Improving the Evidence Base for Maternal Health Outcomes Worldwide

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A dissertation
submitted in partial fulfillment of the
requirements for the degree of

Doctor of Philosophy

University of Washington

2012

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School of Public Health – Health Services

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Abstract

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Maternal health is a key priority for the international community, as evidenced by commitment to Millennium Development Goal 5. However, evidence on maternal mortality is weak. This thesis addresses the shortcomings in the measurement of maternal mortality through three components. First, it presents a systematic assessment and analysis of all data available for the measurement of maternal mortality over the period 1980-2008, resulting in new estimates of maternal mortality for 181 countries with quantified uncertainty. The results show a remarkable decline in maternal deaths, from 526,300 in 1980 to 342,900 in 2008, an average annual decline of 1.5%. This new evidence suggests there is cause for greater optimism than generally perceived, and that substantial declines in the MMR are possible over relatively short periods of time. Second, the thesis presents an innovative, replicable, and generalizable approach to selecting the multivariable model for the trend analysis of maternal mortality. The third component presents the results of a comprehensive search for maternal deaths in Mexico over the period 2006-2010. This study shows encouraging progress towards the more complete and accurate assessment of causes of maternal mortality in a middle-income country, and offers a useful strategy for improving detailed, cause-specific maternal

mortality data at the country level. The results also highlight the growing importance of indirect obstetric causes, which requires rethinking the health system response to maternal mortality, with health personnel trained to treat the entire woman, not just her pregnancy. Together, this dissertation fills important gaps in the maternal health field, providing new evidence and approaches to the measurement issues that have hampered progress in the past.

ACKNOWLEDGMENTS

I would like to sincerely thank the members of my dissertation committee, who provided guidance, mentorship, and support at every stage. I have been indescribably lucky to work with Emmanuela Gakidou for many years, and she has always provided me with a curious, critical foundation from which to build, as well as good-natured, firm prodding to get things done. Rafael Lozano has been an invaluable resource for the policy, clinical, and practical implications of my work, and has been a reliable source of much-needed humor and balance. Without my weekly Skype calls with Julie Rajaratnam, I have no doubts that this thesis, if I ever finished it, would be a much lesser product; her motivating words propelled me forward when I wanted to step away. Jaime Sepulveda has reminded me to ensure that the research I do has real and lasting impact, and for this I am grateful. I would also like to thank Steven Goodreau, my GSR, who had extremely helpful comments at both my oral exam and final defense.

In addition to the authors listed within this dissertation, I would like to thank two individuals in particular who made enormous intellectual contributions to this work: Kyle J. Foreman and Christopher J. L. Murray.

Without the camaraderie and good humor of my friends and colleagues in the health services program, I would have languished years ago, writing code in a vacuum. I am eternally, inexpressibly grateful for the love, unconditional support, and curiosity of my parents, brother, and all my wonderful in-laws (2 sisters, a brother and another mom and dad!). Most of all, thanks to Steve, for seeing me through this entire process with his usual good humor, patience, and grace. And Sabine: this might have taken a bit longer to finish because you came along, but becoming a mom is the best possible thing that could ever have happened to me, both for my research and my life. I love you all.

I would also like to acknowledge the financial support I received in this doctoral program. I was supported for four years as a research assistant and teaching assistant at the Institute for Health Metrics and Evaluation at the University of Washington. I also received the Warren G. Magnuson Scholarship for the 2011-2012 academic year, an award presented for academic excellence. Partial support for this research came from a Eunice Kennedy Shriver National Institute of Child Health and Human Development research infrastructure grant, 5R24HD042828, to the Center for Studies in Demography & Ecology at the University of Washington

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CHAPTER ONE

Introduction

Background

Maternal mortality as a global priority. Global attention to maternal mortality, defined as the death of a woman while pregnant, during childbirth, or in the 42 days after delivery, began intensifying with the Safe Motherhood Initiative in the late 1980's (Starrs 2006). This increasing focus was largely a response to the sense that maternal health was being neglected in primary health care (Rosenfield and Maine 1985). Several international conferences, including the 1994 International Conference on Population and Development in Cairo and the 1995 Beijing Conference on Women, made clear that maternal health was a key priority for the international community.

When United Nations member states signed the Millennium Declaration in 2000, the prominence of maternal health was solidified as it became one of eight goals for development, Millennium Development Goal 5 (MDG 5) (United Nations General Assembly 2000). The target for MDG 5 is to reduce the maternal mortality ratio (MMR) by three quarters from 1990 levels by 2015. There has been increasing policy attention towards the need to accelerate progress on maternal mortality, as for example with the Obama administration's proposed Global Health Initiative (www.pepfar.gov/ghi/index/htm), as well as active, high-profile civil society groups like the White Ribbon Alliance for Safe Motherhood (www.whiteribbonalliance.org) and Every Mother Counts (everymothercounts.org). Despite this prominence, maternal mortality has largely been seen as an intractable problem, with progress lagging behind

other key health indicators (Hill et al. 2007; Countdown Coverage Writing Group et al. 2008; United Nations 2006).

Maternal mortality measurement. Both the global health community as well as country governments have a strong need for accurate monitoring of maternal mortality. This need is complicated by the widespread perception that maternal mortality is very difficult to measure (Graham et al. 2008; Yazbeck 2007; Campbell 1999; AbouZahr and Wardlaw 2001; Ronsmans 2001). Maternal mortality is a rare event, even where maternal mortality ratios (MMRs) are very high, which can result in enormous sampling error and stochastic variation. In addition, a range of biases and measurement errors can crop up, even in countries with complete vital registration systems (Naghavi et al. 2010).

It is an opportune time to develop new estimates of maternal mortality for four major technical reasons: (1) a detailed analysis of vital registration data, carried out under the Global Burden of Disease Study (Naghavi et al. 2010), has corrected for several known issues; (2) recent work (Gakidou and King 2006; Obermeyer et al. 2010) provides a correction for the problem of survivor bias in sibling history data; (3) there is a growing literature of population-based national and subnational studies of maternal mortality; and (4) new all-cause mortality estimates are available from a systematic assessment of adult female mortality (Rajaratnam, Marcus, Levin-Rector, et al. 2010). Together, these factors provide a key opportunity to advance the field of maternal health and produce trend estimates based on improved technical approaches.

Prior to the work presented in this dissertation, there had been no systematic attempt to develop estimates of maternal mortality for all years in the period relevant for

MDG monitoring. Between 1990 and 2005, the World Health Organization and its partners produced single-year estimates every five years (World Health OrganizationUnited Nations 1996; World Health Organization, United Nations, and UNFPA 2001; United Nations, UNFPA, World Health Organization 2004; World Health Organization et al. 2007), but the estimates were not comparable over time, were controversial with countries, and used a subjective approach to develop uncertainty intervals. In the time since the first component of this dissertation was published (in 2010, in the *Lancet* (Hogan et al. 2010)), WHO and partners have released new time trend estimates (WHO et al. 2012; WHO et al. 2010) which confirm the broad findings of this dissertation.

The measurement of time trends in maternal mortality requires innovative statistical methods. Objective assessment of the performance of any approach is essential, and has been lacking in previous cross-sectional analyses of maternal mortality (Hill et al. 2007; World Health Organization et al. 2007). The growing use of predictive models in global health as a result of the focus on the Millennium Development Goals (i.e., (Rajaratnam, Marcus, Flaxman, et al. 2010; Lim et al. 2008; Glaziou et al. 2011; Mariel M Finucane AB et al. 2011)) has highlighted the need for approaches to choose the "best-performing" models in the context of scanty, mixed-source data. However, despite this need, the process by which the final model is selected is rarely discussed in the literature (i.e., (Mathers and Loncar 2006; Black et al. 2010)). Generalized approaches that allow the researcher to assess a suite of candidate models, and choose the most appropriate based on its performance in tests that are relevant to the specific research question, have not been adequately incorporated into the global health field.

Evidence on cause-specific maternal mortality. In addition to the need for timely, accurate estimates of the umbrella MMR metric, appropriate health system response depends upon more detailed, cause-specific information (Schutte et al. 2010; Berg et al. 2011). The International Classification of Diseases (ICD-10) defines two broad categories of maternal deaths: direct and indirect obstetric deaths (World Health Organization 2004). Direct deaths encompass those causes that result from obstetric complications of the pregnant state, while indirect deaths are those that result from disease or conditions aggravated by the physiologic effects of pregnancy (World Health Organization 2012). The relative burden of these two broad causes of maternal death is a critical distinction for health systems, however in many parts of the world, evidence on specific causes of maternal mortality is very weak (Khan et al. 2006).

Mexico as a case study in maternal mortality measurement. Mexico provides a useful case study for examining the role of indirect obstetric deaths relative to direct. Mexico is a large, federal state with a strong commitment to health, as evidenced by a universal right to health care in the constitution (Frenk et al. 2006). Mexican policies related to maternal mortality in the 1980s were largely shaped by the broader international consensus that population growth was an overarching concern (Finkle and Crane 1985). The focus on population was carried into the 1980s, with both the 1980-82 Global Development Plan and the 1984-88 National Population Plan incorporating targets for population growth as well as contraceptive coverage (Perea and Guillermo 1996).

In the later 1980s and into the early 1990s, maternal mortality emerged as a health issue, and reproductive health became more prominent in the international health agenda (Mills 2006). This was reflected in Mexico in 1993 with the creation of the Department of Reproductive Health within the Ministry of Health (MOH), which was charged with integrating health services for women (Langer and Catino 2006; Perez-Palacios 1996). 1993 also saw the Mexican Declaration for Safe Motherhood, which set up a commission that undertook improving surveillance and data collection, including the pregnancy "checkbox" on the death certificate, and incorporating pregnancy complication checks into National Health Weeks (Langer and Lozano 1996). The early 1990s saw further decentralization, as well as a program (Program for Extension of Coverage, or PAC) to extend a dozen basic services, including family planning and prenatal, perinatal and postnatal care, to the uninsured in poor, rural areas of the country (Frenk et al. 2003; Mills 2006). The 1995 National Development Plan included a new National Reproductive Health Program with safe motherhood as a cornerstone of the plan (Perez-Palacios 1996). Maternal mortality committees were set up in each state to review each case (Langer and Lozano 1996).

In 1997, a major cash transfer program was introduced, PROGRESA. While the primary purpose of the program was poverty alleviation and opportunities for children, there was a health component that ensured that pregnant beneficiaries received regular prenatal checks, nutritional supplements and health education (Latapi and Gonzalez de la Rocha 2008; Nanda, Switlick, and Lule 2005). The election of the opposition Fox government in 2000 led to the expansion of PAC as well as the introduction of a new scheme, "A Fair Start in Life" (APV). APV's primary purpose was to improve maternal

outcomes and newborn health via increasing in-facility births, improving the training of health personnel including traditional birth attendants, and improving medical infrastructure and facilities (Mills 2006; Layton et al. 2008). In 2002, PROGRESA was relaunched and scaled up, as Opportunidades (Latapi and Gonzalez de la Rocha 2008; Molyneux 2006), and in 2004, the major health reform was launched, largely absorbing APV (Layton et al. 2008), with Seguro Popular (SP) expanding coverage for the uninsured (Barber 2006). The SP core benefits package incorporates a range of maternal health services, and the program has invested in improving secondary care, including obstetrics (Sosa-Rubi, Galarraga, and Harris 2009). Between 2004 and 2006, there was a substantial increase in the number of municipalities (12 to 118) providing transport to women needing emergency obstetric care (EmOC); in 2007, the MOH introduced a plan to further improve EmOC throughout the country (Gay and Billings 2009).

As described, the Mexican health system response to maternal mortality has largely focused on those deaths traditionally thought of as "maternal": direct obstetric deaths. However, the epidemiologic transition from communicable to non-communicable disease, well underway in Mexico, has important implications for the distribution of causes of maternal deaths. Mexico has undergone dramatic increases in the prevalence of obesity, particularly in women of lower socioeconomic status (Uauy, Albala, and Kain 2001; Monteiro, Conde, and Popkin 2007; Monteiro et al. 2004; Barquera et al. 2009). This puts the population of reproductive aged women at higher risk for pre-existing hypertensive disorders and diabetes mellitus, as well as a range of obsesity-related complications.

Mexico's strong commitment to improving the evidence base of reproductive health allows for more detailed examination of maternal causes of death. In 2002, a project was introduced to trace back deaths occurring in women of reproductive ages, in order to identify misclassified or miscoded maternal deaths (Anon. 2009). This project provides a rich source of information about the distribution of causes of maternal death in a middle-income country, as well as useful lessons learned for other health systems looking to improve their maternal health evidence base.

Statement of the problem

In summary, the global maternal health field suffers from a lack of evidence. Without strong evidence on time trends, with quantified uncertainty, health systems cannot prioritize their limited resources appropriately. Maternal mortality presents a measurement challenge that has not been adequately met. Appropriate assessment of candidate statistical approaches must be addressed. Innovative approaches are needed to assess the MMR as well as more detailed cause distributions, with particular attention to the division between direct and indirect obstetric deaths.

Purpose

This dissertation undertakes to address the measurement shortcomings in the global maternal health field. This is accomplished through three distinct components:

- The first component presents a systematic assessment and analysis of all data available for the measurement of maternal mortality over the period 1980-2008, and produces new estimates of maternal mortality (both the MMR and the number of maternal deaths) for 181 countries with uncertainty.
- The second component presents an innovative approach to selecting the multivariable model for the trend analysis of maternal mortality, which presents an array of technical modeling challenges.
- Finally, the third component presents a detailed analysis of a single maternal mortality dataset from a middle-income country, Mexico, highlighting the importance of continued work towards cause-specific maternal mortality estimates. It also provides a comparison of the socio-demographic characteristics and health services use of direct and indirect decedents, as well as a descriptive analysis of disparities in direct and indirect mortality outcomes.

References

AbouZahr, C, and T Wardlaw. 2001. "Maternal Mortality at the End of a Decade: Signs of Progress?." *Bulletin of the World Health Organization* 79 (6): 561–568.

Anon. 2009. *Busqueda Intencionada De Muertes Maternas en Mexico*. Mexico: Secretaria de Salud.

Barber, S. 2006. "Does the Quality of Prenatal Care Matter in Promoting Skilled Institutional Delivery? a Study in Rural Mexico." *Maternal & Child Health Journal* 10 (5): 419–425.

Barquera, S, I Campos-Nonato, L Hernández-Barrera, M Flores, R Durazo-Arvizu, R Kanter, and J A Rivera. 2009. "Obesity and Central Adiposity in Mexican Adults: Results From the Mexican National Health and Nutrition Survey 2006." *Salud Pública De México* 51: 595–603.

Berg, Cynthia J, William M Callaghan, Zsakeba Henderson, and Carla Syverson. 2011. "Pregnancy-Related Mortality in the United States, 1998 to 2005.." *Obstetrics &*

Gynecology 117 (5) (May): 1230. doi:10.1097/AOG.0b013e31821769ed.
Black, Robert E, Simon Cousens, Hope L Johnson, Joy E Lawn, Igor Rudan, Diego G Bassani, Prabhat Jha, et al. 2010. "Global, Regional, and National Causes of Child Mortality in 2008: a Systematic Analysis.." *Lancet* 375 (9730) (June 5): 1969–1987. doi:10.1016/S0140-6736(10)60549-1.
Campbell, O M R. 1999. "Measuring Progress in Safe Motherhood Programmes: Uses and Limitations of Health Outcome Indicators." *Safe Motherhood Initiatives: Critical Issues*.
Countdown Coverage Writing Group, Countdown to 2015 Core Group, J Bryce, B Daelmans, A Dwivedi, V Fauveau, J E Lawn, et al. 2008. "Countdown to 2015 for Maternal, Newborn, and Child Survival: the 2008 Report on Tracking Coverage of Interventions." *The Lancet* 371 (9620) (April): 1247–1258. doi:10.1016/S0140-6736(08)60559-0.
Finkle, J L, and B B Crane. 1985. "Ideology and Politics at Mexico City: the United States at the 1984 International Conference on Population." *Population and Development Review* 11 (1): 1–28.
Frenk, J, E Gonzalez-Pier, O Gomez-Dantes, M A Lezana, and F M Knaul. 2006. "Comprehensive Reform to Improve Health System Performance in Mexico." *Lancet* 368 (9546) (October 1): 1524–1534.
Frenk, J, J Sepúlveda, O Gómez-Dantés, and F Knaul. 2003. "Evidence-Based Health Policy: Three Generations of Reform in Mexico." *The Lancet* 362 (9396): 1667–1671.
Gakidou, E, and G King. 2006. "Death by Survey: Estimating Adult Mortality Without Selection Bias From Sibling Survival Data." *Demography* 43 (3) (August 1): 569–585.
Gay, J, and D Billings. 2009. *Evolution of the MacArthur Foundation's Work in Mexico to Reduce Maternal Mortality, 2002-2008*. *Techreport*.
Glaziou, Philippe, Katherine Floyd, Eline L Korenromp, Charalambos Sismanidis, Ana L Bierrenbach, Brian G Williams, Rifat Atun, and Mario Raviglione. 2011. "Lives Saved by Tuberculosis Control and Prospects for Achieving the 2015 Global Target for Reducing Tuberculosis Mortality." *Bulletin of the World Health Organization* 89 (8) (May 31): 573–582. doi:10.2471/BLT.11.087510.
Graham, W J, S Ahmed, C Stanton, C L Abou-Zahr, and OMR Campbell. 2008. "Measuring Maternal Mortality: an Overview of Opportunities and Options for Developing Countries." *BMC Medicine* 6 (1): 12. doi:10.1186/1741-7015-6-12.
Hill, K, K Thomas, C AbouZahr, N Walker, L Say, M Inoue, E Suzuki, and Maternal Mortality Working Group. 2007. "Estimates of Maternal Mortality Worldwide Between 1990 and 2005: an Assessment of Available Data." *Lancet* 370 (9595) (October 19): 1311–1319. doi:10.1016/S0140-6736(07)61572-4. http://linkinghub.elsevier.com/retrieve/pii/S0140673607615724.
Hogan, Margaret C, Kyle J Foreman, Mohsen Naghavi, Stephanie Y Ahn, Mengru Wang, Susanna M Makela, Alan D Lopez, Rafael Lozano, and Christopher J L Murray. 2010. "Maternal Mortality for 181 Countries, 1980-2008: a Systematic Analysis of Progress Towards Millennium Development Goal 5.." *Lancet* 375 (9726) (May 8): 1609–1623. doi:10.1016/S0140-6736(10)60518-1.
Khan, Khalid S, Daniel Wojdyla, Lale Say, A Metin Gulmezoglu, and Paul FA Van

Look. 2006. “WHO Analysis of Causes of Maternal Death: a Systematic Review.” *The Lancet* 367 (9516) (April): 1066–1074. doi:10.1016/S0140-6736(06)68397-9.
Langer, A, and J Catino. 2006. *The Health of Women in Mexico: Opportunities and Challenges*. *Book*.
Langer, A, and R Lozano. 1996. “The Health of Women in Mexico: Current Panorama and Future Prospects.” *Changing Structure of Mexico: Political, Social, and Economic Prospects*: 333–48.
Latapi, A E, and M Gonzalez de la Rocha. 2008. *Girls, Mothers, and Poverty Reduction in Mexico: Evaluating Progresa-Opportunidades*. *Book*.
Layton, M D, B Campillo Carrete, I A Terrazas, and A M Sanchez Rodriguez. 2008. *Reducing Maternal Mortality in Mexico*. *Techreport*.
Lim, S S, D B Stein, A Charrow, and C J L Murray. 2008. “Tracking Progress Towards Universal Childhood Immunisation and the Impact of Global Initiatives: a Systematic Analysis of Three-Dose Diphtheria, Tetanus, and Pertussis Immunisation Coverage.” *The Lancet* 372 (9655): 2031–2046.
Mariel M Finucane AB, Gretchen A Stevens DSc, Melanie J Cowan MPH, Goodarz Danaei MD, John K Lin AB, Christopher J Paciorek PhD, Gitanjali M Singh PhD, et al. 2011. “National, Regional, and Global Trends in Body-Mass Index Since 1980: Systematic Analysis of Health Examination Surveys and Epidemiological Studies with 960 Country-Years and 9Â·1 Million Participants.” *Lancet* 377 (9765) (February 12): 557–567. doi:10.1016/S0140-6736(10)62037-5.
Mathers, Colin D, and Dejan Loncar. 2006. “Projections of Global Mortality and Burden of Disease From 2002 to 2030..” *PLoS Medicine* 3 (11) (November): e442. doi:10.1371/journal.pmed.0030442.
Mills, L. 2006. “Maternal Health Policy and the Politics of Scale in Mexico.” *Social Politics: International Studies in Gender, State & Society* 13 (4): 487.
Molyneux, M. 2006. “Mothers at the Service of the New Poverty Agenda: Progresa/Oportunidades, Mexico's Conditional Transfer Programme.” *Social Policy & Administration* 40 (4): 425–449.
Monteiro, C A, W L Conde, and B M Popkin. 2007. “Income-Specific Trends in Obesity in Brazil: 1975 2003.” *American Journal of Public Health* 97 (10): 1808.
Monteiro, C A, W L Conde, B Lu, and B M Popkin. 2004. “Obesity and Inequities in Health in the Developing World.” *International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity* 28 (9) (September 1): 1181–1186.
Naghavi, M, S Makela, K Foreman, J O'Brien, F Pourmalek, and R Lozano. 2010. “Algorithms for Enhancing Public Health Utility of National Causes-of-Death Data.” *Population Health Metrics* 8 (May 1): 9.
Nanda, G, K Switlick, and E Lule. 2005. *Accelerating Progress Towards Achieving the MDG to Improve Maternal Health: a Collection of Promising Approaches*. *Techreport*.
Obermeyer, Ziad, Julie Knoll Rajaratnam, Chang H Park, Emmanuela Gakidou, Margaret C Hogan, Alan D Lopez, and Christopher J L Murray. 2010. “Measuring Adult Mortality Using Sibling Survival: a New Analytical Method and New Results for 44 Countries, 1974-2006..” *PLoS Medicine* 7 (4) (April): e1000260. doi:10.1371/journal.pmed.1000260.

Perea, F, and J Guillermo. 1996. *Three Comments on Population Policies in Mexico From a Reproductive Rights Approach*. *Book*.

Perez-Palacios, G. 1996. "Reproductive Health in Mexico and Latin America." *Advances in Contraception* 12 (4): 251–256.

Rajaratnam, J K, J R Marcus, A D Flaxman, H Wang, A Levin-Rector, L Dwyer, M Costa, A D Lopez, and C J L Murray. 2010. "Neonatal, Postneonatal, Childhood, and Under-5 Mortality for 187 Countries, 1970-2010: a Systematic Analysis of Progress Towards Millennium Development Goal 4." *The Lancet*.

Rajaratnam, J K, J R Marcus, A Levin-Rector, A N Chalupka, H Wang, L Dwyer, M Costa, A D Lopez, and C J Murray. 2010. "Worldwide Mortality in Men and Women Aged 15-59 Years From 1970 to 2010: a Systematic Analysis." *Lancet* 375 (9727) (May 1): 1704–1720.

Ronsmans, C. 2001. "How Can We Monitor Progress Towards Improved Maternal Health." *Studies in Health Services Organisation and Policy* 17: 313–338.

Rosenfield, A, and D Maine. 1985. "Maternal Mortality--a Neglected Tragedy. Where Is the M in MCH?." *Lancet* 2 (8446) (July 13): 83–85.

Schutte, Joke M, Layla de Jonge, Nico W E Schuitemaker, Job G Santema, Eric A P Steegers, and Jos van Roosmalen. 2010. "Indirect Maternal Mortality Increases in the Netherlands." *Acta Obstetricia Et Gynecologica Scandinavica* 89 (6) (June): 762–768. doi:10.3109/00016341003657876.

Sosa-Rubi, S G, O Galarraga, and J E Harris. 2009. "Heterogeneous Impact of the 'Seguro Popular' Program on the Utilization of Obstetrical Services in Mexico, 2001–2006: a Multinomial Probit Model with a Discrete Endogenous Variable." *Journal of Health Economics* 28 (1): 20.

Starrs, Ann M. 2006. "Safe Motherhood Initiative: 20 Years and Counting." *The Lancet* 368 (9542) (September): 1130–1132. doi:10.1016/S0140-6736(06)69385-9.

Uauy, R, C Albala, and J Kain. 2001. "Obesity Trends in Latin America: Transiting From Under-to Overweight." *Journal of Nutrition* 131 (3): 893S.

United Nations. 2006. *The Millennium Development Goals Report 2006*. *Techreport*.

United Nations General Assembly. 2000. "United Nations Millennium Declaration." *Miscellaneous* A/RES/55/2.

United Nations, UNFPA, World Health Organization. 2004. *Maternal Mortality in 2000: Estimates Developed by WHO, UNICEF, UNFPA*. *Techreport*.

WHO, UNICEF, UNFPA, The World Bank. 2012. *Trends in Maternal Mortality: 1990 to 2010*. World Health Organization.

WHO, United Nations, UNFPA, The World Bank. 2010. *Trends in Maternal Mortality: 1990 to 2008*. *Techreport*.

World Health Organization. 2004. *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision Instruction Manual. Book*. Vol. 2.

World Health Organization. 2012. *The WHO Application of ICD-10 to Deaths During Pregnancy, Childbirth and the Puerperium: ICD-MM*. Geneva, Switzerland: World Health Organization.

World Health Organization, United Nations. 1996. *Revised 1990 Estimates of Maternal Mortality: a New Approach by WHO and UNICEF*. *Techreport*.

World Health Organization, United Nations, and UNFPA. 2001. *Maternal Mortality in 1995: Estimates Developed by WHO, UNICEF, and UNFPA*. *Techreport*.

World Health Organization, United Nations, UNFPA, World Bank. 2007. *Maternal Mortality in 2005: Estimates Developed by WHO, UNICEF, UNFPA and the World Bank. Techreport*.
Yazbeck, Abdo S. 2007. "Challenges in Measuring Maternal Mortality.." *Lancet* 370 (9595) (October 13): 1291–1292. doi:10.1016/S0140-6736(07)61553-0.

CHAPTER TWO

Maternal mortality for 181 countries, 1980-2008: a systematic analysis of progress towards Millennium Development Goal 5

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Abstract

Background: Maternal mortality remains a major challenge to health systems worldwide. Reliable information on the levels and trends in maternal mortality is essential for resource mobilization, planning and evaluating progress towards Millennium Development Goal 5 (MDG5), the target for which is a three quarters reduction in the maternal mortality ratio (MMR) from 1990 to 2015.

Methods: We constructed a database of 2,656 observations of maternal mortality for 181 countries for the period 1980-2008 from vital registration data, censuses, surveys and verbal autopsy studies. We use robust analytical methods to generate estimates of maternal deaths and the MMR for each year between 1980 and 2008. We explored the sensitivity of our numbers to model specification and demonstrate the out-of-sample predictive validity of our methods.

Findings: Global maternal deaths in 2008 are estimated to be 342,900 (302,100-394,300) down from 526,300 (446,400-629,600) in 1980. The global MMR declined from 422 (358-505) in 1980, to 320 (272-388) in 1990, and was 251 (221-289) per 100,000 live births in 2008. The annualized rate of decline of the global MMR since 1990 is 1.3%. Rates of annual decline in the MMR vary across countries from 8.8%to an increase of 5.5% over the period 1990 to 2008. HIV is responsible for 61,400 maternal deaths in 2008, while more than 50% of all maternal deaths are concentrated in only six countries.

Interpretation: Contrary to prior studies, we find that there has been substantial, albeit varied, progress towards MDG5. Even though only 23 countries are on track to achieve a 75% decline by 2015, countries such as Egypt, China, Ecuador and Bolivia have been achieving accelerated progress. These findings are encouraging and highlight the need for further in-depth studies and continued, improved measurement of maternal mortality.

Funding: Bill and Melinda Gates Foundation

Introduction

Maternal mortality, the death of women during pregnancy, childbirth or in the 42 days after delivery, remains a major challenge to health systems worldwide. Global initiatives to intensify policy intervention on maternal mortality began with the Safe Motherhood Initiative in 1987 (Starrs 2006), responding to a growing recognition that primary health care programs in many developing countries were not adequately focused on maternal health (Rosenfield and Maine 1985). The 1994 International Conference on Population and Development confirmed international commitment to reproductive health (Development; Obaid 2009). The focus on maternal mortality was heightened in development circles when reducing maternal mortality became one of eight goals for development in the Millennium Declaration (MDGs): MDG 5 (Ronsmans, Graham, and group 2006). The target for MDG5 is to reduce the maternal mortality ratio by three quarters from 1990 to 2015 (United Nations General Assembly 2000). It is widely perceived that progress on maternal mortality has been slow, and in many places nonexistent (Hill et al. 2007; Countdown Coverage Writing Group et al. 2008; United Nations 2009). Accelerating progress on maternal mortality has received renewed policy attention in the US through the Obama administration's proposed Global Health Initiative (www.pepfar.gov/ghi/index/htm). High profile civil society groups such as the White Ribbon Alliance continue to bring further attention.

The need for accurate monitoring of maternal mortality has long been recognized, both to advocate for resources and policy attention as well as to track progress (Graham, Foster, et al. 2008; Graham and Hussein 2006; Shiffman 2000). Maternal mortality, however, is considered very difficult to measure (Yazbeck 2007; Graham 2002; Graham, Ahmed, et al. 2008; Campbell 1999; AbouZahr and Wardlaw 2001; AbouZahr 2003). Several efforts have been made over

nearly three decades to improve the quality of information on maternal mortality, including the incorporation of sibling history modules in the Demographic and Health Surveys (DHS) and similar surveys (Graham, Brass, and Snow 1989; Stanton, Abderrahim, and Hill 2000), the inclusion of questions on whether recent deaths were related to pregnancy in censuses (Stanton et al. 2001; Hill 2009), and the use of record linkage or confidential enquiry to identify under-registration of maternal deaths in vital registration systems (Atrash, Alexander, and Berg 1995; Schuitemaker et al. 2004).

Beginning in 1996, WHO sponsored the development of country estimates of maternal mortality for the years 1990, 1995, 2000, and 2005 (World Health OrganizationUnited Nations 1996; World Health Organization, United Nations, and UNFPA 2001; World Health Organization et al. 2007; United Nations, UNFPA, World Health Organization 2004). The most recent assessment of maternal mortality jointly sponsored by WHO, UNICEF, UNFPA, and the World Bank reported 576,300 maternal deaths globally in 1990 and 535,900 maternal deaths in 2005, a 0.48% annual rate of decline (Hill et al. 2007). The corresponding decline in the global maternal mortality ratio (the number of maternal deaths per 100,000 live births) was 0.37% per annum. As a separate analysis, Hill et al. estimated an annual rate of decline of 2.5% per year for a subset of 125 countries with more than one observation. For the two results to be consistent, a substantial fraction of countries without multiple observations must have been experiencing increases in the MMR.

Given the continued prominence of maternal mortality as a health and development goal, it is timely to reassess the global levels and trends in maternal mortality. Recent developments provide an opportunity for substantially improved estimates of maternal mortality. First, the Global Burden of Disease study has undertaken extensive analysis of vital registration data to

identify misclassified deaths from causes such as maternal mortality (Naghavi et al. 2010). Second, methodological advances allow for the correction of known biases in survey sibling history data including whether sibling deaths are from maternal causes (Gakidou and King 2006). Third, there is a growing literature of population-based verbal autopsy studies that measure maternal mortality at the national and sub-national level. Fourth, a systematic assessment of data sources on adult female mortality provides estimates of mortality for reproductive aged women from 1970 to 2010 (Rajaratnam et al. 2010). Finally, methodological developments in other fields provide improved tools for estimation. In this study, we take advantage of these developments and use all available data to assess levels and trends in maternal mortality from 1980 to 2008 for 181 countries.

Methods

Definitions. Table 1 classifies, by timing and cause, the types of deaths of pregnant or recently pregnant women that may be captured by different data systems. Deaths during pregnancy or less than 42 days after termination of pregnancy are *early*, those after 42 days up to one year are *late*. Four groups of causes can also be identified: direct obstetric causes, causes aggravated by pregnancy (often called indirect), HIV, and incidental causes unrelated to pregnancy. Vital registration systems using ICD 10 assign deaths in A, B, E, and F to Chapter O. The ICD Manual (World Health Organization 2004) and the MDG manual (United Nations Development Program 2003) recommend that the maternal mortality rate include deaths in categories A, B and C. Late maternal deaths and deaths from incidental causes other than HIV should not to be included in international comparisons of the MMR.

Data. We systematically searched for data on maternal mortality from 1980 to present. Data can be divided into four types: vital registration systems; sibling history data from household surveys; data from censuses and surveys on deaths in the household; and published studies reporting population-based studies of maternal mortality, both national and sub-national. Vital registration of cause of death data is the richest resource for measuring maternal mortality. We constructed a dataset based primarily on the World Health Organization Mortality Database (World Health Organization), and supplemented by a web search of country statistical offices. Several issues with vital registration data must be taken into consideration when constructing a time series. First, periodic changes in the ICD rules and codes can lead to discontinuities that do not reflect true trends. ICD9 introduced two changes: clear definition of the 42-day period for a maternal death and the inclusion of indirect causes of maternal death. ICD10 explicitly added codes for late maternal deaths and made some changes in the coding practice for indirect causes. Second, maternal deaths can be incorrectly assigned to other causes (Pattinson et al. 2009). Causes which often include misclassified maternal deaths include disseminated intravascular coagulation (D65), peritonitis (K65), septicaemia (A41, A42), pulmonary embolism (I26), acute and chronic renal failure (N18 and N19), acute abdomen (R10) and hypovolaemic shock (R57.1) (Schuitemaker et al. 2004; Naghavi et al. 2010; Turner et al. 2002; Kao et al. 1997; Ordi et al. 2009). In addition, some maternal deaths can be assigned to ill-defined causes of death such as "other ill-defined and unspecified causes of mortality" (R99), "unattended death" (R98) and "respiratory arrest" (R09.2). Naghavi et al. have produced a corrected vital registration dataset which provides 2,186 country-years covering the period 1980-2008 (Naghavi et al. 2010). Correcting for misclassification on average increases maternal deaths in the vital registration country-years by 42%. This is consistent with literature examining under-registration of maternal

deaths (Karimian-Teherani et al. 2002; Horon 2005; Deneux-Tharaux et al. 2005). Care must be taken in interpreting previous studies as some also include as under-registered deaths suicides and later maternal deaths which are not included in the official maternal death definition for the MMR. In this analysis, we count all deaths coded to the maternal chapter in the ICD as maternal deaths, encompassing codes O00-O99. It is important to note that the addition of late maternal deaths in ICD-10 (Laurenti and Buchalla 2001) may lead to some inconsistencies in time trends, but this effect will be small in most places. On average in ICD10 datasets, less than 2% of maternal deaths are coded as late maternal, but there are some important exceptions, such as the United States.

