rapid testing:** Germany's robust and rapid testing programme was helped by the use of a distributed network of testing through individual hospitals, clinics and laboratories, instead of relying on tests from a single government resource (Bwire & Paulo, 2020). Germany has carried out more diagnostic swab tests (PCR tests) than any other major European nation. A total of 132 labs across the country have conducted on average 116,655 swab tests per day (Morris, 2020). Over 200 laboratories across Germany have become involved in the rapid testing scheme since February (Eckner, 2020). Special drive-in test stations have also been used to perform tests in addition to hospitals and doctors' practices (Hall & Buck, 2020).
- **Extensive contact tracing:** Extensive contact tracing was implemented by public health offices. Close contacts were quarantined (in Germany, close contact means either that the person spoke with the sick person for at least 15 minutes or was coughed or sneezed on at a time when the sick person was infectious i.e. two days before the first symptoms) (Hall & Buck, 2020).

Singapore

First case of COVID-19 was confirmed in Singapore on 23 January 2020. As of 21 April 2020, Singapore has 9,125 total cases, with total of 11 deaths. (Eckner, 2020) Singapore, a city-state and global travel hub in Southeast Asia, was one of the first countries to be affected by COVID-19, and for a while was the country with the highest COVID-19 numbers outside of China from 5 to 18 February 2020 (D. Kim, 2020).

- **Surveillance system:** Success of Singapore's COVID-19 is supposed to be largely because of strong surveillance system. Singapore's surveillance for COVID-19 aimed to identify as many cases as possible. Apart from suspected cases, Singapore enhanced its surveillance system to detect COVID19 among all cases of pneumonia in hospital and primary care, severely ill patients in hospital ICUs and deaths with possible infectious cause, and influenza-like illness (ILI) in sentinel primary care clinics.
- **Rapid scaling up of testing capacity:** SARS-CoV2 reverse transcription-polymerase chain reaction (RT-PCR) testing capacity was scaled up rapidly in all public hospitals in Singapore and is able to handle 2,200 tests a day for a population of 5.7 million. Singapore also strengthened contact tracing system placing close contacts under mandatory quarantine for 14 days. (Lee et al., 2020)

India

India reported its first COVID-19 positive patient on 31 January (Pulla, 2020). As of 23 April 2020, India had 21,370 cases with total of 681 deaths (Indian Council of Medical Research [ICMR], 2020). India has attempted to expanding the testing capacity through combination of rapid tests and RT-PCR. The strategies adopted by India in expansion of testing capacity could be more relevant in Nepalese context because of similar socio-cultural, demographic and health system capacity.

- **Use of rapid diagnostic test:** The ICMR has published an advisory on 4 April 2020 which suggests that rapid antibody tests will be used to test all symptomatic cases of Influenza-Like Illness (ILI) at the health facility level. If the antibody test turns out negative, then if considered necessary real-time RT-PCR will be used to for confirmation by using throat/nasal swab (ICMR & Department of Health Research [DHR], 2020a). On 16 April 2020, ICMR has released a list of validated antibody test which are considered satisfactory for use and are presented as follows (ICMR, 2020). ICMR states that positive test indicates exposure to SARS-CoV-2, however, a negative test does not rule out COVID-19 infection.

Table 2: Rapid diagnostic tests (antibody test) considered to have satisfactory quality after validation by ICMR

S.N.	Kit name and company	S.N.	Kit name and company
1	SARS-CoV-2 Antibody test (Lateral flow method): Guangzhou Wondfo Biotech,Mylan Laboratories Limited (CE-IVD),M R Roofs Private Ltd,Abbott Laboratories,Zydus Cadilla	8	ACCUCARE IgM/IgG Lateral Flow Assay kit: LAB-CARE Diagnostics (India Pvt. Ltd)
2	COVID-19 IgM IgG Rapid Test: BioMedomics (CE-IVD)	9	Abchek COVID-19 IgM/IgG Antibody Rapid Test: NuLifecare
3	COVID-19 IgM/IgG Antibody Rapid Test: ZHUHAI LIVZON DIAGNOSTICS (CE-IVD)	10	One Step Corona Virus (COVID-19) IgM/IgG Antibody Test: ALPINE BIOMEDICALS
4	New Coronavirus (COVID-19) IgG/IgM Rapid Test: Voxtur Bio Ltd, India	11	COVID 19 IgM/IgG Rapid Test Kit; Medsource Ozone Biomedicals (ver 2.0)
5	COVID-19 IgM/IgG Antibody Detection Card Test: VANGUARD Diagnostics, India	12	Immuno Quick Rapid Test for Detection of Novel Coronavirus (COVID-19) IgM/IgG Antibodies: Immuno Science India Pvt. Ltd
6	Makesure COVID-19 Rapid test: HLL Lifecare Limited, India	13	Standard Q Covid -19 IgM/IgG Duo test – One Step Rapid Antibody test: SD Biosensors
7	YHLO iFlash-SARS-CoV-2 IgM and IgG detection kit (additional equipment required): CPC Diagnostics	14	COVID-19 IgG/IgM Rapid Test Kit Rafael Diagnostic: BMT Diagnostics

