

Take2

Take2 Health Limited



Company Overview

Company overview



- Headquartered in Hong Kong SAR, China
- Founded by world-class scientists from The Chinese University of Hong Kong
- Licensed Nasopharyngeal Cancer (NPC) technologies from a leading cancer detection company in Silicon Valley, US

Our vision

“Empowering · Actionable · Timely”

Take2 delivers empowering, actionable and timely information and solutions for individuals and communities to maintain health and combat diseases.

Common Blood Tests for EBV Detection

Common blood tests for EBV detection

1. EBV Serological Test:
 - Viral Capsid Antigen (VCA) IgA
 - Early Antigen (EA) IgA
 - Epstein-Barr Nuclear Antigen 1 (EBNA1) IgA
2. Plasma EBV DNA:
 - Quantitative PCR

EBV serological test

Hong Kong experience: Screening for family members of NPC patients by VCA IgA and EBNA1 IgA.

- Relative risk for positive serology: 30.2
- Stage I disease: 41% (screening) vs 2% (hospital referral)
- Sensitivity: 75%
- Specificity: 92%

Serological status	Number of subjects	NPC detected at first visit	NPC detected at subsequent visits
Positive	84	6	3
Negative	845	0	3
Total	929	6	6

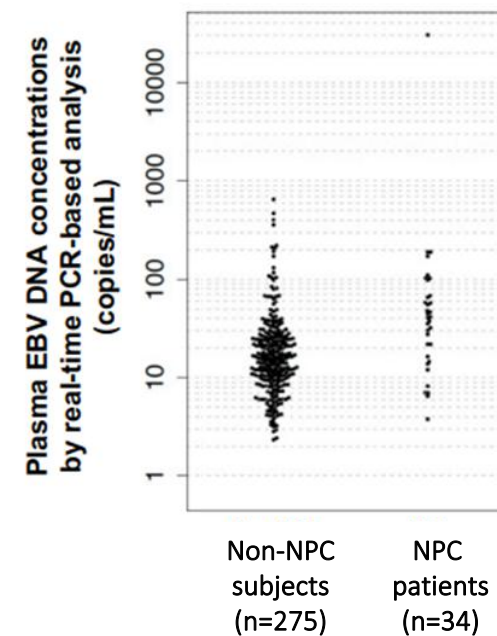
Int. J. Cancer, 113, 2005.

Plasma EBV DNA: Quantitative PCR

- Sensitivity: 81.4%
- Specificity: 96.6%
- PPV: 3.1%
- False positive rate: 3.4%

Limitation:

- Cannot rule out transient infection.



Oral Oncology, 44(8), 2008.
Proc. Natl. Acad. Sci. USA, 115(22), 2018.

Common blood tests for EBV detection

- EBV serology test and quantitative EBV DNA test are commonly used for the characterization of EBV infection
- EBV infection \neq NPC
- There was no large-scale clinical study on the application of EBV serology and quantitative EBV DNA tests for early NPC screening in asymptomatic individuals

Technologies of Take2 Prophecy

Take2 Prophecy's uniqueness lies in our state-of-the-art technologies

A combination of both NGS and qPCR is required for an accurate test with fast result reporting; and only a single blood draw is needed

Real-time PCR
(qPCR)

traditional
testing method

Take2
Prophecy

NPC early
detection test

Next-Generation
Sequencing (NGS)