We analyzed sibling history microdata from the DHS (DHS) and the US Centers for Disease Control and Prevention (CDC) International Reproductive Health Surveys (Centers for Disease Control and Prevention), totaling 97 surveys from 53 countries. Sibling histories ask respondents to report on all of their siblings, including sex, date of birth, current status (alive or dead), and current age or age at death. Among sisters who died between the ages of 15 and 49, questions identify whether the death occurred during pregnancy, childbirth or within six weeks or two months after the termination of pregnancy. In this analysis, we pool surveys together within countries and apply Gakidou-King weights to correct for survivor bias (Gakidou and King 2006; Obermeyer et al. 2010). Using these weights, we estimate the age-specific proportion maternal among deaths in women of reproductive age (PMDF) for five year periods going back from the time of the most recent survey in each country, for a maximum of three periods prior to the most distant survey in each country.

A further 26 observations are based on survey or census information on deaths in households and whether the death occurred during pregnancy, childbirth or within six weeks of

delivery for women of reproductive age. Both the sibling history data and the household death data capture pregnancy related deaths (categories A, B, C and D in Table 1) and thus may be an overestimate of the fraction of deaths due to maternal causes.

We also undertook a literature review to identify published estimates of maternal mortality. We searched PubMed for the search terms "maternal mortality AND country name" for all non-Organization for Economic Co-operation and Development (OECD) countries; we excluded OECD countries from the literature search because most of these countries have high quality vital registration data. We also reviewed all citations in the WHO publication "Maternal Mortality: A Global Factbook" (World Health Organization 1991). This search produced 9,659 titles; from these, 593 abstracts were identified as potentially relevant. 209 papers were identified from these abstracts, from which 61 studies were extracted and added to the database. In addition, we searched using the term "verbal autopsy" and identified 1,042 titles, which yielded a further 22 studies with data on maternal causes. We also searched the Chinese language website Wanfang Data for "maternal mortality surveillance" and identified eight papers. Studies were excluded if they were hospital or clinic-based, intervention studies, used the indirect sisterhood method, or judged to be of low quality. Indirect sisterhood studies were excluded because at best, they provide a summary assessment of maternal mortality covering a long time period prior to the survey (Hill et al. 2006; Garenne and Friedberg 1997).

Before undertaking statistical analysis of the dataset combining all the data sources listed above, implausible values or outliers in the data were identified via qualitative review. 314 (11.8% (314/2656)) site-years of data were excluded via expert review using the following criteria: outliers relative to other measurements in the same country, outliers relative to what would be expected based on the model predictions, and outliers relative to MMRs observed in

countries with similar levels of development and health system access. Many of these outliers are from sub-national studies with implausibly low rates. These points are plotted on the graphs, but do not contribute to the estimation process.

Analysis

From each of the data sources described above, we extract the proportion of all female deaths which are due to maternal causes for five-year age groups in the reproductive age period (15-49). These proportions were applied to the new time series of adult female mortality based on a systematic assessment of all adult mortality sources for each country 1970-2010 (Rajaratnam et al. 2010). For computation of maternal mortality ratios, we use population and live births from the UN Population Division (United Nations Population Division 2009).

We modeled both the count of maternal deaths using generalized negative binomial regression and the log of the maternal death rate using ordinary least squares (OLS) and robust regression – details on the sensitivity analysis are presented in the Web appendix. We also tested Poisson regression to model the count but found its performance to be dramatically worse than the generalized negative binomial. Based on tests of predictive validity (see below), we selected the modeling strategy with the best out-of-sample performance. Our modeling strategy is a variant of spatial-temporal regression used in fields as disparate as geology, agriculture, and meteorology (Handcock and Wallis 1994; Landagan and Barrios 2007). The basic form of the model is:

$$\ln(\mu_{a,i,t}) = \beta X_{a,i,t} + M_{a,i,t} + e$$

Where μ is the maternal death rate, a is age, i is country, t is a year. $X_{a,i,t}$ is a vector of covariates that explain variation in maternal mortality rates. Substantial variation in the maternal mortality

rate is not explained by these covariates, and the unexplained component, $M_{a,i,t}$, varies systematically over time and across countries. Spatial-temporal regression models capture this systematic variation through local regression with weights on time and space (Knotters, Brus, and Voshaar 1995). Loess regression (Cleveland and Devlin 1988) is a special case where weighting only occurs in time and not across countries. □ is the stochastic error in the maternal mortality rate due to sampling and to unmeasured factors that are not correlated in time and space.

The model is estimated in two stages: we first estimate the linear model $\beta X_{a,i,t}$ and then use spatial-temporal local regression to estimate $M_{a,i,t}$. Our choice for the linear model depends on available covariates; included covariates must be a comparable, complete time series for the period 1980-2008. Based on the published literature and prior theory, we selected the total fertility rate (TFR), GDP per capita, HIV seroprevalence, neonatal mortality, and age-specific female education, as well as indicators for 5-year age groups (15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49). We considered including skilled birth attendance, but found that it was collinear with other covariates (r=0.73 with neonatal mortality, r=0.72 with education, r=0.67 with GDP per capita) and did not improve model performance. We examined the univariate relationship of each covariate with the dependent variable as well as with the model residuals to select the appropriate transformation of each covariate. We use robust regression, which uses Huber and biweights to minimize the influence of outliers on the parameter estimates (LP 2009).

To estimate $M_{a,i,t}$, we apply spatial-temporal regression to the residuals over space and time from this first-stage model. Details of the time weights used for the spatial-temporal local regression are provided in Appendix A1. Weights are also included across age-groups to borrow strength across ages. Spatial correlation was only allowed within the 21 GBD regions used in this

study. If a given country has both national and subnational data, we assign a total of one-fifth of the weight in the local regression to sub-national studies and four fifths of the weight to national studies to prevent subnational studies from overly influencing the national assessment. Each local regression was estimated using OLS. We truncated observed residuals to three standard deviations of the mean of the residuals to reduce the impact of extreme outliers on the spatial temporal regression.

To validate our modeling approach, we conducted extensive tests of predictive validity. Four different types of predictive validity tests were undertaken: a) holding out a random sample of 20% of country-years of data; b) holding out all data from a random sample of 20% of countries; c) holding out the first 20% of years of data for all countries; and d) holding out the last 20% of years for all countries. For each of these datasets where samples of the data have been withheld, we estimate our model including the linear and spatial-temporal local regression components and compare predictions of the MMR to the real data in the 20% of the sample held out. We repeat these tests 30 times to ensure our results are not an artifact of a given random sample of the data being withheld. In Appendix A1, we also examine the predictive validity of a range of alternative model specifications and model families; in the body of the paper we only present results for the linear component and the full model for the best performing strategy. Our uncertainty estimates incorporate four sources of uncertainty: sampling uncertainty in the underlying measurements of the maternal mortality rate from each data source; parameter uncertainty in both the linear model and the spatial-temporal local regressions (Tomz, Wittenberg, and King 2003); and an estimate of fundamental uncertainty incorporating both the impact of non-sampling variance and systematic variation in the expected value not captured in the model. This is a conservative approach that overestimates uncertainty because in principle,

we would not want to propagate non-sampling variance into the estimate of uncertainty in the expected value of the maternal death rate. We provide further details in the technical appendix. HIV-related maternal deaths are of particular interest. We carried out a counterfactual analysis, exploring the effect of removing HIV from the population on maternal mortality. We generate counterfactual estimates of HIV by using the final estimated model (including both the linear and $M_{a,i,t}$ components) but set the HIV and HIV-squared covariates to zero.

All of the analysis was done in Stata/MP 11.0 (Stata Corporation).

Role of the funding source

The funders had no role in study design, data collection and analysis, interpretation of data, decision to publish, or preparation of the manuscript. The corresponding author had full access to all data analysed and had final responsibility for the decision to submit this original research paper for publication.

Results

Table 2 shows the source of the 2,656 observations included in the dataset for the period 1980-2008. Vital registration data is the dominant source, accounting for 82% of the total observations. Other sources contribute 470 observations. Figure 1 shows that 21 countries have no empirical observations over the period, the largest of which are Angola and Saudia Arabia in terms of births; together these countries account for 2.2% of global births. As a region, North Africa and the Middle East is particularly weak in terms of data density except for Egypt, Kuwait and Iran. Because of the availability of sibling history data, many countries in sub-Saharan Africa have more than five observations. Most high-income countries have a nearly complete

time series of vital registration data, while other lower income settings, such as Bangladesh and Tanzania, have substantial data from surveys and sub-national studies.

Figure 2 (A-D) shows four different data scenarios along with our final predictions for the maternal mortality ratio (MMR). We have a complete time series of vital registration data from Mexico (Figure 2A), which shows a consistent, downward trend in the MMR from 1980 to 1995 and then a period of minimal change. Figure 2B shows a mix of vital registration and sibling history data from the Dominican Republic. In this case, the results of the sibling histories show higher rates in each year. Our model estimates reflect both sources of data. India (Figure 2C) has the largest number of maternal deaths of any country in the world, and there are numerous data sources available to estimate maternal mortality in the country. The figure illustrates marked inconsistencies between sources. In some cases, sources cover only a component of the national population, which may explain these patterns. For example, the Survey of Causes of Death, Rural covers only rural populations and the Medical Certification of Causes of Death covers largely urban populations. We have chosen to use only national sources with the least apparent bias: the sample registration system (Registrar General 2006), the National Family Health Surveys (NFHS rounds 1 and 2) and the District Level Household Surveys (DLHS rounds 2 and 3). Together, these sources suggest a substantial decline in maternal mortality, though there is considerable variation among the sources for any given year. The most recent round of the DLHS provides substantially higher estimates than do the previous rounds, but is in line with the NFHS 2. Figure 2D shows estimates from Mali, where we have three DHS that include a sibling history module (in 1995, 2001 and 2006). Similar data plots, along with the final estimates, are available for all countries in the appendix.

The β-coefficients from the linear model are presented in Webtable 2. TFR exhibits the strongest relationship with maternal mortality of all the covariates, with higher fertility associated with higher maternal mortality. Of the covariates included in the model GDP per capita has the next strongest relationship, with higher GDP being associated with lower rates of maternal mortality. All of the covariates were highly significant in the linear model with a p-value<0.001, and were in the expected direction.

Predictive validity results for the four out-of-sample tests are presented in Table 3. All measures of out-of-sample performance demonstrate improved performance using the spatial-temporal model compared to the linear model. In terms of median relative error, which is resistant to extreme outliers, for improvements relevant to 160 countries with some data, there is a 61% reduction in the error rate for predicting missing country years, a 49% reduction for forecasting, and a 54% reduction for back-casting. Average relative error is higher than the other measures, but also shows the dramatic improvement using spatial-temporal regression methods.

We estimate that there were 342,900 (302,100-394,300) maternal deaths worldwide in 2008, down from 526,300 (446,400-629,600) in 1980, an annualized rate of decline of 1.5%. In a counterfactual scenario of a global HIV seroprevalence of zero, this number would be 281,500 (243,900-327,900), as compared to 526,200 (444,500-633,900) in 1980, a more substantial rate of decline of 2.2%. Figure 3a shows the trends in the global number of deaths. It is clear that with the onset of the HIV epidemic in the early 1990s, there was a slowing in the decline of global maternal deaths, with a rate of decline of 1.8% between 1980 and 1990 and a rate of decline of 1.4% from 1990 to 2008. The maternal mortality ratio shows a similar consistent decline; we estimate the global MMR to be 251 (221-289) per 100,000 live births in 2008, down from 422 (358-505) in 1980, an annual rate of decline of 1.8%. For comparison, the MDG target

of a 75% reduction from 1990 MMR levels by 2015 would require an annual rate of decline of 5.5%. In the absence of HIV, we estimate that the global MMR in 2008 would be 206 (179-240).

Figures 4a and 4b provide insights into the changing regional composition of maternal deaths. The number of births globally has varied only between 124 million in 1980 to 136 million in 2008. The regional composition has shifted slowly towards sub-Saharan Africa with the most noticeable change being the reduction in the number of births in East Asia. Figure 4b shows the distribution of maternal deaths by region over time. The fraction of global maternal deaths in sub-Saharan Africa has increased from 23% in 1980 to 52% in 2008, resulting from both the accelerated increase in the number of maternal deaths in the early 1990s as well as declines in Asia.

Figure 5 shows how trends in the MMR have been markedly different across regions. Five regions have MMRs below 20 per 100,000 in 2008: Australasia, Western Europe, Asia-Pacific High-Income, Central Europe and North America High-Income. In this group, the most impressive declines have occurred in Central Europe, with more than a two-thirds decline since 1980. The second group of regions has MMRs less than 60 in 2008, including Eastern Europe, East Asia, Southern Latin America, Central Asia, Tropical Latin America and Central Latin America. East Asia has had a greater than three-quarters decline over the period, though there is substantial heterogeneity between countries, whereas Eastern Europe has experienced only a slow reduction over the same period. The third cluster of regions has MMRs under 280 in 2008, and includes North Africa and the Middle East, Latin America Andean, Southeast Asia, Oceania, and the Caribbean. Rates of decline have been consistent in these regions, except for the slowdown in the Caribbean that is related to HIV, as shown in the HIV counterfactual analysis. Both South Asia and all regions of sub-Saharan Africa have MMRs higher than 250 in 2008, but

South Asia has experienced a dramatic decline since 1980, while rates have increased in the 1990s in all parts of sub-Saharan Africa. Trends in the MMR excluding deaths from HIV show declines through the period in Eastern and Southern Africa and a slower decline in Central and Western Africa.

Table 4 presents the maternal mortality ratio with uncertainty bounds, for each country, in the years 1980, 1990, 2000, and 2008. The results for 2008 are also shown in Figure 6. In 2008, the highest MMR in Afghanistan (1,575 per 100,000 live births) is about 394 times higher than the lowest MMR, in Italy (4). There is also noticeable variation within regions. Within Latin America and the Caribbean, Paraguay, Bolivia, Guyana, Haiti, Nicaragua, Honduras, and Suriname have MMRs above 100 per 100,000. Ratios are noticeably low in North Africa and the Middle-East with the exception of Iraq, Yemen, and Morocco, though data is more limited in this region. While ratios are much higher throughout sub-Saharan Africa, they range from 75 in Cape Verde to 1,570 in Central African Republic, a ratio of 21. The range across South Asia is dramatic, ranging from 1,575 in Afghanistan to 240 in Nepal; the MMR in India is 254. South-East Asia also demonstrates huge heterogeneity with the highest ratios reported in Timor-Leste and the lowest in Mauritius.

The 21 countries with the highest number of maternal deaths in the year 2008 are presented in Table 5. Together, these countries represent 79.4% of total global maternal deaths and 60.6% of global live births. While Table 4 demonstrates that MMRs are substantially higher in Sub-Saharan Africa than other regions, South Asia remains a major contributor in terms of total numbers of maternal deaths.

We focus on the period of the MDGs when considering trends in the time series. Figure 7a provides the annualized rate of change in the MMR for the period 1990 to 2008. To

understand the impact of the HIV epidemic on the MMR, Figure 7b provides the annualized rates of change if we remove HIV from the estimated MMR. These figures highlight the marked variation in performance across countries in reducing the MMR. Countries in North Africa and the Middle East, parts of Latin America and South and East Asia have had the most impressive decline. Increases in the MMR have been documented in countries with large HIV epidemics in Southern Africa but also in Nigeria, Chad, Gabon, and Central African Republic. Examination of the rates of change excluding HIV show that Southern Africa would have experienced declines, but that increases in many parts of Central and West Africa are not solely related to the HIV epidemic.

Figure 7 also highlights the rise in the MMR seen in the USA, Canada, Norway, and Afghanistan. While the rise in Afghanistan may be interpreted as a real trend, improved ascertainment of maternal deaths and the inclusion of late maternal deaths in ICD-10, may explain these increases. Other countries with relatively low MMR, such as Cuba and Thailand, have seen minimal change in the MMR over the MDG period.

Discussion

Our analysis of all available data on maternal mortality from 1980-2008 for 181 countries shows a remarkable decline in maternal deaths, from 526,300 in 1980 to 342,900 in 2008, an average annual decline of 1.5%. Progress overall would have been larger if the HIV epidemic had not contributed to significant increases in maternal mortality in Eastern and Southern Africa. Global progress on reducing the MMR, an average annual decline from 1980 to 2008 of 1.8%, has been similar to progress on maternal death numbers, as the size of the global birth cohort has changed little over this period. Across countries, average annual rates of decline from 1980-2008 in the

MMR have differed widely, ranging from a greater than 9.5% decrease in the Maldives to a 3.7% increase in Zimbabwe. This new evidence suggests there is a much greater reason for optimism than generally perceived, and that substantial declines in the MMR are possible over relatively short periods of time.

Global progress on reducing the MMR should perhaps not be seen as surprising. Four powerful drivers of maternal mortality are improving in most countries. First, the global total fertility rate has dropped from 3.70 in 1980, to 3.26 in 1990 and 2.56 in 2008. Despite rising numbers of women of reproductive age, the decline in the TFR has kept the global birth cohort size stable. In addition to the direct impact of fertility on exposure to risk of maternal death (Fortney and Leong 2009), there is a strong correlation between the MMR and the TFR (Ronsmans, Graham, and group 2006; Vahidnia 2007). Societies where the TFR decreases are also places with declines in the MMR – whether this relationship is causal or mediated through social change that drives both is not clear. Second, income per capita, which can influence maternal mortality through multiple channels from nutritional status of mothers to physical and financial access to healthcare (Borghi et al. 2006), has been rising particularly in Asia and Latin America. Third, levels of maternal education, another strong correlate of maternal mortality, have been rising; for example, average years of schooling of women aged 25-44 in sub-Saharan Africa increased from 1.5 in 1980 to 4.4 in 2008. Finally, although we did not include the fraction of women giving birth with a skilled attendant as a covariate in our model due to collinearity, the steady, albeit slow, rise in skilled birth attendance coverage may also have contributed to maternal mortality declines (Lim, Myerson, et al. 2010). Further, some large countries such as India have witnessed quite rapid increases in SBA in recent years (Lim,

Dandona, et al. 2010). The combination of these factors suggest that it would in fact be more surprising if the global MMR was not declining.

Our analysis, echoing previous studies (Ronsmans, Graham, and group 2006; Bicego, Boerma, and Ronsmans 2002; McIntyre 2003), highlights the important adverse effect of the HIV epidemic on the MMR, especially in East and Southern Africa. In the absence of HIV, progress even in sub-Saharan Africa on reducing the MMR would have been much more extensive. The counterfactual analysis of the MMR without HIV has important implications for intervention policy. The set of interventions for dealing with HIV in pregnant or post-partum women would include access to ARVs, not part of the set of maternal health interventions targeting women who are HIV negative. Tracking HIV-related maternal mortality is important, but challenging in settings without vital registration. In countries with quite complete vital registration systems, including South Africa (Rajaratnam et al. 2010), the use of a checkbox to identify women who were pregnant at the time of death or within 42 days prior to the death may be a useful adjunct (Atrash, Alexander, and Berg 1995; MacKay et al. 2000).

Some countries have had marked success in reducing the MMR. If we focus on the period 1990 to 2008, countries with substantial declines in MMR include Egypt, Romania, Bangladesh, India, and China. In some cases, policy case studies have been written about these countries (Campbell et al. 2005; Mills et al. 2007; Li et al. 2007; Fang and Kaufman 2008; Chowdhury et al. 2007; Yadamsuren et al. 2010). In others, no policy analyses have yet been published in the scientific literature. While this analysis does not provide explanations for these accelerated declines, we hope the results will stimulate further detailed policy reviews. In contrast, some countries that are counted as success stories, such as Indonesia, have not had particularly rapid declines in the MMR (Goodburn and Campbell 2001). In these cases, it will be important to

explore whether there are other data sources missing that would change the estimated trend or whether there is a disconnect between increases in SBA or other maternal health interventions and actual changes in the MMR.

Comparison of pairs of countries reveals the complexity of understanding trends in the MMR. From 1990 to 2008, the MMR declined 1.9% annually in Mexico and 3.9% annually in Brazil. Both are large complex federal states that have experienced marked improvements in adult mortality mediated through social, economic and health system change. Both have placed substantial policy emphasis on reducing maternal mortality (Frenk 2006; Research 2004), but Brazil has outperformed Mexico in terms of declines. In Asia, India and Indonesia have achieved dramatically different rates of decline. In 1980, India's MMR was 677, substantially higher than Indonesia's of 423. Over the MDG period, India has seen an annual rate of decline of 4.0%, while Indonesia has lagged with an annual decline of only 0.6%. This differential performance means that the two countries now have comparable MMRs.

Egypt and Turkey provide another interesting comparison. Egypt has seen an impressive improvement from 1990 to 2008, with an annual decrease of 8.4%, while Turkey has seen a slower rate of decline of only 4.2%. In 1990, the ratio of the MMRs in Egypt as compared to Turkey was 1.6, but after nearly 20 years of steady progress in Egypt, Turkey now has a higher MMR than Egypt, with a ratio of 1.3.

One of the most surprising results is the apparent rise in the MMR in the United States, Canada and Norway. This is likely to be partly explained by the introduction of late maternal deaths in the ICD-10, and the inclusion of a separate pregnancy status question on the US death certificate (Hoyert 2007). This addition to the US death certificate was intended to improve ascertainment of pregnancy-related deaths, which our results suggest it has done. However, it

raises important questions about how these maternal deaths were being coded prior to the introduction of the pregnancy status question on the death certificate.

Our results for 2005 are markedly different from the assessment undertaken by Hill et al (Hill et al. 2007). There are several reasons that this may be the case. First, we have used a dataset with nearly three times as many observations. Second, Hill et al model the proportion of deaths among women of reproductive age, which is likely confounded by the rise of HIV. Other authors have questioned the choice of the proportion as the dependent variable (Hakkert 2001); we model the maternal mortality rate. Third, our method captures systematic spatial and temporal variation, demonstrated by improved performance in predictive validity tests. Fourth, this study uses improved adult mortality estimates based on a systematic assessment of all available data. Finally, Hill et al developed subjective uncertainty intervals for each country and then made the unusual assumption that uncertainty across countries was perfectly correlated in generating global and regional uncertainty intervals; we have taken an approach grounded in a statistical framework.

Our study has a number of important limitations. In countries with complete vital registration systems, we may be over-estimating maternal deaths. We have used cause of death data where the misclassification of maternal deaths to causes such as septicemia has been carefully corrected. Vital registration data, however, also includes late maternal deaths that occur after 42 days. The UN MDG and ICD manuals recommend that late maternal deaths should not be counted in the MMR, but in most countries, we are unable to identify these deaths from the vital registration data. The fraction of late maternal deaths is likely higher in low MMR countries (Turner et al. 2002; Hoyert 2007).

In countries with incomplete vital registration systems, we may be underestimating the proportion of deaths due to maternal causes. While vital registration data used in our model have been corrected for misclassification, if an incomplete system excludes populations at higher risk of maternal death, then the proportion may be biased downwards.

For countries where the primary source is surveys or censuses, our numerator includes incidental deaths among pregnant women from causes such as motor vehicle accidents, burning or drowning. These should not be counted as maternal deaths. This will bias our estimates upwards, but there is no clear analytical strategy to identify the fraction of pregnancy related deaths that are incidental. Other analysts have suggested that any over-counting resulting from the incidental deaths captured by these methods may be offset by under-counting due to respondents not knowing about the pregnancy or not wishing to identify a pregnancy (Hill et al. 2007; Stecklov 1995), however, there is little evidence for this claim.

Another important limitation is the lack of any data for 21 countries for the entire time period 1980 to 2008. However, the predictive validity results suggest that our model performs reasonably well out of sample. Countries with no data may be particularly affected by uncertainty in the covariates, which we have not incorporated into our estimates of uncertainty. Lastly, for countries which do have data from multiple sources such as India, there can be marked non-sampling error across data sources. Inconsistencies between different data have required informed, but arbitrary, choices about which set to include. Future data collection or studies may provide new insights that could change the identification of which sources are outliers.

Compared to prior assessments of maternal mortality, we have narrowed the uncertainty around global and national estimates of the MMR. This reflects a more extensive database and

the use of analytical methods with increased explanatory power and improved out-of-sample predictive validity. Nevertheless, as noted in the methods section, our uncertainty intervals are biased towards being too large. Based on our systematic assessment, we are optimistic about the ability to monitor maternal mortality over time. Compared to other key causes of child or adult death, there is much more data available for maternal mortality. For example, WHO estimates just over 100 thousand deaths from tuberculosis in reproductive aged-women (World Health Organization 2008), yet the number of data points directly measuring tuberculosis as a cause of death is dramatically lower in low and lower-middle income countries as compared to maternal mortality. A comparison of the information base for maternal mortality compared to HIV and many causes of child mortality is similarly favourable (Morris, Black, and Tomaskovic 2003; Boschi-Pinto, Velebit, and Shibuya 2008). Put simply, among leading causes of death in children and adults in developing countries, there are more empirical observations for maternal mortality than for any other cause. Continued efforts at strengthening vital registration and the expansion of data collection on pregnancy related mortality through household surveys and censuses should further strengthen the global database. It is important to note, however, the critical importance of ongoing surveillance of all-cause adult female mortality as an input to tracking maternal mortality.

This analysis has shown that while countries can achieve significant progress in reducing maternal deaths, far too many have not. In five years, the global health community and country governments will be held accountable for their achievement of the MDGs. There is an urgent need to accelerate progress where further significant reductions in maternal mortality ought to be achievable with heath system reform. Delivering interventions to women when and where they need them ought to be a purposeful policy of all countries.

Author contributions

MCH analyzed the data, carried out the literature review, contributed to the methods development, and wrote the first draft. KJF contributed to the development of the methodological approach and implemented the statistical analysis. MN interpreted results and carried out the garbage code redistribution. SYA and MW carried out the verbal autopsy literature review and contributed to the figures and tables. SMM analyzed the vital registration data and contributed to the figures and tables. ADL provided conceptual and technical guidance and made contributions in the manuscript revisions. RL interpreted results, provided feedback on model development, and contributed to the first draft. CJLM conceptualized the methodology and guided the analysis, interpretation of data and results, and contributed to the first draft and revisions.

Conflict of Interest Statement

All authors declare that the answers to the questions on your competing interest form (http://www.icmje.org/coi_disclosure.pdf) are all No and therefore have nothing to declare with the exception of stating our core grant funding from the Bill & Melinda Gates Foundation.

Role of Funding Sources

This research was supported by funding from the Bill & Melinda Gates Foundation (http://www.gatesfoundation.org). The funders had no role in study design, data collection and analysis, interpretation of data, decision to publish, or preparation of the manuscript. The corresponding author had full access to all data analysed and had final responsibility for the decision to submit this original research paper for publication.

Ethics Committee Approval

No primary data were collected for this study. The study used country-level data which were completely anonymous.

Acknowledgments

We would like to thank Janaki O'Brien for assistance with data preparation, Emmanuela Gakidou for valuable inputs on the final draft, Julie K. Rajaratnam and Stephen S. Lim for contributions to the analytical process, and Haidong Wang, Krycia Cowling, Jacob Marcus, Rebecca Myerson, Katherine Andrews, Laura Dwyer and Alison Levin-Rector for assistance with data.

AbouZahr, C. 2003. "Global Burden of Maternal Death and Disability." *British Medical Bulletin* 67 (1) (December 1): 1–11. doi:10.1093/bmb/ldg015.

AbouZahr, C, and T Wardlaw. 2001. "Maternal Mortality at the End of a Decade: Signs of Progress?." *Bulletin of the World Health Organization* 79 (6): 561–568.

Atrash, H K, S Alexander, and C J Berg. 1995. "Maternal Mortality in Developed Countries: Not Just a Concern of the Past." *Obstetrics & Gynecology* 86 (4 Pt 2) (October 1): 700–705.

Bicego, G, J T Boerma, and C Ronsmans. 2002. "The Effect of AIDS on Maternal Mortality in Malawi and Zimbabwe." *AIDS (London, England)* 16 (7) (May 1): 1078–1081.

Borghi, JO, Tim Ensor, Aparnaa Somanathan, Craig Lissner, Anne Mills, and Lancet Maternal Survival Series steering group. 2006. "Mobilising Financial Resources for Maternal Health." *Lancet* 368 (9545) (October 1): 1457–1465.

Boschi-Pinto, Cynthia, Lana Velebit, and Kenji Shibuya. 2008. "Estimating Child Mortality Due to Diarrhoea in Developing Countries.." *Bulletin of the World Health Organization* 86 (9) (September): 710–717.

Campbell, O M R. 1999. "Measuring Progress in Safe Motherhood Programmes: Uses and Limitations of Health Outcome Indicators." *Safe Motherhood Initiatives: Critical Issues*.

Campbell, O, R Gipson, A H Issa, N Matta, B El Deeb, A El Mohandes, A Alwen, and E Mansour. 2005. "National Maternal Mortality Ratio in Egypt Halved Between 1992-93 and 2000." *Bulletin of the World Health Organization* 83 (6) (June 1): 462–471.

Centers for Disease Control and Prevention. "International Reproductive Health Surveys Program." *Miscellaneous*. http://www.cdc.gov/reproductivehealth/Global/GatherData.htm.

Chowdhury, Mahbub Elahi, Roslin Botlero, Marge Koblinsky, Sajal Kumar Saha, Greet Dieltiens, and Carine Ronsmans. 2007. "Determinants of Reduction in Maternal Mortality in Matlab, Bangladesh: a 30-Year Cohort Study." *The Lancet* 370 (9595) (October 19): 1320–

1328. doi:10.1016/S0140-6736(07)61573-6.
Cleveland, W S, and S J Devlin. 1988. “Locally Weighted Regression: an Approach to Regression Analysis by Local Fitting.” *Journal of the American Statistical Association* 83 (403): 596–610.
Countdown Coverage Writing Group, Countdown to 2015 Core Group, J Bryce, B Daelmans, A Dwivedi, V Fauveau, J E Lawn, et al. 2008. “Countdown to 2015 for Maternal, Newborn, and Child Survival: the 2008 Report on Tracking Coverage of Interventions.” *The Lancet* 371 (9620) (April): 1247–1258. doi:10.1016/S0140-6736(08)60559-0.
Deneux-Tharaux, C, C Berg, M H Bouvier-Colle, M Gissler, M Harper, A Nannini, S Alexander, K Wildman, G Breart, and P Buekens. 2005. “Underreporting of Pregnancy-Related Mortality in the United States and Europe.” *Obstetrics & Gynecology* 106 (4) (October 1): 684–692.
Development, International Conference on Population and. *Summary of the ICPD Program of Action*. http://www.unfpa.org/icpd/summary.cfm.
DHS, Measure. “Demographic and Health Surveys.” *Book*. http://measuredhs.com/.
Fang, Jing, and Joan Kaufman. 2008. “Reproductive Health in China: Improve the Means to the End..” *Lancet* 372 (9650) (November 8): 1619–1620. doi:10.1016/S0140-6736(08)61356-2.
Fortney, J A, and M Leong. 2009. “Saving Mother's Lives: Programs That Work.” *Clinical Obstetrics and Gynecology* 52 (2): 224.
Frenk, J. 2006. “Bridging the Divide: Global Lessons From Evidence-Based Health Policy in Mexico.” *The Lancet* 368 (9539): 954–961.
Gakidou, E, and G King. 2006. “Death by Survey: Estimating Adult Mortality Without Selection Bias From Sibling Survival Data.” *Demography* 43 (3) (August 1): 569–585.
Garenne, M, and F Friedberg. 1997. “Accuracy of Indirect Estimates of Maternal Mortality: a Simulation Model.” *Studies in Family Planning* 28 (2) (June 1): 132–142.
Goodburn, E, and O Campbell. 2001. “Reducing Maternal Mortality in the Developing World: Sector-Wide Approaches May Be the Key.” *British Medical Journal* 322 (7291): 917.
Graham, W J, and J Hussein. 2006. “Universal Reporting of Maternal Mortality: an Achievable Goal?.” *International Journal of Gynaecology and Obstetrics: the Official Organ of the International Federation of Gynaecology and Obstetrics* 94 (3) (September 1): 234–242.
Graham, W J, L B Foster, L Davidson, E Hauke, and O M R Campbell. 2008. “Measuring Progress in Reducing Maternal Mortality.” *Best Practice & Research Clinical Obstetrics & Gynaecology* 22 (3): 425–445.
Graham, W J, S Ahmed, C Stanton, C L Abou-Zahr, and OMR Campbell. 2008. “Measuring Maternal Mortality: an Overview of Opportunities and Options for Developing Countries.” *BMC Medicine* 6 (1): 12. doi:10.1186/1741-7015-6-12.
Graham, W, W Brass, and R W Snow. 1989. “Estimating Maternal Mortality: the Sisterhood Method.” *Studies in Family Planning* 20 (3) (May 1): 125–135.
Graham, Wendy J. 2002. “Now or Never: the Case for Measuring Maternal Mortality.” *The Lancet* 359 (9307): 701–704. doi:10.1016/S0140-6736(02)07817-0. http://linkinghub.elsevier.com/retrieve/pii/S0140673602078170.
Hakkert, R. 2001. “Country Estimates of Maternal Mortality: an Alternative Model.” *Statistics in Medicine* 20 (23) (December 1): 3505–3524.
Handcock, M S, and J R Wallis. 1994. “An Approach to Statistical Spatial-Temporal Modeling of Meteorological Fields..” *Journal of the American Statistical Association* 89 (426).
Hill, K, K Thomas, C AbouZahr, N Walker, L Say, M Inoue, E Suzuki, and Maternal Mortality

Working Group. 2007. “Estimates of Maternal Mortality Worldwide Between 1990 and 2005: an Assessment of Available Data.” *Lancet* 370 (9595) (October 19): 1311–1319. doi:10.1016/S0140-6736(07)61572-4. http://linkinghub.elsevier.com/retrieve/pii/S0140673607615724.

