Contents

1 Model Overview **2**
- 1.1 Hierarchical Models . . . 2
- 1.2 Cancer Incidence . . . 3
- 1.3 Stage Distribution . . . 3
- 1.4 Maximum Achievable Survival . . . 9
- 1.5 Modality Efficacy . . . 10
  - 1.5.1 Priors . . . 10
  - 1.5.2 Consensus Results . . . 11
  - 1.5.3 Modern Modalities . . . 11
- 1.6 Treatment Availability . . . 12
- 1.7 Imaging Availability . . . 13
- 1.8 Quality of Care . . . 13

2 Model Calibration **14**
- 2.1 Calibration Overview . . . 14
- 2.2 Model Performance . . . 14
  - 2.2.1 Training Set Comparisons . . . 14
  - 2.2.2 Testing Set Comparisons . . . 17

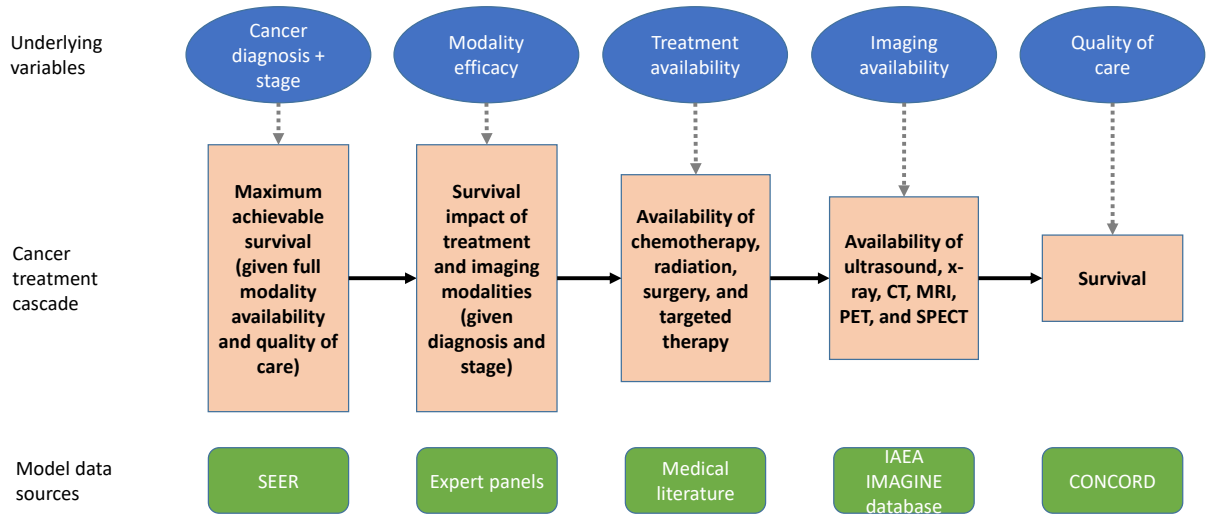
3 Calibrated Treatment Impact Parameters **18**

4 Additional Results **20**

1 Model Overview

We briefly describe here a previously developed microsimulation (individual-level) model of global cancer survival - see Ward 2020 for more details. The model simulates survival for 11 cancers in 200 countries/territories. The cancer sites were selected based on which comparable topography codes from the International Classification of Diseases for Oncology (3rd edition) were available in both GLOBOCAN 2018 and CONCORD-3: oesophagus (C15), stomach (C16), colon (C18), rectum (C19–20), anus (C21), liver (C22), pancreas (C25), lung (C33–34), breast (C50), cervix uteri (C53), and prostate (C61). The model simulates the number of incident (diagnosed) cancer cases in each country/territory and models the individual-level cancer treatment cascade and survival outcome for each patient with cancer.

Here we present an overview of the conceptual model, along with the data sources used to inform various aspects of the model development.



Reference: Ward ZJ, Scott AM, Hricak H, et al. Estimating the impact of treatment and imaging modalities on 5-year net survival of 11 cancers in 200 countries: a simulation-based analysis. Lancet Oncol 2020; 21: 1077-88.

1.1 Hierarchical Models

We use Bayesian hierarchical models to synthesize data from multiple sources and estimate parameters for countries for which no data are available. In contrast to no pooling (i.e. every country is different), or complete pooling (i.e. every country is the same), hierarchical models allow for partial pooling of information (i.e. countries in similar income groups and geographic regions likely have similar parameters), which allows for 'borrowing' of information from multiple sources. This approach also helps to provide estimates that are more robust to outliers by smoothing, or 'regularizing' the country-specific parameters by virtue of the hierarchical structure. For more information on Bayesian data analysis, see Gelman et al. 2014.

We use vertical density plots to display the probability distributions of the model priors and the calibrated posteriors for each country. In these plots, the value of interest (i.e. parameter value) is plotted on the y-axis, with the probability density plotted symmetrically around the origin for visual balance - wider curves correspond to higher probability density.

Reference: Gelman A, Carlin JB, Stern HS, Rubin DB. Bayesian data analysis, 3rd edn. Boca Raton, Florida: CRC Press, 2014.

1.2 Cancer Incidence

Estimated breast cancer incidence was obtained from GLOBOCAN 2018, and was available for 178 countries. Estimates were not available for countries with small populations, so we imputed incidence rates from similar countries (ie, similar region and income group). Estimated number of breast cancers were then calculated based on the UN Medium Population estimates for females in 2018.

Missing	Match
Andorra	Spain
Antigua and Barbuda	Bahamas
Belize	Guatemala
Bermuda	Bahamas
Bhutan	Nepal
Brunei Darussalam	Malaysia
Cabo Verde	Senegal
Cayman Islands	Bahamas
Comoros	Madagascar
Djibouti	Eritrea
Dominica	Jamaica
Faroe Islands	Iceland
Gambia	Senegal
Greenland	Iceland
Grenada	Jamaica
Iceland	Norway
Kiribati	Fiji
Liechtenstein	Switzerland
Maldives	Sri Lanka
Marshall Islands	Fiji
Micronesia (Fed. States of)	Fiji
Monaco	France
Nauru	Fiji
Palau	Fiji
Saint Kitts and Nevis	Bahamas
Saint Vincent and the Grenadines	Jamaica
Samoa	Fiji
San Marino	Italy
Sao Tome and Principe	Equatorial Guinea
Seychelles	Comoros
Taiwan	South Korea
Timor-Leste	Indonesia
Tonga	Samoa
Tuvalu	Samoa
Vanuatu	Papua New Guinea

1.3 Stage Distribution

Due to the paucity of data on cancer stage distribution at diagnosis, we performed a literature review to obtain estimates of country-specific and cancer-specific stage distribution, which yielded estimates from 162 studies in 84 countries.

We used a hierarchical modelling approach to regularize the stage distribution estimates, and to make

estimates for countries with no data.

Stage at Diagnosis

G = Global $\alpha_i^G \sim N(\widehat{\alpha_i^G}, \widehat{\sigma_i^G})$ (Empirical mean and SE)

I = Income Group $\beta_i^I \sim N(\widehat{\alpha_i^I}, \widehat{\sigma_i^I})$ (Empirical mean and SE)

A = Area $\gamma_i^A \sim N(\widehat{\alpha_i^A}, \widehat{\sigma_i^A})$ (Empirical mean and SE)

R = Region $\delta_i^R \sim N(\widehat{\alpha_i^A}, \widehat{\sigma_i^R})$ (Empirical mean and SE)

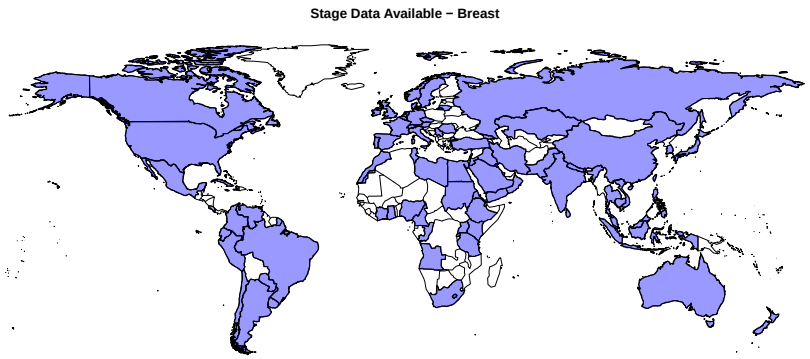
C = Country $\epsilon_i^C \sim N\left(\widehat{\epsilon_i^C}, 0.01\right)$ (Country residual)

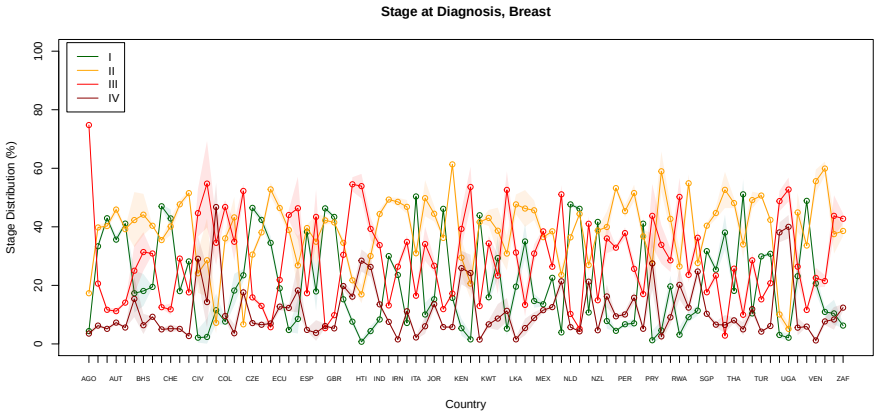
$$\lambda_i^C = \frac{1}{1 + \exp\left(-\left(\alpha_i^G + \beta_i^I + \gamma_i^A + \delta_i^R + \epsilon_i^C\right)\right)}$$