New & advanced
method

Take2 Prophecy was proven robust in a large-scale prospective clinical study

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

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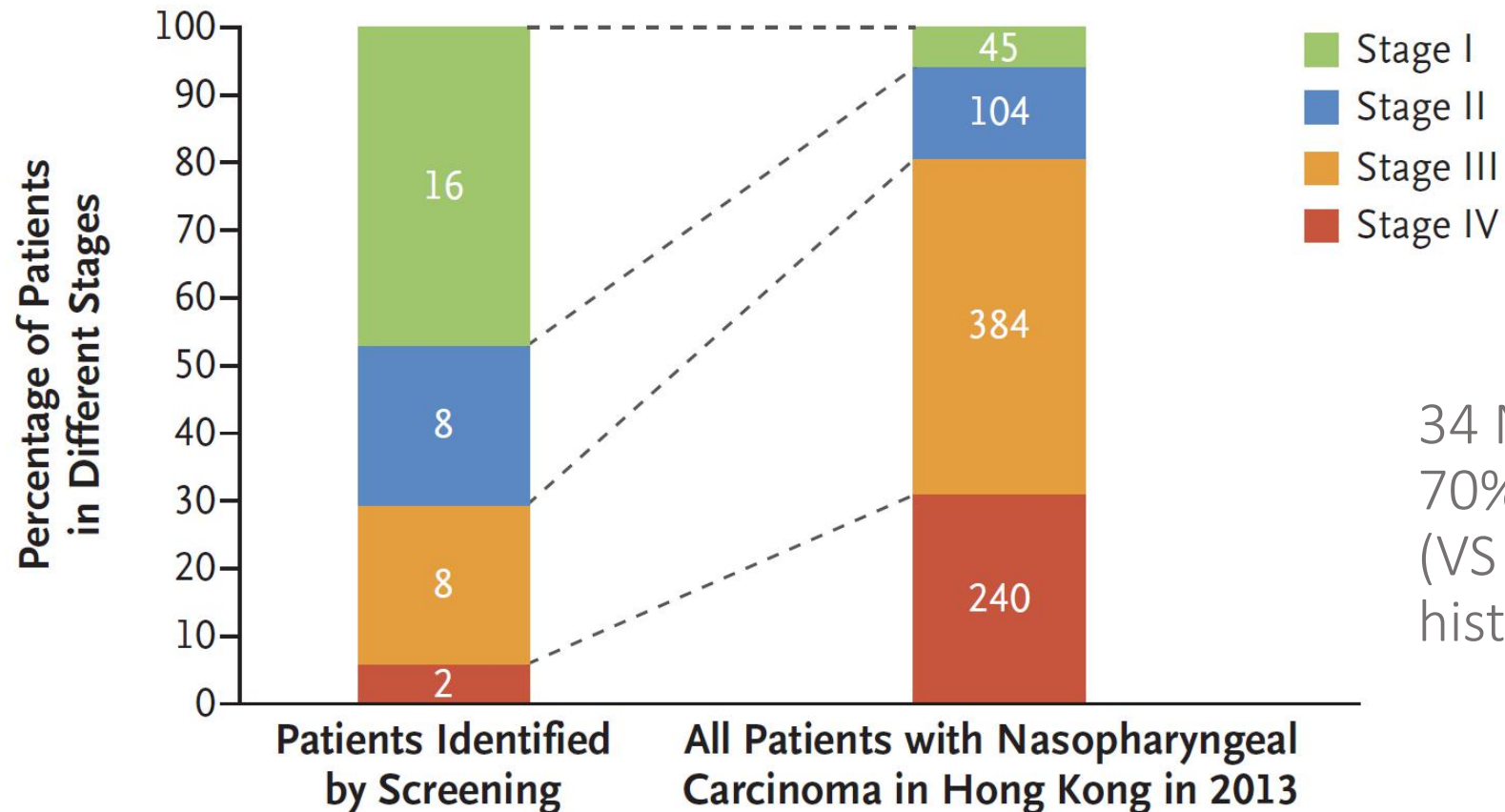
Analysis of Plasma Epstein–Barr Virus DNA to Screen for Nasopharyngeal Cancer

K.C. Allen Chan, F.R.C.P.A., John K.S. Woo, F.R.C.S., Ann King, F.R.C.R., Benny C.Y. Zee, Ph.D., W.K. Jacky Lam, F.R.C.S., Stephen L. Chan, F.R.C.P., Sam W.I. Chu, B.Sc., Constance Mak, B.S.N., Irene O.L. Tse, B.N., Samantha Y.M. Leung, B.N., Gloria Chan, R.N., Edwin P. Hui, F.R.C.P., Brigette B.Y. Ma, M.D., Rossa W.K. Chiu, F.R.C.P.A., Sing-Fai Leung, F.R.C.R.,* Andrew C. van Hasselt, F.R.C.S., Anthony T.C. Chan, F.R.C.P., and Y.M. Dennis Lo, F.R.S.

- >20,000 tested subjects
- No symptoms of NPC at enrollment
- Screened positive subjects were all investigated with endoscopy and/ MRI for confirmation
- Longitudinal follow-up for at least 3 years after testing