Hill, Kenneth. 2009. “Estimating Pregnancy-Related Mortality From Census Data: Experience From Latin America.” *Bulletin of the World Health Organization* 87 (4) (April 1): 288–295. doi:10.2471/BLT.08.052233.

Hill, Kenneth, Shams el Arifeen, Michael Koenig, Ahmed Al-Sabir, Kanta Jamil, and Han Raggers. 2006. “How Should We Measure Maternal Mortality in the Developing World? a Comparison of Household Deaths and Sibling History Approaches.” *Bulletin of the World Health Organization* 84 (3) (March 1): 173–180.

Horon, Isabelle L. 2005. “Underreporting of Maternal Deaths on Death Certificates and the Magnitude of the Problem of Maternal Mortality.” *American Journal of Public Health* 95 (3) (March): 478–482. doi:10.2105/AJPH.2004.040063.

Hoyert, Donna L. 2007. “Maternal Mortality and Related Concepts..” *Vital & Health Statistics. Series 3, Analytical and Epidemiological Studies / [U.S. Dept. of Health and Human Services, Public Health Service, National Center for Health Statistics]* (33) (February): 1–13.

Kao, S, L M Chen, L Shi, and M C Weinrich. 1997. “Underreporting and Misclassification of Maternal Mortality in Taiwan.” *Acta Obstetricia Et Gynecologica Scandinavica* 76 (7) (August 1): 629–636.

Karimian-Teherani, D, G Haidinger, T Waldhoer, A Beck, and C Vutuc. 2002. “Under-Reporting of Direct and Indirect Obstetrical Deaths in Austria, 1980-98.” *Acta Obstetricia Et Gynecologica Scandinavica* 81 (4) (April 11): 323–327.

Knotters, M, D J Brus, and J H Oude Voshaar. 1995. “A Comparison of Kriging, Co-Kriging and Kriging Combined with Regression for Spatial Interpolation of Horizon Depth with Censored Observations.” *Geoderma* 67 (3-4): 227–246.

Landagan, O Z, and E B Barrios. 2007. “An Estimation Procedure for a Spatial-Temporal Model.” *Statistics & Probability Letters* 77 (4): 401–406.

Laurenti, R, and C M Buchalla. 2001. “Indicators of Maternal and Infant Health: Implications of the 10th Revision of the International Classification of Diseases.” *Revista Panamericana De Salud Publica = Pan American Journal of Public Health* 1 (1) (November 28): 18–22.

Li, J, C Luo, R Deng, P Jacoby, and N de Klerk. 2007. “Maternal Mortality in Yunnan, China: Recent Trends and Associated Factors.” *BJOG an International Journal of Obstetrics and Gynaecology* 114 (7) (July): 865–874. doi:10.1111/j.1471-0528.2007.01362.x.

Lim, S S, L Dandona, J A Hoisington, S L James, M C Hogan, and E Gakidou. 2010. “India's Janani Suraksha Yojana, a Conditional Cash Transfer Programme to Increase Births in Health Facilities: an Impact Evaluation.” *The Lancet* 375 (9730): 2009–2023.

Lim, S S, R Myerson, L C Rosenfeld, and C J L Murray. 2010. “Safe Pregnancy and Delivery: a Systematic Analysis of Trends in the Coverage of Antenatal and Intra-Partum Care.”

LP, StataCorp. 2009. *Stata Base Reference Manual: Release 11*. *Book*.

MacKay, A P, R Rochat, J C Smith, and C J Berg. 2000. “The Check Box: Determining Pregnancy Status to Improve Maternal Mortality Surveillance..” *American Journal of Preventive Medicine* 19 (1 Suppl) (July): 35–39.

McIntyre, James. 2003. “Mothers Infected with HIV..” *Br Med Bull* 67: 127–135.

Mills, Samuel, John E Williams, George Wak, and Abraham Hodgson. 2007. “Maternal

Mortality Decline in the Kassena-Nankana District of Northern Ghana." *Maternal & Child Health Journal* 12 (5) (October 23): 577–585. doi:10.1007/s10995-007-0289-x.
Morris, Saul S, Robert E Black, and Lana Tomaskovic. 2003. "Predicting the Distribution of Under-Five Deaths by Cause in Countries Without Adequate Vital Registration Systems.." *International Journal of Epidemiology* 32 (6) (December): 1041–1051.
Naghavi, M, S Makela, K Foreman, J O'Brien, F Pourmalek, and R Lozano. 2010. "Algorithms for Enhancing Public Health Utility of National Causes-of-Death Data." *Population Health Metrics* 8 (May 1): 9.
Obaid, Thoraya Ahmed. 2009. "Fifteen Years After the International Conference on Population and Development: What Have We Achieved and How Do We Move Forward?." *International Journal of Gynaecology and Obstetrics: the Official Organ of the International Federation of Gynaecology and Obstetrics* 106 (2) (August): 102–105. doi:10.1016/j.ijgo.2009.03.017.
Obermeyer, Ziad, Julie Knoll Rajaratnam, Chang H Park, Emmanuela Gakidou, Margaret C Hogan, Alan D Lopez, and Christopher J L Murray. 2010. "Measuring Adult Mortality Using Sibling Survival: a New Analytical Method and New Results for 44 Countries, 1974-2006.." *PLoS Medicine* 7 (4) (April): e1000260. doi:10.1371/journal.pmed.1000260.
Ordi, J, M R Ismail, C Carrilho, C Romagosa, N Osman, F Machungo, J A Bombi, J Balasch, P L Alonso, and C Menendez. 2009. "Clinico-Pathological Discrepancies in the Diagnosis of Causes of Maternal Death in Sub-Saharan Africa: Retrospective Analysis." *PLoS Medicine* 6 (2) (February 1): e1000036.
Pattinson, R, L Say, J P Souza, N Broek, C Rooney, WHO working group on Maternal Mortality, and Morbidity Classifications. 2009. "WHO Maternal Death and Near-Miss Classifications." *Bulletin of the World Health Organization* 87 (10) (October 1): 734.
Rajaratnam, J K, J R Marcus, A Levin-Rector, A N Chalupka, H Wang, L Dwyer, M Costa, A D Lopez, and C J Murray. 2010. "Worldwide Mortality in Men and Women Aged 15-59 Years From 1970 to 2010: a Systematic Analysis." *Lancet* 375 (9727) (May 1): 1704–1720.
Registrar General, India. 2006. "Sample Registration System (SRS)." New Delhi: India Registrar General.
Research, Institute for Applied Economic. 2004. *Brazilian Monitoring Report on the Millennium Development Goals*. *Techreport*.
Ronsmans, C, W J Graham, and Lancet Maternal Survival Series steering group. 2006. "Maternal Mortality: Who, When, Where, and Why." *Lancet* 368 (9542) (September 1): 1189–1200.
Rosenfield, A, and D Maine. 1985. "Maternal Mortality--a Neglected Tragedy. Where Is the M in MCH?." *Lancet* 2 (8446) (July 13): 83–85.
Schuitemaker, N, J van Roosmalen, G Dekker, P van Dongen, H Van Geijn, and J B Gravenhorst. 2004. "Underreporting of Maternal Mortality in the Netherlands." *Obstetrics & Gynecology* 90 (1) (November 18): 78–82.
Shiffman, J. 2000. "Can Poor Countries Surmount High Maternal Mortality?." *Studies in Family Planning* 31 (4) (December 1): 274–289.
Stanton, C, J Hobcraft, K Hill, N Kodjogbe, W T Mapeta, F Munene, M Naghavi, V Rabeza, B Sisouphanthong, and O Campbell. 2001. "Every Death Counts: Measurement of Maternal Mortality via a Census." *Bulletin of the World Health Organization* 79 (7): 657–664.
Stanton, C, N Abderrahim, and K Hill. 2000. "An Assessment of DHS Maternal Mortality Indicators." *Studies in Family Planning* 31: 111–123.

Starrs, Ann M. 2006. “Safe Motherhood Initiative: 20 Years and Counting.” *The Lancet* 368 (9542) (September): 1130–1132. doi:10.1016/S0140-6736(06)69385-9.
Stecklov, G. 1995. “Maternal Mortality Estimation: Separating Pregnancy-Related and Non-Pregnancy-Related Risks.” *Studies in Family Planning* 26 (1): 33–38.
Tomz, M, J Wittenberg, and G King. 2003. “CLARIFY: Software for Interpreting and Presenting Statistical Results.” *Miscellaneous* Version 2.1.
Turner, L A, M Cyr, R A Kinch, R Liston, M S Kramer, M Fair, M Heaman, Maternal Mortality, and Morbidity Study Group of the Canadian Perinatal Surveillance System. 2002. “Under-Reporting of Maternal Mortality in Canada: a Question of Definition.” *Chronic Diseases in Canada* 23 (1): 22–30.
United Nations. 2009. *The Millenium Development Goals Report 2009*. New York: United Nations.
United Nations Development Program. 2003. *Indicators for Monitoring the Millennium Development Goals: Definitions, Rationale, Concepts, and Sources*. *Techreport*.
United Nations General Assembly. 2000. “United Nations Millennium Declaration.” *Miscellaneous* A/RES/55/2.
United Nations Population Division. 2009. “World Population Prospects: the 2008 Revision Population Database.” *Miscellaneous*. http://www.un.org/esa/population/.
United Nations, UNFPA, World Health Organization. 2004. *Maternal Mortality in 2000: Estimates Developed by WHO, UNICEF, UNFPA*. *Techreport*.
Vahidnia, F. 2007. “Case Study: Fertility Decline in Iran.” *Population & Environment* 28 (4): 259–266.
World Health Organization. 1991. *Maternal Mortality: a Global Factbook*. *Book*.
World Health Organization. 2004. *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision Instruction Manual. Book*. Vol. 2.
World Health Organization. 2008. *The Global Burden of Disease: 2004 Update*. Geneva, Switzerland: World Health Organization.
World Health Organization. “WHO Mortality Database.” http://www.who.int/whosis/mort/download/en/index.htm.
World Health Organization, United Nations. 1996. *Revised 1990 Estimates of Maternal Mortality: a New Approach by WHO and UNICEF*. *Techreport*.
World Health Organization, United Nations, and UNFPA. 2001. *Maternal Mortality in 1995: Estimates Developed by WHO, UNICEF, and UNFPA*. *Techreport*.
World Health Organization, United Nations, UNFPA, World Bank. 2007. *Maternal Mortality in 2005: Estimates Developed by WHO, UNICEF, UNFPA and the World Bank*. *Techreport*.
Yadamsuren, Buyanjargal, Mario Merialdi, Ishnyam Davaadorj, Jennifer Harris Requejo, Ana Pilar Betrán, Asima Ahmad, Pagvajav Nymadawa, et al. 2010. “Tracking Maternal Mortality Declines in Mongolia Between 1992 and 2007: the Importance of Collaboration..” *Bulletin of the World Health Organization* 88 (3) (March): 192–198. doi:10.2471/BLT.08.061747.
Yazbeck, Abdo S. 2007. “Challenges in Measuring Maternal Mortality..” *Lancet* 370 (9595) (October 13): 1291–1292. doi:10.1016/S0140-6736(07)61553-0.

Figure 1. Density of Site-Years of Observation, 1980 to 2008

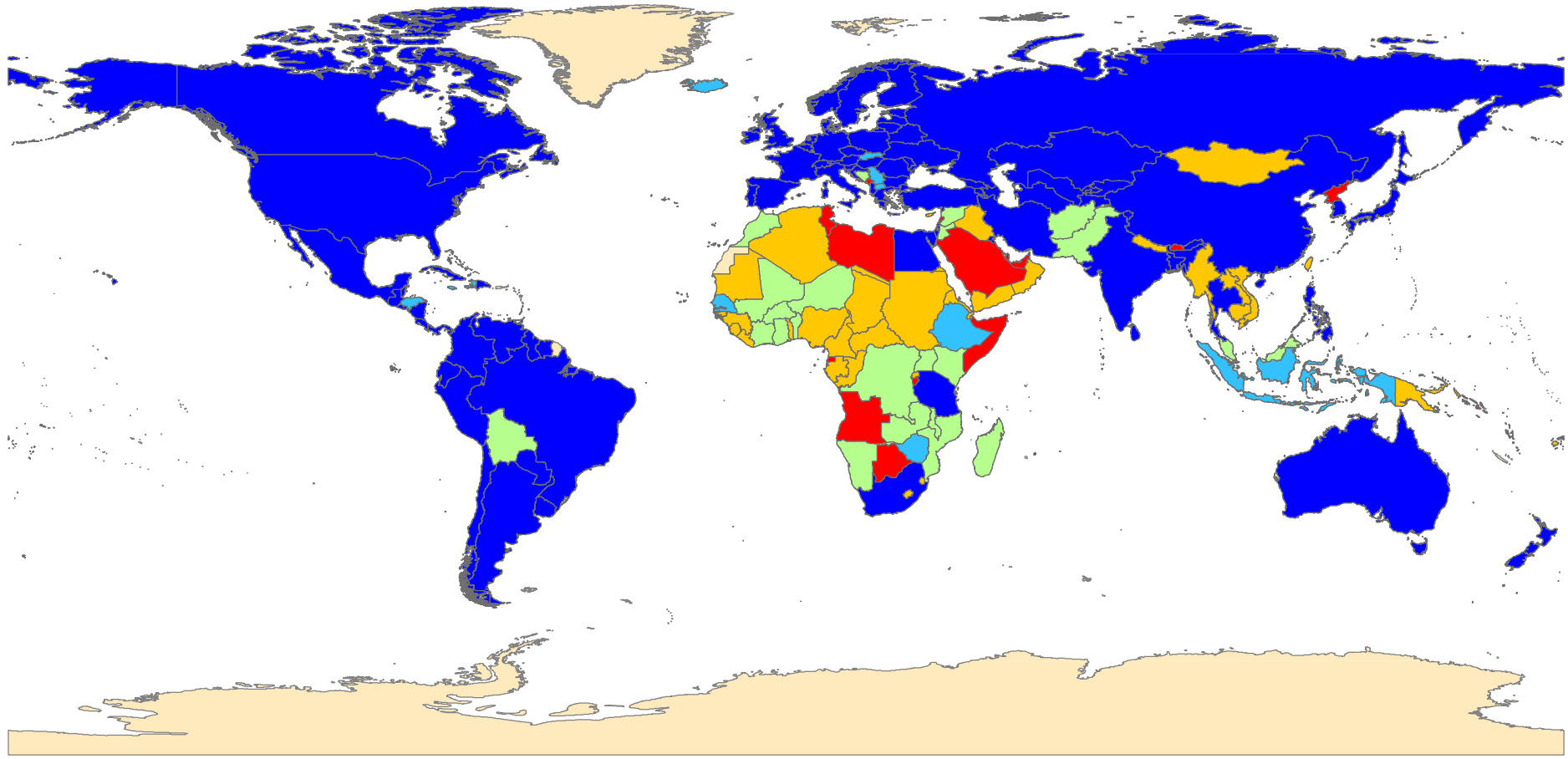
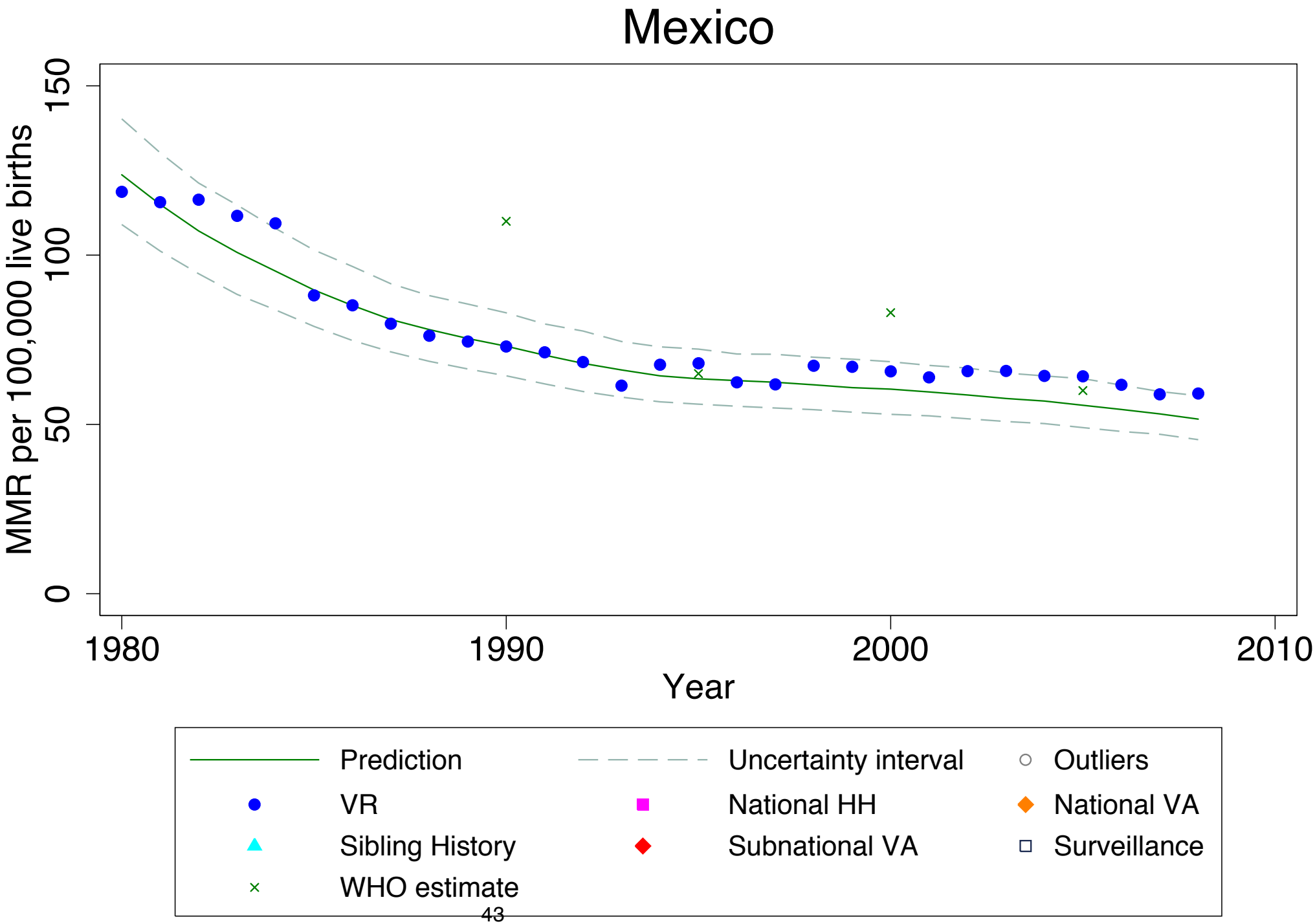
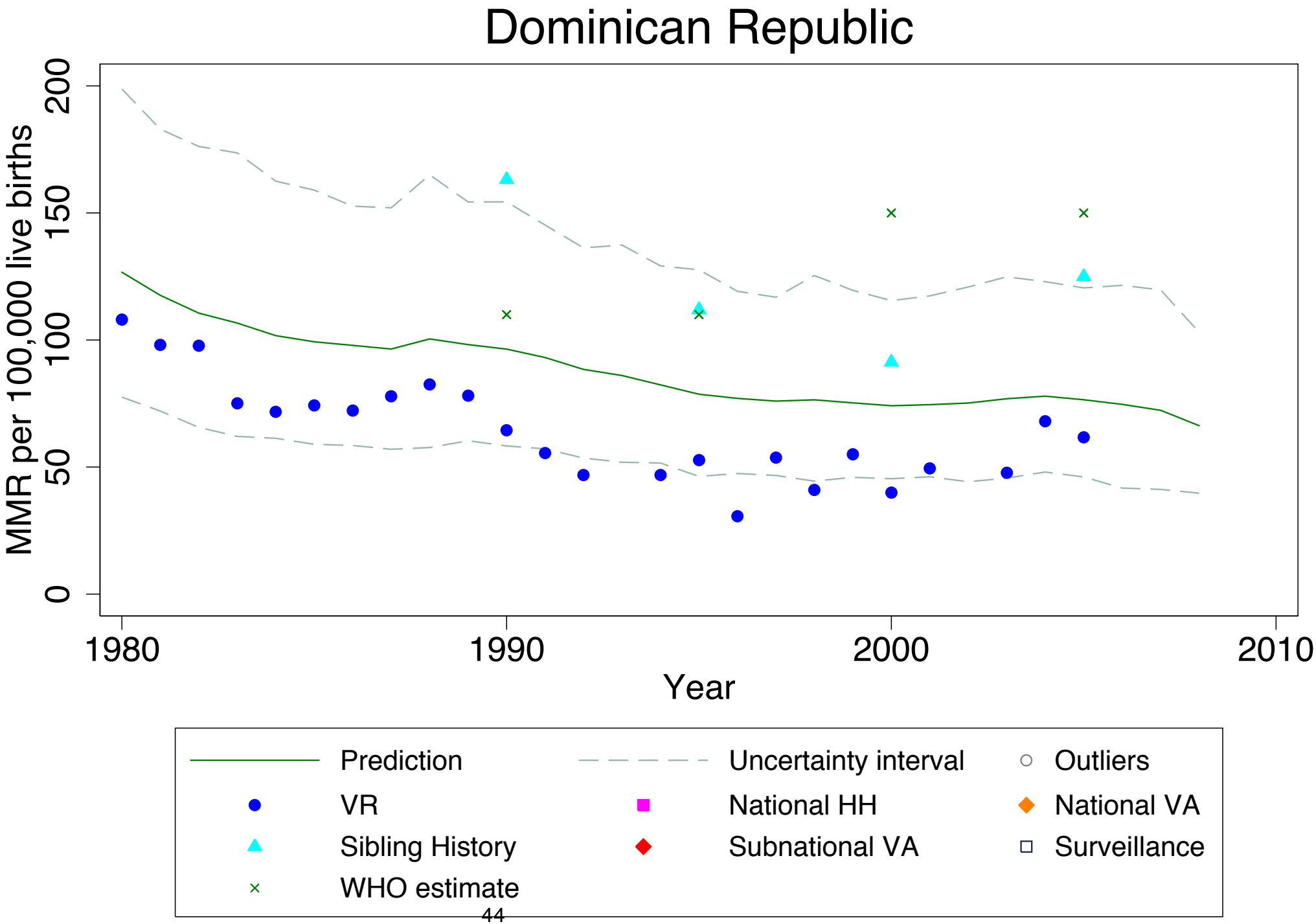
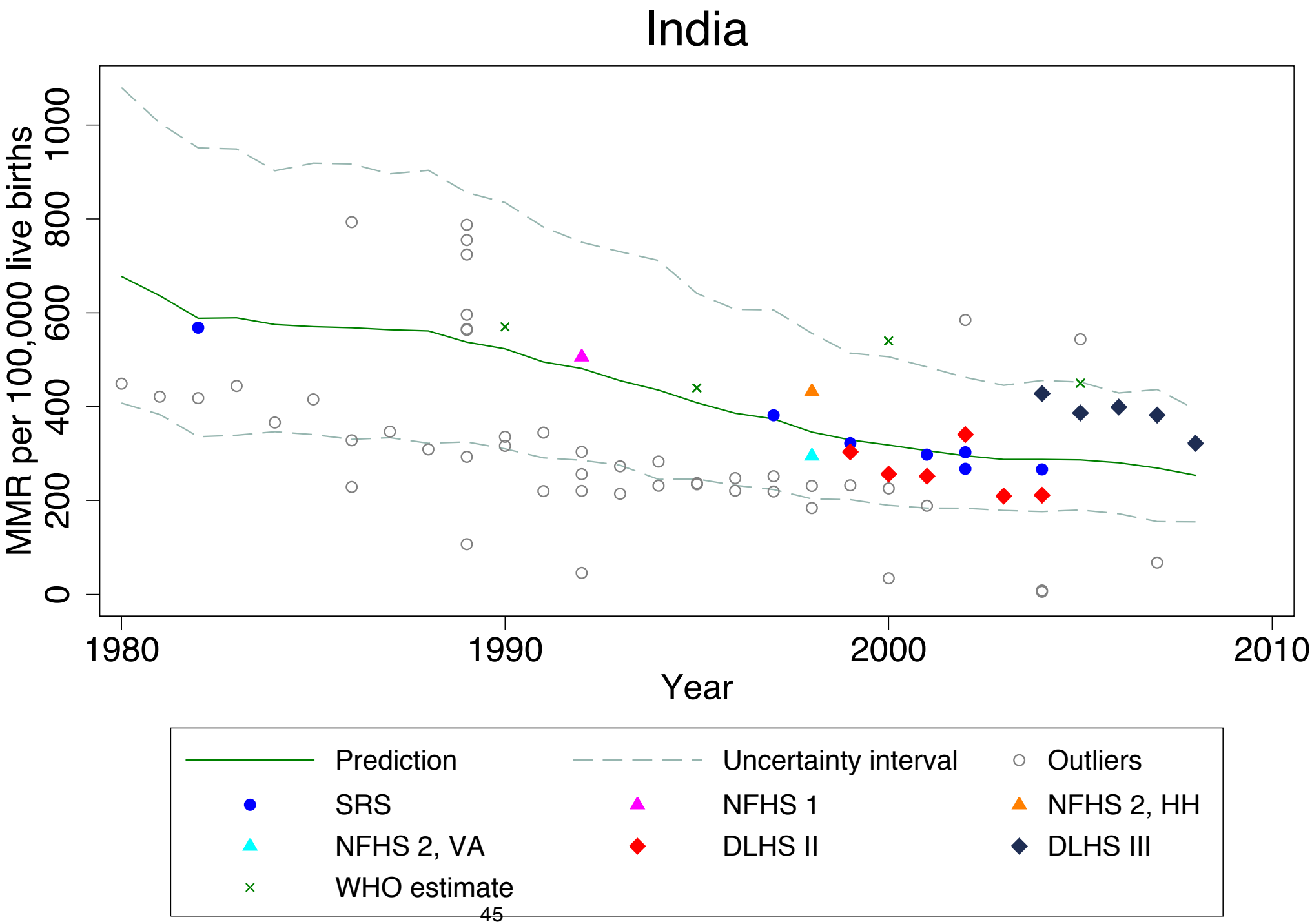


Figure 2a-d. Predicted MMR per 100,000 live births with uncertainty for Mexico, Dominican Republic, India, and Mali


Mexico
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Dominican Republic
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


India
MMR per 100,000 live births
0
200
400
600
800
1000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
SRS
NFHS 1
NFHS 2, HH
NFHS 2, VA
DLHS II
DLHS III
WHO estimate

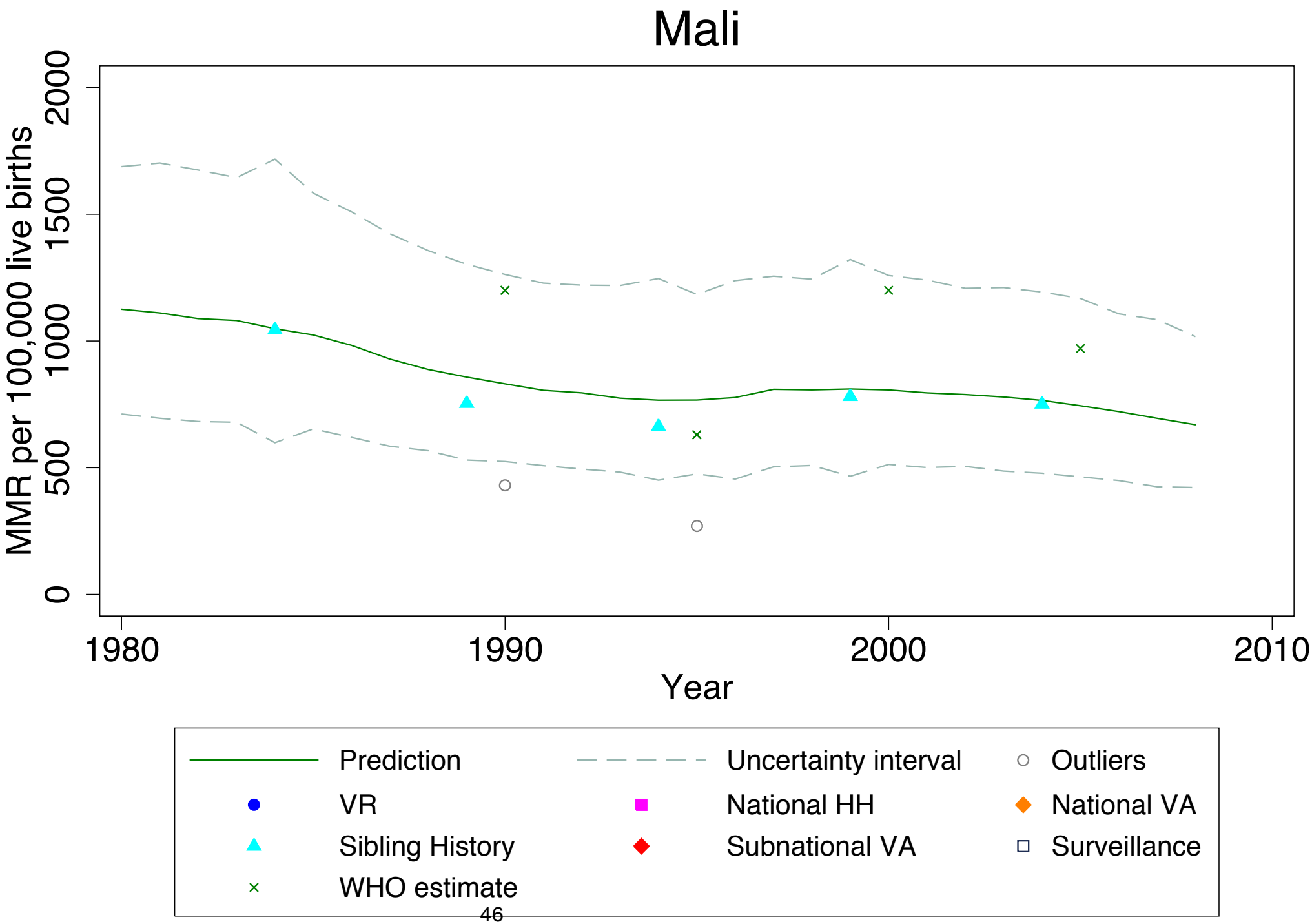

Mali
MMR per 100,000 live births
0
500
1000
1500
2000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