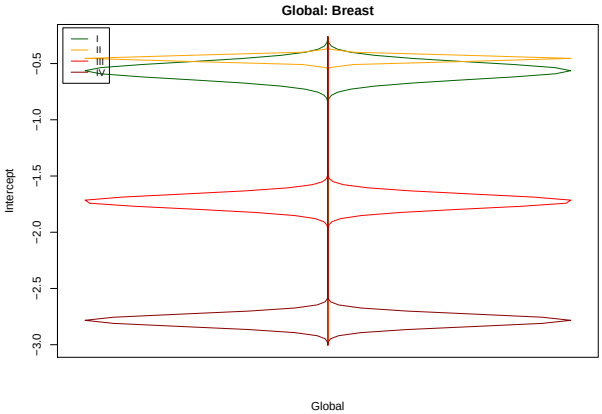
Probability $\pi_i^C = \frac{\lambda_i^C}{\sum_{j=1}^4 \lambda_j^C}$

We weighted the estimates by the total number of cases for which stage was reported. To guard against over-fitting to individual country data we reduced the magnitude of the country-level residuals by 75%.

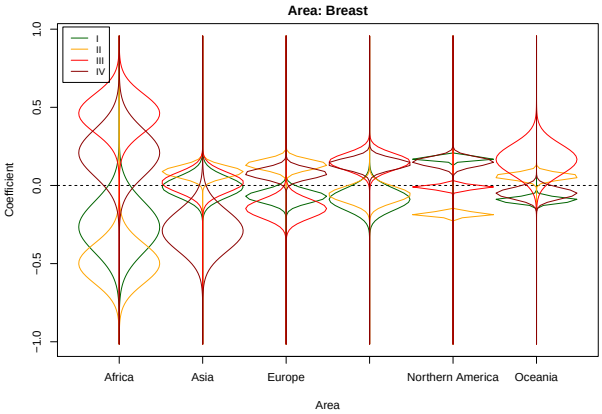
When drawing stage in the model, we used raking to estimate joint probabilities of stage and age. Initial joint probabilities of age and stage were estimated from SEER 2010-16 data using AJCC stage groups, 7 edition. Raking was then performed until convergence was achieved with the target marginal distributions: 1) estimated stage distribution and 2) age distribution from GLOBOCAN. Uniform priors were put on age distribution by stage (i.e. Beta$(1, 1)$) to avoid initial weights of 0 for raking.

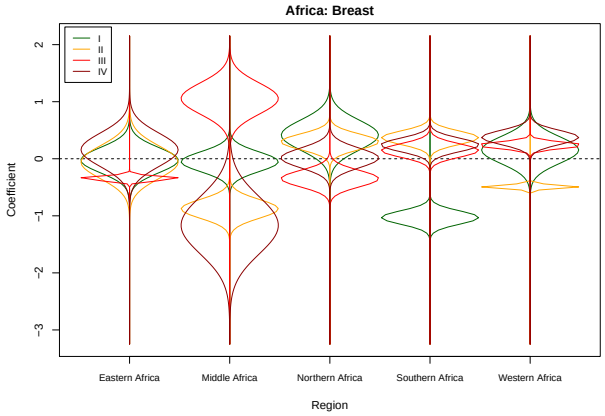


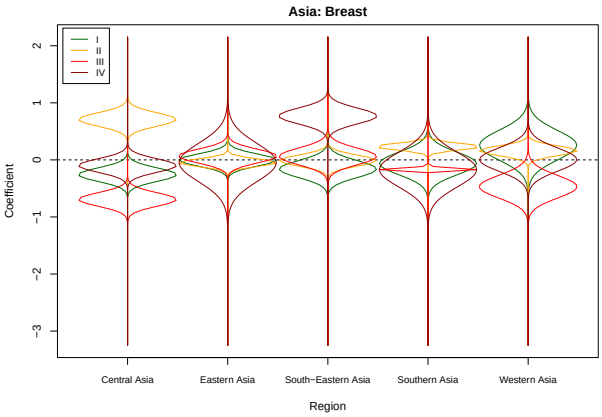

Stage at Diagnosis, Breast
Stage Distribution (%)
0
20
40
60
80
100
I
II
III
IV
AGO AUT BHS CHE CIV COL CZE ECU ESP GBR HTI IND IRN ITA JOR KEN KWT LKA MEX NLD NZL PER PRY RWA SGP THA TUR UGA VEN ZAF
Country

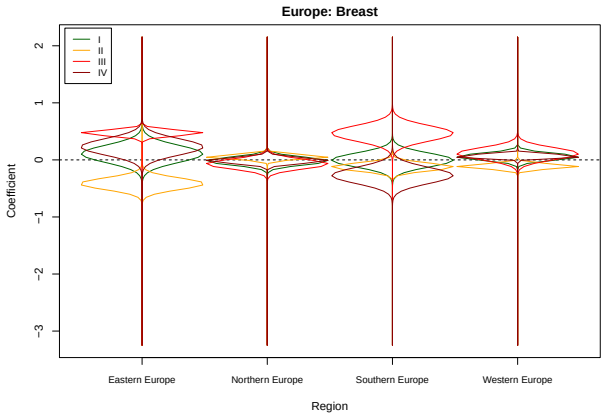

Global: Breast
Intercept
−0.5
−1.0
−1.5
−2.0
−2.5
−3.0
I
II
III
IV
Global

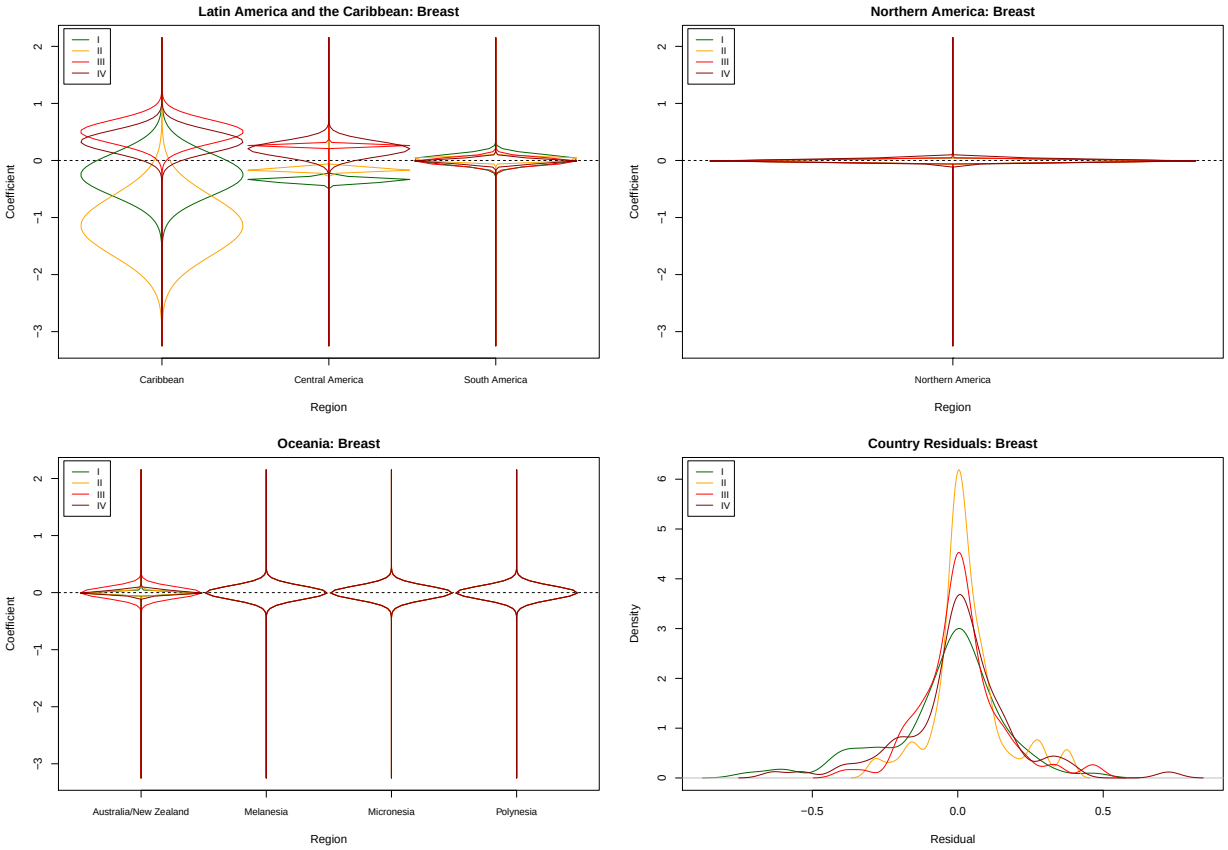

Income Group: Breast
Coefficient
2
1
0
−1
−2
−3
−4
I
II
III
IV
Low
Lower−middle
Upper−middle
High
Income Group