Take2 Prophecy demonstrated a stage shift

A Stage Distribution of Patients with Nasopharyngeal Carcinoma

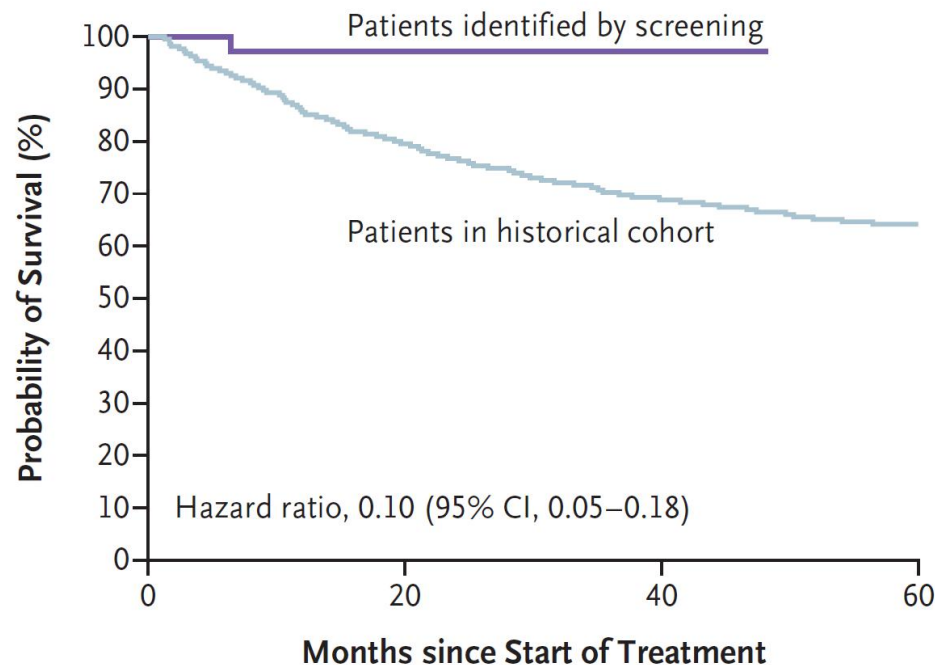


34 NPC cases diagnosed and 70% were early stage NPC (VS 70% were late stage in historical cohort)

Chan, KC Allen, et al. "Analysis of plasma Epstein–Barr virus DNA to screen for nasopharyngeal cancer." New England Journal of Medicine 377.6 (2017): 513-522.

Patients identified through early cancer screening had a significantly better prognosis

B Progression-free Survival



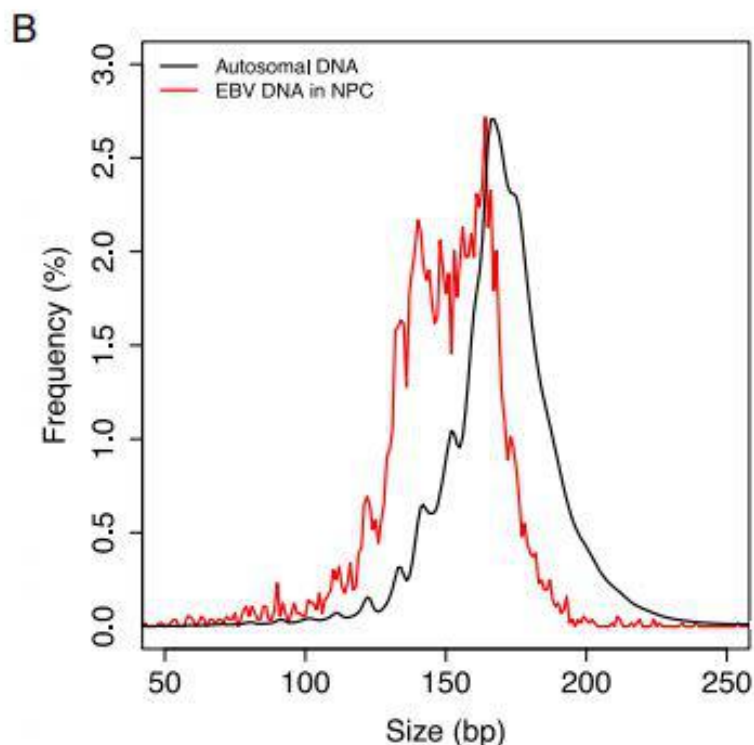
The 3-year progression-free survival of patients identified by screening was superior

No. at Risk

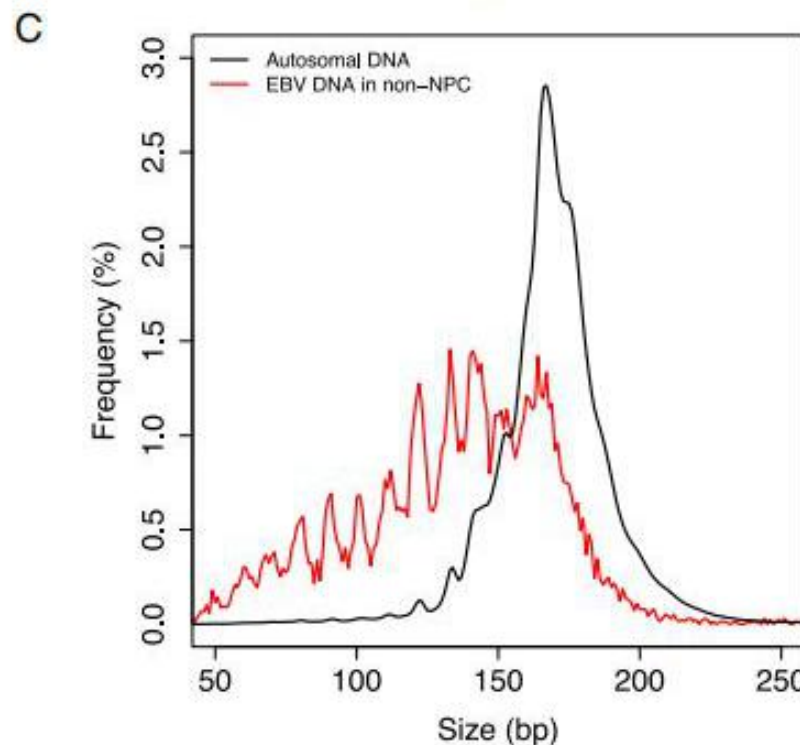
	0	20	40	60
Patients identified by screening	34	28	9	0
Patients in historical cohort	1278	902	520	241