- **Pool testing:** ICMR suggested pool testing to increase testing capacity in the country. Recommendation from ICMR's feasibility study on pool testing makes the following suggestion (ICMR & DHR, 2020b).
  - Number of samples to be pooled in a PCR test should not exceed 5 to avoid false negatives.
  - Recommended in areas where prevalence of positive cases is low, and not for the areas with positivity rates of >5%
  - Can be considered for community survey or surveillance among asymptomatic individuals, excluding individuals who have reported to have direct contact with confirmed cases, health workers involved in treatment and screening. In those case individual samples should be tested.
- The Indian state of Uttar Pradesh will be the first state in the country to attempt pool testing to expedite the COVID-19 testing process. Likewise, another state of Maharashtra has also sought permission to adopt this modality of mass testing. The method involves placing multiple swabs together in a pool to test using a single RT-PCR test. (Gaur, 2020)
- **Collaboration with private laboratories:** The Indian government has decided to engage available private laboratories (BSL 2 following BSL 3 precautions) along with government laboratories to collect/test samples following quality assurance and safety protocols (Government of India, 2020). As of 13 April 2020, ICMR has listed 70 private sector laboratories for sample collection and testing in addition to 159 government facilities (ICMR & DHR, 2020a).

Reference

Abbott Molecular Inc. (2020). Abbott RealTime SARS-CoV-2. Retrieved from https://www.molecular.abbott/sal/9N77-095_SARS-CoV-2_US_EUA_Amp_PI.pdf?fbclid=IwAR2iiMOqLkjurqIioOEw76VqQc7UfgEN1X4w76crOV8Vj6nHJzxzCLXC_dc.

Bwire, G. M., & Paulo, L. S. (2020). Coronavirus disease-2019: is fever an adequate screening for the returning travelers? *Tropical Medicine and Health, 48*(1), 14. doi:10.1186/s41182-020-00201-2

Cepheid. (2020). Xpert® Xpress SARS-CoV-2. Retrieved from https://www.fda.gov/media/136314/download

Duchâtel, M., Godement, F., Trichard, F., & Zhu, V. (2020). Fighting the Coronavirus Pandemic, East Asian Responses - Republic of Korea: Mass-testing, targeted investigations and the transparency issue. Retrieved from https://www.institutmontaigne.org/en/blog/fighting-coronavirus-pandemic-east-asian-responses-republic-korea-mass-testing-targeted