Area: Breast
Coefficient
1.0
0.5
0.0
−0.5
−1.0
I
II
III
IV
Africa
Asia
Europe
Northern America
Oceania
Area


Africa: Breast
Coefficient
2
1
0
−1
−2
−3
I
II
III
IV
Eastern Africa
Middle Africa
Northern Africa
Southern Africa
Western Africa
Region


Asia: Breast
Coefficient
2
1
0
−1
−2
−3
I
II
III
IV
Central Asia
Eastern Asia
South−Eastern Asia
Southern Asia
Western Asia
Region


Europe: Breast
Coefficient
2
1
0
−1
−2
−3
I
II
III
IV
Eastern Europe
Northern Europe
Southern Europe
Western Europe
Region



References

Country	Cases	Years	Source	Reference
AGO	162	2011	National Oncology Centre of Luanda	Armando 2015
AGO	1323	2006-2014	Tertiary hospital in Luanda	Lopes 2015
AGO	132	2011-2014	Angolan Institute of Cancer Control and Clínica Sagrada Esperança, Luanda	Miguel 2017
ARG	2457	2012-2016	Institutional Tumor Registry of Argentina (RITA)	Abriata 2019
ARG	3383		[Systematic review: de Lemos 2019]	Elizalde 2013
ARG	303		[Systematic review: de Lemos 2019]	Grippo 2015
ARG	281		[Systematic review: de Lemos 2019]	Juarez 2009
AUS	3935	2017	Victoria Cancer Registry	Victoria Cancer Registry 2019
AUS	4457	2011	New South Wales Cancer Registry	Lawrance 2019
AUT	3913	1988-2000	Cancer Registry of Tyrol	Oberaigner 2006
BEL	25178	2004-2006	Three databases were linked at the patient level: the Cancer Registry, the population and the claims databases	Vrijens 2012
BHR	104	2010-2013	Salmaniya Medical Complex, Manama	AlZaman 2016
BHS	188	2009-2011	National Oncology Board of the Bahamas	Mungrue 2016
BRA	201079	2001-2014	A network of SUS-affiliated hospital-based cancer registries (Registros hospitalares de cancer [RHC])	Dos-Santos-Silva 2019
CAN	16407	2011-2015	Canadian Cancer Registry	Canadian Cancer Statistics 2018
CHE	1017	2003-2007	Ticino Cancer Registry	Spitale 2009
CHL	4693	2000-2010	Six public hospitals	Del Castillo Sm 2017
CHN	288	2004-2006	First Affiliated Hospital of Inner Mongolia Medical College	Kang 2012
CHN	4187	2006-2010	Four hospitals: Cancer Hospital/Chinese Academy of Medical Sciences, Peking University Cancer Hospital, Beijing Obstetrics and Gynecology Hospital, and Shunyi Maternal and Child Health Care Hospital	Zuo 2017
CHN	1997	2008-2010	Hong Kong Breast Cancer Registry	Cheung 2012
CHN	3455	1999-2008	Nationwide multi-center study from 7 geographic regions across China (North, North-East, Central, South, East, North-West, and South-West)	Li 2011
CIV	141	2008-2009	Abidjan cancer registry	Islami 2015
CMR	42	2006-2009	Douala General Hospital	Nguefack 2012
COG	139	2008-2009	Brazzaville cancer registry	Islami 2015
COL	1548	2007-2012	Instituto Nacional de Cancerología of Colombia	Pardo 2018
COL	233	2003-2007	Manizales population-based Cancer Registry	Arias-Ortiz 2018

(continued)

Country	Cases	Years	Source	Reference
CRI	192	2009-2010	San Juan de Dios Hospital of the Costa Rican Social Security System (Caja Costarricense del Seguro Social)	Srur-Rivero 2014
CUB	54		[Systematic review: de Lemos 2019]	Milián-Mosquera 2015
CUB	141		[Systematic review: de Lemos 2019]	Viera-Hernández 2011
CUB	1315		[Systematic review: de Lemos 2019]	Gómez-Delgado 2017
CZE	7419	2015	Modelled estimates based on data from Czech National Cancer Registry	Dusek 2015
DEU	4383	2001-2013	Population-based Cancer Registry, Dresden	Kast 2017
DNK	1735	1996-1997	Danish Cancer Registry	Jensen 2003
ECU	302		[Systematic review: de Lemos 2019]	Martínez 2015
ECU	1158		[Systematic review: de Lemos 2019]	Cueva and Yepez 2014
ECU	621		[Systematic review: de Lemos 2019]	Cueva and Yepez 2009
EGY	3027	2004-2008	Gharbiah cancer registry	Schlichting 2015
ERI	82	2007-2008	General Surgical Units of 3 hospitals: Orotta Medical Surgical National Referral Hospital, Halibet Hospital, and Sembel Hospital	Tesfamariam 2013
ESP	2662	2000-2014	Hospital del Mar Tumour Registry	Parés-Badell 2017
ESP	4944	2000-2012	Population-based cancer registry in Granada (southern Spain)	Baeyens-Fernandez 2018
ETH	106	2012-2015	Tikur Anbessa Specialized Hospital	Hadgu 2018
FRA	3978	1990-1997	Cancer Registry of Isere	Cluze 2009
GBR	191086	2013-2017	England ONS	ONS 2019
GBR	13998	2009-2012	Scotland Cancer Registry	McMenamin 2017
GEO	3580	2006-2015	National population-based cancer registry	Vashakidze 2018
GHA	56	2013-2016	Komfo Anokye Teaching Hospital (KATH)	Gyedu 2018
GHA	179	2013	Korle Bu Teaching Hospital	Dedey 2016
GHA	463	2008-2011	Komfo Anokye Teaching Hospital (KATH)	Scherber 2014
GHA	564	2005-2009	Department of Pathology, University of Ghana Medical School	Edmund 2013
GHA	330	2004-2009	Komfo Anokye Teaching Hospital (KATH)	Ohene-Yeboah 2012
HTI	445	2013-2017	Port-au-Prince	Degennaro 2018
HTI	93	2013-2015	Innovating Health International Women's Cancer Center (IHI-WCC) in Port-au-Prince	Gomez 2016
IDN	421	2010	Dharmais Cancer Centre (DCC)	Ng 2011
IDN	195	1998-2002	Dharmais Cancer Hospital	Irawan 2008
IND	132	2010-2011	University Teaching and Tertiary Referral Hospital, Kashmir	Wani 2012
IND	2425	2005-2014	Population Based Cancer Registry, Trivandrum	Mathew 2016
IND	906	2010-2012	Hospital based cancer registry of a regional cancer center of North-East India	Krishnatreya 2014
IRL	20816	1999-2008	Irish National Cancer Registry	Walsh 2014
IRN	4748	Not reported	Shiraz Breast Cancer Registry	Akrami 2018
IRQ	479	2018	Duhok	Mohammed 2019
IRQ	30	Not reported	College of Medicine, Al-Nahrain University, Baghdad	Abdulhussain 2019
IRQ	996	2011-2015	Basra Oncology Center	Abood 2018
IRQ	242	2006-2008	Hewa Hematology and Oncology Hospital, Sulaimaniyah province	Majid 2009
ITA	138	2003-2010	Morgagni-Pierantoni Hospital (Forli)	Amadori 2014
ITA	1764	2003-2009	Varese section of the Lombardy Cancer Registry	Tagliabue 2016
JAM	65	2006-2007	Hospital-based specialist clinic in Kingston, Jamaica	Chin 2014
JAM	184	2002-2009	University Hospital of the West Indies	Alfred 2012
JOR	348	2004-2014	Jordan University of Science and Technology (JUST) and King Abdullah Teaching University Hospital (KAUH)	Ayoub 2019
JOR	151	2013-2014	Three hospitals in Central and Northern Jordan	Obeidat 2015
JOR	721	1997-1998	Jordan Cancer Registry	Arkoob 2010
JOR	98	2000-2002	Al-Basheer Governmental Hospital	Atoum 2010
JPN	157292	2012-2015	Nationwide hospital-based cancer registries	Okuyama 2018
KAZ	4210	2014	Registry data from fourteen regions and two major cities	Chukmaitov 2018
KEN	125	2012-2018	Aga Khan University Hospital, Nairobi	Ekpe 2019
KEN	99	2011-2012	Aga Khan University Hospital, Nairobi	Sayed 2014
KHM	194	2008-2011	Sihanouk Hospital Center of Hope, Phnom Penh	Ley 2016
KOR	86784	1996-2015	Korean Breast Cancer Society Registry	Park 2019
KWT	353	1999-2009	Kuwait Cancer Control Center	Fayaz 2013
KWT	902	1999-2004	Clinical oncologists' data	Elbasmi 2010
LBN	150	2009-2014	American University of Beirut Medical Center (AUBMC)	Akel 2017
LBY	100	2000-2007	National Cancer Institute, Sabratha	Ermiah 2012
LBY	130	2000-2006	African Oncology Institute, Sabratha and Tripoli Medical Center, Tripoli	Boder 2012
LKA	833	2006-2012	University of Ruhuna	Peiris 2017
LTU	240	2008	Kaunas region	Ivanauskiene 2012
MAR	560	2005-2008	Rabat Cancer Registry	Mechita 2016
MAR	279	2010-2015	Oncology Clinic Al Amal of Tangier	Derkaoui 2016
MEX	397		[Systematic review: de Lemos 2019]	Pérez-Michel 2009
MEX	816		[Systematic review: de Lemos 2019]	Ángeles-Llerenas 2016
MEX	2075		[Systematic review: de Lemos 2019]	Lara-Medina 2011