Chan, KC Allen, et al. "Analysis of plasma Epstein–Barr virus DNA to screen for nasopharyngeal cancer." New England Journal of Medicine 377.6 (2017): 513-522

Sequencing-based counting and size profiling of plasma Epstein–Barr virus DNA enhance population screening of NPC



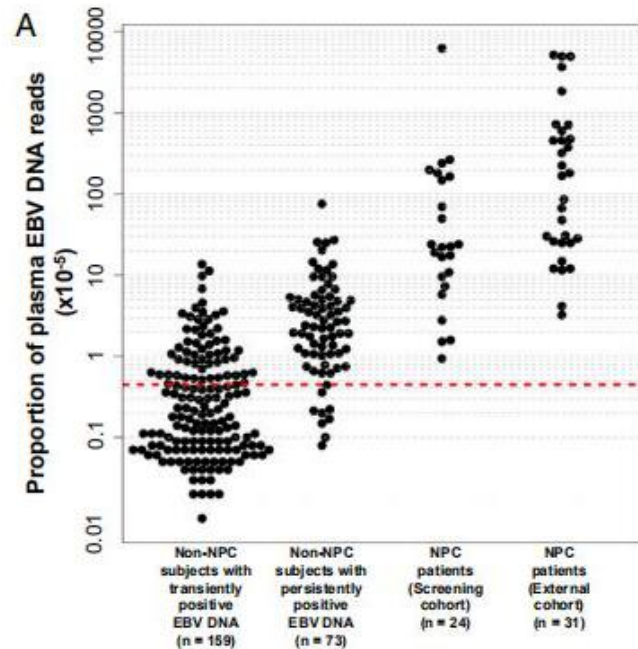
(B) Size distributions of EBV DNA (red curve) and autosomal DNA (black curve) in the plasma of a patient with NPC.



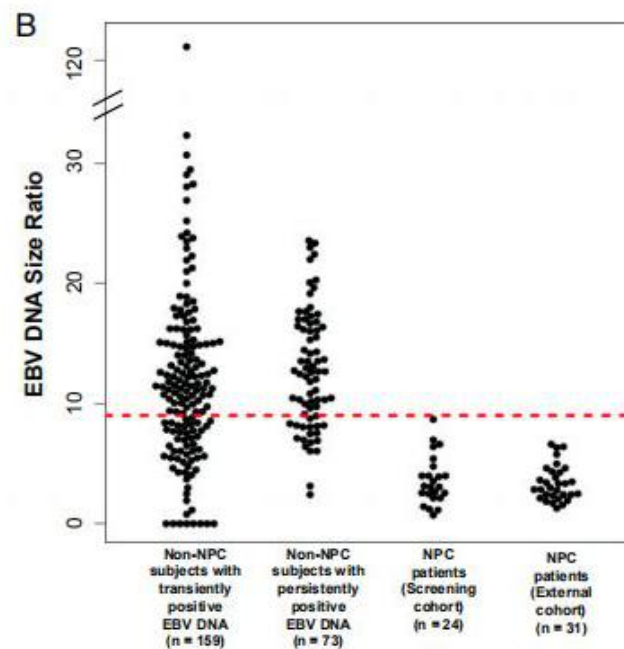
Size distributions of EBV DNA (red curve) and human autosomal DNA (black curve) in a non-NPC subject with persistently positive plasma EBV DNA results.

The size profile of the EBV DNA in NPC patient is different from non-NPC patient

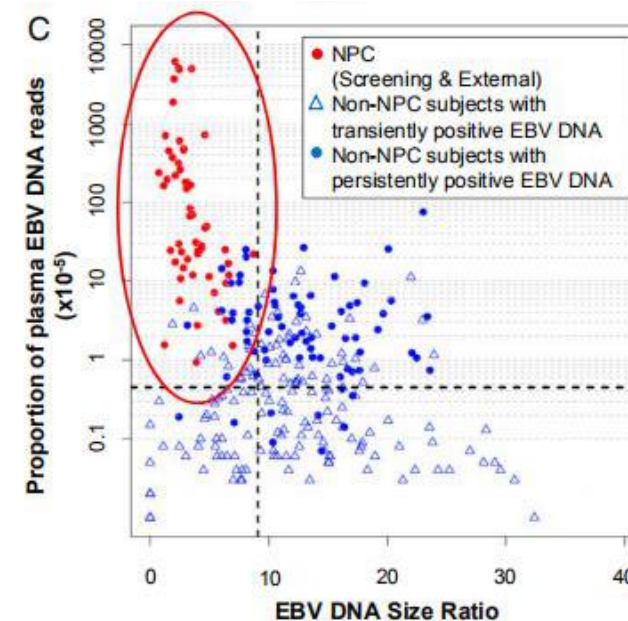
A modified analysis combining sequencing-based counting and size profiling further reduces false positive rate



(A) The proportions of plasma EBV DNA reads of the NPC patients and non-NPC subjects are shown. The same cutoff value of 4.5×10^{-6} defined in exploratory dataset is denoted by the red dotted line.