Eckner, C. (2020). How Germany has managed to perform so many Covid-19 tests. Retrieved from https://www.spectator.co.uk/article/how-germany-has-managed-to-perform-so-many-covid-19-tests
Gaur, V. (2020). Uttar Pradesh to start pool testing for Covid-19 to expedite process. Retrieved from https://economictimes.indiatimes.com/news/politics-and-nation/uttar-pradesh-to-start-pool-testing-for-covid-19-to-expedite-process/articleshow/75122742.cms
Gostic, K., Gomez, A. C. R., Mummah, R. O., Kucharski, A. J., & Lloyd-Smith, J. O. (2020). Estimated effectiveness of symptom and risk screening to prevent the spread of COVID-19. *eLife, 9*, e55570. doi:10.7554/eLife.55570
Hall, B., & Buck, T. (2020). Germany conducting more than 50,000 coronavirus tests a day. Retrieved from https://www.ft.com/content/6a8d66a4-5862-4937-8d53-b2d10794e795
Hohn, C. (2020). Rapid COVID-19 diagnostic test developed by Cambridge team to be deployed in hospitals. Retrieved from https://www.cam.ac.uk/research/news/rapid-covid-19-diagnostic-test-developed-by-cambridge-team-to-be-deployed-in-hospitals
Indian Council of Medical Research, & Department of Health Research. (2020a). Advisory to start rapid antibody based blood test for COVID-19 (4 April 2020). Retrieved from https://www.mohfw.gov.in/pdf/Advisory&StrategyforUseofRapidAntibodyBasedBloodTest.pdf
Indian Council of Medical Research, & Department of Health Research. (2020b). Advisory on feasibility of using pooled samples for molecular testing of COVID-19. Retrieved from https://icmr.nic.in/sites/default/files/upload_documents/Advisory_on_feasibility_of_sample_pooling.pdf
Indian Council of Medical Research [ICMR]. (2020). Guidance on Rapid antibody kits for COVID-19. Retrieved from https://icmr.nic.in/sites/default/files/upload_documents/Antibody_based_tests_16042020.pdf
Jiang, G., Ren, X., Liu, Y., Chen, H., Liu, W., Guo, Z., . . . Shan, H. (2020). Application and optimization of RT-PCR in diagnosis of SARS-CoV-2 infection. *medRxiv*, 2020.2002.2025.20027755. doi:10.1101/2020.02.25.20027755
Johns Hopkins Center for Health Security. (2020). Serology-based tests for COVID-19. Retrieved from https://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html?fbclid=IwAR169Mh16Lix_r6dQe9iGH01G0BkzBAxt-wkN05l_BcSdizE0bMqgqsq9vs
Kim, D. (2020). The Story Behind South Korea's 'Aggressive' COVID-19 Testing. Retrieved from https://www.asiapacific.ca/publication/story-behind-south-koreas-aggressive-covid-19-testing
Kim, M. S. (2020). South Korea is watching quarantined citizens with a smartphone app. Retrieved from https://www.technologyreview.com/2020/03/06/905459/coronavirus-south-korea-smartphone-app-quarantine/
Lee, V., Chiew, C., & Khong, W. (2020). Interrupting transmission of COVID-19: lessons from containment efforts in Singapore. *Journal of Travel Medicine*. doi:10.1093/jtm/taaa039
Li, Z., Yi, Y., Luo, X., Xiong, N., Liu, Y., Li, S., . . . Chen, W. J. J. o. m. v. (2020). Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis.
Ministry of Health and Family Welfare, & Government of India. (2020). Containment Plan for Large Outbreaks Novel Coronavirus Disease 2019 (COVID-19). Retrieved from https://www.mohfw.gov.in/pdf/3ContainmentPlanforLargeOutbreaksofCOVID19Final.pdf
Republic of Korea. (2020). *Current Status of Response to COVID-19 and Future Plans*. Republic of Korea: Ministry of Health and Welfare Retrieved from http://ncov.mohw.go.kr/en/infoBoardView.do?brdId=15&brdGubun=151&dataGubun=&ncvContSeq=1267&contSeq=1267&board_id=&gubun=.
Morris, C. (2020). Coronavirus: What can the UK learn from Germany on testing? Retrieved from https://www.bbc.com/news/health-52234061
PharmACT. (2020). SARS COV-2 Rapid test. Retrieved from https://pharmact-health.com/en/sars-cov-2-rapid-test/
Pulla, P. (2020). Covid-19: India imposes lockdown for 21 days and cases rise. In: British Medical Journal Publishing Group.
Reisinger, D. (2020). Germany has remarkably few COVID-19 deaths. Its healthcare system shows how Germany prevented a runaway death toll. *Business insiders*. Retrieved from https://www.businessinsider.com/why-germany-has-a-low-covid-19-mortality-rate-2020-4
Sugentech. (2020). COVID-19 IgM/IgG. Retrieved from https://sugentech.com/products/products-view.php?ct=7&target=32
University of Oxford. (2020). Oxford scientists develop rapid testing technology for COVID-19. Retrieved from http://www.ox.ac.uk/news/2020-03-18-oxford-scientists-develop-rapid-testing-technology-covid-19#
Zhang, Y., Odiwuor, N., Xiong, J., Sun, L., Nyaruaba, R. O., Wei, H., & Tanner, N. A. (2020). Rapid Molecular Detection of SARS-CoV-2 (COVID-19) Virus RNA Using Colorimetric LAMP. *medRxiv*, 2020.2002.2026.20028373. doi:10.1101/2020.02.26.20028373
Zhao, R., Li, M., Song, H., Chen, J., Ren, W., Feng, Y., . . . Sun, L. (2020). Serological diagnostic kit of SARS-CoV-2 antibodies using CHO-expressed full-length SARS-CoV-2 S1 proteins. *medRxiv*, 2020.2003.2026.20042184. doi:10.1101/2020.03.26.20042184
Zhihua, L. (2020). Chinese testing kit exports soar as COVID-19 spreads. Retrieved from https://en.wondfo.com.cn/2020/03/18/chinese-testing-kit-exports-soar-as-covid-19-spreads/

Acknowledgement

This evidence note is the product of the knowledge café meeting presentation and discussion organized by the knowledge café secretariat at PPMD, MoHP on 17 April 2020. Under the aegis of PPMD, DFID Nepal Health Sector Programme 3 (NHSP3), Monitoring, Evaluation and Operational Research (MEOR) project provided technical assistance to produce the evidence note. The views expressed in the material do not necessarily reflect the views of DFID nor the UK Government.