(continued)

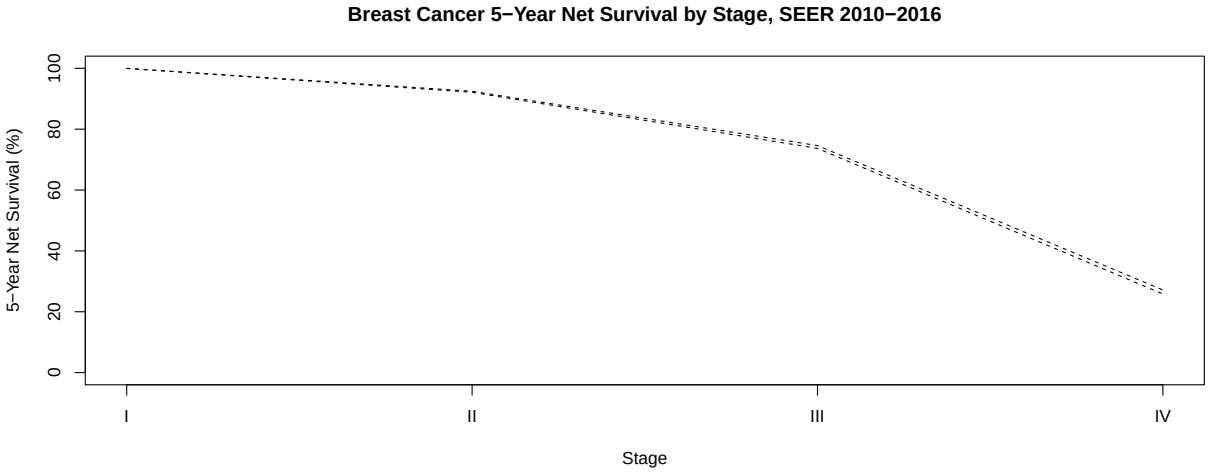
Country	Cases	Years	Source	Reference
MEX	4301		[Systematic review: de Lemos 2019]	Reynoso-Noverón 2017
MYS	328	2005-2007	Three referral medical centres in the East Coast of Malaysia and two government hospitals in Kuala Lumpur	Norsa'adah 2011
MYS	447	2010	University Malaya Medical Centre (UMMC), Kuala Lumpur	Ng 2011
MYS	824	2014-2015	Three large hospitals: University Malaya Medical Centre (UMMC), Kuala Lumpur; Tengku Ampuan Rahimah Hospital (TARH), Klang, Selangor; Queen Elizabeth Hospital (QEH), Kota Kinabalu, Sabah	Wong 2019
MYS	121	2007-2013	Hospital Sultanah Nora Ismail Batu Pahat, Johor	Balasundram 2018
MYS	549	2007-2011	Kelantan Cancer Registry	Nordin 2018
MYS	446	2010-2015	Sarawak General Hospital	Yang 2017
MYS	3959	2001-2011	University Malaya Breast Cancer Registry	Kong 2017
NGA	85	2016	Lagos University Teaching Hospital (LUTH)	Awofeso 2018
NGA	105	2015	University College Hospital, Ibadan	Hafiz 2018
NGA	300	2014-2016	Six secondary and tertiary hospitals in Nigeria	Jedy-Agba 2017
NGA	200	2005-2008	Lagos State University Teaching Hospital (LASUTH) Cancer Registry	Makanjuola 2014
NGA	103	2001-2005	Ahmadu Bello University Teaching Hospital (ABUTH) , Zaria, Kaduna State	Kene 2010
NGA	34	1999-2001	Jos University Teaching Hospital	Gukas 2008
NGA	89	2004-2005	Oncology Clinic of the Department of Surgery, University College Hospital, Ibadan	Adebamowo 2008
NLD	31277	2015-2016	Netherlands Cancer Registry	Walraven 2019
NOR	14890	2005-2010	Norwegian Cancer Registry	Lousdal 2014
NPL	85	2016-2017	Three cancer hospitals of Kathmandu, Nepal	Bhandari 2017
NPL	114	2007-2008	Bir Hospital, Kathmandu and BP Koirala Memorial Cancer Hospital, Bharatpur	Acharya 2012
NPL	1141	1999-2006	Tertiary care center	Jah 2010
NZL	13644	2000-2014	Auckland and Waikato Breast Cancer Registers	Tin Tin 2018
OMN	65	2015-2016	Sultan Qaboos University Hospital	Naik 2017
OMN	118	2003-2008	Sultan Qaboos University Hospital	Kumar 2011
OMN	150	1996-2002	Sultan Qaboos University Hospital and the Royal Hospital	Al-Moundhri 2004
PAK	261	2012-2013; 2013-2015	Institute of Nuclear Medicine and Oncology Lahore (INMOL); Services Hospital Lahore (SHL)	Khokher 2016
PAK	834	1999-2008	A university hospital in Southern Pakistan	Kumar 2016
PAK	1299	2001-2010	Aga Khan University Hospital (AKUH) in Karachi	Zeeshan 2019
PAK	9461	1994-2016	Liaquat National Hospital, Karachi	Soomro 2018
PAK	6214	2004-2012	Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore	Badar 2015
PER	91	2015	Tertiary care referral cancer center in Trujillo, Peru	Romanoff 2017
PER	75		[Systematic review: de Lemos 2019]	Larrea-Fernández 2016
PER	545		[Systematic review: de Lemos 2019]	Díaz-Vélez 2013
PER	1505		[Systematic review: de Lemos 2019]	Gutiérrez and Alarcón 2008
PHL	1166	1993-2002	Philippine Cancer Society-Manila Cancer Registry and the Department of Health-Rizal Cancer Registry	Laudico 2009
PRT	1229	2005	Southern Portugal Cancer Registry (ROR-Sul)	Andre 2014
PRT	551	2000-2007	North Region Cancer Registry	Jose Bento 2014
PRY	80		[Systematic review: de Lemos 2019]	Yoffe de Quiroz 2005
ROU	173	2000-2005	Municipal Clinical Hospital, Timisoara	Zaha 2010
ROU	22	Not reported	Not reported	Suciu 2008
RUS	473	2009-2012	N. N. Blokhin Russian Cancer Research Center	Filipenko 2017
RWA	42	Not reported	King Faisal Hospital and Kigali Teaching Hospital, Kigali	Habyarimana 2018
RWA	39	2016	Rwanda Military Hospital and King Faysal Hospital, Kigali	Habyarimana 2018
RWA	142	2014-2015	Butaro Cancer Center of Excellence	Schleimer 2019
SAU	535	2007-2012	Oncology Department at King Faisal Specialist Hospital & Research Center (KFSH&RC), Riyadh	Elkum 2014
SAU	449	Not reported	King Abdulaziz University Hospital	Khabaz 2017
SDN	1249	1999-2006	Institute of Nuclear Medicine, Molecular Biology and Oncology (INMO) at Gezira University, Wadmedani, al-Gezira State	Elgaili 2010
SGP	8773	2011-2015	Singapore Cancer Registry	Annual Report, 2017
SGP	1165	1990-2002	National University Hospital Breast Cancer Registry	Lim 2007
SRB	2252	1985-1990	Surgical and Oncological Clinic in Nis	Djordjevic 2004
SWE	247	1996-1997	Swedish Cancer Registry	Jensen 2003
THA	3251	2006-2015	Chiang Mai cancer registries	Chitapanarux 2019
TTO	362		[Systematic review: de Lemos 2019]	Raju and Naraynsingh 1989
TUN	70	2016-2017	Fattouma Bourguiba University Hospital of Monastir	Daldoul 2018
TUN	1082	2003-2007	Cancer Registry of the Center of Tunisia	Missaoui 2011
TUR	18586	2005-2017	National Breast Cancer Registry Program of Turkish Federation of Breast Diseases Societies	Ozmen 2019
TWN	29152	2004-2008	Taiwan Cancer Registry	Chiang 2016

(continued)

Country	Cases	Years	Source	Reference
TZA	74	2016-2017	Muhimbili National Hospital	Mansouri 2019
TZA	384	2002-2011	Bugando Medical Center, Mwanza	Mabula 2012
TZA	327	2007-2009	Ocean Road Cancer Institute (ORCI)	Burson 2010
UGA	194	2003-2010	Kampala Cancer Registry	Menon 2018
UGA	162	2014	Mulago National Referral Hospital	Odongo 2015
UGA	209	2014	Mulago National Referral Hospital and Ugandan Cancer Institute	Galukande 2015
URY	107		[Systematic review: de Lemos 2019]	Malvasio 2017
URY	109		[Systematic review: de Lemos 2019]	Camejo 2013
USA	293629	2010-2016	SEER	SEER 2019
VEN	179		[Systematic review: de Lemos 2019]	Rebolledo 2012
VEN	411		[Systematic review: de Lemos 2019]	Ferri 2012
VNM	1574	2001-2006	Hue Central Hospital and the Cancer Registry in Ho Chi Minh City	Lan 2013
YEM	192	1998-2002; 2005-2007	Registry of Algamhouria teaching hospital; Aden public and private hospitals	Harhra 2012
ZAF	231	2016-2017	Urban South African open-access breast care clinic	Rayne 2019
ZAF	1006	2015-2017	Charlotte Maxeke Johannesburg Academic Hospital and Chris Hani Baragwanath Academic Hospital, Johannesburg	Phakathi 2019
ZAF	586	2010-2011	Tygerberg Hospital, Cape Town	Langenhoven 2016
ZAF	1051	2006-2012	Chris Hani Baragwanath Academic Hospital, Soweto, Johannesburg	Dickens 2014

1.4 Maximum Achievable Survival

To account for variation in the curability of different cancers, we estimated maximum achievable survival probabilities using 2010–16 data from the Surveillance, Epidemiology, and End Results (SEER) Program by cancer type and stage. We inflated the SEER estimates to account for the possibility of non-optimal service delivery in the USA. This model parameter is used to estimate relative differences in survival by cancer site and stage, and represents the highest possible survival given current knowledge and medical technology.