(B) The EBV DNA size ratios of the NPC patients and non-NPC subjects are shown. The same cutoff value of 9.1 defined in the exploratory dataset is denoted by the red dotted line.



(C) Plot of the proportions of plasma EBV reads and corresponding size ratio values for all of the cases in the validation sample set. The same cutoff values in the count- and size-based analyses defined in the exploratory sample set are denoted by the gray dotted lines. The red oval highlights the quadrant with cases that passed the cutoffs in the combined count- and size-based analysis.

The viral load of EBV DNA in NPC patients is different from that in non-NPC patients

Lam, WK Jacky, et al. "Sequencing-based counting and size profiling of plasma Epstein-Barr virus DNA enhance population screening of nasopharyngeal carcinoma." Proceedings of the National Academy of Sciences 115.22 (2018): E5115-E5124.

Comparison between Take2 Prophecy and other EBV blood tests

	Detection Technologies		
Name or description of the test	Take2 Prophecy Test for NPC	Other tests for viral DNA of EBV without clinical validation for NPC early detection	EBV Serology Test
Key feature	NPC-associated genomic signatures of human and EBV DNA	EBV DNA quantitative results	EBV IgA-VCA (Antibody testing)
False positive rate	0.7%	3.4%	1-40%
Detection rate	97.1%	81.4%	42.9-92.7%
	Validated for early NPC screening with large-scale clinical trial		

Lam, WK Jacky, et al. "Sequencing-based counting and size profiling of plasma Epstein-Barr virus DNA enhance population screening of nasopharyngeal carcinoma." *Proceedings of the National Academy of Sciences* 115.22 (2018): E5115-E5124.

Chan, KC Allen, et al. "Analysis of plasma Epstein-Barr virus DNA to screen for nasopharyngeal cancer." *New England Journal of Medicine* 377.6 (2017): 513-522. Lam, WK Jacky, et al. "Sequencing-based counting and size profiling of plasma Epstein-Barr virus DNA enhance population screening of nasopharyngeal carcinoma." *Proceedings of the National Academy of Sciences* 115.22 (2018): E5115-E5124.

Tay JK, Lim MY, Kanagalingam J. Screening in Nasopharyngeal Carcinoma: Current Strategies a Future Directions. *Current Reports*. 2013;2(1):1-7. doi:10.1007/s40136-013-0035-4.

Value propositions

 is an early cancer detection test for NPC. It is clinically proven to detect early stage cancers in asymptomatic individuals which

- ✓ Reduce complexity of possible forth-coming cancer treatment and thus total medical expense
- ✓ Improve survival rate of NPC patients



隱形殺手
鼻咽癌

正視鼻咽癌風險

在東南亞和南中國，特別是廣東，廣西和香港，鼻咽癌(NPC)的發病率特別高，所以鼻咽癌被稱為“廣東癌”。香港每年有超過800名新的鼻咽癌病例，因此鼻咽癌是不可忽視的十大癌症殺手之一。

The test was proven robust and the technology was published in medical/scientific journals

Non-invasiveness

Requires a single blood draw only

High accuracy

Demonstrates 97% sensitivity at 99% specificity

World-leading technology

Applies patented sequencing technology

Clinical application

Validated in large-scale clinical study on asymptomatic population



Analysis of Plasma Epstein–Barr Virus DNA to Screen for Nasopharyngeal Cancer

K.C. Allen Chan, F.R.C.P.A., John K.S. Woo, F.R.C.S., Ann King, F.R.C.R., Benny C.Y. Zee, Ph.D., W.K. Jacky Lam, F.R.C.S., Stephen L. Chan, F.R.C.P., Sam W.I. Chu, B.Sc., Constance Mak, B.S.N., Irene O.L. Tse, B.N., Samantha Y.M. Leung, B.N., Gloria Chan, R.N., Edwin P. Hui, F.R.C.P., Brigitte B.Y. Ma, M.D., Rossa W.K. Chiu, F.R.C.P.A., Sing-Fai Leung, F.R.C.R.,[†] Andrew C. van Hasselt, F.R.C.S., Anthony T.C. Chan, F.R.C.P., and Y.M. Dennis Lo, F.R.S.