Figure 3a. Global Maternal Deaths, 1980–2008

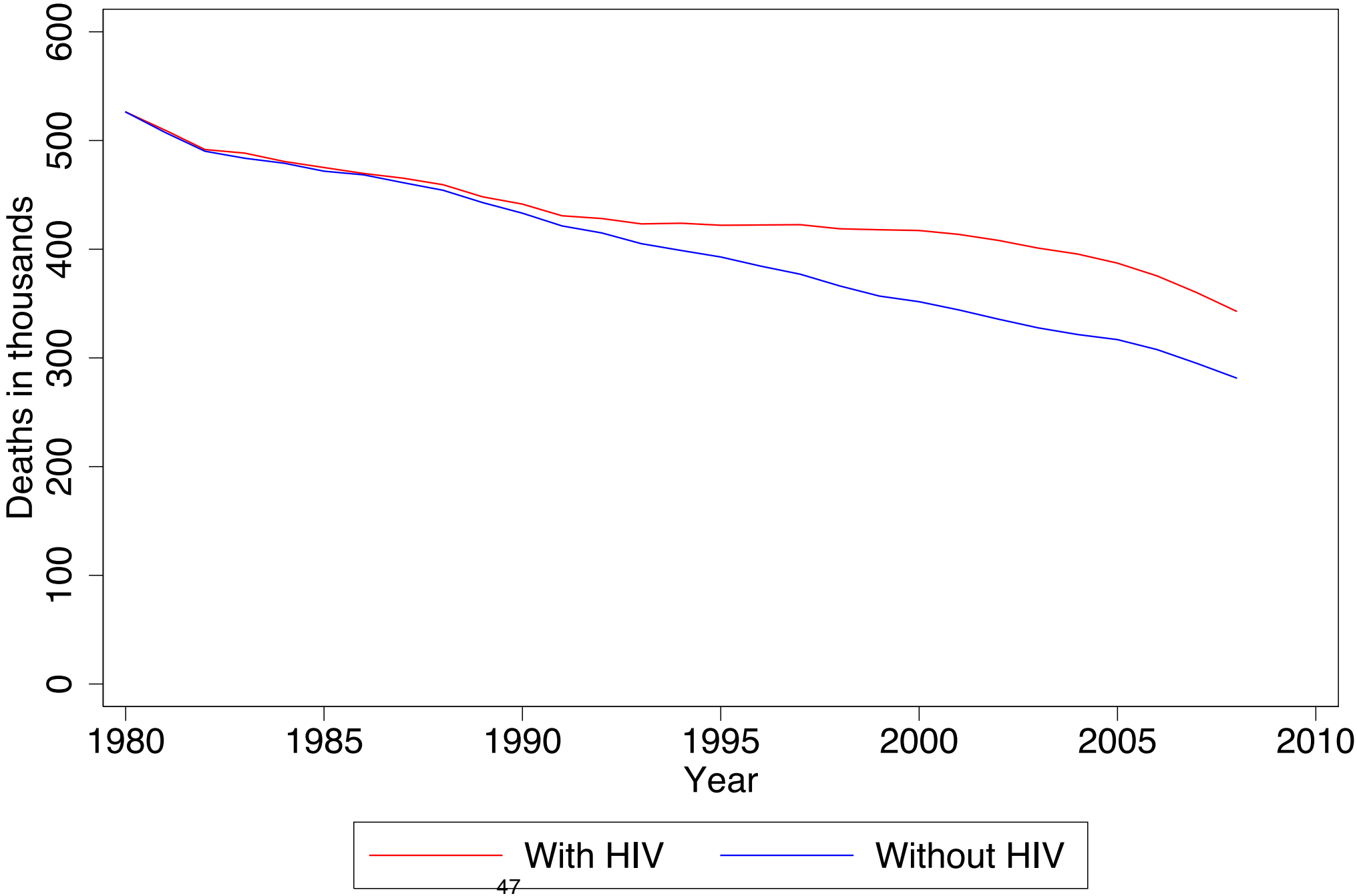


Figure 3b. Global MMR, 1980–2008

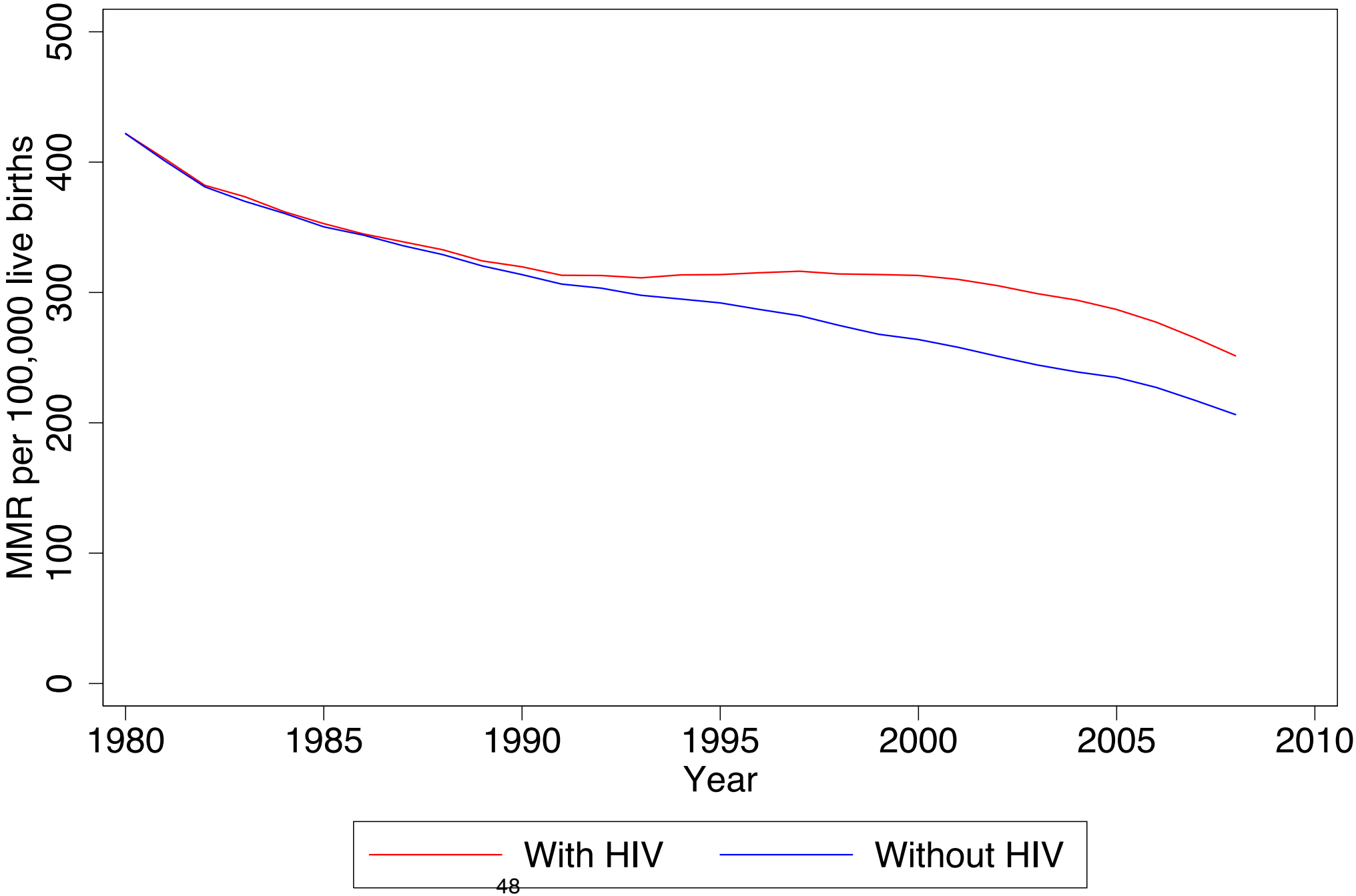


Figure 4a. Births by Region, 1980-2008

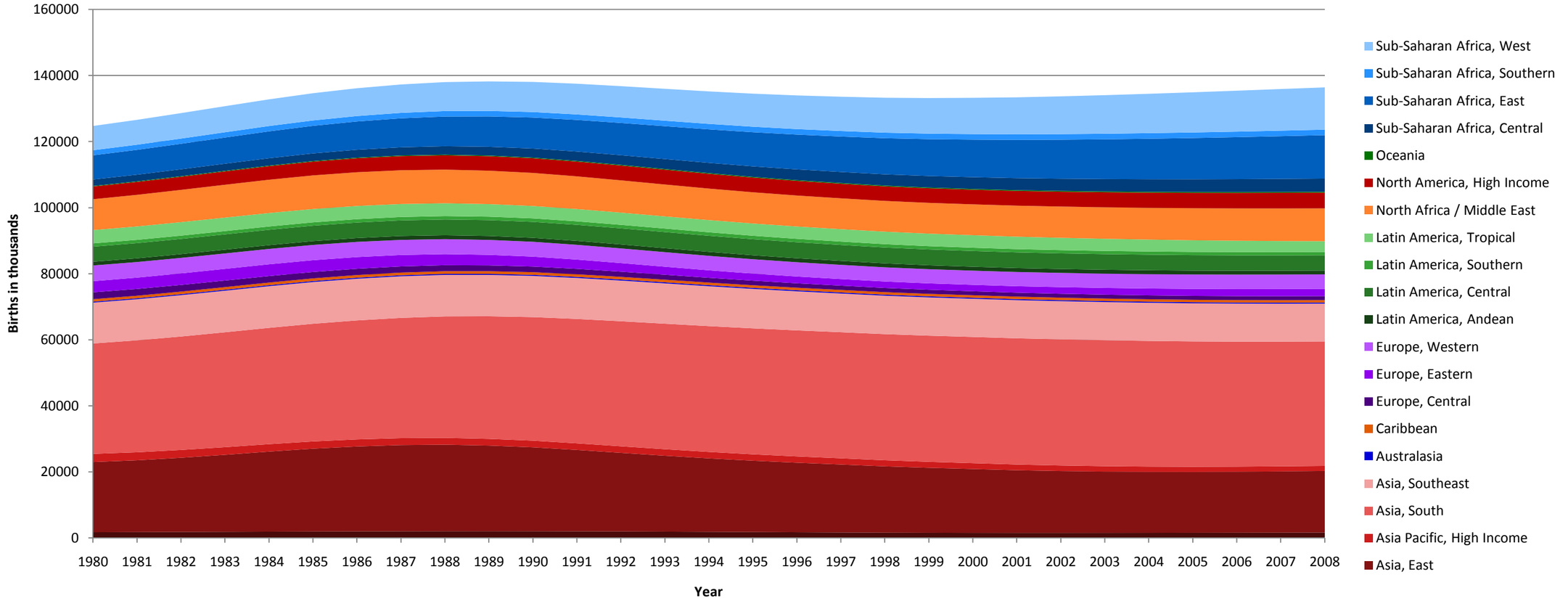


Figure 4b. Maternal Deaths by Region, 1980-2008

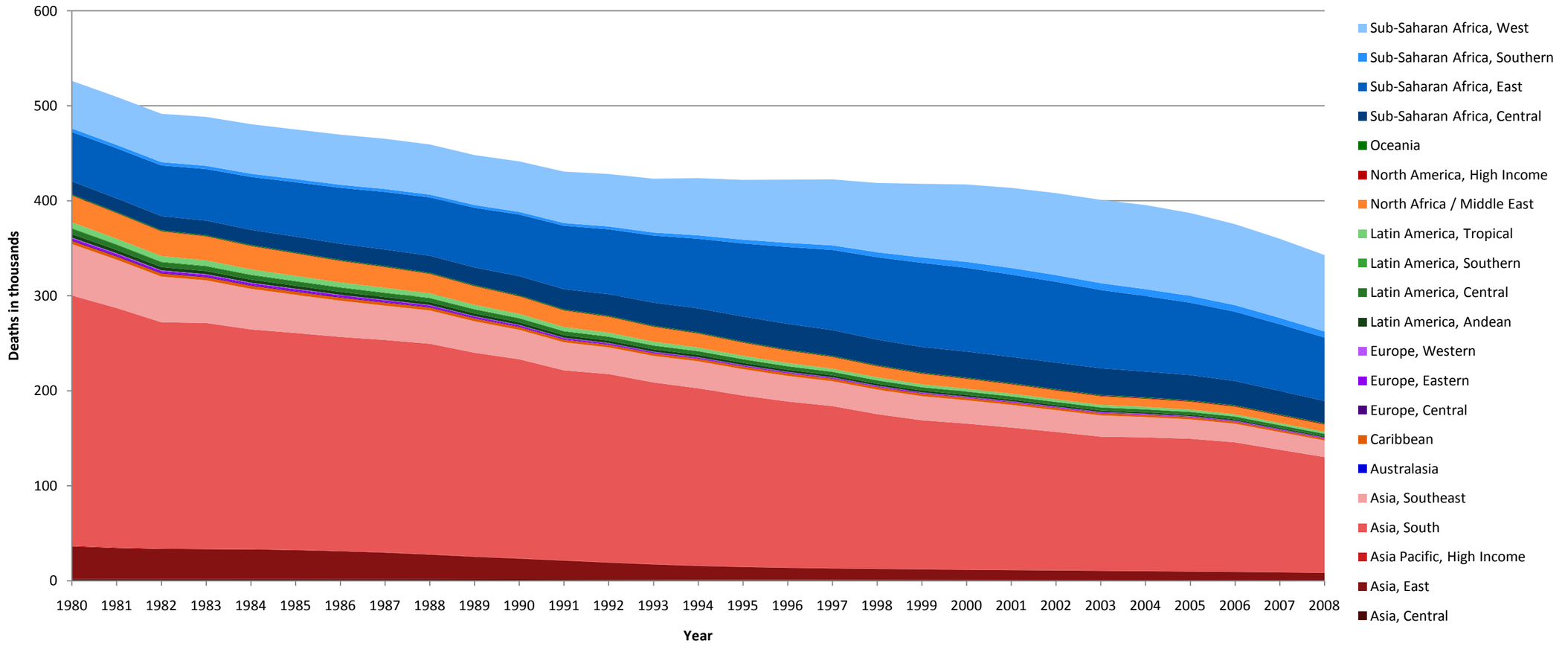
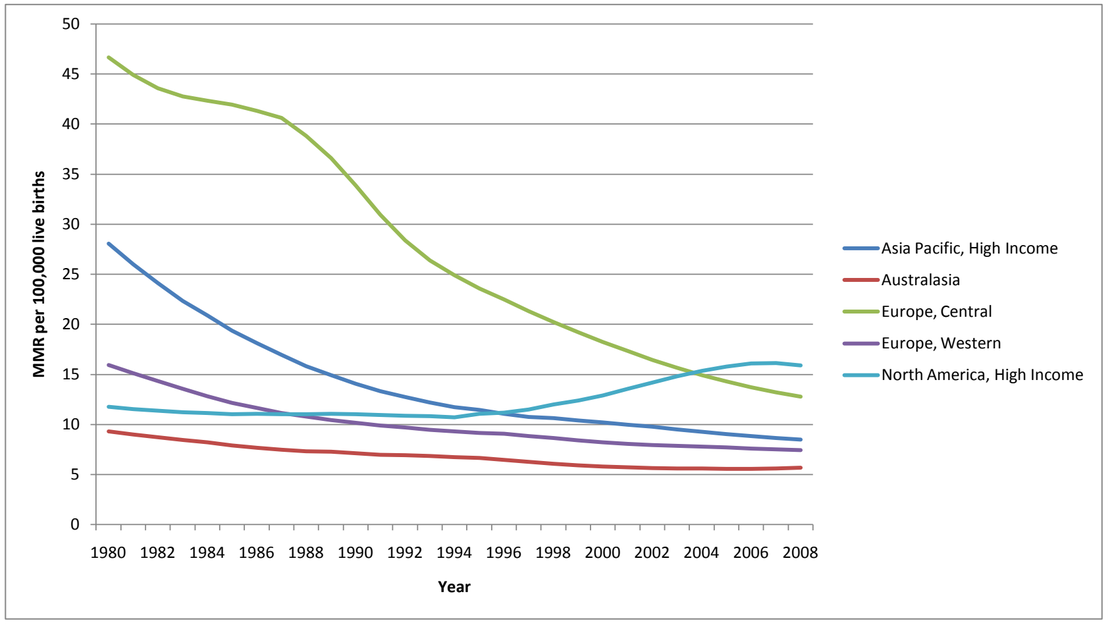
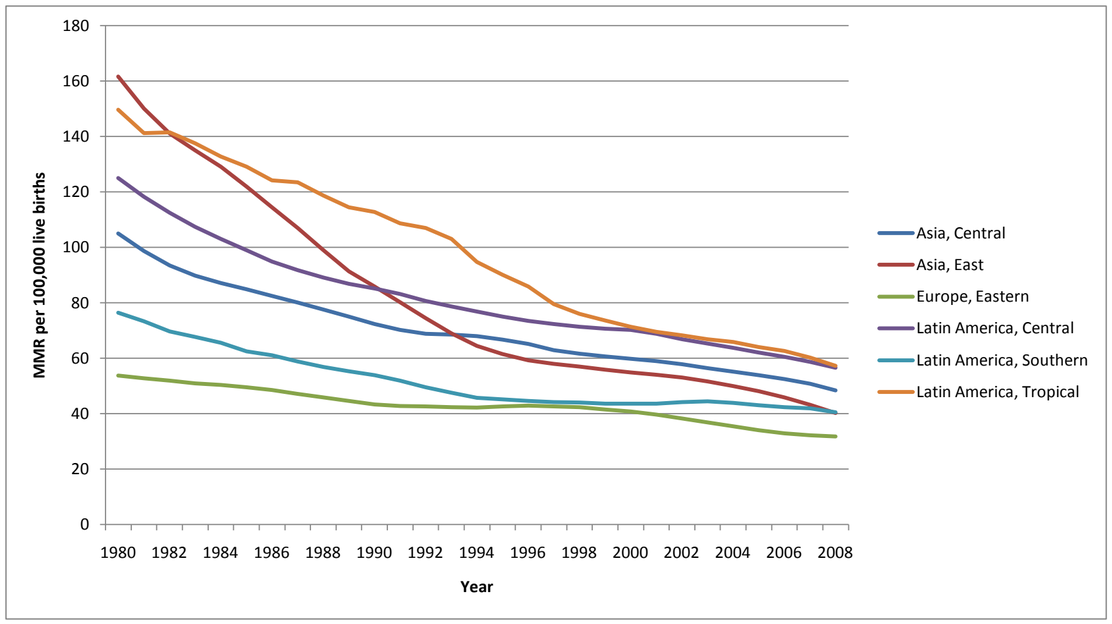
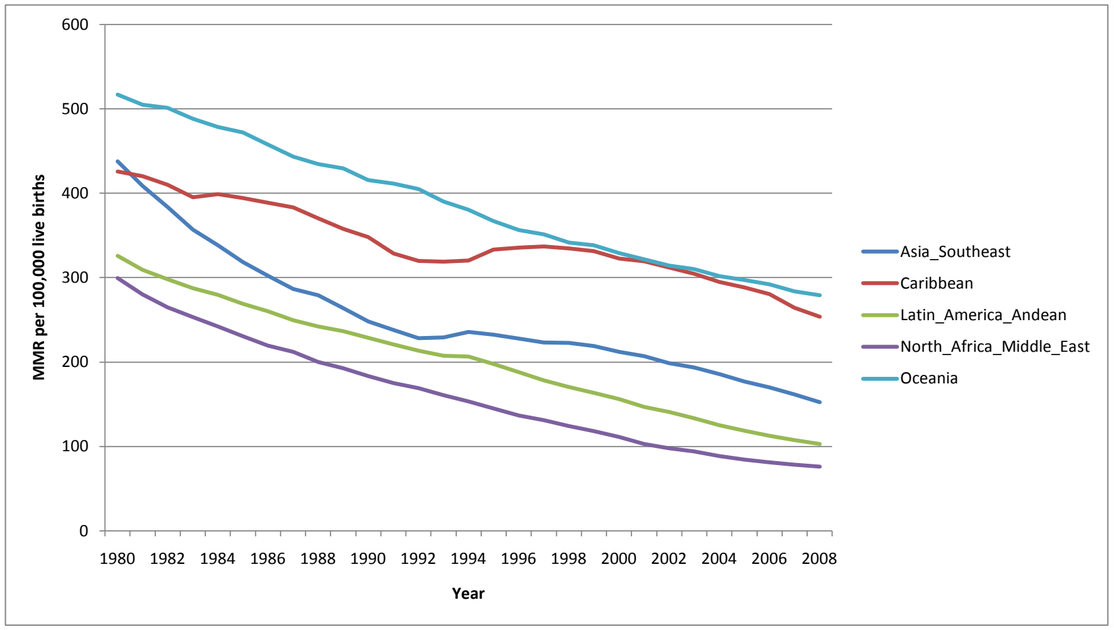


Figure 5. Maternal Mortality Ratio per 100, 000 live births by Region, 1980 to 2008







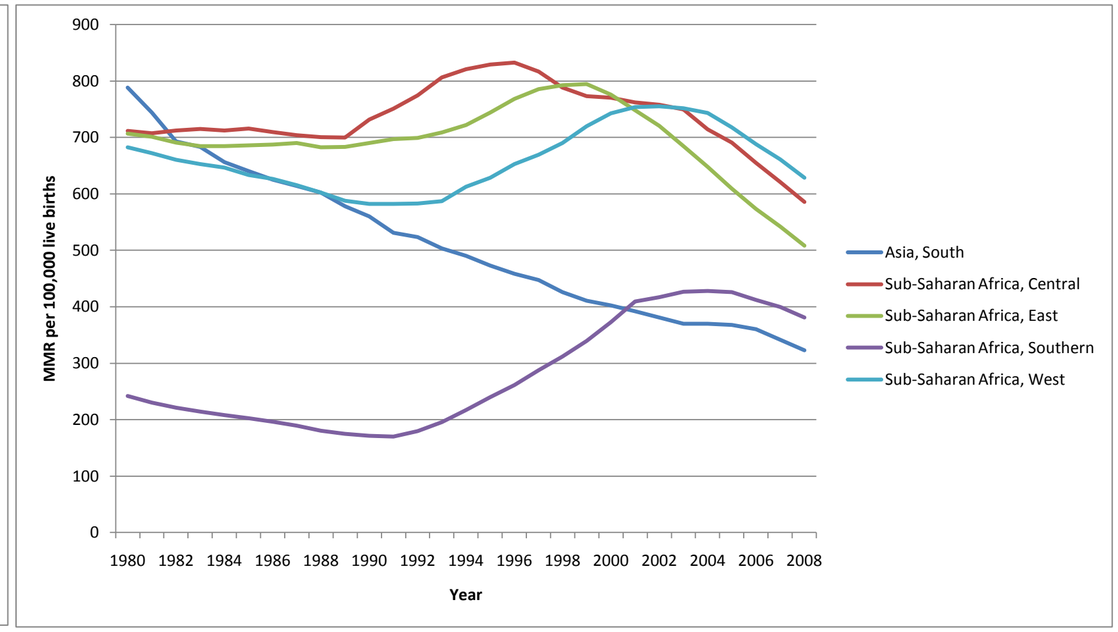
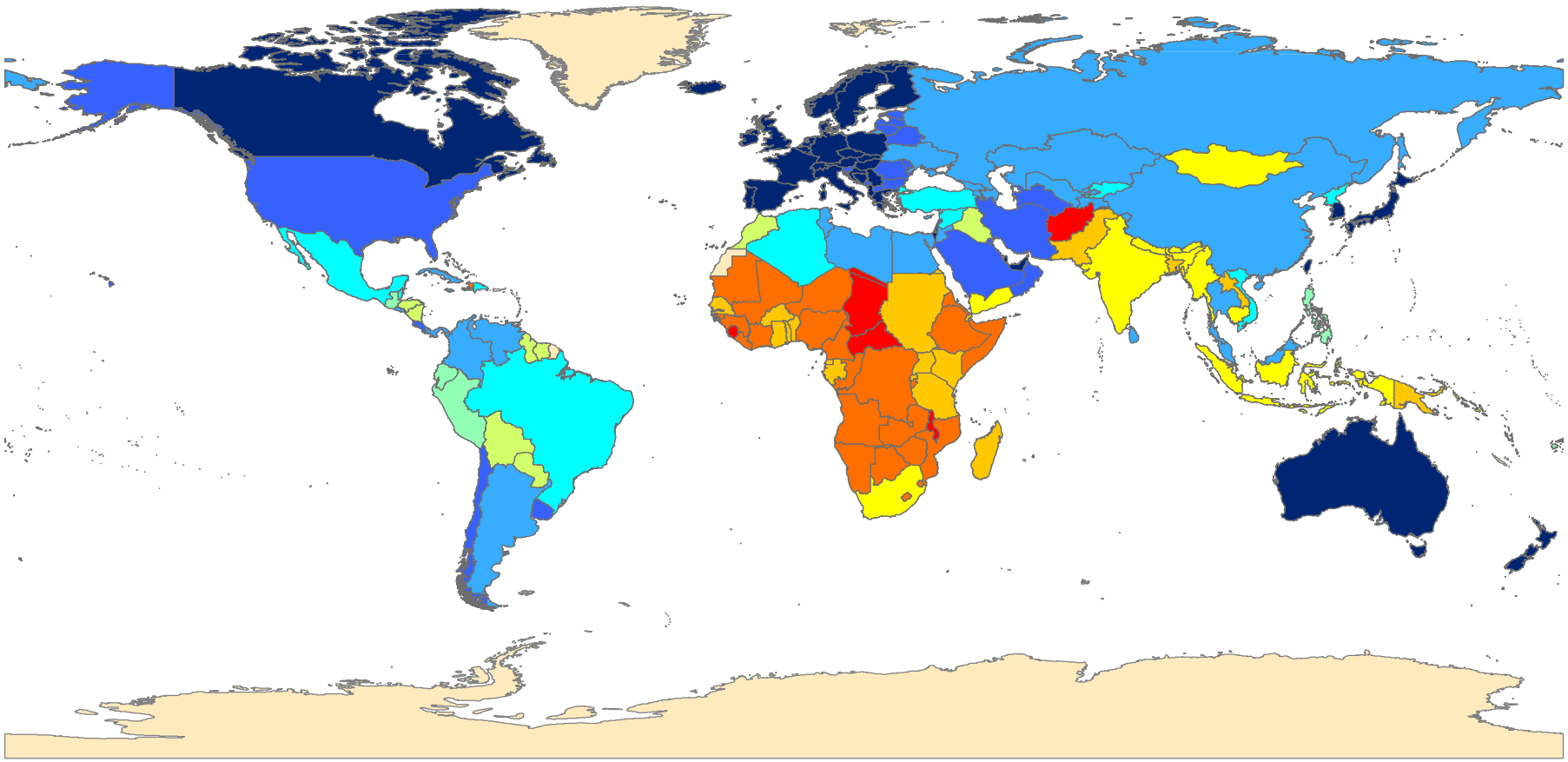


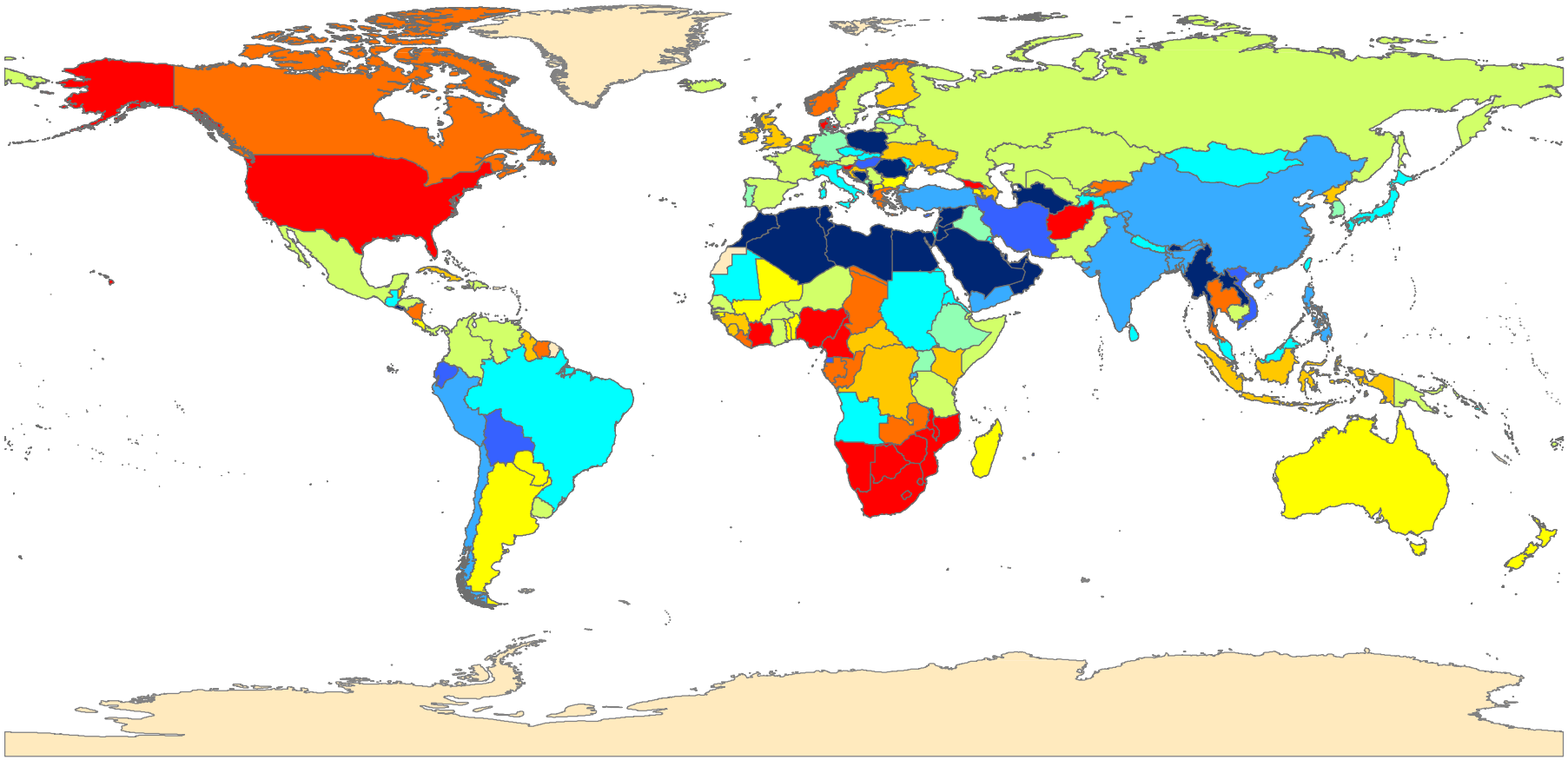
Figure 6. MMR per 100,000 live births, 2008



MMR per 100,000 live births

- <15
- 15 - 29
- 30 - 49
- 50 - 74
- 75 - 99
- 100 - 199
- 200 - 299
- 300 - 499
- 500 - 999
- 1000 - 1575

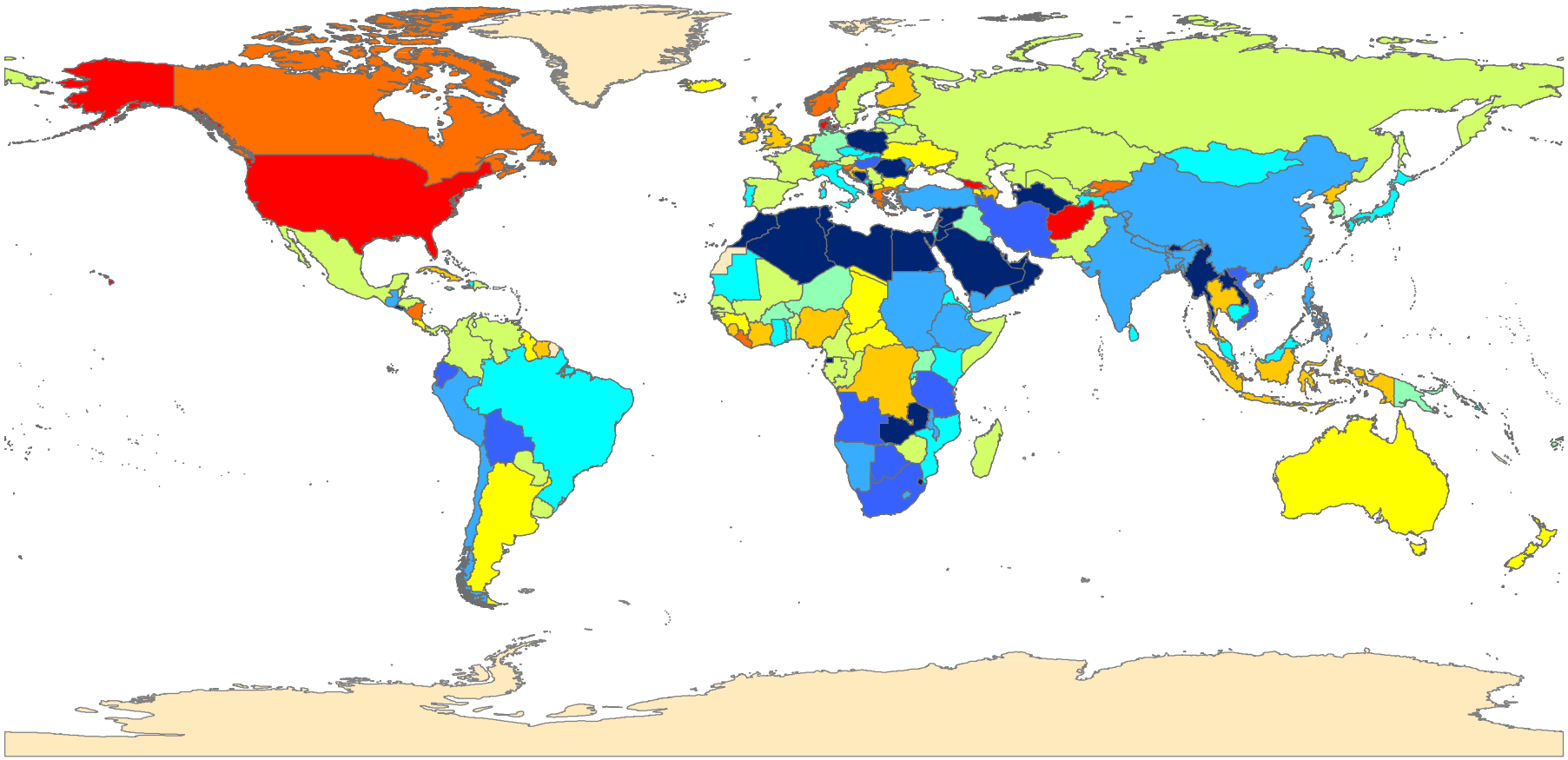
Figure 7a. Annualized Rate of Decline in MMR, 1990 to 2008



Annualized percent rate of decline in MMR (%)

- < -5.5
- -5.5 to -4.5
- -4.5 to -4.0
- -4.0 to -3.0
- -3.0 to -2.5
- -2.5 to -1.5
- -1.5 to -1.0
- -1.0 to 0.0
- 0.0 to 1.0
- > 1

Figure 7b. Annualized Rate of Decline in MMR, excluding HIV, 1990 to 2008



Annualized percent rate of decline in MMR (%)

- < -5.5
- -5.5 to -4.5
- -4.5 to -4.0
- -4.0 to -3.0
- -3.0 to -2.5
- -2.5 to -1.5
- -1.5 to -1.0
- -1.0 to 0.0
- 0.0 - 1.0
- > 1

Table 1. Definitions of Maternal Death and Maternal Mortality

	Direct	Indirect	HIV	Incidental
Early maternal (<42 weeks)	A	B	C	D
Late maternal (> 42 weeks & < 1 year)	E	F		

Table 2. Summary of Site-Years of Observation by Source, 1980 to 2008

Source of Data	Site-Years of Observation
Vital registration	2186
Sibling Histories	209
Surveillance Systems	20
Census/Survey Deaths in Household	26
National VA	35
Subnational VA	180
Total	**2656**

Table 3. Predictive Validity for Robust Regression:

Out-of-sample model performance measured by root mean squared error (SE), root median SE, mean relative error (RE) and median RE for the following hold-out scenarios: (i) withholding all information for 20% of countries; (ii) withholding the first 20% of years of data for every country; (iii) withholding the last 20% of years of data for every country; and (iv) withholding 20% of all datapoints.