Dashed lines indicate 95% CI.

We inflated these priors by 3 percentage points (up to maximum of 100%) to account for the potential for non-optimal service delivery in the US. When sampling we enforced constraints to ensure that survival was non-increasing by stage.

Reference:

Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2018 Sub (2000-2016) - Linked To County Attributes - Total U.S., 1969-2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2019, based on the November 2018 submission.

1.5 Modality Efficacy

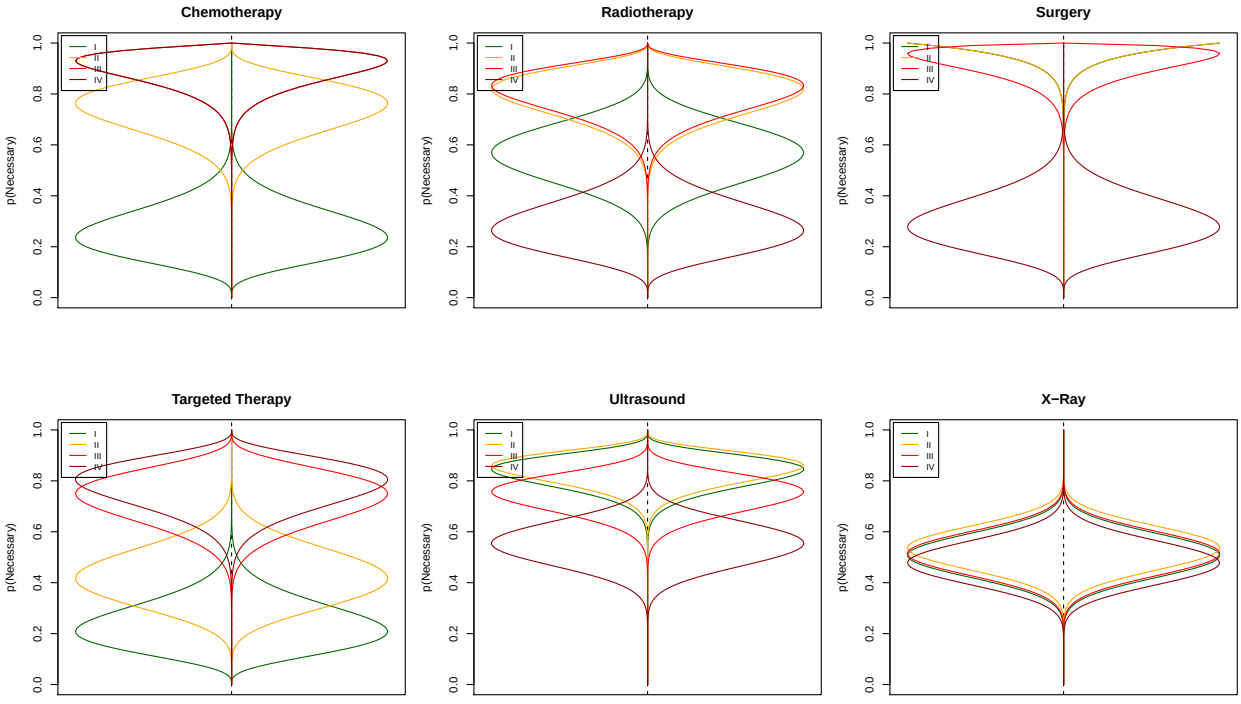
To set prior probability distributions for the impact of treatment and imaging modalities on stage-specific cancer survival, we used a two-stage survey to elicit expert opinion. A sample of actively practising physicians (33 imaging experts and 22 therapy experts) was selected, based on expertise in their field, both in high-income and low-income settings.

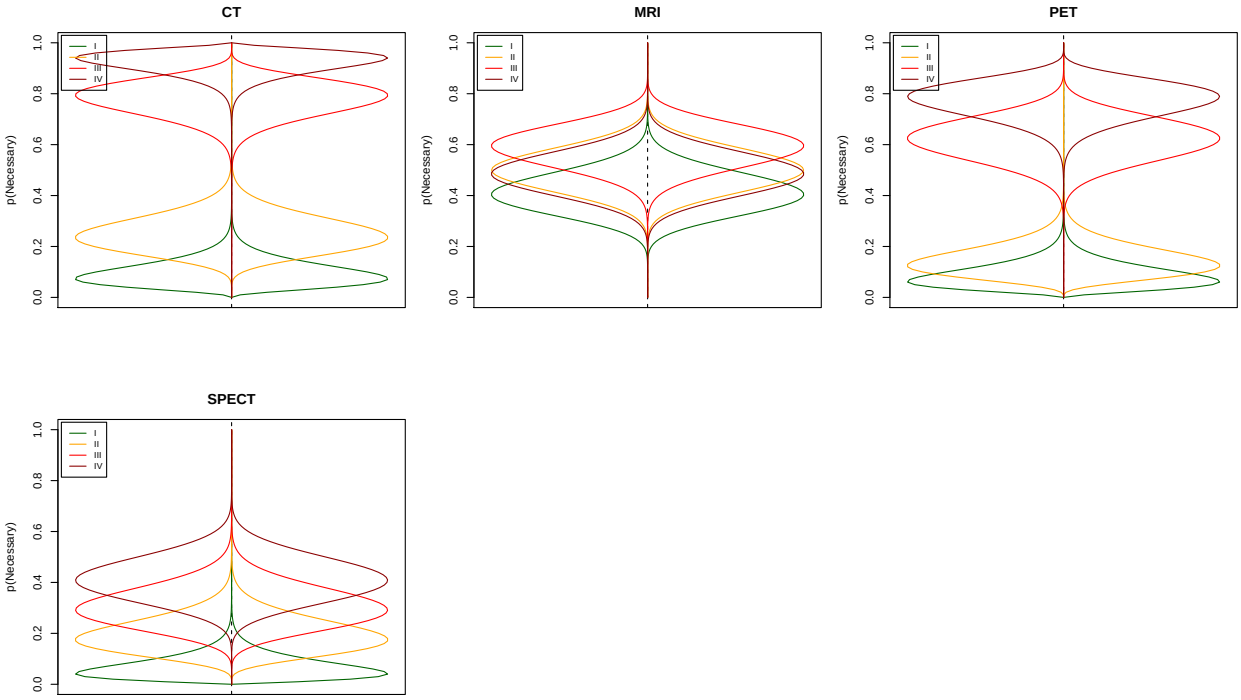
Respondents were asked to indicate the impact of each treatment/imaging modality on 5-year net survival for each cancer/stage using a four-point scale, ranging from necessary for 5-year survival to no impact on 5-year survival. To estimate prior probability distributions for the probability that each modality was necessary, we weighted the responses as follows and estimated Beta distributions with the sum of the weighted estimates.

Response	Description	Weight
No impact/Not indicated	Not expected to affect 5-yr survival at all	0.0
Small impact	May improve the probability of 5-yr survival in some cases	0.25
Moderate impact	Likely to improve the probability of 5-yr survival in most cases	0.75
Necessary	Use is necessary to achieve 5-yr survival	1.00

1.5.1 Priors

We plot the estimated priors by stage below.