Sequencing-based counting and size profiling of plasma Epstein–Barr virus DNA enhance population screening of nasopharyngeal carcinoma

W. K. Jacky Lam^{a,b,c,d,1}, Peiyong Jiang^{a,b,c,1}, K. C. Allen Chan^{a,b,c,1}, Suk H. Cheng^{a,b}, Haiqiang Zhang^{a,b}, Wenlei Peng^{a,b}, O. Y. Olivia Tse^{a,b}, Yu K. Tong^{a,b}, Wanxia Gai^{a,b}, Benny C. Y. Zee^e, Brigitte B. Y. Ma^{c,f}, Edwin P. Hui^{c,f}, Anthony T. C. Chan^{c,f}, John K. S. Woo^d, Rossa W. K. Chiu^{a,b,c}, and Y. M. Dennis Lo^{a,b,c,2}

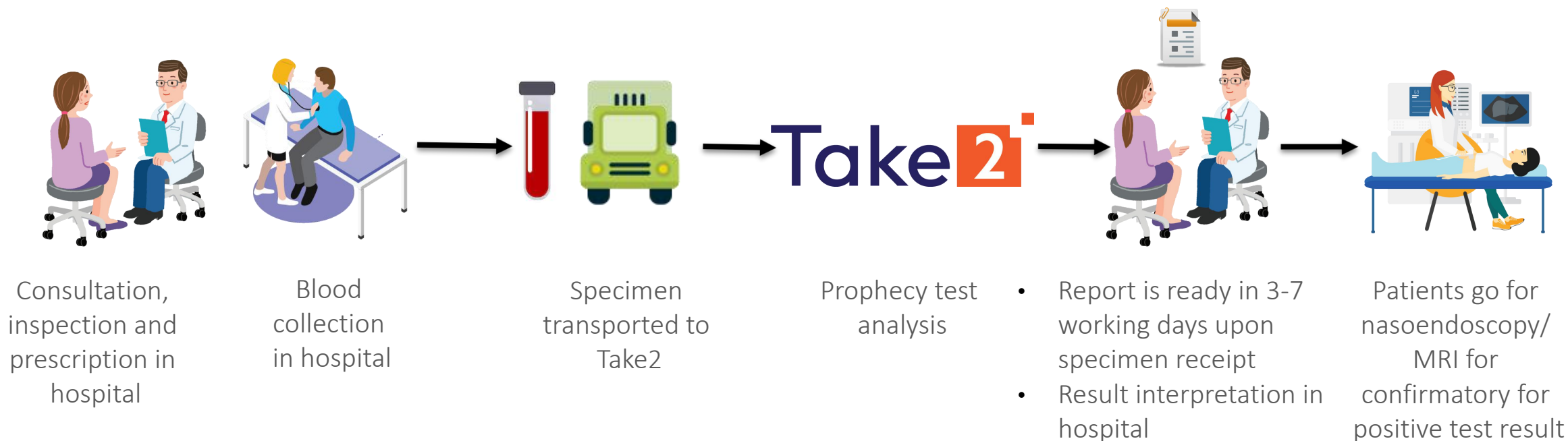
^aLi Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong; ^bDepartment of Chemical Pathology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong; ^cState Key Laboratory in Oncology in South China, Sir Y. K. Pao Centre for Cancer, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong; ^dDepartment of Otorhinolaryngology, Head and Neck Surgery, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong; ^eJockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong; and ^fDepartment of Clinical Oncology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong

Contributed by Y. M. Dennis Lo, April 26, 2018 (sent for review March 13, 2018; reviewed by Luis Diaz and Klaus Pantel)

Usage angles of doctors in different specialties

Specialty	Examples of how doctors use Prophecy	Reasons
General Practitioners & Family Medicine doctors	Use as regular health checks especially for men	Clinically proven for asymptomatic individuals for early NPC screening <ul style="list-style-type: none"> Targeted healthy middle-aged men in NEJM study More accurate blood-based screening test <ul style="list-style-type: none"> False positive rate <0.7% Positive Predictive Value(PPV):19.5%
	Use for suspected cases to replace serology and EBV DNA test	
Otorhinolaryngologists (ENT)	Offer the test with nasal endoscopy as a package	To minimize missing cases in 5-10% submucosal conditions
	Offer another option for high risk family members without symptoms	More accurate blood-based screening test <ul style="list-style-type: none"> False positive rate <0.7% Positive Predictive Value(PPV): 19.5%
	Use for suspected NPC patients who do not want to have nasal endoscopy	Clinically proven for asymptomatic individuals for early NPC screening

Patient journey



- “Positive” result: “NPC-associated DNA patterns were DETECTED.”
- “Negative” result: “NPC-associated DNA patterns were NOT DETECTED.”