Robust Regression: 20% of Countries				
Regression	Root Mean SE*	Root Median SE	Mean RE**	Median RE
Linear	214.84	27.00	0.604	0.417
Spatio-Temporal	189.27	25.34	0.521	0.357

Robust Regression: First 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	208.28	22.04	0.702	0.437
Spatio-Temporal	129.32	11.92	0.392	0.199

Robust Regression: Last 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	158.86	13.23	0.538	0.421
Spatio-Temporal	104.08	7.46	0.284	0.213

Robust Regression: Random 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	215.44	24.22	0.619	0.419
Spatio-Temporal	125.34	10.36	0.286	0.165

*SE = Squared Error

** RE = Relative Error

Table 4. Maternal Mortality Ratio per 100,000 live births by Country

		MMR (UI)			
GBD Region	**Country Name**	**1980**	**1990**	**2000**	**2008**
Asia Pacific, High Income	Brunei Darussalam	77 (47-126)	62 (39-97)	44 (29-66)	37 (25-54)
Asia Pacific, High Income	Japan	20 (17-22)	12 (10-13)	8 (7-9)	7 (6-8)
Asia Pacific, High Income	Korea, Republic of	45 (39-52)	18 (16-21)	14 (13-16)	11 (10-13)
Asia Pacific, High Income	Singapore	18 (13-23)	12 (9-16)	14 (10-18)	16 (11-21)
Asia Pacific, High Income	**Total**	**28 (26-31)**	**14 (13-15)**	**10 (9-11)**	**8 (8-9)**
Asia, Central	Armenia	31 (24-38)	36 (31-41)	39 (30-49)	30 (21-39)
Asia, Central	Azerbaijan	71 (59-83)	39 (33-44)	50 (43-58)	37 (30-45)
Asia, Central	Georgia	40 (32-48)	28 (24-33)	27 (21-32)	37 (27-48)
Asia, Central	Kazakhstan	62 (54-71)	61 (54-69)	58 (51-66)	44 (38-51)
Asia, Central	Kyrgyzstan	71 (60-83)	65 (57-75)	71 (61-83)	69 (58-82)
Asia, Central	Mongolia	959 (745-1193)	404 (316-501)	257 (203-320)	207 (163-255)
Asia, Central	Tajikistan	128 (110-148)	90 (78-101)	72 (62-84)	46 (38-55)
Asia, Central	Turkmenistan	77 (64-90)	67 (58-77)	41 (33-50)	22 (18-26)
Asia, Central	Uzbekistan	72 (62-83)	61 (54-69)	49 (43-56)	45 (39-51)
Asia, Central	**Total**	**105 (96-115)**	**72 (68-77)**	**60 (56-64)**	**48 (45-52)**
Asia, East	China	165 (144-187)	87 (77-99)	55 (49-62)	40 (35-46)
Asia, East	Korea, Democratic People's Republic of	130 (47-298)	68 (27-148)	70 (26-154)	64 (24-143)
Asia, East	Taiwan, Province of China	38 (23-56)	26 (15-37)	12 (7-16)	14 (8-20)
Asia, East	**Total**	**162 (142-183)**	**86 (76-98)**	**55 (48-62)**	**40 (35-46)**
Asia, South	Afghanistan	1640 (632-3527)	1261 (491-2703)	1957 (729-4356)	1575 (594-3396)
Asia, South	Bangladesh	1329 (800-2105)	724 (420-1196)	574 (344-900)	338 (195-546)
Asia, South	Bhutan	2116 (814-4749)	1145 (437-2539)	481 (186-1063)	255 (100-561)
Asia, South	India	677 (408-1080)	523 (310-835)	318 (190-506)	254 (154-395)
Asia, South	Nepal	865 (536-1351)	471 (290-722)	343 (213-533)	240 (149-370)
Asia, South	Pakistan	746 (411-1267)	541 (327-848)	415 (235-679)	376 (230-587)
Asia, South	**Total**	**788 (568-1099)**	**560 (391-794)**	**402 (293-555)**	**323 (232-444)**
Asia, Southeast	Cambodia	499 (324-751)	409 (237-658)	511 (322-786)	266 (171-398)
Asia, Southeast	Indonesia	423 (274-631)	253 (148-411)	290 (166-477)	229 (133-379)
Asia, Southeast	Lao People's Democratic Republic	1780 (1172-2715)	1215 (796-1816)	630 (377-996)	339 (215-511)
Asia, Southeast	Malaysia	137 (118-160)	76 (66-89)	59 (51-67)	42 (37-49)
Asia, Southeast	Maldives	1057 (405-2277)	366 (145-776)	125 (48-272)	75 (28-167)
Asia, Southeast	Mauritius	122 (100-144)	65 (53-77)	34 (26-43)	28 (21-36)
Asia, Southeast	Myanmar	1052 (401-2171)	662 (249-1484)	411 (155-874)	219 (87-495)
Asia, Southeast	Philippines	443 (289-661)	174 (112-261)	103 (65-160)	84 (53-130)
Asia, Southeast	Sri Lanka	92 (81-105)	52 (46-60)	40 (36-46)	30 (25-35)
Asia, Southeast	Thailand	115 (101-131)	44 (39-50)	43 (38-48)	47 (42-53)
Asia, Southeast	Timor-Leste	1445 (549-3201)	1016 (402-2184)	953 (363-2081)	929 (374-2077)
Asia, Southeast	Viet Nam	336 (218-504)	158 (102-233)	84 (55-125)	64 (42-95)
Asia, Southeast	**Total**	**438 (337-573)**	**248 (187-337)**	**212 (155-293)**	**152 (112-212)**
Australasia	Australia	9 (7-10)	6 (5-7)	5 (4-6)	5 (4-6)
Australasia	New Zealand	12 (9-16)	11 (8-14)	8 (6-10)	8 (6-11)
Australasia	**Total**	**9 (8-11)**	**7 (6-8)**	**6 (5-7)**	**6 (5-7)**
Caribbean	Bahamas	120 (81-163)	80 (56-104)	66 (50-86)	59 (45-77)

Caribbean	Barbados	99 (72-133)	86 (65-110)	94 (68-121)	78 (54-104)
Caribbean	Belize	120 (83-168)	88 (65-120)	87 (68-107)	74 (55-94)
Caribbean	Cuba	62 (54-71)	47 (41-54)	51 (45-59)	40 (34-46)
Caribbean	Dominican Republic	127 (78-199)	96 (58-154)	74 (45-116)	66 (40-103)
Caribbean	Grenada	155 (60-341)	99 (38-217)	66 (24-143)	47 (18-102)
Caribbean	Guyana	216 (161-281)	162 (134-192)	164 (139-191)	143 (110-178)
Caribbean	Haiti	1122 (708-1726)	898 (562-1413)	783 (488-1244)	582 (352-902)
Caribbean	Jamaica	82 (69-97)	50 (40-61)	37 (29-47)	34 (27-44)
Caribbean	Saint Lucia	162 (61-369)	92 (33-197)	57 (22-125)	46 (18-99)
Caribbean	Saint Vincent and the Grenadines	174 (64-374)	82 (31-181)	59 (23-130)	45 (17-97)
Caribbean	Suriname	175 (140-216)	106 (82-131)	128 (102-159)	116 (91-145)
Caribbean	Trinidad and Tobago	68 (55-82)	66 (55-78)	52 (40-64)	40 (30-51)
Caribbean	**Total**	**426 (293-613)**	**348 (234-518)**	**323 (218-483)**	**254 (168-372)**
Europe, Central	Albania	58 (49-69)	36 (31-43)	12 (9-15)	8 (6-11)
Europe, Central	Bosnia and Herzegovina	58 (45-73)	32 (25-40)	20 (15-26)	12 (9-15)
Europe, Central	Bulgaria	36 (31-43)	34 (29-39)	36 (30-42)	28 (22-35)
Europe, Central	Croatia	21 (15-27)	15 (11-19)	15 (11-19)	14 (11-19)
Europe, Central	Czech Republic	20 (16-25)	12 (10-15)	7 (5-9)	7 (5-9)
Europe, Central	Hungary	22 (18-26)	16 (14-19)	10 (8-12)	7 (5-9)
Europe, Central	Macedonia, the Former Yugoslav Republic of	28 (20-38)	20 (14-27)	19 (13-25)	17 (11-23)
Europe, Central	Montenegro	79 (31-178)	33 (13-72)	27 (10-60)	19 (8-41)
Europe, Central	Poland	22 (19-25)	21 (19-24)	10 (9-12)	7 (6-9)
Europe, Central	Romania	139 (122-157)	92 (80-104)	42 (37-48)	26 (22-31)
Europe, Central	Serbia	15 (11-20)	12 (8-16)	10 (8-13)	9 (6-11)
Europe, Central	Slovakia	19 (14-25)	13 (9-18)	8 (6-11)	7 (5-9)
Europe, Central	Slovenia	30 (20-43)	16 (11-22)	21 (15-29)	19 (13-26)
Europe, Central	**Total**	**47 (43-51)**	**34 (31-37)**	**18 (17-20)**	**13 (12-14)**
Europe, Eastern	Belarus	30 (24-35)	28 (24-32)	26 (21-31)	19 (15-23)
Europe, Eastern	Estonia	34 (26-46)	28 (22-36)	24 (18-33)	22 (16-33)
Europe, Eastern	Latvia	37 (30-45)	30 (24-36)	24 (18-31)	18 (13-25)
Europe, Eastern	Lithuania	33 (26-40)	22 (18-27)	18 (13-22)	16 (12-21)
Europe, Eastern	Moldova	58 (49-68)	42 (36-48)	31 (25-37)	20 (16-26)
Europe, Eastern	Russian Federation	60 (52-68)	48 (43-55)	45 (39-51)	34 (30-39)
Europe, Eastern	Ukraine	44 (38-50)	35 (31-40)	35 (31-40)	30 (26-34)
Europe, Eastern	**Total**	**54 (49-60)**	**43 (39-48)**	**41 (37-45)**	**32 (29-35)**
Europe, Western	Austria	14 (11-17)	8 (6-10)	5 (4-7)	6 (4-7)
Europe, Western	Belgium	13 (10-16)	8 (7-10)	10 (8-13)	9 (7-12)
Europe, Western	Cyprus	148 (18-278)	98 (12-184)	57 (7-109)	41 (5-78)
Europe, Western	Denmark	7 (5-10)	7 (5-9)	7 (5-9)	9 (6-13)
Europe, Western	Finland	7 (5-9)	7 (6-10)	7 (5-9)	7 (5-9)
Europe, Western	France	19 (17-22)	14 (12-16)	11 (10-13)	10 (9-12)
Europe, Western	Germany	20 (18-23)	12 (10-13)	8 (7-9)	7 (6-8)
Europe, Western	Greece	18 (15-22)	8 (6-9)	8 (7-10)	8 (6-11)
Europe, Western	Iceland	11 (4-24)	9 (4-20)	8 (3-18)	7 (3-16)
Europe, Western	Ireland	11 (8-13)	7 (5-9)	7 (5-10)	6 (4-8)
Europe, Western	Israel	9 (7-11)	11 (9-13)	8 (6-9)	6 (4-8)
Europe, Western	Italy	14 (12-16)	7 (6-8)	5 (4-6)	4 (3-5)
Europe, Western	Luxembourg	9 (4-19)	7 (2-15)	6 (2-13)	5 (2-11)

Europe, Western	Malta	21 (8-45)	15 (6-33)	9 (4-20)	6 (2-13)
Europe, Western	Netherlands	10 (8-11)	9 (8-11)	10 (8-11)	8 (6-9)
Europe, Western	Norway	7 (5-10)	7 (5-9)	7 (5-10)	8 (5-10)
Europe, Western	Portugal	29 (25-33)	16 (13-19)	12 (9-14)	10 (7-12)
Europe, Western	Spain	18 (16-21)	9 (8-10)	7 (6-8)	7 (6-8)
Europe, Western	Sweden	6 (5-7)	6 (5-8)	5 (4-6)	5 (3-6)
Europe, Western	Switzerland	9 (7-11)	7 (5-9)	7 (5-9)	7 (5-9)
Europe, Western	United Kingdom	10 (9-12)	8 (7-10)	8 (7-10)	8 (7-10)
Europe, Western	**Total**	**16 (15-17)**	**10 (10-11)**	**8 (8-9)**	**7 (7-8)**
Latin America, Andean	Bolivia	547 (344-845)	439 (276-666)	269 (168-413)	180 (110-284)
Latin America, Andean	Ecuador	288 (178-443)	181 (114-281)	121 (69-196)	77 (48-119)
Latin America, Andean	Peru	268 (165-406)	172 (110-262)	125 (79-195)	81 (50-123)
Latin America, Andean	**Total**	**326 (248-426)**	**229 (176-295)**	**156 (116-205)**	**103 (77-134)**
Latin America, Central	Colombia	115 (102-130)	71 (62-81)	61 (54-70)	46 (41-53)
Latin America, Central	Costa Rica	39 (33-46)	32 (27-37)	32 (27-38)	25 (21-30)
Latin America, Central	El Salvador	216 (139-325)	135 (85-203)	63 (38-99)	37 (23-57)
Latin America, Central	Guatemala	189 (113-296)	178 (108-279)	111 (68-170)	88 (55-141)
Latin America, Central	Honduras	174 (104-279)	164 (100-254)	169 (106-257)	105 (66-162)
Latin America, Central	Mexico	124 (109-140)	73 (64-83)	60 (53-69)	52 (45-58)
Latin America, Central	Nicaragua	145 (90-224)	101 (60-159)	124 (75-196)	103 (63-162)
Latin America, Central	Panama	80 (67-92)	61 (51-72)	51 (44-59)	44 (35-54)
Latin America, Central	Venezuela	74 (65-83)	66 (58-75)	56 (49-63)	48 (42-55)
Latin America, Central	**Total**	**125 (114-137)**	**85 (77-94)**	**70 (64-78)**	**57 (51-63)**
Latin America, Southern	Argentina	80 (71-91)	60 (53-68)	52 (46-59)	49 (43-55)
Latin America, Southern	Chile	70 (62-80)	44 (38-50)	24 (21-28)	21 (18-25)
Latin America, Southern	Uruguay	55 (46-64)	33 (27-39)	26 (21-32)	25 (18-31)
Latin America, Southern	**Total**	**76 (69-84)**	**54 (49-60)**	**44 (39-49)**	**41 (36-45)**
Latin America, Tropical	Brazil	149 (84-242)	112 (64-186)	69 (43-106)	55 (34-86)
Latin America, Tropical	Paraguay	185 (111-288)	146 (92-224)	129 (80-200)	113 (70-173)
Latin America, Tropical	**Total**	**150 (87-240)**	**113 (66-184)**	**71 (47-107)**	**57 (37-87)**
North Africa / Middle East	Algeria	396 (336-464)	189 (159-219)	94 (80-109)	66 (56-77)
North Africa / Middle East	Bahrain	132 (84-204)	89 (58-138)	49 (30-70)	36 (23-52)
North Africa / Middle East	Egypt	352 (217-550)	195 (120-312)	74 (46-114)	43 (25-71)
North Africa / Middle East	Iran, Islamic Republic of	101 (65-155)	64 (40-96)	35 (21-53)	28 (17-43)
North Africa / Middle East	Iraq	241 (136-404)	212 (131-335)	174 (107-270)	130 (73-211)
North Africa / Middle East	Jordan	214 (133-327)	103 (63-155)	59 (37-91)	35 (19-59)
North Africa / Middle East	Kuwait	51 (36-67)	48 (34-65)	31 (22-42)	26 (18-36)
North Africa / Middle East	Lebanon	124 (49-269)	76 (30-168)	37 (14-78)	24 (9-53)
North Africa / Middle East	Libyan Arab Jamahiriya	148 (58-319)	124 (46-271)	63 (24-140)	40 (15-89)
North Africa / Middle East	Morocco	601 (396-885)	384 (240-570)	262 (165-402)	124 (70-200)
North Africa / Middle East	Occupied Palestinian Territory	181 (114-275)	92 (57-144)	52 (30-84)	46 (27-71)
North Africa / Middle East	Oman	174 (102-256)	85 (49-126)	41 (26-59)	24 (16-33)
North Africa / Middle East	Qatar	52 (21-114)	49 (18-107)	26 (9-62)	14 (5-31)
North Africa / Middle East	Saudi Arabia	135 (52-297)	94 (36-208)	47 (19-104)	28 (11-61)
North Africa / Middle East	Syrian Arab Republic	251 (143-411)	156 (92-251)	67 (39-108)	50 (28-84)
North Africa / Middle East	Tunisia	294 (111-643)	141 (57-312)	56 (22-121)	36 (14-79)
North Africa / Middle East	Turkey	251 (143-412)	121 (73-188)	69 (41-108)	58 (32-101)
North Africa / Middle East	United Arab Emirates	41 (15-91)	31 (12-66)	14 (5-30)	9 (3-19)

North Africa / Middle East	Yemen	808 (479-1273)	582 (337-921)	383 (227-606)	269 (162-435)
North Africa / Middle East	**Total**	**299 (250-355)**	**183 (154-218)**	**111 (92-135)**	**76 (61-94)**
North America, High Income	Canada	7 (6-9)	6 (5-7)	6 (5-7)	7 (5-8)
North America, High Income	United States	12 (11-14)	12 (10-13)	13 (12-15)	17 (15-19)
North America, High Income	**Total**	**12 (10-13)**	**11 (10-12)**	**13 (11-15)**	**16 (14-18)**
Oceania	Fiji	178 (66-397)	133 (50-285)	111 (41-244)	85 (32-194)
Oceania	Micronesia, Federated States of	378 (142-825)	227 (87-488)	164 (61-381)	127 (48-279)
Oceania	Papua New Guinea	585 (343-956)	476 (267-782)	371 (212-603)	312 (184-507)
Oceania	Samoa	246 (91-554)	173 (65-386)	154 (57-345)	104 (39-236)
Oceania	Solomon Islands	719 (274-1606)	500 (188-1081)	330 (126-747)	284 (102-638)
Oceania	Tonga	359 (129-826)	189 (70-400)	130 (48-279)	113 (42-250)
Oceania	Vanuatu	509 (192-1147)	336 (127-725)	230 (84-505)	178 (66-400)
Oceania	**Total**	**517 (334-784)**	**416 (252-649)**	**329 (202-518)**	**279 (174-434)**
Sub-Saharan Africa, Central	Angola	1309 (492-2909)	1156 (447-2571)	1105 (425-2466)	593 (236-1282)
Sub-Saharan Africa, Central	Central African Republic	990 (623-1512)	1757 (1084-2731)	1988 (1161-3220)	1570 (981-2407)
Sub-Saharan Africa, Central	Congo	897 (558-1395)	616 (356-1039)	850 (521-1336)	617 (378-972)
Sub-Saharan Africa, Central	Congo, the Democratic Republic of the	498 (321-746)	550 (314-906)	607 (379-927)	534 (311-856)
Sub-Saharan Africa, Central	Equatorial Guinea	663 (271-1459)	775 (283-1661)	670 (258-1447)	302 (115-655)
Sub-Saharan Africa, Central	Gabon	403 (247-622)	422 (248-692)	637 (408-970)	493 (310-742)
Sub-Saharan Africa, Central	**Total**	**711 (487-1072)**	**732 (488-1101)**	**770 (535-1108)**	**586 (392-839)**
Sub-Saharan Africa, East	Burundi	776 (291-1713)	712 (279-1560)	904 (346-1996)	570 (221-1240)
Sub-Saharan Africa, East	Comoros	699 (268-1520)	450 (175-989)	293 (110-642)	225 (89-488)
Sub-Saharan Africa, East	Djibouti	641 (384-1025)	607 (356-961)	565 (337-897)	462 (274-738)
Sub-Saharan Africa, East	Eritrea	1436 (841-2371)	1293 (790-1970)	874 (526-1389)	751 (442-1210)
Sub-Saharan Africa, East	Ethiopia	1061 (665-1639)	968 (600-1507)	937 (543-1537)	590 (358-932)
Sub-Saharan Africa, East	Kenya	494 (307-768)	452 (263-732)	730 (437-1157)	413 (236-678)
Sub-Saharan Africa, East	Madagascar	490 (308-747)	484 (305-746)	505 (313-781)	373 (229-574)
Sub-Saharan Africa, East	Malawi	632 (395-966)	743 (457-1127)	1662 (1034-2551)	1140 (675-1813)
Sub-Saharan Africa, East	Mozambique	411 (228-668)	385 (241-591)	505 (311-796)	599 (359-957)
Sub-Saharan Africa, East	Rwanda	755 (468-1171)	813 (508-1223)	952 (610-1449)	383 (249-584)
Sub-Saharan Africa, East	Somalia	1061 (405-2308)	963 (380-2105)	837 (329-1856)	675 (263-1501)
Sub-Saharan Africa, East	Sudan	639 (395-971)	593 (367-908)	490 (308-741)	306 (195-463)
Sub-Saharan Africa, East	Tanzania, United Republic of	603 (380-925)	610 (375-940)	714 (411-1162)	449 (273-721)
Sub-Saharan Africa, East	Uganda	435 (258-709)	571 (355-893)	604 (366-963)	352 (215-558)
Sub-Saharan Africa, East	Zambia	599 (359-950)	594 (365-932)	914 (555-1421)	603 (376-928)
Sub-Saharan Africa, East	**Total**	**707 (586-854)**	**690 (574-842)**	**776 (639-948)**	**508 (430-610)**
Sub-Saharan Africa, Southern	Botswana	424 (166-891)	237 (90-529)	655 (255-1468)	519 (199-1133)
Sub-Saharan Africa, Southern	Lesotho	588 (369-896)	363 (227-555)	1021 (655-1519)	964 (599-1482)
Sub-Saharan Africa, Southern	Namibia	397 (235-639)	354 (226-525)	558 (355-853)	586 (363-899)
Sub-Saharan Africa, Southern	South Africa	208 (131-316)	121 (73-190)	155 (95-248)	237 (146-372)
Sub-Saharan Africa, Southern	Swaziland	559 (314-923)	359 (208-587)	609 (369-945)	736 (460-1124)
Sub-Saharan Africa, Southern	Zimbabwe	219 (135-334)	232 (143-362)	819 (474-1342)	624 (371-976)
Sub-Saharan Africa, Southern	**Total**	**242 (184-319)**	**171 (132-222)**	**373 (280-499)**	**381 (288-496)**
Sub-Saharan Africa, West	Benin	829 (476-1370)	588 (343-947)	551 (341-842)	469 (294-716)
Sub-Saharan Africa, West	Burkina Faso	541 (342-830)	488 (307-745)	456 (286-707)	332 (208-522)
Sub-Saharan Africa, West	Cameroon	810 (507-1254)	523 (308-845)	886 (549-1415)	705 (393-1155)
Sub-Saharan Africa, West	Cape Verde	528 (289-854)	229 (118-384)	139 (75-223)	75 (41-120)
Sub-Saharan Africa, West	Chad	978 (629-1473)	891 (562-1358)	1205 (746-1880)	1065 (661-1636)

Sub-Saharan Africa, West	Côte d'Ivoire	590 (378-884)	580 (350-916)	1116 (719-1643)	944 (566-1500)
Sub-Saharan Africa, West	Gambia	898 (516-1464)	628 (404-936)	396 (246-610)	281 (171-441)
Sub-Saharan Africa, West	Ghana	731 (444-1157)	549 (336-857)	538 (329-819)	409 (248-633)
Sub-Saharan Africa, West	Guinea	1140 (726-1722)	965 (610-1453)	976 (616-1491)	860 (529-1314)
Sub-Saharan Africa, West	Guinea-Bissau	1155 (644-1890)	966 (589-1510)	809 (486-1246)	804 (454-1332)
Sub-Saharan Africa, West	Liberia	645 (394-1005)	729 (446-1130)	1055 (651-1642)	859 (547-1289)
Sub-Saharan Africa, West	Mali	1125 (712-1688)	831 (525-1263)	807 (513-1258)	670 (422-1017)
Sub-Saharan Africa, West	Mauritania	1491 (948-2265)	1295 (761-2099)	866 (505-1386)	712 (451-1119)
Sub-Saharan Africa, West	Niger	1083 (669-1696)	890 (526-1483)	754 (470-1176)	601 (373-927)
Sub-Saharan Africa, West	Nigeria	516 (334-757)	473 (306-703)	694 (435-1041)	608 (372-946)
Sub-Saharan Africa, West	Sao Tome and Principe	607 (241-1312)	531 (210-1188)	420 (164-912)	296 (112-607)
Sub-Saharan Africa, West	Senegal	670 (395-1064)	542 (352-822)	491 (306-765)	401 (252-622)
Sub-Saharan Africa, West	Sierra Leone	1240 (800-1880)	1044 (685-1592)	1200 (745-1824)	1033 (635-1627)
Sub-Saharan Africa, West	Togo	600 (388-906)	540 (351-819)	552 (352-837)	447 (289-672)
Sub-Saharan Africa, West	**Total**	**683 (577-818)**	**582 (485-709)**	**742 (608-915)**	**629 (508-787)**

Table 5. Number and Proportion of Maternal Deaths and Live Births for Top 21 Countries, 2008

Order	Country	Deaths in 1000s (UI)	%	Cumulative %	Births (%)	Cumulative %
1	India	68.3 (41.6-106.2)	19.9	19.9	19.7	19.7
2	Nigeria	36.7 (22.4-57.0)	10.7	30.6	4.4	24.1
3	Pakistan	20.1 (12.3-31.3)	5.9	36.5	3.9	28.0
4	Afghanistan	20.0 (7.5-43.1)	5.8	42.3	0.9	28.9
5	Ethiopia	18.2 (11.1-28.8)	5.3	47.6	2.3	31.2
6	Congo, the Democratic Republic of the	15.4 (9.0-24.7)	4.5	52.1	2.1	33.3
7	Bangladesh	11.6 (6.7-18.7)	3.4	55.5	2.5	35.8
8	Indonesia	9.6 (5.6-16.0)	2.8	58.3	3.1	38.9
9	Tanzania, United Republic of	8.0 (4.8-12.8)	2.3	60.6	1.3	40.2
10	China	7.3 (6.4-8.3)	2.1	62.7	13.3	53.5
11	Malawi	6.8 (4.0-10.9)	2.0	64.7	0.4	53.9
12	Côte d'Ivoire	6.8 (4.1-10.8)	2.0	66.7	0.5	54.4
13	Kenya	6.2 (3.6-10.2)	1.8	68.5	1.1	55.5
14	Chad	5.3 (3.3-8.2)	1.5	70.0	0.4	55.9
15	Mozambique	5.2 (3.1-8.4)	1.5	71.5	0.6	56.5
16	Uganda	5.2 (3.1-8.2)	1.5	73.0	1.1	57.6
17	Cameroon	5.0 (2.8-8.1)	1.4	74.4	0.5	58.1
18	Niger	4.7 (3.0-7.3)	1.4	75.8	0.6	58.7
19	Angola	4.6 (1.8-9.9)	1.3	77.1	0.6	59.3
20	Sudan	4.0 (2.5-6.0)	1.2	78.3	0.9	60.2
21	Mali	3.6 (2.3-5.5)	1.1	79.4	0.4	60.6
	All other countries (160)	70.3 (43.0-112.2)	20.5	100.0	39.3	100.0
Total		**342.9**	**100.0**	**100.0**	**100.0**	**100.0**

CHAPTER THREE

Predictive validity for model selection: a test case of maternal mortality

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Introduction

Model selection is a rich field in statistics. A wide range of approaches has been developed to help a researcher identify the model, or models, that best addresses the research question. The approach to developing the "best" model depends on the purpose for that model: whether a model is intended to explain an observed phenomenon or to predict that phenomenon is crucial to how a model is constructed, and how its performance is assessed. A good explanatory model will approximate the true underlying model for the observed data, whereas a good predictive model will predict new values accurately (Shmueli 2010). A model with good explanatory power will not necessarily have good predictive ability, though the two are often conflated (Shmueli 2010).

The role of prediction models in global health has grown with the intensifying focus on the Millennium Development Goals (MDGs). This set of eight goals, agreed to by UN member states in 2000, has spurred the need for high quality time trends of key indicators related to, among other things, child and maternal health, health service access, and the prevalence of HIV/AIDS, malaria and other key diseases among the world's poor. The MDGs outline specific, empirical goals for indicators, and as such, require accurate and timely estimates of trends in these indicators for all countries of the world (United Nations General Assembly 2000; United Nations Development Program 2003).

A growing literature has responded to this need, and relies on the use of statistical models to inform predictions (i.e. (Mariel M Finucane AB et al. 2011; Rajaratnam et al. 2010; Lim et al. 2010; Glaziou et al. 2011)). For most indicators in global health, the data are of mixed quality and availability, and modeling is necessary to construct a complete time series. However, despite the growing attention and publication of predictive models in global health, the selection of model form receives scant attention in the global health literature (i.e. (Mathers and Loncar 2006; Black et al. 2010; de Onis, Blossner, and Borghi 2010)). While researchers likely consider a range of models, the process by which the final model is chosen is rarely discussed in the scientific literature.

A complete review of the vast literature on model selection is beyond the scope of this paper, but some background is useful. Widely used measures of goodness of fit, such as the R-squared or adjusted R-squared (which measure the explained variance), are useful for selecting an explanatory model, but they are not appropriate for selecting the model with the best predictive ability. Another commonly used model selection metric is the Akaike Information Criteria (AIC), and its derivations such as the AICc, for small sample sizes, and the QAIC, for over-dispersed count data (Burnham, Anderson, and Burnham 2002; McQuarrie and Tsai 1998). The AIC can be thought of as an estimate of the distance between the unknown, true model that generated the observed data and the proposed, fitted model (Burnham, Anderson, and Burnham 2002). The AIC is often used interchangeably with the BIC (the Schwarz Bayesian Information criteria), but the AIC is actually more appropriate for predictive model selection, as it was developed to measure predictive accuracy (Sober 2002), whereas the BIC was developed to measure goodness of fit (Shmueli 2010). The predicted residual sum of squares (PRESS) and the Akaike

final prediction-error criterion (FPE) are two other metrics appropriate for predictive model selection (Forster 2000; Cawley and Talbot 2007; McQuarrie and Tsai 1998).

However, empirical approaches, such as the bootstrap, jackknife and, in particular, cross-validation, offer the most natural route for predictive model selection, because they offer a way to directly test precisely how well a given model predicts new values (Babu 2011; Sewell 2008; McQuarrie and Tsai 1998). Cross-validation is a widely used approach wherein part of the dataset is withheld as the test set, and the rest of the dataset is used to "train" the models. Summary metrics are then computed to compare performance across models. There are several approaches to cross-validation, including k-fold, repeated random sub-sampling, and leave-one-out (Shao 1996).

Futher, some disciplines, including meterology and financial analysis, have moved away from the selection of a single "best" model (Hsieh and Benyang 1998; Lu, Wang, and Lai 2008). This shift has grown out of the recognition that there is rarely a single "best" model choice across all tests, and that even if there were, the other intermediate models also contain valuable information (Barai and Reich 1999). In ensemble modeling, a range of plausible models is fitted to the data, and each of the models' results is combined to create the final predictions (Sharkey 1996). This approach was used to win the "Netflix Prize" in 2009 (http://www.netflixprize.com/). In this framework, some method is needed to combine the component models.

This paper presents the use of predictive validity for predictive model selection. Predictive validity uses a cross-validation approach to identify the model that best performs in specific tests, tailored to address the needs of a specific analysis. It can also be used to weight the component models in an ensemble modeling approach, as in a

recent publication on causes of death modeling, part of the Global Burden of Disease project (Foreman et al. 2012). Similar to repeated random sub-sampling cross-validation (Shao 1993; Babu 2011; Browne 2000), predictive validity is an approach that uses withheld components of the dataset to identify the best-performing model from a range of candidates trained on the remaining data. The innovation of predictive validity is to identify a range of tests for what the model needs to do well.

As a test case, this paper explores the use of predictive validity in a specific dataset of maternal mortality over the period 1980-2010, first presented in Hogan et al (Hogan et al. 2010). Maternal mortality (defined as the death of a woman while pregnant, during childbirth, or in the 42 days after delivery (World Health Organization 2012)) is highlighted in MDG 5, with the target of reducing the maternal mortality ratio (the number of maternal deaths per 100,000 live births, the MMR) by three-quarters from 1990 to 2015 {UnitedNationsDevelopmentGroup:2003th}(United Nations Development Program 2003; Graham, Foster, et al. 2008). Maternal mortality has long been perceived as very difficult to measure (Graham, Foster, et al. 2008; Graham, Ahmed, et al. 2008; Yazbeck 2007; Campbell 1999; AbouZahr and Wardlaw 2001; Ronsmans 2001), largely because even where MMRs are very high, maternal mortality is rare.

Hogan et al (2010) present a detailed description of the data, data correction, and two-stage statistical analysis used to construct complete time trends of maternal mortality for 1980-2010 in 181 countries. The authors used predictive validity at several stages of the analysis, but this paper will focus on the use of predictive validity to select the type of first stage regression model. The dataset constructed for the analysis of this trend presents several challenges, and the model needs to be accurate when forecasting, backcasting,

and when predicting out of sample, both within countries with missing years of data, and into countries that have no data at all. This paper presents predictive validity as a tool to help identify the model that best accomplishes these specific goals.

Methods

Data. To explore the use of predictive validity for model selection, a dataset first presented in Hogan et al (2010) is used as an example case. That dataset is the result of a systematic assessment of all available data for the estimation of maternal mortality over the period 1980-2010 for all countries of the world. The data are from varied sources: vital registration data, sibling history data from surveys, household death data from censuses and surveys, and published national and subnational population-based verbal autopsy studies. Each data point is one country-year-age estimate, for a total of 2,651 country-years in the dataset. The dataset presents several challenges: the data are relatively sparse; in many country-year-age groups there are small numbers of maternal deaths which results in substantial stochastic measurement error; there is large and often country-specific non-sampling error; and covariates can only explain a portion of the variance across age, country and year. Hogan et al (2010) used a two-stage modeling approach, with a first-stage linear model followed by a spatial-temporal step to improve the predictions. This paper will focus on the selection of the type of model used in the first stage.