1.5.2 Consensus Results

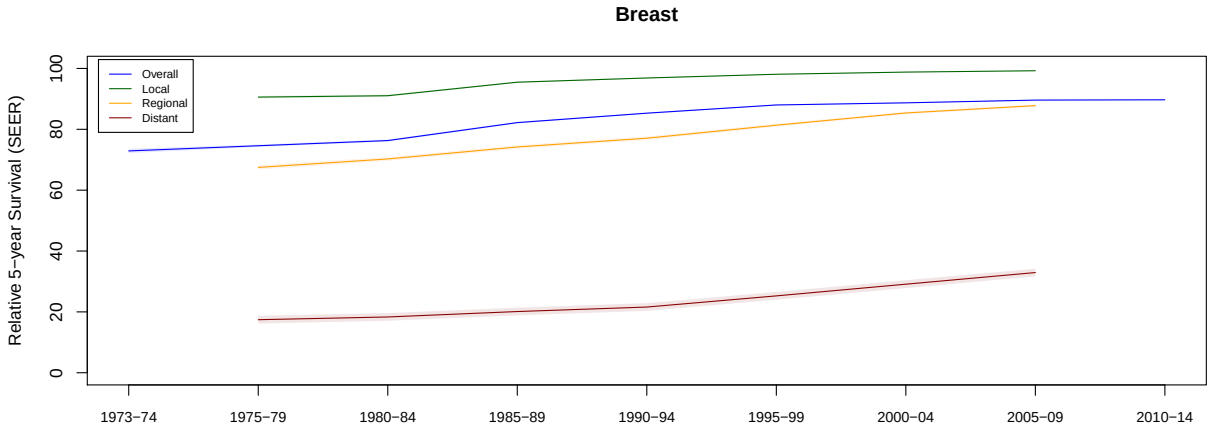
Expert opinion consensus of impact of treatment and imaging modalities on 5-year breast cancer net survival given initial stage at diagnosis

Modality	Stage I	Stage II	Stage III	Stage IV
Treatment				
Chemotherapy	Small impact	Necessary	Necessary	Necessary
Radiotherapy	Small impact	Necessary	Necessary	No impact
Surgery	Necessary	Necessary	Necessary	No impact
Targeted therapy	Small impact	Moderate impact	Necessary	Necessary
Imaging				
Ultrasound	Necessary	Necessary	Necessary	Necessary
X-ray	No impact	No impact	No impact	No impact
CT	No impact	No impact	Moderate impact	Necessary
MRI	Moderate impact	Moderate impact	Moderate impact	Necessary
PET	No impact	No impact	Moderate impact	Necessary
SPECT	Small impact	Small impact	Moderate impact	Necessary

1.5.3 Modern Modalities

We also estimated the proportion of cancer cases expected to benefit from modern modalities (i.e. targeted therapy, CT, MRI, PET, and SPECT). Because these modalities were generally not available until the late 1970s or early 1980s, we analysed trends in stage-specific survival using SEER data between 1973 and 2014 to estimate the level of survival achievable before the introduction of modern modalities.

Here we plot the trends in survival based on SEER data. We used SEER Historic Stage A (Local/Regional/Distant) as it was the only staging system available for historic data.



1.6 Treatment Availability

To estimate the availability of traditional treatment modalities (chemotherapy, radiotherapy, and surgery), we relied on previously published estimates. We estimated priors of the availability of chemotherapy using data for 94 countries from a published global survey of oncologists (Cohen 2018). Estimates of radiotherapy coverage were available for 173 countries, based on the Lancet Oncology Commission on Expanding Global Access to Radiotherapy (Atun 2015). Surgery estimates were available for 184 countries, based on a modelling study of the Lancet Commission on Global Surgery (Alkire 2015).

Data on the availability of targeted therapy in low- and middle-income countries are scarce, but estimates that are available suggest that patients have limited access to targeted therapy, usually because of the high cost of these therapies (Yip 2015). For example, among 49 new oncology medicines launched between 2010 and 2014, patients in only 6 countries had access to at least half of these drugs (IMS 2016). Furthermore, such drugs are often only accessible for a privileged minority of the population with private health insurance (Ruiz 2017). We therefore set wide priors by income group, centered at 5%, 25%, 75%, and 95%. When sampling parameters we ensured that the probabilities of targeted therapy availability were lower than for chemotherapy in each country to account for the lack of access to targeted therapy.

References:

Alkire BC, Raykar NP, Shrime MG, et al. Global access to surgical care: a modelling study. Lancet Glob Health 2015; 3: e316–23.

Atun R, Jaffray DA, Barton MB, et al. Expanding global access to radiotherapy. Lancet Oncol 2015; 16: 1153–86.

Cohen P, Friedrich P, Lam C, et al. Global access to essential medicines for childhood cancer: a cross-sectional survey. J Glob Oncol 2018; 4: 1–11.

IMS Institute for Healthcare Informatics. Global Oncology Trend Report: A Review of 2015 and Outlook to 2020. 2016. Available at: https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/global-oncology-trend-report-2016.pdf.

Ruiz R, Strasser-Weippl K, Touya D, et al. Improving access to high-cost cancer drugs in Latin America: Much to be done. Cancer 2017; 123(8): 1313-1323.

Yip CH, Buccimazza I, Hartman M, Deo SV, Cheung PS. Improving outcomes in breast cancer for low and middle income countries. World J Surg 2015; 39(3): 686-92.

1.7 Imaging Availability

We obtained coverage estimates for each imaging modality (i.e. equipment per million population) from the International Atomic Energy Agency IMAGINE database. To estimate probabilities of availability, we set thresholds of minimum coverage density needed to ensure availability. Because there are no general guidelines regarding the ideal number of imaging units per population, we set thresholds based on observed data in high-income countries with relatively low coverage so as not to overestimate the thresholds needed to ensure availability.

The following thresholds were used to estimate priors for the probability that each modality was available:

Modality	Threshold (per million)	HIC Mean	Country Examples
Ultrasound	40	132.0	Puerto Rico: 16.6, Bahamas: 25.9
X-ray	30	110.2	Puerto Rico: 16.9, Trinidad and Tobago: 21.6
CT	10	25.4	Canada: 15.1, UK: 14.5
MRI	10	16.3	Canada: 9.9, Czechia: 10.4
PET	1	2.1	Canada: 1.5, UK: 0.5
SPECT	5	7.7	UK: 5.7, France: 6.1

(Note: Estimates based on IAEA IMAGINE database estimates as of Jan 14, 2020)

Note however that country-level density thresholds do not take into account how imaging equipment and human resources are distributed within countries, nor potential differences in the availability of imaging for diagnostics versus treatment planning. Therefore, there may not be a direct relationship between imaging density and probabilities of availability, which we fitted via model calibration to observed survival estimates.

Reference: International Atomic Energy Agency. IMAGINE—IAEA Medical imAGIng and Nuclear mEdicine global resources database. https://humanhealth.iaea.org/HHW/DBStatistics/IMAGINE.html

1.8 Quality of Care

We also included country-specific parameters for quality of care, defined by the Institute of Medicine as the "degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge" (IOM 1990). This parameter captures health-system and facility-level factors that account for residual differences in survival not explained by cancer stage or treatment and imaging availability. We set wide priors with increasing probability of quality by income group (25%, 50%, 75%, 95%), and zero-mean priors for the other levels in the hierarchical model.

Adequate quality of care is assumed to be a prerequisite for survival in the model. This parameter can therefore be interpreted as the probability that the quality of care available is adequate to ensure 5-year survival, given the availability of all necessary treatment and imaging modalities.

Reference: Institute of Medicine. Medicare: a strategy for quality assurance. Washington, DC: National Academy Press, 1990.

2 Model Calibration

2.1 Calibration Overview

As described above, we used Bayesian hierarchical models with four levels (income group, geographical area, geographical region, and country) to synthesise all available estimates and generate prior probability distributions, allowing us to regularise the reported estimates and estimate priors for countries for which no data were available. We used these priors as initial sampling distributions for model calibration and enforced non-decreasing income group intercepts when sampling from the hierarchical models (see Ward 2020).

To ensure our model results were consistent with reported survival data, we calibrated the model to survival estimates from CONCORD-3 (Allemani 2018), reserving a set of randomly sampled estimates as a validation test set. We calibrated the model using a Bayesian approach in which the observed data (i.e. CONCORD survival estimates) are considered fixed, and the model parameters are random variables. To fit the parameters we used a simulated annealing search algorithm (a stochastic optimization approach) to identify good-fitting parameter sets. A goodness-of-fit score for each proposed parameter set was calculated as the sum of the squared distance between the predicted and reported 5-year survival estimates. We weighted each survival target inversely proportional to the width of its confidence interval to allow more precise estimates to have larger influence in the calibration.

We ran 2,000 independent search chains of 1,000 iterations each, and selected the final 100 best-fitting parameter sets to account for uncertainty around the model parameters. When running the final 1,000 simulations we sampled a parameter set (from the best-fitting 100 sets) at random, accounting for both first-order (patient-level stochastic) and second-order (parameter) uncertainty. Our estimated 95% UIs, reported for all model outcomes, therefore indicate the sensitivity of our results to different parameter values and account for their joint distribution.

References:

Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 2018; 391: 1023–75.