Materials for requesting a test

Take2 Prophecy Test for NPC

Test Requisition Form

SPECIMEN INFORMATION (To be completed by blood draw site)

BLOOD DRAW DATE (dd-mm-yyyy) _____ BLOOD DRAW TIME (hh:mm) _____
 AM PM

PATIENT INFORMATION (Affix label if available)

PATIENT NAME (Surname, Given Name(s)) _____ SEX (Check one box only)
 Male Female

DATE OF BIRTH (dd-mm-yyyy) _____ OTHER REFERENCE ID (Patient) _____
 MRN No. or PASSPORT No. _____ HKID No. Passport No. (Country: _____)

TEST ORDERED

NPCGSA - Take2 Prophecy for NPC
 NPCGSA - Take2 Prophecy for NPC plus pHLBiotomy
 NPCD2 - Take2 NPC Monitoring Test (reporting quantitative result of gPCR only)

NPCD2P - Take2 Cancer Screening Package (Please perform the pHLBiotomy service on one of the partnering labs, as indicated in the list of partnering labs for cancer screening package)

AUTHORIZATION

I, the undersigned, certify that I have explained to the patient the nature and purpose of the testing to be performed, including the risks, benefits, limitations, and alternatives, and have obtained informed consent to permit TAKE2 Health Ltd. or its affiliates to perform the testing and use the patient's specimens, results, and data as specified herein and in the Take2 Prophecy consumer educational brochure. I acknowledge the terms and conditions located at take2.health/terms-and-conditions.

ORDERING CLINICIAN (Signature) _____ DATE OF AUTHORIZATION (dd-mm-yyyy) _____
 ORDERING CLINICIAN (Print name) _____ INSTITUTION _____
 ORDERING CLINICIAN ADDRESS (If different from specimen pickup site) _____

TAKE2 Customer Support
 Tel: +852 3633 0534
 Fax: +852 3633 0534
 Email: customer.support@take2.health

LABORATORY USE ONLY
 PATIENTS LAB ID: _____

Test Requisition Form (TRF)

Take2 Participant's Profile Number: _____
 (for Take2 Use 僅供Take2內部使用)

Consent Form 同意書

Take2 Health Limited ("Take2") requires your written consent to perform the "Take2 Prophecy Test for NPC" & "Take2 Prophecy Early Cancer Detection Package", 詳情請參閱取樣公司（「取樣機構」）索取您的取樣指南才能執行「Take2 Prophecy 早期癌篩檢服務」及「Take2 Prophecy 早期腫瘤偵測服務」。

Participant Information 參與者資料

Name 姓名: _____
 (Surname 姓氏) (Given Name 名字) (Chinese Name 中文姓名)

HKID Card No. 香港身份證號碼 (7位或8位數的號碼): _____

Passport No. & Place of Issuance 護照號碼及簽發地方: _____
 (Please provide your passport number if you do not have an HKID card 請提供護照號碼，如沒有香港身份證)

Birth Month and Year 出生月份及年份: _____ Gender 性別: _____

Contact Number 聯絡電話: _____ Email 電郵地址: _____

By signing this Consent Form, I confirm receipt of the Take2 Welcome Pack, which contains information concerning the "Take2 Prophecy Test for NPC" and "Take2 Prophecy Early Cancer Detection Package". I understand that the Take2 Welcome Pack and related documents are for informational purposes only and acknowledge that they do not constitute and are never intended to be a substitute for qualified medical advice. I have sought professional advice and acknowledge the nature, purpose and limitations of such relevant tests. I have also read the Personal Information Collection Statement and Privacy Policy Statement of Take2, and consent to the collection, use, processing and/or transfer of my personal data by Take2 in accordance with the terms thereof, including Take2's use of my blood specimen for conducting the relevant tests and any deidentified results and residual specimen for internal evaluation, education and/or medical research purposes.

透過簽署本同意書，本人確認收到包含「Take2 Prophecy 早期癌篩檢服務」及「Take2 Prophecy 早期腫瘤偵測服務」之工具的「Take2 歡迎包」。本人了解該歡迎包及相關文件僅供參考用途，並非構成或應被視為合格醫療人員的醫療建議。本人已閱讀本人之同意書並知悉有關醫療服務的性質、效用以及其限制。本人亦已閱讀得悉有關服務個人資料收集聲明及隱私政策聲明，並同意將血液樣本用於相關測試、教育及/或醫學研究之用。

I further agree to receive and participate in the selected services and products below. (Please put a ✓ in the appropriate box to opt-in/opt-out services/products)
 本人進一步同意進行下列本人所選擇之服務或產品。請選擇接受或拒絕，並在相關的方格內填上「✓」。

I agree to join Take2 Extra Care. I have read and accept the Take2 Extra Care Terms & Conditions.
 本人同意加入 Take2 Extra Care 計劃。我已閱讀及接受其相關條款及細則。

I wish to receive health-related information, new product information, marketing communications and promotional materials from Take2 via: (please tick all applicable options)
 本人希望透過以下途徑獲取有關健康服務提供的健康資訊、最新產品、市場推廣及宣傳活動資訊。(請選擇所有適用選項)

Email 電郵 SMS 短訊 Telephone Call 電話 WhatsApp 通訊 WeChat 微信 (WeChat ID 微信號: _____)