For maternal mortality, the ultimate indicator of interest is the maternal mortality ratio: the number of maternal deaths per 100,000 live births (MMR), typically calculated in women aged 15-49. Hogan et al (2010) did not model the MMR directly, because they

were interested in the age-pattern of maternal mortality. Live birth data is not available by five-year age groups. Therefore, the dependent variable was the age-specific maternal mortality rate. There are a range of potential model types that may be appropriate for modeling the maternal mortality rate directly, including ordinary least squares (OLS), quantile regression, and a range of formulations of robust regression. The rate can also be modeled using count models, including Poisson, negative binomial regression, or generalized negative binomial regression. The selection of the type of the first-stage model from these possibilities is the focus of this example.

Predictive validity as a model selection approach could be appropriately used for other applications, such as in the selection of the independent variables to be included, or the appropriate transformation of those independent variables, as applied by Hogan et al. (2010). This application will not be explored in this paper. The independent variables selected in this case were: total fertility rate, GDP per capita, HIV seroprevalence, neo-natal mortality, age-specific female education, and indicators for five-year age groups (15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49).

Maternal mortality is a rare event, even where maternal mortality ratios (MMRs) are very high, which can result in enormous sampling error and stochastic variation. In addition, a range of biases and measurement errors can crop up. Each of these factors can result in the presence of outliers that appear to be implausible given previous knowledge. An outlier can be understood as an atypical observation ((Maronna, Martin, and Yohai 2006) p.1) that appears to be derived from some distribution other than the one of interest ((Barnett, Lewis, and Abeles 1979), p. 7). Numerous methods have been proposed to identify outliers, but most authors agree that some degree of judgment and expert review

is needed to decide how to treat flagged outliers and further, it is unlikely that any approach, whether qualitative or quantitative, will completely solve the issue of outliers (Hodge and Austin 2004)((Altman 1992), p.126). For this reason, it may be necessary for a robust approach to the modeling process itself, hence the inclusion of robust regression approaches in this analysis. In this example, 314 outliers (11.8% of the sample) were identified via expert review. These data points were excluded from the predictive validity analysis on the assumption that the model should not be tested in its ability to predict values not considered plausible.

The estimation of maternal mortality relies on a range of data sources with striking variability in availability and quality across countries and over time. For some countries, particularly in Western Europe and North America, there is a single estimate for every year in the study period from vital registration systems; however, in many places with vital registration, it is only partially available across the study period. In other cases, there are multiple data points available for a single year, such as a value from the vital registration system as well as a sample survey. Some countries have only a few scattered data points from a range of sources, and some (n=21) have no data at all. Figure 1 shows the data available in four countries that illustrate these scenarios.

Analysis. Conceptually, the ideal would be a "gold standard" to which model predictions could be compared, and to select the model that most closely reproduces the gold standard from the available data. However, in the case of this dataset, as well as most datasets in global health, there is no available "gold standard" for comparison. Instead, as in a cross-validation approach, the researcher holds back some of the observed data, and

then sees how well the model, fit to the remaining data, does in predicting the held back data points.

The data available for the estimation of maternal mortality presents four distinct circumstances in which the selected regression model must perform well: gaps within the time series, gaps at the start and end of the time series (forecasting and backcasting), and in countries with no data whatsoever. To test model performance in the case of gaps within the time series, a random sample of country-years is dropped from the dataset. The model is then fit in the remaining sample, predictions are made, and then those predictions are compared to the "true values" in the random holdout sample. This process is repeated several times to ensure that the results are not an artifact of a particular random sample. Similarly, to test model performance in the case where there is no data whatsoever, a random sample of countries is dropped, the model fitted to the remaining data, and then predictions made and compared with the withheld data points. To test backcasting and forecasting, within each country, a portion of the earliest and latest years of data, respectively, are withheld and compared against after predicting.

Seven model forms were considered: ordinary least squares (OLS), quantile regression (QUANTILE), robust regression using Huber iterations only (MREGRESS), robust regression using Huber and biweight iterations (RREG), poisson regression (POISSON), negative binomial regression (NBREG), and generalized negative binomial regression (GNBREG).

After fitting these models, the predicted age-specific mortality rates were converted to the MMR, as this is the primary indicator on which the models should perform well. Four summary metrics of performance were calculated after the holdout

procedure described above in MMR space: absolute average relative error (AARE), absolute median relative error (AMRE), root mean square error (RMSE), and root median square error (RMEDSE). The median versions of these metrics (AMRE and RMEDSE) are less subject to the influence of extreme outliers.

The procedure described above has two components that require further investigation: first, the appropriate number of random draws for the model fit and prediction must be determined, and second, the fraction of the data to be withheld as the comparison group. To address the former, the process of model fit, prediction, and comparison to the holdout sample was undertaken one through 100 times. In other words, in the first test, there was no correction for the fact that the results may be an artifact of a particular random sample, as a single sample was dropped, the model estimated and the predicted results compared to the single holdout sample. In the 100^{th} test, the model was estimated and predicted results compared in 100 different random samples, and then the mean performance metrics calculated across all samples. This is only applicable in the tests where the countries and country-years are dropped; forecasting and backcasting are not subject to the random sampling issue because the samples for testing are fixed by their timing.

For the latter issue, that of what proportion of the data to be withheld as the comparison group, a sensitivity analysis was undertaken to assess what proportion of the data should be dropped for these tests. 10%, 20%, 30% and 50% were sequentially dropped, and the metrics of fit were examined in each.

All analysis was undertaken in Stata MP/12.0 (Stata Corp).

Results

Figure 2 shows selected results for the sensitivity analysis of 10%, 20%, 30%, and 50% random samples for the dropped countries and dropped country year tests. The figure shows results for all models. Across most tests, for all models and all metrics, dropping more data leads to higher errors, but the relative performance of the models is consistent across the samples. The one exception is the backcasting tests, which show more variability, particularly in the AARE and RMEDSE metrics (not shown in the figure below).

Figure 3 shows selected results from the analysis of the number of random samples that should be dropped. When 20 or fewer random samples were dropped, and the performance metrics averaged, there is substantial variability in the metrics. With more than 30 random samples, the variability declines substantially. This is a consistent finding across all combinations of metrics, models and tests, though only a subsample of four is shown below. There are higher mean errors and substantially more variability in the country as opposed to the country-year tests. This relatively wider variability in the dropped country tests remains when many samples have been averaged.

Based on the analyses above, a 20% random sample and 40 random draws for the dropped countries and dropped country-years tests were used in the final assessment of model performance. Table 1 shows the metrics of performance for the different model forms in the four tests.

Table 1 suggests that several different model forms may be appropriate and justifiable based on the predictive validity tests. The highest performing models are OLS and the three robust regression approaches, and there is very little difference between

them. No single model outperforms all others in all tests and in all metrics. For example, OLS is the best-performing model across all tests when looking at the AARE, but its performance is poorer when looking at the RMSE. The three robust regression approaches each perform relatively well across all tests, with none a clearly superior form. Poisson, on the other hand, consistently performs very poorly in most metrics, but has the best performance in the RMSE metric in three of the tests. Among the count models, the generalized negative binomial marginally outperforms the negative binomial in most tests, and both outperform the Poisson. The table shows that the count model forms generally perform more poorly than the robust and OLS models.

Table 1 also demonstrates that all the models do best in the forecasting test, with substantially lower errors in all metrics, suggesting that this is the "easiest" test. The other three tests show a mix of performance across all models and metrics.

It should be noted that predictive validity is useful for assessing both the relative performance of one model to another, as well as for assessing the absolute performance of a single model. Table 1 shows that when examining the AMRE and the RMSE, no model does particularly well. Recall that these metrics are calculated in maternal mortality ratio (MMR) space; the lowest RMSE across all models and tests is 143, which is very high. The RMEDSE tells a different story, with the lowest RMEDSE across all models and tests as 11; it is likely that some extreme outliers in the errors are affecting the RMSE.

Discussion

This paper outlines a transparent, replicable approach to model selection that can be tailored to help a researcher choose a model that best answers the research question, or questions, at hand. In this example of a time series, cross-country dataset of maternal mortality, predictive validity demonstrated that a range of models is justifiable. No single model out-performed every other model in all tests or all metrics, which is perhaps not surprising given the breadth of what the model is being asked to do. The predictive validity analysis outlined above does suggest that modeling the count of maternal deaths using Poisson, negative binomial, or generalized negative binomial would be a poor choice. Instead, the more appropriate modeling approach would be the use of OLS or one of three robust modeling approaches.

In the paper that this example is based upon, Hogan et al. (2010) used robust regression with Huber and biweight iterations (RREG), and applied a second stage of modeling to exploit the additional information in relationships across geographic space and over time, which substantially improved model performance, as assessed by predictive validity (Hogan 2010). The authors would have been equally justified in choosing one of the other robust regression approaches, or even OLS, though OLS performs poorly in RMSE space.

The approach outlined above provides a useful approach for other researchers looking to identify the most appropriate model for their research questions. While this paper demonstrated the use of predictive validity for the selection of model form, other applications exist. The approach could be used to select among a range of independent variables, to select the set of covariates that best predicts the outcome. It could also be

used to identify the form of the dependent variable (such as whether a log transformation is appropriate).

Predictive validity is a useful tool to assist researchers in assessing model performance, but it cannot be used as the sole approach to model selection. Clearly, distributional assumptions must be met for any of the proposed models (McQuarrie and Tsai 1998; Burnham, Anderson, and Burnham 2002). In this example, Poisson regression, with its strict distributional assumptions, could be excluded based on the fact that the variance of the dependent variable does not equal its mean; it was included here for illustrative purposes. The suite of potential models must be based upon a thorough understanding of the data for which it is intended.

In the Hogan (2010) publication, predictive validity as outlined in this paper was used to identify a single model. However, an alternative approach would be to use multiple models and then average across them, as in an ensemble modeling strategy (Burnham, Anderson, and Burnham 2002; Foreman et al. 2012; Lozano et al. 2011; Murray et al. 2012). In this example, predictive validity demonstrated that several different models performed relatively well, and there was no clear single preferred model form across all tests and all metrics. A model-averaging approach may be particularly attractive in a case like this, where there is no clear "winner."

There are several limitations to a predictive validity approach to model selection. First, the accuracy of the end result from predictive validity will only be as good as the candidate models allow it to be. If the models being tested all give poor predictions, predictive validity will only pick the relatively best performing of the suite of these poor performing models. Second, the approach is computationally intensive, requiring much

iteration. For complex models, this is a particular issue. This approach may not be feasible where computing power is limited. Third, at the time of writing, there is no canned software approach to implementing predictive validity, which implies that more sophisticated programming skills are needed by researchers hoping to use this approach.

Despite these limitations, predictive validity offers a useful, transparent approach to model selection that allows the researcher to identify the key attributes that they desire in their model and identify the model that best meets those attributes. Global health, and public health research more broadly, would be well-served by the wider adoption of this method.

References

AbouZahr, C, and T Wardlaw. 2001. "Maternal Mortality at the End of a Decade: Signs of Progress?." *Bulletin of the World Health Organization* 79 (6): 561–568.

Altman, D G. 1992. *Practical Statistics for Medical Research*. *Book*. Chapman & Hall/CRC Press.

Babu, G Jogesh. 2011. "Resampling Methods for Model Fitting and Model Selection." *Journal of Biopharmaceutical Statistics* 21 (6) (November): 1177–1186. doi:10.1080/10543406.2011.607749.

Barai, S V, and Y Reich. 1999. "Ensemble Modelling or Selecting the Best Model: Many Could Be Better Than One." *Ai Edam* 13 (05): 377–386.

Barnett, V, T Lewis, and F Abeles. 1979. "Outliers in Statistical Data." *Physics Today* 32: 73.

Black, Robert E, Simon Cousens, Hope L Johnson, Joy E Lawn, Igor Rudan, Diego G Bassani, Prabhat Jha, et al. 2010. "Global, Regional, and National Causes of Child Mortality in 2008: a Systematic Analysis.." *Lancet* 375 (9730) (June 5): 1969–1987. doi:10.1016/S0140-6736(10)60549-1.

Browne, M W. 2000. "Cross-Validation Methods." *Journal of Mathematical Psychology* 44 (1): 108–132.

Burnham, Kenneth P, David R Anderson, and Kenneth P Model selection and inference Burnham. 2002. *Model Selection and Multimodel Inference : a Practical Information-Theoretic Approach*. New York : Springer.

Campbell, O M R. 1999. "Measuring Progress in Safe Motherhood Programmes: Uses and Limitations of Health Outcome Indicators." *Safe Motherhood Initiatives: Critical Issues*.

Cawley, G C, and N L C Talbot. 2007. “Preventing Over-Fitting During Model Selection via Bayesian Regularisation of the Hyper-Parameters.” *The Journal of Machine Learning Research* 8: 841–861.

de Onis, M, M Blossner, and E Borghi. 2010. “Global Prevalence and Trends of Overweight and Obesity Among Preschool Children.” *American Journal of Clinical Nutrition* 92 (5) (October 20): 1257–1264. doi:10.3945/ajcn.2010.29786.

Foreman, Kyle J, Rafael Lozano, Alan D Lopez, and Christopher JL Murray. 2012. “Modeling Causes of Death: an Integrated Approach Using CODEm.” *Population Health Metrics* 10 (1): 1. doi:10.1186/1478-7954-10-1.

Forster, M R. 2000. “Key Concepts in Model Selection: Performance and Generalizability.” *Journal of Mathematical Psychology* 44 (1): 205–231.

Glaziou, Philippe, Katherine Floyd, Eline L Korenromp, Charalambos Sismanidis, Ana L Bierrenbach, Brian G Williams, Rifat Atun, and Mario Raviglione. 2011. “Lives Saved by Tuberculosis Control and Prospects for Achieving the 2015 Global Target for Reducing Tuberculosis Mortality.” *Bulletin of the World Health Organization* 89 (8) (May 31): 573–582. doi:10.2471/BLT.11.087510.

Graham, W J, L B Foster, L Davidson, E Hauke, and O M R Campbell. 2008. “Measuring Progress in Reducing Maternal Mortality.” *Best Practice & Research Clinical Obstetrics & Gynaecology* 22 (3): 425–445.

Graham, W J, S Ahmed, C Stanton, C L Abou-Zahr, and OMR Campbell. 2008. “Measuring Maternal Mortality: an Overview of Opportunities and Options for Developing Countries.” *BMC Medicine* 6 (1): 12. doi:10.1186/1741-7015-6-12.

Hodge, V, and J Austin. 2004. “A Survey of Outlier Detection Methodologies.” *Artificial Intelligence Review* 22 (2): 85–126.

Hogan, Margaret C, Kyle J Foreman, Mohsen Naghavi, Stephanie Y Ahn, Mengru Wang, Susanna M Makela, Alan D Lopez, Rafael Lozano, and Christopher J L Murray. 2010. “Maternal Mortality for 181 Countries, 1980-2008: a Systematic Analysis of Progress Towards Millennium Development Goal 5..” *Lancet* 375 (9726) (May 8): 1609–1623. doi:10.1016/S0140-6736(10)60518-1.

Hsieh, W W, and T Benyang. 1998. “Applying Neural Network Models to Prediction and Data Analysis in Meteorology and Oceanography.” *Bulletin of the American Meteorological Society* 79 (9): 1855.

Lim, S S, R Myerson, L C Rosenfeld, and C J L Murray. 2010. “Safe Pregnancy and Delivery: a Systematic Analysis of Trends in the Coverage of Antenatal and Intra-Partum Care.”

Lozano, Rafael, Haidong Wang, Kyle J Foreman, Julie Knoll Rajaratnam, Mohsen Naghavi, Jake R Marcus, Laura Dwyer-Lindgren, et al. 2011. “Progress Towards Millennium Development Goals 4 and 5 on Maternal and Child Mortality: an Updated Systematic Analysis.” *The Lancet* 378 (9797) (September): 1139–1165. doi:10.1016/S0140-6736(11)61337-8.

Lu, Y, S Wang, and K K Lai. 2008. “Credit Risk Assessment with a Multistage Neural Network Ensemble Learning Approach.” *Expert Systems with Applications* 34 (2): 1434–1444.

Mariel M Finucane AB, Gretchen A Stevens DSc, Melanie J Cowan MPH, Goodarz Danaei MD, John K Lin AB, Christopher J Paciorek PhD, Gitanjali M Singh PhD, et al. 2011. “National, Regional, and Global Trends in Body-Mass Index Since 1980:

Systematic Analysis of Health Examination Surveys and Epidemiological Studies with 960 Country-Years and 9Â·1 Million Participants." *Lancet* 377 (9765) (February 12): 557–567. doi:10.1016/S0140-6736(10)62037-5.
Maronna, R A, D R Martin, and V J Yohai. 2006. *Robust Statistics: Theory and Methods*. *Book*.
Mathers, Colin D, and Dejan Loncar. 2006. "Projections of Global Mortality and Burden of Disease From 2002 to 2030.." *PLoS Medicine* 3 (11) (November): e442. doi:10.1371/journal.pmed.0030442.
McQuarrie, Allan D R, and Chih-Ling Tsai. 1998. *Regression and Time Series Model Selection*. Singapore ; River Edge, N.J. : World Scientific.
Murray, C J L, L C Rosenfeld, S S Lim, K G Andrews, K J Foreman, D Haring, N Fullman, M Naghavi, R Lozano, and A D Lopez. 2012. "Global Malaria Mortality Between 1980 and 2010: a Systematic Analysis." *Lancet* 379 (9814) (February 4): 413–431. doi:10.1016/S0140-6736(12)60034-8.
Rajaratnam, J K, J R Marcus, A D Flaxman, H Wang, A Levin-Rector, L Dwyer, M Costa, A D Lopez, and C J L Murray. 2010. "Neonatal, Postneonatal, Childhood, and Under-5 Mortality for 187 Countries, 1970-2010: a Systematic Analysis of Progress Towards Millennium Development Goal 4." *The Lancet*.
Ronsmans, C. 2001. "How Can We Monitor Progress Towards Improved Maternal Health." *Studies in Health Services Organisation and Policy* 17: 313–338.
Sewell, Martin. 2008. *Model Selection*. http://www.modelselection.org/model-selection.pdf.
Shao, J. 1993. "Linear Model Selection by Cross-Validation." *Journal of the American Statistical Association* 88 (422): 486–494.
Shao, J. 1996. "Bootstrap Model Selection." *Journal of the American Statistical Association*: 655–665.
Sharkey, A J C. 1996. "Combining Artificial Neural Nets: Modular."
Shmueli, Galit. 2010. "To Explain or to Predict?." *Statistical Science* 25 (3) (August): 289–310. doi:10.1214/10-STS330.
Sober, E. 2002. "Instrumentalism, Parsimony, and the Akaike Framework." *Philosophy of Science* 69 (S3): S112–S123.
United Nations Development Program. 2003. *Indicators for Monitoring the Millennium Development Goals: Definitions, Rationale, Concepts, and Sources*. *Techreport*.
United Nations General Assembly. 2000. "United Nations Millennium Declaration." *Miscellaneous* A/RES/55/2.
World Health Organization. 2012. *The WHO Application of ICD-10 to Deaths During Pregnancy, Childbirth and the Puerperium: ICD-MM*. Geneva, Switzerland: World Health Organization.
Yazbeck, Abdo S. 2007. "Challenges in Measuring Maternal Mortality.." *Lancet* 370 (9595) (October 13): 1291–1292. doi:10.1016/S0140-6736(07)61553-0.

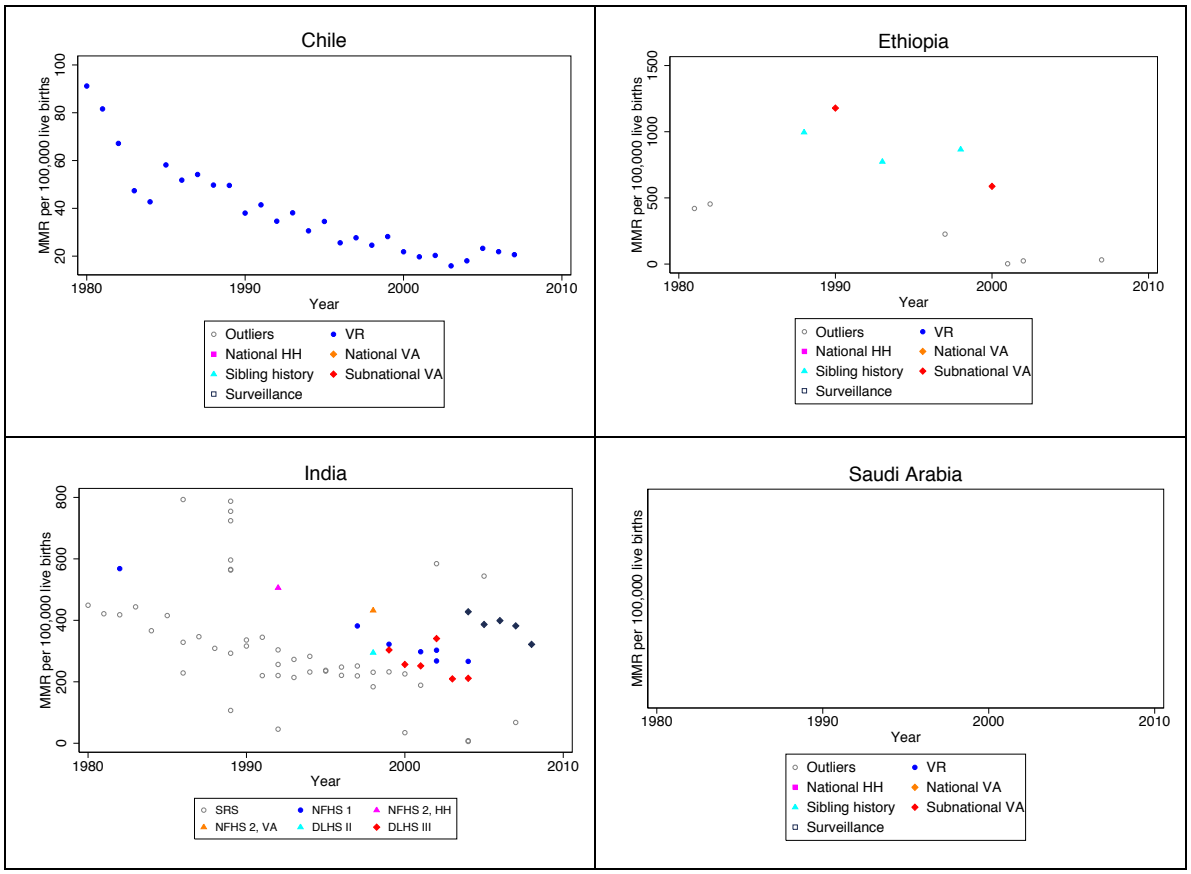

Figure 1. Four examples of data available by country: Chile, Ethiopia, India and Saudi Arabia

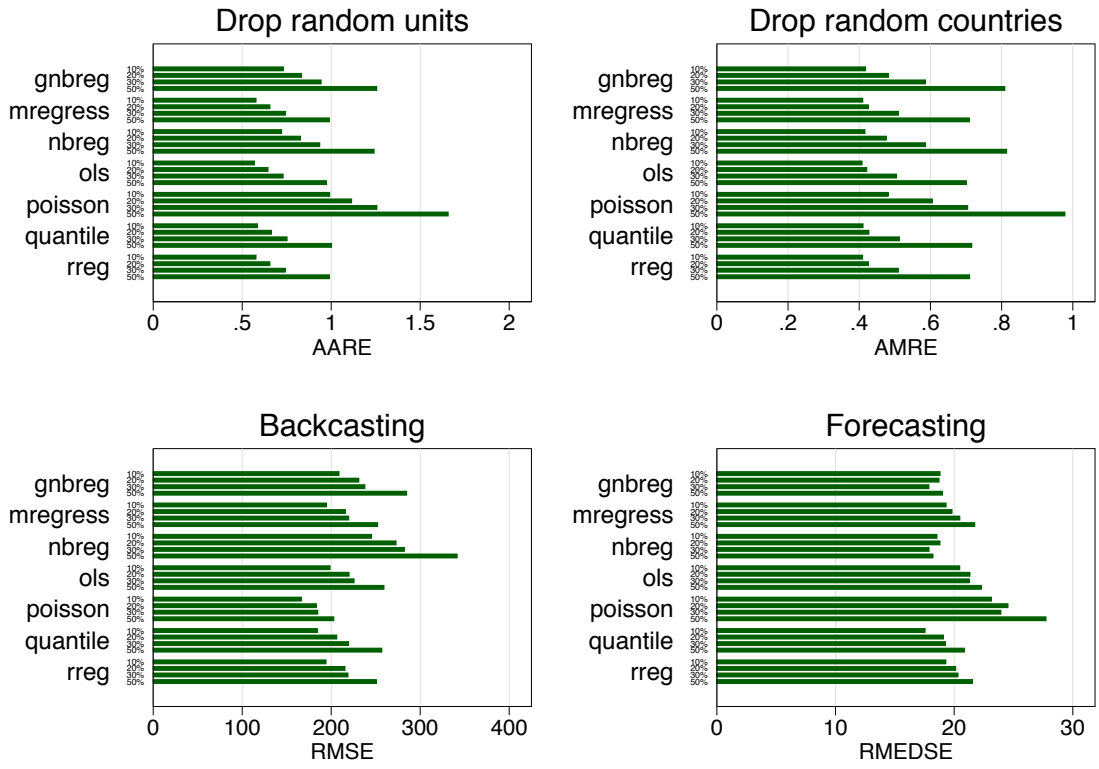

Figure 2. Selection of results from predictive validity tests, showing the comparative performance of seven regression models with different fractions of dropped data.

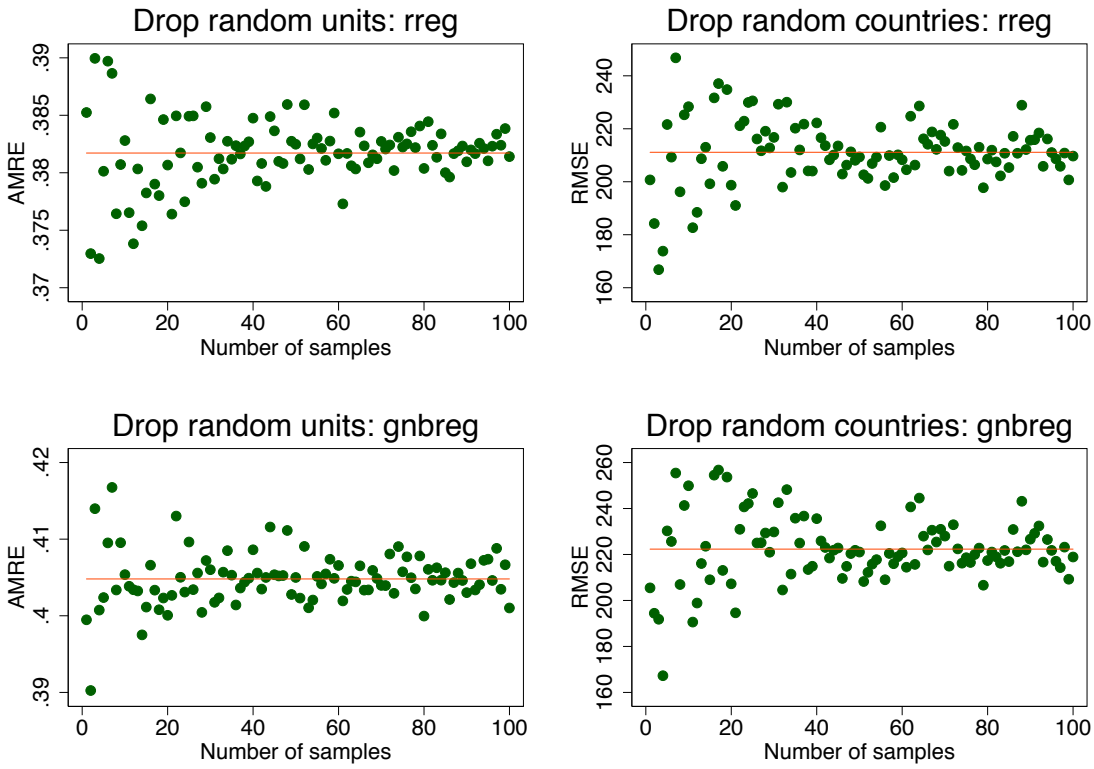

Figure 3. Selected results for convergence tests

Table 1. Four metrics of performance, for all models, across all four tests

Test	Model	AARE	AMRE	RMEDSE	RMSE
Drop random units	gnbreg	0.86	0.49	31.18	258.02
	mregress	0.68	0.43	25.86	234.65
	nbreg	0.85	0.49	30.57	283.07
	ols	0.67	0.43	25.74	236.91
	poisson	1.15	0.61	45.14	204.89
	quantile	0.69	0.43	25.91	233.58
	rreg	0.68	0.43	25.89	234.87
Drop random country	gnbreg	0.88	0.51	33.75	270.63
	mregress	0.69	0.45	28.78	246.00
	nbreg	0.87	0.50	33.78	295.97
	ols	0.68	0.45	28.38	248.25
	poisson	1.18	0.65	48.63	211.24
	quantile	0.70	0.46	28.86	245.81
	rreg	0.69	0.45	28.79	246.49
Backcasting	gnbreg	0.99	0.55	32.61	209.71
	mregress	0.77	0.45	23.63	199.19
	nbreg	1.01	0.58	33.82	250.54
	ols	0.76	0.45	23.70	204.20
	poisson	1.19	0.72	40.78	157.56
	quantile	0.77	0.44	23.19	182.33
	rreg	0.77	0.45	23.60	198.59
Forecasting	gnbreg	0.57	0.36	11.15	168.25
	mregress	0.47	0.40	12.63	143.12
	nbreg	0.55	0.38	12.10	175.46
	ols	0.47	0.40	12.77	143.50
	poisson	0.90	0.45	21.72	152.60
	quantile	0.48	0.39	12.63	150.98
	rreg	0.47	0.40	12.77	143.05

CHAPTER FOUR

Indirect and direct obstetric deaths in Mexico: results from an intentional search for maternal deaths

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Abstract

Objective. Cause-specific maternal cause of death data is not available in many countries. In Mexico, the "Búsqueda intencionada y reclasificación de muertes maternas" (BIRMM) project provides a comprehensive examination of maternal mortality. This paper provides a descriptive analysis of maternal mortality from this intentional search, with particular attention to indirect obstetric deaths and socio-economic disparities.
Methods. Investigators identified and reviewed supporting documentation for all deaths in women of reproductive age whose deaths were coded to a subset of 46 codes suspected of "hiding" maternal deaths, as well as all deaths coded to the maternal chapter of the ICD. Tabulations, tests of proportions, t-tests, and chi square tests were used to compare proportions, means and ratios.
Findings. 5,886 deaths were subjected to the review process over the period 2006-2010, and 1,192 (20.3%) were reclassified between four broad groups: direct, indirect, non-maternal, and late maternal. There was a 12% increase in all maternal deaths identified. Direct deaths are declining, but indirect are not. As compared to those dying of direct causes, women dying of indirect causes have fewer pregnancies, are slightly younger, are better educated, and are more likely to live in richer municipalities.
Conclusion. The modified RAMOS approach used in BIRMM may make correcting maternal death statistics more feasible in other settings with limited resources. The spike of indirect deaths in 2009 highlights the importance of attention towards maternal mortality in the case of epidemics like H1N1. The growing importance of indirect obstetric causes requires rethinking the health system response to maternal mortality, with health personnel trained to treat the entire woman, not just her pregnancy.

Introduction

Maternal mortality – the death of a woman during pregnancy, childbirth, or in the 42 days after delivery – is a critical outcome for any health system, but evidence on specific causes of maternal mortality is very weak in many parts of the world (Khan et al. 2006).

The overall maternal mortality ratio (MMR – the number of maternal deaths per 100,000 live births) itself has been considered very difficult to measure due to the relative rarity of maternal deaths even where the maternal mortality ratio (MMR) is very high (Graham, Foster, et al. 2008; Yazbeck 2007; Campbell 1999; AbouZahr and Wardlaw 2001; Ronsmans 2001). Even very high quality vital registration systems are known to "miss" maternal deaths (Graham, Ahmed, et al. 2008). This, coupled with the challenges in causes of death data, means that accurate estimates of cause-specific maternal mortality are often not available.

The ICD-10 manual divides the causes of maternal mortality into two broad categories: direct obstetric deaths and indirect obstetric deaths (World Health Organization 2004). Direct deaths are those more traditionally thought of as "maternal", resulting from obstetric complications of the pregnant state (such as hemorrhage, sepsis, unsafe abortion, or eclampsia). Indirect obstetric deaths are those resulting from disease, often pre-existing, which was aggravated by the physiologic effects of pregnancy (such as diabetes, cardiovascular diseases, or infectious disease such as tuberculosis or influenza) (World Health Organization 2012; Graham, Ahmed, et al. 2008). The average contribution of indirect maternal deaths to a country's overall maternal mortality ratio is often reported to be about 20% (Tinker, Koblinsky, and Daly 1993; Nour 2008; Chowdhury et al. 2009), but this fraction is believed to vary considerably across settings.

Indirect causes are particularly likely to be misclassified as non-maternal deaths, making measurement difficult (Ronsmans, Graham, and group 2006; Khan et al. 2006). A study in the 1990s found that in more than half of 60 countries reporting maternal cause of death data from vital registration systems, no deaths at all were registered as indirect

maternal deaths (AbouZahr 2003). Even very high quality vital registration systems suggest wide variation in the fraction of maternal deaths attributable to indirect causes. Studies in the United States suggest that indirect causes account for between 33% and 43% of all maternal deaths in that country (Clark et al. 2008; Berg et al. 2011). A 2011 confidential enquiry in the UK found more than half of maternal deaths were due to indirect causes (Center for Maternal and Child Enquiries 2011), while a similar study in the Netherlands in 2010 showed that 23% were due to indirect causes (Schutte et al. 2010); this marked discrepancy may be due in part to a better health system response to indirect deaths in the Netherlands. However, it is also likely the result of differing interpretations of what constitutes an indirect obstetric death, as there were a much higher number of suicides coded as indirect deaths in the UK (7% of indirect deaths were attributed to mental disorders in the Netherlands study, while 44% of indirect deaths were attributed to psychiatric disorders in the UK study (Schutte et al. 2010; Center for Maternal and Child Enquiries 2011)).