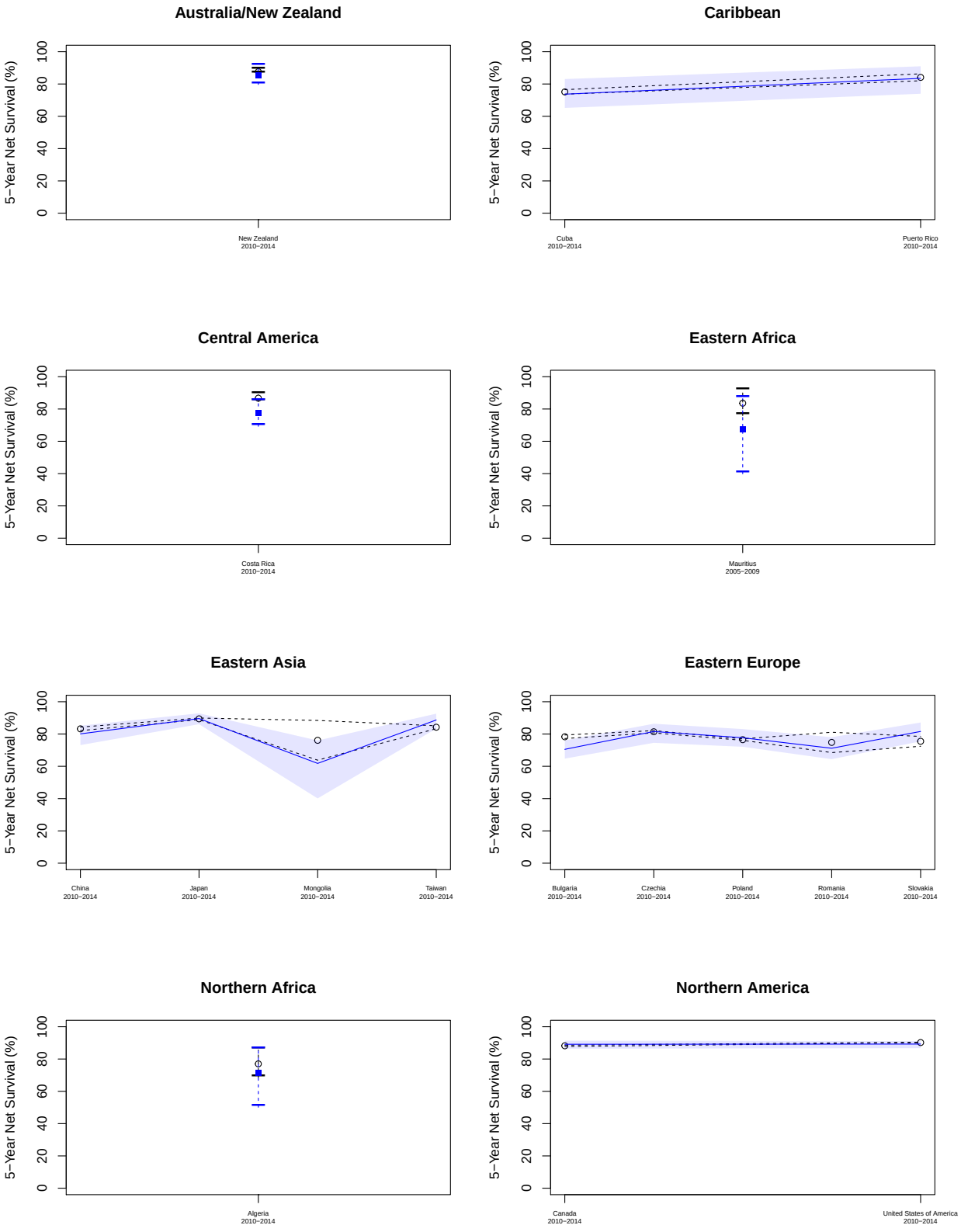
Ward ZJ, Scott AM, Hricak H, et al. Estimating the impact of treatment and imaging modalities on 5-year net survival of 11 cancers in 200 countries: a simulation-based analysis. Lancet Oncol 2020; 21: 1077-88.

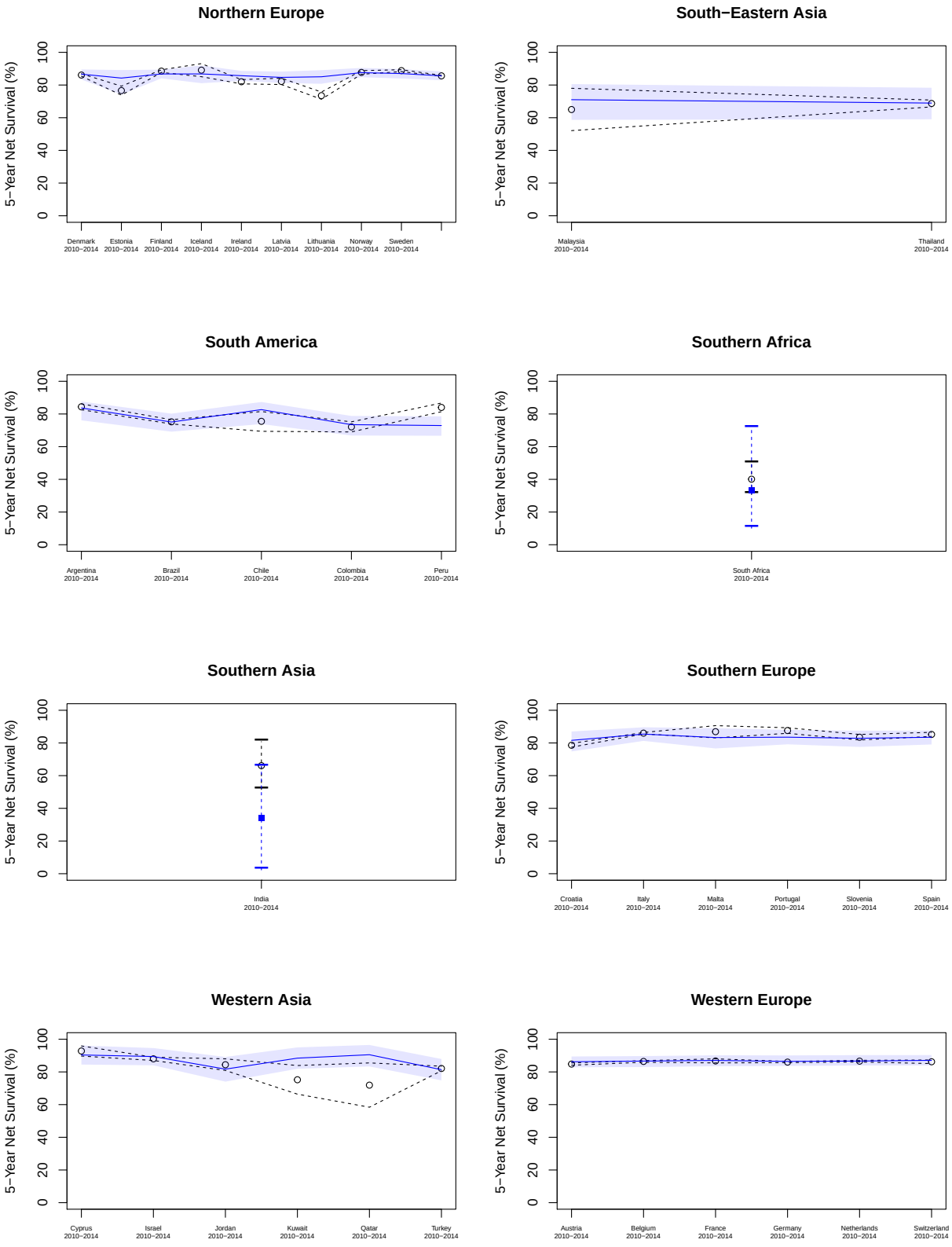
2.2 Model Performance

Comparing our model results with the CONCORD-3 estimates for breast cancer, our posterior predictive checks of our training set found that our 95% UIs overlapped with the CONCORD 95% CIs $94 \cdot 2\%$ of the time and contained the reported point estimate $80 \cdot 9\%$ of the time. Our validation checks of our test set found that $96 \cdot 0\%$ of our 95% UIs overlapped the CONCORD 95% CIs, with a coverage probability of $82 \cdot 0\%$.

2.2.1 Training Set Comparisons

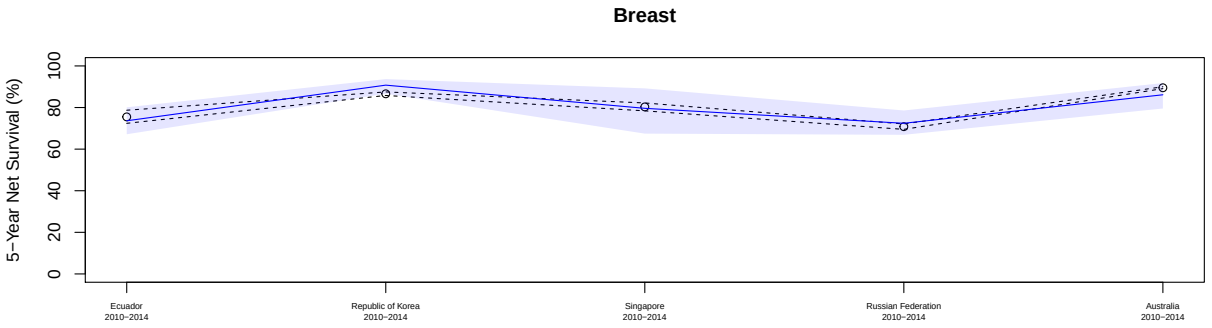
Here we plot our modeled breast cancer survival estimates (mean and 95% UI of the posterior predicted estimates) compared to the CONCORD estimates used to calibrate the model (i.e. training set).
Black lines indicate CONCORD estimates and 95% CI. Blue lines and shaded regions indicate modeled means and 95% UI.