If the Participant is below 18 years old or a mentally incapacitated person, this Consent Form should be signed by the legal guardian. As the legal guardian, by signing this Consent Form and providing the Participant's personal data, you hereby consent to our processing of his/her personal data as set forth in this Consent Form and agree to be bound by the terms hereof.
 如果參與者是未滿 18 歲或精神上無行為能力的人，則此同意書應由法定代理人簽署。作為法定代理人，簽署此同意書或提供參與者的個人資料，即表示你同意我們按照此同意書中所列的方式處理個人資料，並同意接受本同意書的條款。

In the event of any inconsistency between the English version and the Chinese version of this Consent Form, the English version shall prevail.
 如本同意書的英文版本與中文版本存在任何歧義，則以英文版本為準。

Participant's / Guardian's Name in Print _____ Signature of Participant or Guardian _____ Date of Signature _____
 參與者 / 監護人姓名：_____ 參與者 / 監護人簽署：_____ 簽署日期：_____

PH-19-0023-01

Consent Form



2 x 8.5ml Roche Cell-Free DNA Collection tubes

Take2 Prophecy reports

“Positive” result: “NPC-associated DNA patterns were **DETECTED**.”

“Negative” result: “NPC-associated DNA patterns were **NOT DETECTED**.”

- Follow-up consultation with ENT doctors if the result is positive
- Regular screening if the result is negative

Confirmatory test for NPC such as nasal endoscopy is recommended

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Page 1 of 1

PATIENT NAME	HO, TAK YEE CUTIE
DATE OF BIRTH	01 Jan 1982
HKID No./ PASSPORT No.	2123456(7)
OTHER REFERENCE ID	-
REPORT ID	20F000-0-01
BLOOD DRAW DATE/ TIME	11 May 2020 15:06
REPORT DATE/ TIME	15 May 2020 15:06

CLINICAL INFORMATION

ORDERING CLINICIAN	ORDERING SITE
DR. ABC	Medical Centre

SAMPLE TYPE

Plasma DNA

TEST RESULT

NPC-associated DNA patterns were **DETECTED.**

“Take2 Prophecy Test for NPC” is a test that analyzes blood to detect the presence of DNA patterns associated with nasopharyngeal carcinoma (NPC). Based on NPC screening clinical studies carried out by The Chinese University of Hong Kong^{1,2} on 20,174 asymptomatic male subjects with age between 40 - 62, the performance is as follows:

Sensitivity 97.1%
Specificity 99.3%
Positive predictive value 19.5%
*(i.e. 19.5% subjects **WITH DETECTABLE** NPC-associated DNA patterns were confirmed to have NPC.)*

COMMENTS

Further confirmatory test for NPC, for example nasal endoscopy, is recommended.

This test was performed by The Chinese University of Hong Kong. This is a transcribed report based on the result from University Pathology Service, The Chinese University of Hong Kong.

Please contact Take2 at +852 3613 0536 to discuss any questions regarding this result. The patient's clinical history and test results are private information, and should not be disclosed to a third party, without the patient's authorization, except where permitted by law. The result of this lab report should be interpreted in the context of the patient's medical history and other diagnostic evidence. For more information concerning the limitations of the Take2 Prophecy Test for NPC, please refer to our website at www.take2.health or the Take2 Prophecy consumer educational brochure. It is strongly recommended that these results be communicated to the patient together with medical advice on the required follow-up actions.

References:

1. Chan et al. (2017) *N Engl J Med* 377(6):513-522.
2. Lam et al. (2018) *PLoS ONE* 13(2): e0181151.

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REPORT DATE/ TIME	15 May 2020 15:06

CLINICAL INFORMATION

ORDERING CLINICIAN	ORDERING SITE
DR. ABC	Medical Centre

SAMPLE TYPE

Plasma DNA

TEST RESULT

NPC-associated DNA patterns were **NOT DETECTED.**

“Take2 Prophecy Test for NPC” is a test that analyzes blood to detect the presence of DNA patterns associated with nasopharyngeal carcinoma (NPC). Based on NPC screening clinical studies carried out by The Chinese University of Hong Kong^{1,2} on 20,174 asymptomatic male subjects with age between 40 - 62, the performance is as follows:

Sensitivity 97.1%
Specificity 99.3%
Negative predictive value >99.99%
*(i.e. only 1 out of approximately 20,000 subjects with **NO DETECTABLE** NPC-associated DNA patterns was confirmed of having NPC within 1 year of testing.)*

COMMENTS

NIL

This test was performed by The Chinese University of Hong Kong. This is a transcribed report based on the result from University Pathology Service, The Chinese University of Hong Kong.

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References:

1. Chan et al. (2017) *N Engl J Med* 377(6):513-522.
2. Lam et al. (2018) *PLoS ONE* 13(2): e0181151.

Please contact our Sales Team for details. Thank you for your kind consideration.

Anne Tam

Sales Manager

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Email: annebelle.tam@take2.health