While direct obstetric deaths still receive most attention, the growing burden of non-communicable diseases and risk factors in low- and middle-income countries has led some to argue that indirect maternal deaths are an increasing concern in these settings, as the health status of reproductive age women may be compromised (Maina 2011). The rising prevalence of obesity in particular has raised a red flag for some researchers (Center for Maternal and Child Enquiries 2011; Guelinckx et al. 2008).

Mexico provides an interesting and relevant case study in indirect maternal deaths. The epidemiologic transition from communicable to non-communicable disease, well underway in Mexico ((Bobadilla et al. 1993)), has important implications for the

distribution of the causes of maternal deaths. Mexico has seen a rapid increase in diabetes, hypertension, and hypercholesterolaemia (Stevens et al. 2008; Rojas et al. 2010; Rivera, Barquera, and Campirano 2002; Barquera et al. 2003; Gómez et al. 2009), as well as striking increases in the prevalence of obesity, particularly in women of lower socioeconomic status (Uauy, Albala, and Kain 2001; Monteiro et al. 2004; Barquera et al. 2009; Rivera et al. 2004; Flores et al. 2010; Instituto Nacional de Salud Publica 2012). This puts the population of reproductive aged women at higher risk for pre-existing hypertensive disorders and diabetes mellitus, which may be complicated by pregnancy. In addition to the rising burden of chronic disease, Mexico was badly affected by the 2009 H1N1 epidemic (Domınguez-Cherit et al. 2009; Echevarría-Zuno et al. 2009), with pregnant women at higher risk of hospitalization, severe illness and death (Valdespino-Gomez, Garcia-Garcia, and de LeOn-Rosales 2009; Mosby, Rasmussen, and Jamieson 2011; Secretaria de Salud 2011).

In the last decades, Mexico has made strides in improving the measurement of maternal mortality, beginning with the 1993 Mexican Declaration for Safe Motherhood, which set up a commission that undertook improving surveillance and data collection, including the pregnancy "checkbox" on the death certificate (Langer and Lozano 1996; Schiavon, Troncoso, and Polo 2012). A few years later, state-level maternal mortality committees were established to review each maternal case (Langer and Lozano 1996). Despite these efforts, problems of underreporting and misreporting are well known in the vital statistics systems of Mexico (Gay and Billings 2009; Lozano 2012; Freyermuth-Enciso and Cárdenas-Elizalde 2009). In response, a new project was undertaken in 2002, to identify all maternal deaths in Mexico using an intentional search approach (similar to

some reproductive-age mortality surveys (RAMOS)). The project, referred to as "Búsqueda intencionada y reclasificación de muertes maternas", BIRMM, (originally "Búsqueda intencionada de muertes maternas", or BIMM) provides a comprehensive examination of maternal mortality in Mexico (CONEVAL 2012).

This analysis describes the maternal deaths identified through this intentional search, with particular attention to the misclassification and miscoding of indirect obstetric deaths. This analysis also provides a comparison of the socio-demographic characteristics and health services use of direct and indirect decedents, as well as a descriptive analysis of disparities in direct and indirect mortality outcomes. The BIRMM project offers useful lessons for other countries looking to improve their maternal mortality statistics.

Data

The BIRMM project was introduced in 2002 to identify all maternal deaths in Mexico using a variety of data sources (Secretaria de SaludCEMECE 2011). While death registration is thought to be virtually complete in Mexico (Mathers et al. 2005), many deaths are misclassified or coded to unspecified or poorly defined causes (Lozano 2012). The BIRMM project undertook to recapture those miscoded maternal deaths by investigating deaths in women of reproductive ages (10-54) that had been assigned to a subset of 46 ICD codes that were suspected might be "hiding" maternal deaths (see (Secretaria de SaludCEMECE 2011), Annex 11.1). Deaths assigned maternal codes (the O-chapter of the ICD codebook), those with suspicious or incomplete codes, and all death certificates with the pregnancy checkbox ticked were also investigated.

The death records were obtained from SEED (the Ministry of Health's Epidemiological and Statistical Mortality System) and INEGI (Instituto Nacional de Estadística y Geografía), and for each, a range of materials were sought out and reviewed by independent coders from the Mexican Centre for Disease Classification (CEMECE). The research team then requested a range of additional documents from the states to help investigate each death, including the death certificate, clinical summary or medical records, verbal autopsy, confidential enquiry, or autopsy report. These documents were assembled to construct a new dataset containing information on the classification of each death before and after review as well as a range of individual-level covariates, including age, marital status, education level, total number of pregnancies, place of delivery, place of care for the first complication, birth attendant, and whether there were any prenatal visits during the pregnancy. For more details on the BIRMM procedures, please see (Secretaria de SaludCEMECE 2011).

Municipality-level deprivation index data (2010 data) and live births data (for 2006-2010) were obtained from the Consejo Nacional de Poblacion's (CONAPO) website. The deprivation index is a state and municipality-level numerical index computed from data on education levels, living standards (i.e. proportion of houses with electricity, running water, or earthen floors), the urban-rural distribution of the population and income (CONAPO 2012). The deprivation index was divided into quintiles and then merged into the individual level dataset based on municipality of residence.

This analysis uses data from 2006-2010, though the project was initiated in 2002. It was the opinion of the BIRMM team that the first four years of the data collection

process was a learning process, and it wasn't until 2006 that the strategy and procedures became more uniform, and there was national agreement on the technical process.

Methods

The definition of "indirect obstetric death" is taken from the ICD-10 manual. Table 1 presents the ICD blocks, detailed codes, and broad cause names for deaths classified as "indirect obstetric deaths". It is important to note that this formal definition represents a new international agreement on what constitutes an "indirect death"; before the ICD-10, countries used variable definitions making comparability challenging. "Late maternal deaths", defined as either direct or indirect obstetric causes occurring more than 42 days but less than one year after termination of pregnancy (ICD code O96) are not included in the ICD definition of "maternal death" but are considered as a separate, important category.

Simple tabulations were used to examine the cause distributions and the reclassification of indirect cases. Tests of proportions, t-tests, and chi square tests were used to compare proportions, means and ratios. Multiple imputation was completed using the Amelia package for R (King et al. 2001) for the imputation model and the "mi" program in Stata for the analysis model. Multiple logistic regression was used to examine associations between indirect deaths and various socio-demographic and health service use covariates. All analyses were done in Stata/MP 11.2, with the exception of the imputation model, which was done in R (version 2.15.1).

Results

A total of 5,886 deaths were subjected to the review process over the period 2006-2010. Appendix 3, figure A3.1 shows the distribution of the documents reviewed; nearly all had the death certificate available for review, and more than half had a clinical summary and/or verbal autopsy.

Table 2 summarizes the reclassification of deaths after the review process to four broad groups: direct, indirect, non-maternal, and late maternal. A total of 1,192 (20.3%) deaths were reclassified between these four groupings. Non-maternal deaths were the largest source for both direct and indirect reclassifications, though there were also a substantial number of direct deaths incorrectly classified as indirect and vice versa. While late maternal deaths are not included in the official definition of "maternal deaths", the number in that category increased by 2.7 times after the review, from 101 to 268, signaling extensive misclassification for late maternal deaths.

Table 2 shows that the review process resulted in an increase in both indirect and direct deaths, with a 10.8% average increase across the five years for indirect deaths and an 11.2% average increase for direct deaths. Including late maternal deaths, the method resulted in a 14.2% increase in deaths classified as due to any of the maternal causes, and excluding them, an 11.1% increase. Comparing the original codes to the codes after review, the uncorrected approach identified the correct groupings for 87% of direct deaths, 69% of indirect deaths, and just 34% of late maternal deaths.

Table 3 shows the original codes of those deaths recoded to indirect maternal deaths. In addition to miscoding within the maternal chapter, many indirect maternal deaths were originally misclassified as diseases of the circulatory system, diseases of the respiratory system, diseases of the digestive system, and neoplasms. This is also reflected

in Appendix 3 table A3.1, which provides tabulations of the detailed indirect causes after the review process. Most recoded deaths were recoded to the O994-O998 codes (other diseases (n=337), and diseases of the circulatory (n=265), respiratory (n=290) or digestive (n=145) systems, complicating pregnancy, childbirth or the puerperium). 189 deaths were recoded to maternal parasitic and infectious diseases. By ICD rules, H1N1 deaths are included within the "diseases of the respiratory system" chapter.

Figure 1 shows the number of direct and indirect deaths per 100,000 live births, by year, both before and after the review process. The review process resulted in an increase in the number of maternal deaths, both direct and indirect, in both years, though with much larger differences for direct deaths. The figure shows a decline in the direct trend, but a slight increase in the indirect, with a spike in 2009 presumably due to the H1N1 epidemic.

A bivariate examination of socio-demographic characteristics and health system use is presented in table 4 (missing rates for the covariates are presented in Appendix 3 table A3.2). As compared to those dying of direct deaths, women dying of indirect deaths have fewer pregnancies, are slightly younger, and are better educated. They are also more likely to have delivered, received care for their first complication, and died in Instituto Mexicano del Seguro Social (IMSS) facilities as compared to direct deaths. Both indirect and direct decedents most frequently delivered, died, and received care in Secretaria de Salud facilities. The data show that skilled attendants were more likely to be present at birth for direct decedents, but this is because indirect decedents were more likely to have died before delivery; 27% of indirect decedents had no delivery versus 9% of direct decedents. Results for a logistic regression controlling for all covariates is included in

Appendix 3 table A3.3; the relationships are the same as in the bivariate analysis, with the exception that, after controlling for all covariates, having a secondary or higher education is associated with lower odds of an indirect as opposed to a direct death.

Quintiles of the municipality-level deprivation index allow for some area-level analysis of the relative contribution of direct and indirect deaths. Table 4 shows that richer municipalities have relatively more indirect than direct deaths, and that most deaths, both direct and indirect, occur in the richest (and most populous) municipalities. After pooling the data across the five years, figure 2A shows the number of indirect and direct deaths per 100,000 live births, by quintile of municipality-level deprivation index. Poorer municipalities see a dramatically higher number of direct deaths per 100,000 live births, but also a slightly higher rate of indirect deaths. Figure 2B highlights the disparities in the number of direct and indirect deaths per 100,000 live births between the richest and poorest quintiles for each of the years in the study period. The disparity between the richest and poorest municipalities is stark for direct deaths. There also appears to be a small but steady increase in the rate of indirect deaths in the poorest municipalities.

Table 5 shows the top five causes of indirect maternal deaths, by highest and lowest municipality-level deprivation index quintile. Diseases of the circulatory and respiratory systems, as well as “other specified diseases” (a vague category) figure prominently in both quintiles, and mental disorders and diseases of the nervous system round out the list in both quintiles.

Discussion

This paper presents the results of a comprehensive search for maternal deaths in Mexico over the period 2006-2010. The intentional search identified an average of 12% additional maternal deaths that had originally been miscoded as non-maternal, as well as many more deaths miscoded within the maternal ICD chapter. This study shows encouraging progress towards the more complete and accurate assessment of causes of maternal mortality in a middle-income country, and offers a useful strategy for improving detailed maternal mortality data at the country level. Several important lessons can be taken from this project.

Feasibility. The 12% increase in the number of maternal deaths (a 1.1 inflation factor) in Mexico resulting from this study suggests that this type of exercise is critical for correcting misclassification. PAHO has advocated for the adoption of similar methods in other countries in the region. Similar projects have been undertaken in other settings and found a range of underreporting; for example, inflation factors of 1.9 in Northeast Brazil (Alves 2007), 3.2 in Menoufia, Egypt (Grubb et al. 1988), and estimates ranging between 0.9 and 2.2 in several high income countries (Hill et al. 2007). This observed variation limits the ability to generalize across settings, and suggests that correction projects such as the BIRMM are essential for all countries in assessing their maternal mortality estimates.

However, the feasibility of implementing such a project is dependent on the scale of the problem of maternal mortality. In countries with relatively few maternal deaths, extensive review of suspected cases may be more feasible than in a country with thousands of suspected maternal deaths each year. In Mexico, the dual registration system

of deaths (wherein both INEGI and the Ministry of Health collect death information) allows for a built in consistency check. The adoption of electronic death registration would allow real-time validation of suspected maternal deaths, lessening the burden on investigators.

In the BIRMM study, investigators elected to use a "modified" RAMOS ("reproductive-age mortality study") approach. In a "traditional" RAMOS, all deaths in women of reproductive age are investigated to identify maternal deaths (Graham, Ahmed, et al. 2008; Campbell et al. 2005). In the modified approach used in this study, only a subset of deaths in women of reproductive ages was investigated, based on the original coded underlying cause of death. While this can be seen as a limitation, it was a cost-saving shortcut to avoid investigating all maternal deaths, and was based on expert opinion regarding likely codes "hiding" maternal deaths (Lozano, Torres-Palacios, and Soliz 2010). This approach may be more palatable in countries where resources are not available for a full RAMOS-style review, or the number of deaths is simply too high to make a full review feasible. Country-specific identification of the appropriate subset of codes is essential as coding practices can differ dramatically between settings.

The BIRMM project also highlights the critical importance of maternal death review in the case of unusual disease patterns, as the 2009 H1N1 epidemic had a disproportionately large group of misclassified (indirect) maternal deaths. This type of temporary, dramatic change in underreporting or misclassification of maternal deaths in the case of epidemics have been observed in Rwanda and South Africa (Cross, Bell, and Graham 2010), and, in the event of an epidemic, this increase in error should be anticipated to ensure the impact on maternal mortality is appropriately assessed.

The BIRMM project was initiated within the Ministry of Health, which reflects a research focus within that institution. By the early 2000s, there was substantial evidence of under-registration of maternal deaths in the country, both through the demographic and health survey program (Encuesta Nacional de Dinamica Demografica (ENADID) from 1992 and 1997), as well as through several smaller studies ((Lezana 1999; Elú 1993; Hernandez et al. 1994; Hernández et al. 1993; Reyes Frausto et al. 1998; Langer et al.)). There was a need for state-level correction factors, as the existing evidence could not be generalized to the entire population, for both technical and political reasons. In 2002, the National Health Program began producing annual accountability reports with indicators of the state health system (D R Secretaría de Salud 2003), but maternal mortality could not be included because the data was so poor at the state level. This incentivized the Ministry to initiate the intentional search project and, in 2003, results were first presented with the misclassification correction.

This type of critical, academic perspective is essential for the adoption of this approach. While this academic approach within the Ministry was critical, other components of the project suggest that the government is the appropriate organization to be carrying out this type of maternal death review, as suggested in a US study as well (Berg 2012). The use of the central power of the Ministry helped to get the project underway, as well as get cooperation (and, as a result, the required validation information) from the states. What started as a single study became an ongoing effort, and now has been incorporated as the norm; this project is now integrated into Mexico's official estimates of maternal mortality, with the annual results used to adjust the official estimates, produced by INEGI. This kind of institutionalization, as well as

implementation of new guidelines or recommendations, is most feasible from within a governmental organization. Integration of such projects into the vital statistics system treats maternal mortality review as a "core public health function" (Berg 2012).

One challenge to the adoption of this type of review can come from the medical/OBGYN community itself, if there is misinterpretation of this type of project as targeting the "guilty". Doctors or OBs may be hesitant to embrace or participate in the review process if they fear legal or professional repercussions, even if it would ultimately improve their practice. Without the appropriate frameworks in place, those fears may be well-founded. The goal of this type of review must be to improve the health system, not to assign blame, and so the appropriate legal protections of anonymity, confidentiality and immunity must be put into place (Berg 2012).

This study highlights the importance of examining maternal death data by sub-national, socio-demographic characteristics. The municipality-level quintile analysis suggests that poorer municipalities have dramatically higher rates of direct maternal deaths, but higher rates of indirect as well, and that these indirect deaths are increasing over time in the poorer municipalities. However, as this is an aggregate, area-level analysis, this must be interpreted with caution; the richest municipalities also likely have some of the greatest disparities in wealth and resource access among individuals. Incorporating individual-level information on wealth or resources into the dataset would allow more careful assessment of disparities.

Despite being based at the Ministry of Health, there is no separate specific budget for the ongoing BIRMM project; it has been treated as a kind of "extra activity" and is largely subsidized by committed individuals and invested groups within the larger

institution (Lozano, Torres-Palacios, and Soliz 2010). The future of the project would certainly be more secure with a specific budget line or guaranteed funding from another source. The resource needs are primarily human resources, both for the coordinating core group, and for the states, as well as the reproductive health programs, researchers, coders, medical units and maternal mortality committees within the states, as they must provide the supporting documentation (Secretaria de SaludCEMECE 2011). There are also the operational costs of computers, storage systems, meetings and trainings and other expenses.

To justify these costs, a convincing case must be made for the added value of this type of maternal death review. In Mexico, this project has resulted in more attention to maternal mortality, better coding practices, and better statistics (Schiavon, Troncoso, and Polo 2012). Perhaps the most important public good from this project is disaggregated maternal cause of death data for Mexico. Cross et al. argue that evaluations of maternal health interventions that use as their outcome all-cause maternal mortality will be inaccurate, because the programs are not in actuality targeting all causes of maternal death (Cross, Bell, and Graham 2010). The ability to drill down to more specific causes is essential to understanding how to tackle the problem, however, this more detailed information is often not reliably available, particularly not comparably over time (Foreman et al. 2012; Naghavi et al. 2010; Mathers et al. 2005).

The best justification for the costs of the project is for maternal deaths to continue to decline. To be truly worthwhile, the data must be used to take appropriate action to avert maternal deaths.

Health policy implications. One of the most policy-relevant findings from the BIRMM project is the role that indirect maternal deaths play in Mexico. Direct deaths are on the decline, but indirect are not, and given the rapid increase in non-communicable disease and risk factors in Mexico, indirect deaths are likely to continue to account for an increasing proportion of maternal deaths. The 2012 ENSANUT survey found a truly alarming prevalence of 73% of overweight and obesity in Mexican women, with 38% in the obese category (Instituto Nacional de Salud Publica 2012). This finding highlights the need for an appropriate health system response.

The focus by the international community on the first target of Millennium Development Goal 5 (the reduction in maternal mortality) has largely eclipsed the other MDG 5 target, MDG 5B, which is to achieve universal access to reproductive health. This exclusive focus on maternal mortality treats women solely as mothers, or mothers-to-be, with little attention paid to their broader reproductive or general health. There is a need for a more "holistic conceptualization" of women as the targets of health interventions (Langer, Frenk, and Horton 2012). A parallel can be drawn between the narrow focus on maternal mortality and the increasing importance of indirect maternal deaths. Most maternal health interventions are focused around the delivery period, as they are related to providing skilled birth attendance or emergency obstetric care. These two interventions have clearly been essential in reducing the maternal mortality ratio, but this is through their impact on *direct* maternal deaths. Indirect deaths are not likely to be averted through these delivery-focused interventions, unless the indirect complication arises during labor (Cross, Bell, and Graham 2010). The results from this study show that 27% of indirect decedents never had a delivery, as compared to just 9% of direct

decedents, underscoring the very different profiles of service need for these two groups of women.

What does a health system response to indirect obstetric deaths look like? This question has not been effectively answered in the literature and it requires much more attention. However, a few general recommendations can be made. First, obstetricians and other health care personnel interacting with pregnant, delivering and post-partum women need to be trained to treat the entire woman, not just her pregnancy (Langer, Frenk, and Horton 2012). This requires the development, dissemination, and adoption of clinical guidelines related to the major causes of indirect deaths (McCaw-Binns et al. 2007). A confidential enquiry in the UK noted that physicians failed to take note of typical CVD risk factors in pregnant women (Center for Maternal and Child Enquiries 2011), which may be indicative of the narrow focus of some obstetricians. Second, this is directly related to the need for more analysis, treatment, and surveillance of pregnant women to identify at-risk pregnancies. The traditional package of services for antenatal care is not adequate to avert indirect deaths. The complexity and diversity of indirect causes of maternal death does not lend itself to the development of such a "package of services" and requires a more holistic, internal medicine approach. Third, better collaboration and referral systems within medical teams are essential, with obstetricians communicating with chronic disease specialists for at-risk cases (Cross, Bell, and Graham 2010). Fourth, there needs to be more health education of women to recognize risk factors for indirect obstetric mortality (McCaw-Binns et al. 2007), particularly for women with pre-existing conditions. Further, this health education should also be provided *prior* to pregnancy, so women are able to make fully informed decisions about their reproductive health. This,

naturally, also requires full access to and education about modern contraception. Finally, there needs to be continued attention paid to the unique risks that pregnant women face in the case of epidemics like H1N1, with information disseminated early and often, to both clinicians and women, about the signs and symptoms of severe cases (Berg 2012).

Limitations. This study has several limitations. First, the review process does not investigate all deaths in women of reproductive age, but instead a subset based on the registered cause of death. While it is believed that these codes make up the vast majority of misclassified or miscoded maternal deaths, there may be others "hidden" in codes not investigated (Freyermuth-Enciso and Cárdenas-Elizalde 2009; Lozano, Torres-Palacios, and Soliz 2010). Second, the review process itself is subject to the availability and quality of additional sources beyond the death certificate. This means that for some deaths, the additional information available to make a reclassification decision was quite limited. Third, while this project has been underway since 2002, the strategy was made more consistent in 2006, making the first four years of data non-comparable and of lesser quality. Fourth, the role of improved ascertainment and categorization must not be overlooked when examining the trends in this analysis. Often, an observed increase in a particular cause of death could plausibly be explained by improvements in the registration system. In this case, because the same procedures are used in each year of the intentional search, it seems unlikely that the observed increase in indirect deaths would be due solely to improved ascertainment. Fifth, a few causes of death, considered to be indirect obstetric causes such as O26.6 (liver disorders), are subsumed within chapters of the ICD broadly considered direct. These very detailed, 4-digit codes were not available for all deaths, and were considered of questionable quality, so the broader 3-digit

categories were used. This means that some (rare) causes of indirect deaths may be grouped in with direct causes, and this analysis may underestimate the contribution of indirect deaths. Sixth, missing data in the covariates is another issue, as highlighted in Appendix 3, table A3.2.

Seventh, as this is a retrospective study, there were a limited number of covariates related to the socio-demographic status and health care service use of the decedents. In order to include some discussion of socioeconomic disparities, the municipality-level deprivation index was used. However, it is likely that the individual women dying of maternal deaths across all quintiles of the deprivation index are the poorer women within those municipalities. The area-level nature of this component of the analysis does not allow for commentary about how an individual's access to resources affects her risk of maternal death.

This study presents the results of a multi-year intentional search for maternal deaths in Mexico. This project represents a useful strategy towards achieving more complete and accurate assessment of the causes of maternal mortality in a country with complete vital registration, provides useful lessons for other countries looking to improve maternal mortality measurement, and highlights the importance of the development of an appropriate health system response to indirect maternal mortality.

Acknowledgments
The authors would like to thank Jaime Sepulveda, Julie Rajaratnam, and Steven Goodreau for thoughtful contributions and suggestions, particularly regarding the discussion.

References

AbouZahr, C. 2003. "Global Burden of Maternal Death and Disability." *British Medical*

Bulletin 67 (1) (December 1): 1–11. doi:10.1093/bmb/ldg015.
AbouZahr, C, and T Wardlaw. 2001. "Maternal Mortality at the End of a Decade: Signs of Progress?." *Bulletin of the World Health Organization* 79 (6): 561–568.
Alves, S V. 2007. "Maternal Mortality in Pernambuco, Brazil: What Has Changed in Ten Years?." *Reproductive Health Matters* 15 (30) (November 1): 134–144.
Anon. "Enadid." ENADID. http://www.inegi.org.mx/est/contenidos/proyectos/encuestas/hogares/especiales/enadid/default.aspx.
Barquera, S, I Campos-Nonato, L Hernández-Barrera, M Flores, R Durazo-Arvizu, R Kanter, and J A Rivera. 2009. "Obesity and Central Adiposity in Mexican Adults: Results From the Mexican National Health and Nutrition Survey 2006." *Salud Pública De México* 51: 595–603.
Barquera, Simón, Víctor Tovar-Guzmán, Ismael Campos-Nonato, Clicerio González-Villalpando, and Juan Rivera-Dommarco. 2003. "Geography of Diabetes Mellitus Mortality in Mexico: an Epidemiologic Transition Analysis." *Archives of Medical Research* 34 (5) (September): 407–414. doi:10.1016/S0188-4409(03)00075-4.
Berg, C J. 2012. "From Identification and Review to Action—Maternal Mortality Review in the United States." *Ysper* 36 (1) (February 1): 7–13. doi:10.1053/j.semperi.2011.09.003.
Berg, Cynthia J, William M Callaghan, Zsakeba Henderson, and Carla Syverson. 2011. "Pregnancy-Related Mortality in the United States, 1998 to 2005.." *Obstetrics & Gynecology* 117 (5) (May): 1230. doi:10.1097/AOG.0b013e31821769ed.
Bobadilla, J L, J Frenk, R Lozano, T Frejka, and C Stern. 1993. "The Epidemiologic Transition and Health Priorities ." In *Disease Control Priorities in Developing Countries*. New York: Oxford University Press.
Campbell, O M R. 1999. "Measuring Progress in Safe Motherhood Programmes: Uses and Limitations of Health Outcome Indicators." *Safe Motherhood Initiatives: Critical Issues*.
Campbell, O, R Gipson, A H Issa, N Matta, B El Deeb, A El Mohandes, A Alwen, and E Mansour. 2005. "National Maternal Mortality Ratio in Egypt Halved Between 1992-93 and 2000." *Bulletin of the World Health Organization* 83 (6) (June 1): 462–471.
Center for Maternal and Child Enquiries. 2011. "Saving Mothers Lives: Reviewing Maternal Deaths to Make Motherhood Safer: 2006-2008" 118 (March): 1–205.
Chowdhury, Mahbub Elahi, Anisuddin Ahmed, Nahid Kalim, and Marge Koblinsky. 2009. "Causes of Maternal Mortality Decline in Matlab, Bangladesh.." *Journal of Health, Population and Nutrition* 27 (2) (April): 108–123.
Clark, Steven L, Michael A Belfort, Gary A Dildy, Melissa A Herbst, Janet A Meyers, and Gary D Hankins. 2008. "Maternal Death in the 21st Century: Causes, Prevention, and Relationship to Cesarean Delivery." *American Journal of Obstetrics and Gynecology* 199 (1) (July): 36.e1–36.e5. doi:10.1016/j.ajog.2008.03.007.
CONAPO. 2012. "Anexo C: Metodología De Estimación Del Índice De Marginación Por Localidad." http://www.conapo.gob.mx/work/models/CONAPO/indices_margina/2010/anexoc/AnexoC.pdf.
CONEVAL. 2012. *Evaluación Estratégica Sobre Mortalidad Materna en México 2010: Características Sociodemográficas Que Obstaculizan a Las Mujeres Embarazadas*

Su Acceso Efectivo a Instituciones De Salud. México.
Cross, Suzanne, Jacqueline S Bell, and Wendy J Graham. 2010. "What You Count Is What You Target: the Implications of Maternal Death Classification for Tracking Progress Towards Reducing Maternal Mortality in Developing Countries." *Bulletin of the World Health Organization* 88 (2) (February 1): 147–153. doi:10.2471/BLT.09.063537.
D R Secretaría de Salud. 2003. *Salud: México 2002. Información Para La Rendición De Cuentas*. 2nd ed. México.
Domınguez-Cherit, G, S E Lapinsky, A E Macias, R Pinto, L Espinosa-Perez, A De la Torre, M Poblano-Morales, J A Baltazar-Torres, E Bautista, and A Martinez. 2009. "Critically Ill Patients with 2009 Influenza a (H1N1) in Mexico." *Jama* 302 (17): 1880–1887.
Echevarría-Zuno, Santiago, Juan Manuel Mejía-Aranguré, Alvaro J Mar-Obeso, Concepción Grajales-Muñiz, Eduardo Robles-Pérez, Margot González-León, Manuel Carlos Ortega-Alvarez, Cesar Gonzalez-Bonilla, Ramón Alberto Rascón-Pacheco, and Víctor Hugo Borja-Aburto. 2009. "Infection and Death From Influenza a H1N1 Virus in Mexico: a Retrospective Analysis." *Lancet* 374 (9707) (December 19): 2072–2079. doi:10.1016/S0140-6736(09)61638-X.
Elú, M C. 1993. "La Luz Enterrada." In *Estudio Antropológico Sobre La Mortalidad Materna en Tlaxcala*, ed. Fondo de Cultura Económica. Mexico.
Flores, Mario, Nayeli Macias, Marta Rivera, Ana Lozada, Simón Barquera, Juan Rivera-Dommarco, and Katherine L Tucker. 2010. "Dietary Patterns in Mexican Adults Are Associated with Risk of Being Overweight or Obese.." *The Journal of Nutrition* 140 (10) (October): 1869–1873. doi:10.3945/jn.110.121533.
Foreman, Kyle J, Rafael Lozano, Alan D Lopez, and Christopher JL Murray. 2012. "Modeling Causes of Death: an Integrated Approach Using CODEm." *Population Health Metrics* 10 (1): 1. doi:10.1186/1478-7954-10-1.
Freyermuth-Enciso, G, and R Cárdenas-Elizalde. 2009. "Evaluación Del Subregistro De La Mortalidad Materna en Los Altos De Chiapas Mediante Las Estrategias RAMOS Y RAMOS Modificada." *Salud Pública De México* 51 (6): 450–457.
Gay, J, and D Billings. 2009. *Evolution of the MacArthur Foundation's Work in Mexico to Reduce Maternal Mortality, 2002-2008*. *Techreport*.
Gómez, Luz María, Bernardo Hernández-Prado, Maria del Carmen Morales, and Teresa Shamah-Levy. 2009. "Physical Activity and Overweight/Obesity in Adult Mexican Population: the Mexican National Health and Nutrition Survey 2006.." *Salud Pública De México* 51 Suppl 4: S621–9.
Graham, W J, L B Foster, L Davidson, E Hauke, and O M R Campbell. 2008. "Measuring Progress in Reducing Maternal Mortality." *Best Practice & Research Clinical Obstetrics & Gynaecology* 22 (3): 425–445.
Graham, W J, S Ahmed, C Stanton, C L Abou-Zahr, and OMR Campbell. 2008. "Measuring Maternal Mortality: an Overview of Opportunities and Options for Developing Countries." *BMC Medicine* 6 (1): 12. doi:10.1186/1741-7015-6-12.
Grubb, G S, J A Fortney, S Saleh, S Gadalla, A el-Baz, P Feldblum, and S M Rogers. 1988. "A Comparison of Two Cause-of-Death Classification Systems for Deaths Among Women of Reproductive Age in Menoufia, Egypt." *International Journal of Epidemiology* 17 (2) (June 1): 385–391.

Guelinckx, I, R Devlieger, K Beckers, and G Vansant. 2008. “Maternal Obesity: Pregnancy Complications, Gestational Weight Gain and Nutrition.” *Obesity Reviews* 9 (2): 140–150.

Hernandez, B, J Chirinos, M Romero, and A Langer. 1994. “Estimating Maternal Mortality in Rural Areas of Mexico: the Application of an Indirect Demographic Method.” *International Journal of Gynaecology and Obstetrics: the Official Organ of the International Federation of Gynaecology and Obstetrics* 46 (3) (September 1): 285–289.

Hernández, B, A Langer, M Romero, and J Chirinos. 1993. “Cálculo De La Subestimación De La Mortalidad Materna en Morelos.” In. Cuernavaca, Morelos, México.

Hill, K, K Thomas, C AbouZahr, N Walker, L Say, M Inoue, E Suzuki, and Maternal Mortality Working Group. 2007. “Estimates of Maternal Mortality Worldwide Between 1990 and 2005: an Assessment of Available Data.” *Lancet* 370 (9595) (October 19): 1311–1319. doi:10.1016/S0140-6736(07)61572-4. http://linkinghub.elsevier.com/retrieve/pii/S0140673607615724.

Instituto Nacional de Salud Publica. 2012. “Encuesta Nacional De Salud Y Nutrición 2012: Evidencia Para La Política Publica en Salud.” http://ensanut.insp.mx.

Khan, Khalid S, Daniel Wojdyla, Lale Say, A Metin Gulmezoglu, and Paul FA Van Look. 2006. “WHO Analysis of Causes of Maternal Death: a Systematic Review.” *The Lancet* 367 (9516) (April): 1066–1074. doi:10.1016/S0140-6736(06)68397-9.

King, G, J Honaker, A Joseph, and K Scheve. 2001. “Analyzing Incomplete Political Science Data: an Alternative Algorithm for Multiple Imputation.” *American Political Science Review* 95 (1): 49–70.

Langer, A, and R Lozano. 1996. “The Health of Women in Mexico: Current Panorama and Future Prospects.” *Changing Structure of Mexico: Political, Social, and Economic Prospects*: 333–48.

Langer, A, B Hernandez, C Garcia-Barrios, and G L Saldanha-Uranga. “The National Safe Motherhood Committee of Mexico. Identifying Interventions to Prevent Maternal Mortality in Mexico: a Verbal Autopsy Study.” *Reproductive Health Matters Initiatives: Critical Issues*: 127–137.

Langer, Ana, Julio Frenk, and Richard Horton. 2012. “Women and Health Initiative: Integrating Needs and Response.” *The Lancet* 380 (9842) (August): 631–632. doi:10.1016/S0140-6736(11)60742-3.

Lezana, M Á. 1999. “Evolución De Las Tasas De Mortalidad Materna en México.” In *Una Nueva Mirada a La Mortalidad Materna en México*, ed. M C Elú and E Santos, 53–70. México.