Australia/New Zealand
5−Year Net Survival (%)
0
20
40
60
80
100
New Zealand
2010−2014
Caribbean
Cuba
2010−2014
Puerto Rico
2010−2014
Central America
Costa Rica
2010−2014
Eastern Africa
Mauritius
2005−2009
Eastern Asia
China
2010−2014
Japan
2010−2014
Mongolia
2010−2014
Taiwan
2010−2014
Eastern Europe
Bulgaria
2010−2014
Czechia
2010−2014
Poland
2010−2014
Romania
2010−2014
Slovakia
2010−2014
Northern Africa
Algeria
2010−2014
Northern America
Canada
2010−2014
United States of America
2010−2014


Northern Europe
5−Year Net Survival (%)
0
20
40
60
80
100
Denmark 2010−2014
Estonia 2010−2014
Finland 2010−2014
Iceland 2010−2014
Ireland 2010−2014
Latvia 2010−2014
Lithuania 2010−2014
Norway 2010−2014
Sweden 2010−2014
South−Eastern Asia
Malaysia 2010−2014
Thailand 2010−2014
South America
Argentina 2010−2014
Brazil 2010−2014
Chile 2010−2014
Colombia 2010−2014
Peru 2010−2014
Southern Africa
South Africa 2010−2014
Southern Asia
India 2010−2014
Southern Europe
Croatia 2010−2014
Italy 2010−2014
Malta 2010−2014
Portugal 2010−2014
Slovenia 2010−2014
Spain 2010−2014
Western Asia
Cyprus 2010−2014
Israel 2010−2014
Jordan 2010−2014
Kuwait 2010−2014
Qatar 2010−2014
Turkey 2010−2014
Western Europe
Austria 2010−2014
Belgium 2010−2014
France 2010−2014
Germany 2010−2014
Netherlands 2010−2014
Switzerland 2010−2014

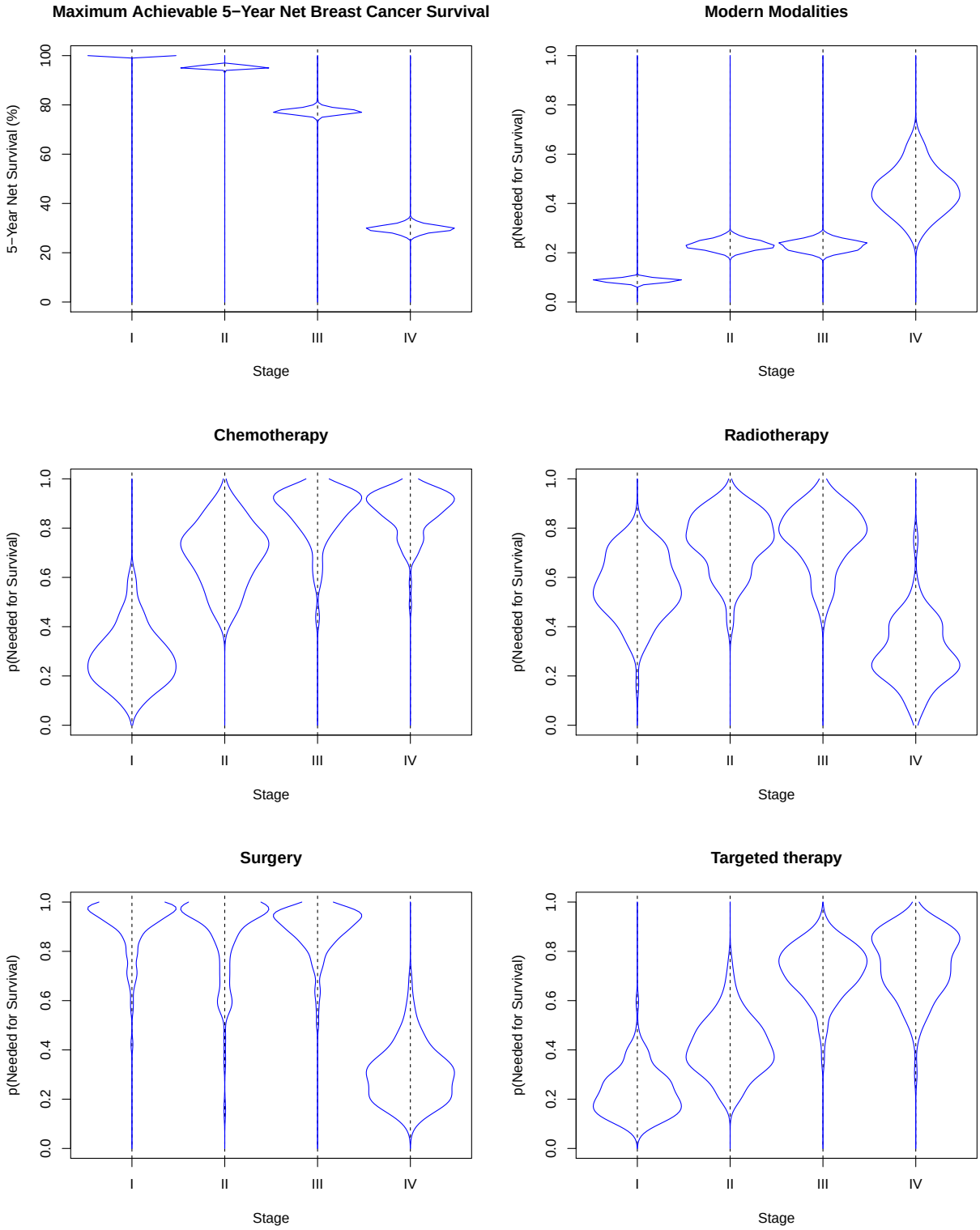
2.2.2 Testing Set Comparisons

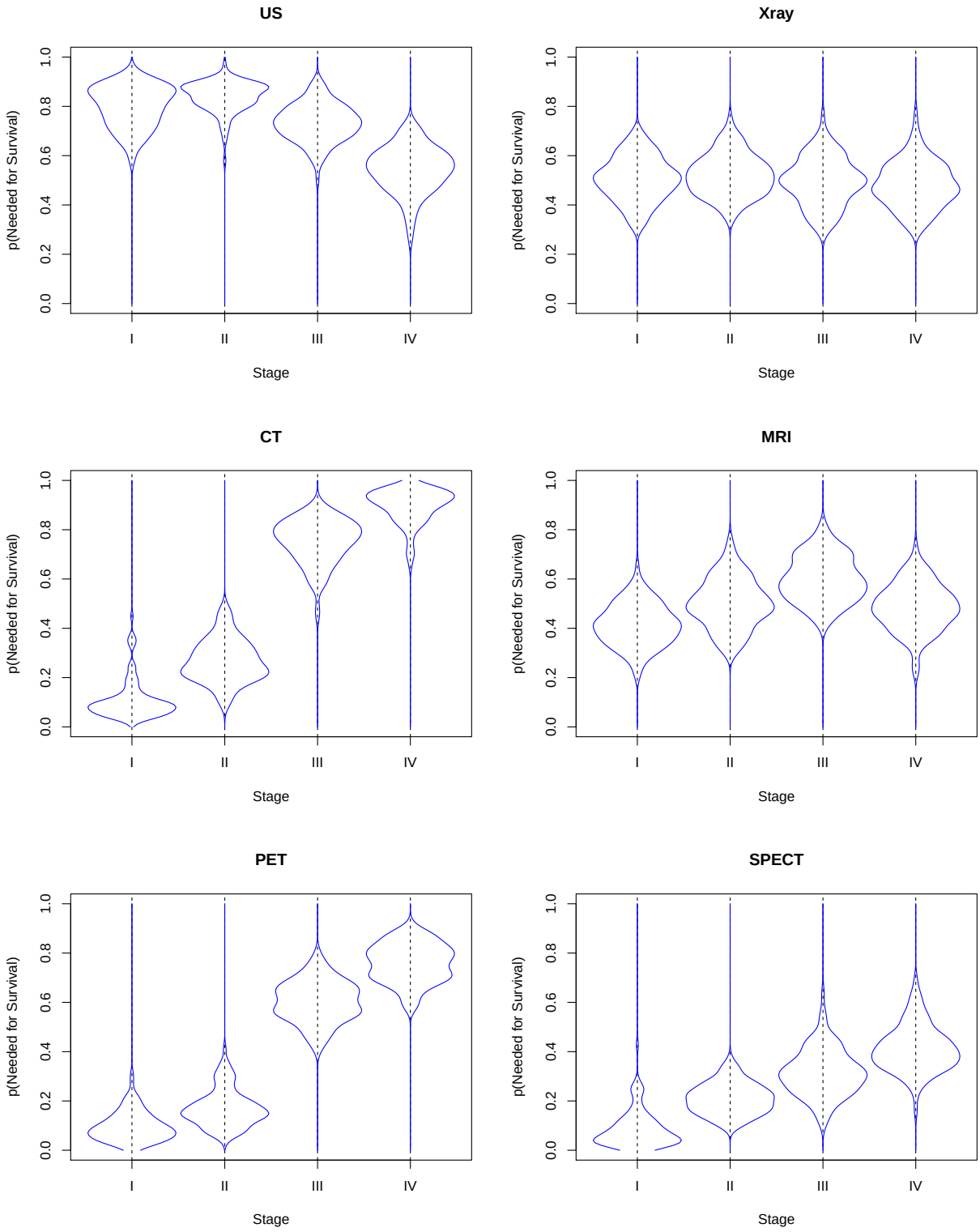
Here we plot our modeled survival estimates (mean and 95% UI of the posterior predicted estimates) compared to the randomly selected CONCORD estimates not used to calibrate the model (i.e. testing set).
Black lines indicate CONCORD estimates and 95% CI. Blue lines and shaded regions indicate modeled means and 95% UI.



3 Calibrated Treatment Impact Parameters

Here we plot the calibrated parameters for the impact of treatment and imaging modalities on breast cancer survival.




US
Xray
CT
MRI
PET
SPECT
p(Needed for Survival)
0.0
0.2
0.4
0.6
0.8
1.0
I
II
III
IV
Stage

4 Additional Results

Estimated Stage III-IV Breast Cancers (%) at Diagnosis