Lozano, R. 2012. “La Carga De La Enfermedad Y Las Desigualdades en Salud De Las Mujeres en México.”

Lozano, Rafael, Luis Manuel Torres-Palacios, and Patricia Soliz. 2010. “Comentarios Al Artículo ‘Evaluación Del Subregistro De La Mortalidad Materna en Los Altos De Chiapas Mediante Las Estrategias RAMOS Y RAMOS Modificada’ De Graciela Freyermuth Y Colaboradores.” *Salud Pública De México* 52 (5): 1–6.

Maina, William K. 2011. “Integrating Noncommunicable Disease Prevention Into Maternal and Child Health Programs: Can It Be Done and What Will It Take?.” *International Journal of Gynaecology and Obstetrics: the Official Organ of the*

International Federation of Gynaecology and Obstetrics 115 Suppl 1 (November): S34–6. doi:10.1016/S0020-7292(11)60010-6.

Mathers, Colin D, Doris Ma Fat, Mie Inoue, Chalapati Rao, and Alan D Lopez. 2005. "Counting the Dead and What They Died From: an Assessment of the Global Status of Cause of Death Data." *Bulletin of the World Health Organization* 83 (3) (March 1): 171–177.

McCaw-Binns, A, S F Alexander, J L M Lindo, C Escoffery, K Spence, K Lewis-Bell, and G Lewis. 2007. "Epidemiologic Transition in Maternal Mortality and Morbidity: New Challenges for Jamaica.." *International Journal of Gynaecology & Obstetrics* 96 (3) (March): 226–232. doi:10.1016/j.ijgo.2006.12.002.

Monteiro, C A, W L Conde, B Lu, and B M Popkin. 2004. "Obesity and Inequities in Health in the Developing World." *International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity* 28 (9) (September 1): 1181–1186.

Mosby, L G, S A Rasmussen, and D J Jamieson. 2011. "2009 Pandemic Influenza a (H1N1) in Pregnancy: a Systematic Review of the Literature." *American Journal of Obstetrics and Gynecology* 205 (1) (July 1): 10–18. doi:10.1016/j.ajog.2010.12.033.

Naghavi, M, S Makela, K Foreman, J O'Brien, F Pourmalek, and R Lozano. 2010. "Algorithms for Enhancing Public Health Utility of National Causes-of-Death Data." *Population Health Metrics* 8 (May 1): 9.

Nour, N M. 2008. "An Introduction to Maternal Mortality." *Reviews in Obstetrics and Gynecology* 1 (2): 77–81.

Reyes Frausto, S, M A Lezana Fernández, M D García Peña, and J L Bobadilla Fernández. 1998. "Maternal Mortality Regionalization and Trend in Mexico (1937-1995)." *Archives of Medical Research* 29 (2): 165–172.

Rivera, J A, S Barquera, and F Campirano. 2002. "Epidemiological and Nutritional Transition in Mexico: Rapid Increase of Non-Communicable Chronic Diseases and Obesity." *Public Health*.

Rivera, Juan A, Simón Barquera, Teresa González-Cossío, Gustavo Olaiz, and Jaime Sepulveda. 2004. "Nutrition Transition in Mexico and in Other Latin American Countries." *Nutrition Reviews* 62 (July): S149–S157. doi:10.1111/j.1753-4887.2004.tb00086.x.

Rojas, Rosalba, Carlos A Aguilar-Salinas, Aída Jiménez-Corona, Teresa Shamah-Levy, Juan Rauda, Leticia Avila-Burgos, Salvador Villalpando, and Eduardo Lazcano Ponce. 2010. "Metabolic Syndrome in Mexican Adults: Results From the National Health and Nutrition Survey 2006.." *Salud Pública De México* 52 Suppl 1: S11–8.

Ronsmans, C. 2001. "How Can We Monitor Progress Towards Improved Maternal Health." *Studies in Health Services Organisation and Policy* 17: 313–338.

Ronsmans, C, W J Graham, and Lancet Maternal Survival Series steering group. 2006. "Maternal Mortality: Who, When, Where, and Why." *Lancet* 368 (9542) (September 1): 1189–1200.

Schiavon, Raffaela, Erika Troncoso, and Gerardo Polo. 2012. "Analysis of Maternal and Abortion-Related Mortality in Mexico Over the Last Two Decades, 1990â€"2008." *International Journal of Gynaecology & Obstetrics* 118 (S2) (August 17): S78–S86. doi:10.1016/S0020-7292(12)60004-6.

Schutte, Joke M, Layla de Jonge, Nico W E Schuitemaker, Job G Santema, Eric A P

Steegers, and Jos van Roosmalen. 2010. “Indirect Maternal Mortality Increases in the Netherlands.” *Acta Obstetricia Et Gynecologica Scandinavica* 89 (6) (June): 762–768. doi:10.3109/00016341003657876.

Secretaria de Salud. 2011. *Mortalidad Materna en Mexico Durante 2009: El Efecto De Las Infecciones Respiratorias Agudas (Neumonia E Influenza)*. Col Juarez: Secretaria de Salud.

Secretaria de Salud, CEMECE. 2011. “Búsqueda Intencionada De Muertes Maternas en México: Informe 2008.” In. Secretaria de Salud. http://www.cemece.salud.gob.mx/descargas/pdf/BIMM_Informe2008.pdf.

Stevens, Gretchen, Rodrigo H Dias, Kevin J A Thomas, Juan A Rivera, Natalie Carvalho, Simón Barquera, Kenneth Hill, and Majid Ezzati. 2008. “Characterizing the Epidemiological Transition in Mexico: National and Subnational Burden of Diseases, Injuries, and Risk Factors.” *PLoS Medicine* 5 (6) (June 17): e125–11. doi:10.1371/journal.pmed.0050125.

Tinker, A G, M A Koblinsky, and P Daly. 1993. *Making Motherhood Safe*. *Book*.

Uauy, R, C Albala, and J Kain. 2001. “Obesity Trends in Latin America: Transiting From Under-to Overweight.” *Journal of Nutrition* 131 (3): 893S.

Valdespino-Gomez, Jose Luis, Lourdes Garcia-Garcia, and Samuel Ponce de LeOn-Rosales. 2009. “Vaccines Against Influenza a (H1N1) Pandemic.” *Archives of Medical Research* 40 (8) (November 1): 693–704. doi:10.1016/j.arcmed.2009.10.008.

World Health Organization. 2004. *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision Instruction Manual. Book*. Vol. 2.

World Health Organization. 2012. *The WHO Application of ICD-10 to Deaths During Pregnancy, Childbirth and the Puerperium: ICD-MM*. Geneva, Switzerland: World Health Organization.

Yazbeck, Abdo S. 2007. “Challenges in Measuring Maternal Mortality..” *Lancet* 370 (9595) (October 13): 1291–1292. doi:10.1016/S0140-6736(07)61553-0.

Table 1: ICD code blocks for indirect causes (World Health Organization 2012)

ICD Block	Detailed codes	Cause name
O10	O10.0-O10.4, O10.9	Pre-existing hypertension complicating pregnancy, childbirth and the puerperium
O24	O24.0-O24.4, O24.9	Diabetes mellitus during pregnancy
O98	O98.0-O98.9	Maternal infectious and parasitic diseases classifiable elsewhere but complicating pregnancy, childbirth and the puerperium
O99	O99.0-O99.8	Other maternal diseases classifiable elsewhere but complicating pregnancy, childbirth and the puerperium

Table 2: Summary of review process, n=5,886

		After review				
		Indirect	Direct	Non-maternal	Late maternal	*Total*
Before review	Indirect	1,006	296	0	13	*1,315*
	Direct	118	3,592	0	26	*3,736*
	Non-maternal	341	252	4	137	*734*
	Late maternal	1	8	0	92	*101*
	Total	*1,466*	*4,148*	*4*	*268*	*5,886*

Table 3: Tabulations of ICD blocks before review for those recoded to indirect maternal deaths

ICD10 codes	Cause group	n
Non-maternal		
A15-B49	Infectious & parasitic diseases	74
A34, O85-O86	Complications predominantly related to the puerperium	13
C15-C96, D10-D48	Neoplasms	37
D55-D89	Diseases of blood and blood-forming organs	6
E00-E90	Endocrine, nutritional and metabolic diseases	20
G00-G99	Diseases of the nervous system	15
I00-I99	Diseases of the circulatory system	65
J00-J99	Diseases of the respiratory system	53
K00-K93	Diseases of the digestive system	29
L00-L08	Infections of the skin and subcutaneous tissue	1
M00-M99	Diseases of the musculoskeletal system and connective tissue	5
N00-N99	Diseases of the genitourinary system	8
Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities	12
R50-R69	General symptoms and signs	4
V01-Y98	External causes	12
Maternal		
O01	Hydatidiform mole	1
O02-O08	Other pregnancy with abortive outcome	7
O10-O16	Oedema, proteinuria and hypertensive disorders in pregnancy, childbirth and the puerperium	26
O20, O45-O46, O67	Premature separation of placenta and other hemorrhage of pregnancy or birth	7
O21, O23-O31, O34	Other complications of pregnancy	16
O22,O87	Other maternal disorders predominantly related to pregnancy	1
O35-O43, O68-O69	Fetal distress and other complications of pregnancy or birth	13
O47-O62, O73-O75	Sepsis and other puerperal infections	5
O72	Postpartum hemorrhage	2
O88	Obstetric embolism	8
O89-O92	Other complications during the puerperium	19
O96-O97	Late maternal death	1
Total		460

Table 4: Characteristics of indirect and direct deaths

Covariate	Indirect	Direct
Number of pregnancies	2.53	3.08†
Age	27.70	28.66†
Any prenatal visit	0.85	0.83
Marital status		
Single	0.17	0.15
Common law, divorced or widowed	0.38	0.38
Married	0.45	0.47
Education		*
< Primary	0.22	0.27
< Secondary	0.28	0.27
Secondary or higher	0.50	0.46
Place of death		**
Secretaria de Salud	0.45	0.46
IMSS	0.21	0.16
IMSS Opportunidades	0.02	0.03
Public worker unit	0.09	0.09
Private medical unit	0.05	0.09
Home, street, other	0.17	0.17
Place of delivery		*
Secretaria de Salud	0.50	0.44
IMSS	0.24	0.15
IMSS Opportunidades	0.02	0.03
Public worker unit	0.08	0.06
Private medical unit	0.09	0.15
Home, street, other	0.07	0.17
Place of care for first complication		*
Secretaria de Salud	0.49	0.49
IMSS	0.23	0.15
IMSS Opportunidades	0.04	0.06
Public worker unit	0.07	0.06
Private medical unit	0.16	0.22
Home, street, other	0.00	0.01
Deprivation index, quintile (municipality)		*
Q1-Rich	0.59	0.48
Q2	0.15	0.13
Q3	0.08	0.1
Q4	0.08	0.11
Q5-Poor	0.09	0.18
Skilled birth attendant		*
Other	0.02	0.06
Doctor, nurse or midwife	0.72	0.85
No delivery	0.27	0.09

† p< 0.005 for the difference in mean or proportion between indirect/direct deaths
* p<0.005, **p<0.05 for the difference between the indirect/direct deaths (using an overall Pearson chi-square)

Table 5: Top five causes of indirect maternal deaths, by highest and lowest municipality-level deprivation index quintile

Q1 - Rich	Number of deaths	Percentage
Other specified diseases and conditions complicating pregnancy, childbirth and the puerperium	219	25.23%
Diseases of the respiratory system complicating pregnancy, childbirth and the puerperium	181	20.85%
Diseases of the circulatory system complicating pregnancy, childbirth and the puerperium	155	17.86%
Diseases of the digestive system complicating pregnancy, childbirth and the puerperium	86	9.91%
Mental disorders and diseases of the nervous system complicating pregnancy, childbirth and the puerperium	42	4.84%
Q5 - Poor		
Diseases of the circulatory system complicating pregnancy, childbirth and the puerperium	36	27.07%
Diseases of the respiratory system complicating pregnancy, childbirth and the puerperium	24	18.05%
Other specified diseases and conditions complicating pregnancy, childbirth and the puerperium	16	12.03%
Tuberculosis complicating pregnancy, childbirth and the puerperium	11	8.27%
Mental disorders and diseases of the nervous system complicating pregnancy, childbirth and the puerperium	10	7.52%

Table 6: Multivariate logistic regression results comparing indirect deaths to direct deaths (n=5,553)

	Coef.	Std. Err.	p-value	95% Conf. Interval	
Marital status					
Single (comparator)					
Common law, divorced or widowed	-0.02	0.10	0.85	-0.21	0.17
Married	0.00	0.10	0.98	-0.19	0.20
Education					
< Primary (comparator)					
< Secondary	-0.10	0.10	0.32	-0.29	0.09
Secondary or higher	-0.24	0.10	0.01	-0.43	-0.06
Place of delivery					
Secretaria de Salud (comparator)					
IMSS	0.08	0.24	0.73	-0.44	0.61
IMSS Opportunidades	-0.23	0.38	0.57	-1.09	0.64
Public worker unit	0.18	0.18	0.32	-0.18	0.54
Private medical unit	-0.60	0.14	0.00	-0.87	-0.33
Home, street, other	-0.83	0.16	0.00	-1.15	-0.50
Place of care for first complication					
Secretaria de Salud (comparator)					
IMSS	0.30	0.23	0.22	-0.21	0.81
IMSS Opportunidades	-0.02	0.23	0.94	-0.51	0.47
Public worker unit	-0.04	0.22	0.87	-0.50	0.43
Private medical unit	0.01	0.13	0.91	-0.24	0.27
Home, street, other	-0.21	0.31	0.50	-0.82	0.40
Deprivation index, quintile (municipality)					
Q1-Rich (comparator)					
Q2	0.03	0.10	0.79	-0.17	0.22
Q3	-0.32	0.12	0.01	-0.56	-0.07
Q4	-0.33	0.12	0.01	-0.57	-0.09
Q5-Poor	-0.63	0.13	0.00	-0.88	-0.38
Skilled birth attendant					
None (comparator)					
Doctor, nurse or midwife	-0.19	0.22	0.40	-0.62	0.25
NA: no delivery	1.21	0.23	0.00	0.76	1.66
Year					
2006 (comparator)					
2007	0.25	0.11	0.02	0.04	0.46
2008	0.20	0.11	0.06	-0.01	0.41
2009	0.82	0.10	0.00	0.62	1.01
2010	0.45	0.11	0.00	0.24	0.66
Number of pregnancies	-0.05	0.02	0.01	-0.09	-0.01
Age	-0.01	0.01	0.06	-0.02	0.00
Any prenatal visit	0.20	0.10	0.05	0.00	0.40
Constant	-0.81	0.30	0.01	-1.39	-0.22

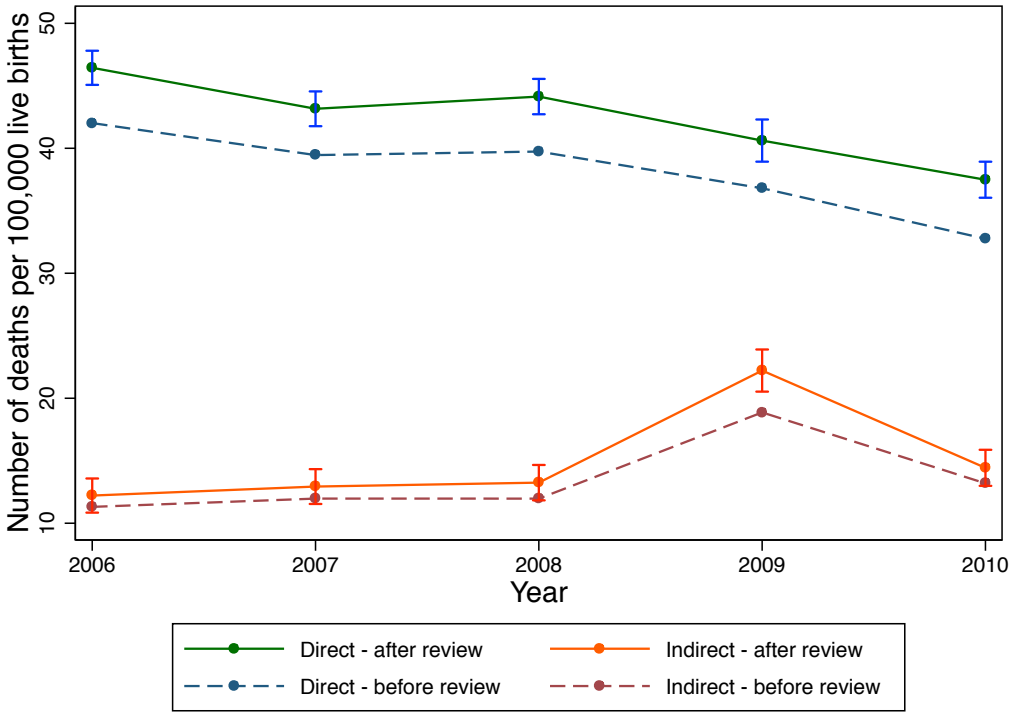


Figure 1: Direct and indirect deaths per 100,000 live births, by year, before and after review process

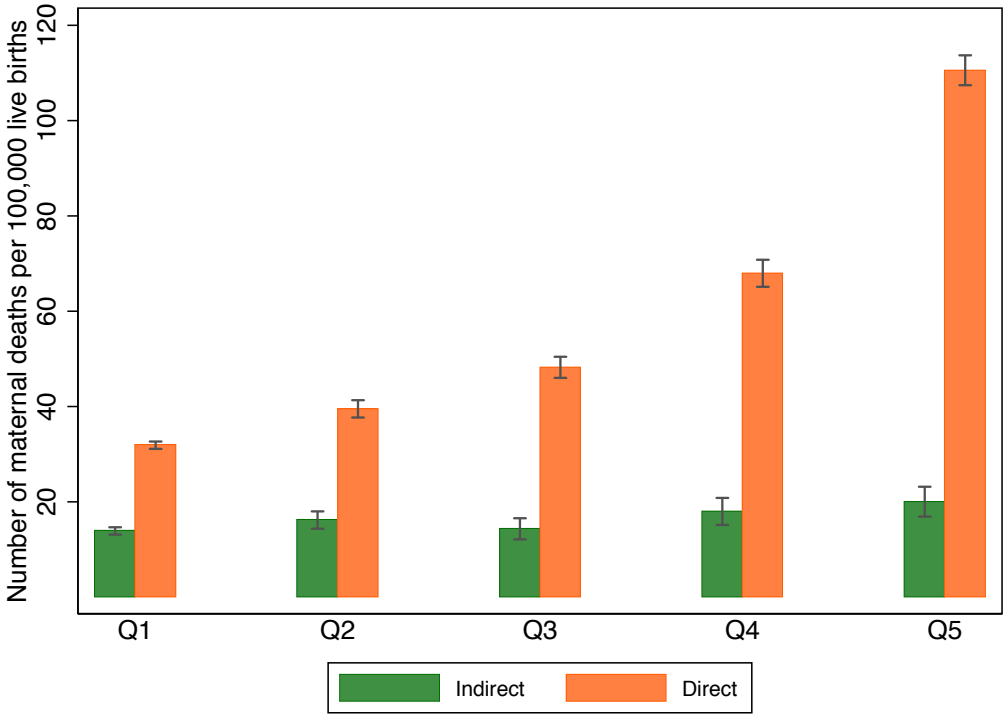


Figure 2A: Number of indirect and direct deaths per 100,000 live births, by quintile of municipality-level deprivation index, pooled 2006-2010

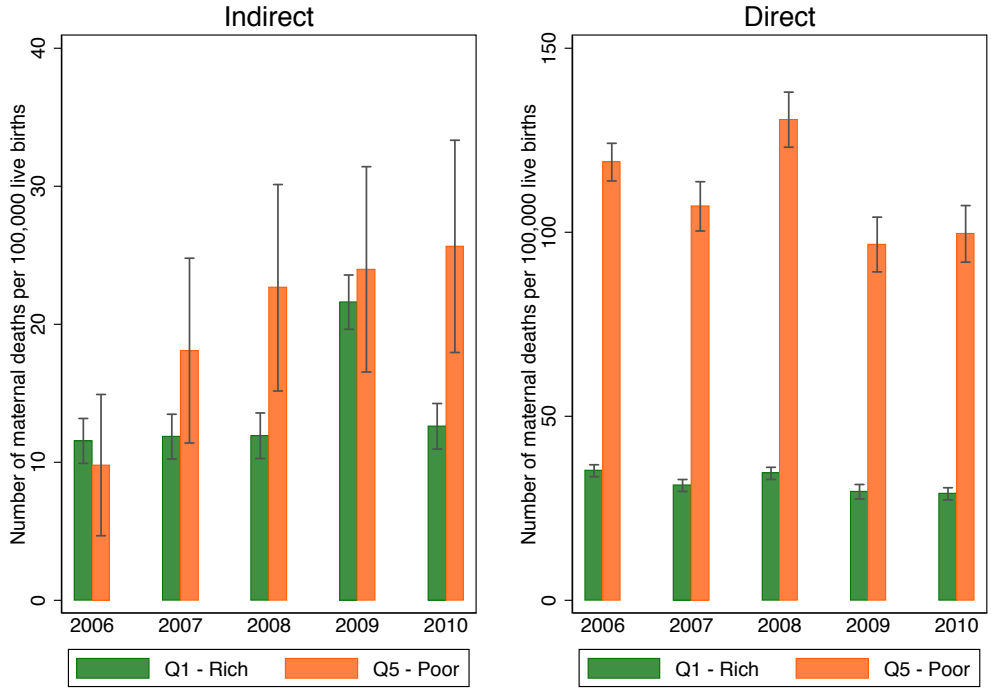


Figure 2B: Number of direct and indirect deaths per 100,000 live births, by year, for the richest and poorest quintile of the municipality-level deprivation index

CHAPTER FIVE

Conclusion

This dissertation addresses key measurement shortcomings in the global maternal health field. It provides the first set of comparable trend estimates for maternal mortality for all countries in the world over the period 1980-2008, the result of a systematic assessment and analysis of all data available for the measurement of maternal mortality in that period. It also suggests an innovative, generalizable approach to selecting the most appropriate multivariable model form for a predictive model. Finally, it presents a detailed analysis of a single maternal mortality dataset from a middle-income country, Mexico, highlighting the importance of continued work towards cause-specific maternal mortality estimates. It also provides a comparison of the socio-demographic characteristics and health services use of direct and indirect decedents, as well as a discussion of the feasibility of adopting a similar correction approach in other contexts and the health system implications of the findings in Mexico.

Summary of findings

The first component of this dissertation, the analysis of all available data on maternal mortality from 1980-2008 for 181 countries, shows a remarkable decline in maternal deaths, from 526,300 in 1980 to 342,900 in 2008, an average annual decline of 1.5%. Progress overall would have been larger if the HIV epidemic had not contributed to significant increases in maternal mortality in Eastern and Southern Africa. Global progress on reducing the MMR, an average annual decline from 1980 to 2008 of 1.8%,

has been similar to progress on maternal death numbers, as the size of the global birth cohort has changed little over this period. Across countries, average annual rates of decline from 1980-2008 in the MMR have differed widely, ranging from a greater than 9.5% decrease in the Maldives to a 3.7% increase in Zimbabwe. This new evidence suggests there is a much greater reason for optimism than generally perceived, and that substantial declines in the MMR are possible over relatively short periods of time. These results have been broadly confirmed by WHO and partners (WHO et al. 2012), and since the time of publication of Paper 1, in 2010, an updated set of estimates has been released by colleagues (Lozano et al. 2011).

The second component outlines a transparent, replicable approach to model selection that can be tailored to help a researcher choose a model that best answers the research question, or questions, at hand. In the cross-country dataset of maternal mortality used as a case study, predictive validity demonstrated that a range of models is justifiable. No single model out-performed every other model in all tests or all metrics, which is perhaps not surprising given the breadth of what the model was asked to do. Predictive validity offers a practical approach to model selection that allows the researcher to identify the key attributes that they desire in their model and identify the model (or models) that best meets those attributes.

The third component presents the results of a comprehensive search for maternal deaths in Mexico over the period 2006-2010. This study shows encouraging progress towards the more complete and accurate assessment of causes of maternal mortality in a middle-income country, and offers a useful strategy for improving detailed maternal mortality data at the country level. The results highlight the need for a strategy to identify

miscoded or misclassified maternal deaths within the vital registration system. The intentional search identified an average of 12% additional maternal deaths that had originally been miscoded as non-maternal, as well as more deaths miscoded within the maternal ICD chapter. This study suggests that in Mexico, while direct maternal deaths are decreasing, indirect maternal deaths may be increasing, particularly in the poor. Examination of the specific causes of indirect obstetric deaths in Mexico reveals that infectious and parasitic diseases complicated by pregnancy contribute more to total indirect maternal deaths than do diabetes and pre-existing hypertension. However, given the rapid rise in obesity and chronic disease in Mexico, it is likely that their role will continue to grow. The project outlined in this paper offers important lessons for the adoption of this approach in other countries: first, the need for an assessment of the scale of the problem; second, the consideration of a "modified" RAMOS approach to reduce costs; third, the importance of maternal death review in the case of unusual disease patterns and epidemics; fourth, the appropriateness of basing such a project within a governmental setting; fifth, the need to establish legal protections for OBGYNs before implementation; and sixth, the importance of continuous, budgeted funding.

Implications for the global maternal health field

Measurement. This dissertation provides new evidence for the global health community on the status of maternal health worldwide: time trends in maternal mortality with quantified uncertainty. To do this, an extensive set of corrections were undertaken to the raw data, and then a two-stage regression modeling procedure was applied. Rigorous testing was undertaken to identify the best-performing modeling approach, using

predictive validity. Four sources of uncertainty were included in the estimation of the confidence intervals. While this represents a breakthrough for the maternal health field, and hopefully will be used to inform policy decisions, it would be a mistake to assume that this ought to be the way forward. What are really needed are not more elaborate and better-performing models, but better data.

Researchers have long called for sustained investment in vital registration systems as the cornerstone to improving understanding of all-cause, as well as cause-specific, mortality. In the long term, this must be a priority for all countries. However this study demonstrates that even complete vital registration systems such as the one in Mexico do not adequately describe maternal mortality: deaths are missed, miscoded, and misclassified. The Mexico BIRMM project represents one approach to ensuring a more accurate and complete estimation of maternal deaths. Investment in vital registration systems must include investment in corrective procedures such as the BIRMM project, recognizing that even high performing systems will not capture all maternal deaths.

Realistically, fully functioning vital registration systems are a long way off in many parts of the world, though efforts to institute them must remain a priority. In the interim, repeated, regularly conducted surveys incorporating a sibling history module, and censuses and surveys with deaths in the household modules, both with maternal death identification, can provide important evidence. These questions should become standard components of census and survey instruments, both to improve maternal mortality estimates, and all-cause adult mortality estimates as well. It is essential that these surveys be conducted regularly, with large sample sizes, and the data be made publicly available with reasonable speed.

Further, in addition to filling important gaps in countries without vital registration systems, the use of these questionnaires in countries with fully functioning vital registration would provide a tremendous public good. The correction approaches applied in this study could be more appropriately validated where a gold-standard, high quality vital registration system is available as the comparator; to date, this comparison has not been possible.

The measurement of cause-specific maternal mortality remains fraught with difficulties. The third paper of this dissertation highlights that the coding rules and definitions within the "maternal mortality" group require further clarification if more detailed cause of death information is to be useful. The new WHO publication (ICD-MM) attempts to clarify the categories and classifications, and it will be important to track whether this new resource assists coders in their work. Qualitative research could play a crucial role in identifying, and addressing, the difficulties faced by coders in their work on maternal mortality.

For countries without vital registration systems, research is needed to identify alternative methods for estimating cause-specific maternal mortality from survey and verbal autopsy data. At present, both of these tools usually group all maternal deaths together, with the identification of a maternal death determined by the timing of a death relative to a pregnancy or live birth. Given the growing burden of indirect maternal deaths and, in particular, the important role of HIV, disaggregating these deaths is essential.

The third paper of this thesis also highlights the need for sub-national estimates of maternal mortality, both geographical and by socio-economic status. Vital registration

systems usually make geographical assessment possible, and some limited socio-economic analysis as well. However, for countries without vital registration systems, there is very limited sub-national data available. For example, the sibling survival approach in surveys does not allow for any socio-economic or geographic breakdown, as information is not collected on the geographical or socio-economic status of the decedent (just the respondent). Research is needed into how this limitation could be addressed.

This thesis presents major progress in the measurement of maternal mortality, but also highlights the limitations of the existing data for the estimation of maternal mortality: improved vital registration is needed to capture all maternal deaths, better approaches are required in countries where vital registration is not performing well or at all, cause-specific data are needed, with new methods particularly in countries with limited vital registration, and sub-national breakdown must be made possible in all contexts.

Health systems. This thesis provides strong evidence that maternal mortality must remain a priority for the international community. While there has been substantial, previously unrecognized progress, the number of maternal deaths is still unacceptably high, and many countries have seen no progress at all. HIV has had a devastating impact on the maternal mortality ratio in sub-Saharan Africa, and increases in other areas require investigation into the causes, as well as rapid reversal.

Overall, the story on maternal mortality is a surprisingly positive one: something that the international community is doing appears to be working in many countries. Further research is needed to understand how that progress can be maintained and

accelerated. The first paper of this thesis presents several hypotheses for the decline in maternal mortality: the global fertility decline must be a driving force, and unpacking the causal web for that relationship (i.e., the relative impact of improved education, access to effective contraception, changing social norms) should remain a research priority.

The focus of the international community on the Millennium Development Goals has likely improved the measurement and perhaps the progress on maternal mortality. However, this thesis raises questions about how realistic those goals are. This work found only 23 countries on track to meet the 2015 target, which is a disappointing finding. However, it may reflect unrealistic goal-setting more than a lack of substantial progress. Finding the balance between ambitious and realistic goals should be a point of discussion before further goals are agreed to; this will be made much easier by the improved international data available after projects such as this one.

The identification of countries seeing enormous progress will be useful for setting realistic goals in the future, and they should also be carefully dissected as case studies to identify lessons learned. Researchers in Mexico, for example, may wish to examine carefully the progress made in Brazil over the same period, to try and unpack the decline and determine what might be applied in Mexico. Comparative studies of countries with similar health systems, epidemiology, resources and systems of government will provide critical insights into differential rates of progress on maternal mortality.

This thesis makes clear that several specific causes of maternal mortality warrant special attention. Perhaps the most striking finding in the first paper is the enormously important role of HIV in maternal mortality. More broadly, it raises the need to assess and respond seriously to non-obstetric maternal deaths. Grouping direct and indirect

maternal deaths together does a disservice to the health systems trying to respond effectively to them. The international community must begin answering the question: what does a health system response to indirect maternal deaths look like? While this thesis does not answer this question, one critical component must be improved screening, surveillance, and treatment for non-obstetric risk factors. The traditional components of prenatal care may not allow health personnel to identify all relevant risk factors. Women require improved education, both prior to conception and during pregnancy, about the risks they face due to any complicating risk factors or disease. The treatment and care a woman receives throughout her pregnancy, delivery, and post-partum period should be appropriate for the challenges her particular pregnancy presents. This will require all health personnel dealing with pregnant and delivering women to have training to recognize non-obstetric risks and emergencies and know how and when to refer these situations to appropriate providers. Finally, there is an urgent need for acute attention to the unique risks that pregnant women face in the case of epidemics like H1N1, with information disseminated early and often to both women and clinicians.

Conclusions

Without strong evidence, health systems cannot prioritize their limited resources appropriately. The global community has long viewed maternal mortality as a stagnant, intractable problem riddled with measurement challenges. This new evidence suggests that many countries have achieved significant progress in reducing maternal deaths, though many have not. This evidence should help arm the international community and country governments as they move forward to address maternal health.

This dissertation also presents a new, generalizable approach to model selection, the adoption of which would increase transparency in the scientific literature and encourage the use of best-performing models, as objectively assessed. The need for models that perform demonstrably well is growing, and this dissertation presents a tool that can be tailored to identify models that perform best on specific research questions.

Finally, the dissertation presents results from a detailed analysis of cause-specific maternal mortality in a middle-income country. It suggests that the relative contribution of indirect deaths to the overall maternal mortality ratio is growing, which should raise concerns about the generally vertical approach taken to maternal mortality.

This dissertation fills important gaps in the maternal health field, providing new evidence and approaches to the measurement issues that have hampered progress in the past. Moving forward, researchers should continue to develop novel approaches to the challenges of measuring maternal mortality, and adopt methods from other fields where appropriate. The transparent measurement of maternal health outcomes will help policy makers and advocacy groups more appropriately target their limited resources.

Lozano, R, H Wang, K J Foreman, J K Rajaratnam, M Naghavi, J R Marcus, L Dwyer-Lindgren, et al. 2011. "Progress Towards Millennium Development Goals 4 and 5 on Maternal and Child Mortality: an Updated Systematic Analysis." *Lancet* 378 (9797) (September 24): 1139–1165. doi:10.1016/S0140-6736(11)61337-8.

WHO, UNICEF, UNFPA, The World Bank. 2012. *Trends in Maternal Mortality: 1990 to 2010*. World Health Organization.

APPENDIX A1

Modeling Maternal Mortality

Introduction

There are particular challenges in modeling maternal mortality over time. At least four aspects of the dataset require special consideration: the available covariates explain only a moderate component of the variance; data are missing for many years; non-sampling error can be large in some settings such as India; and there is marked variation in temporal trends across countries. In the appendix figures, a number of countries such as Kazakhstan or Singapore show how the MMR can accelerate or decelerate; Yemen illustrates a country case where there are only two observations in the 29-year period from 1980 to 2008.

Our general modeling strategy bears some similarity to that used by Rajaratnam et al. (Rajaratnam et al. 2010) for adult mortality. The general model for the expected mortality rate from maternal causes is of the form:

$$\ln(\mu_{a,i,t}) = \beta X_{a,i,t} + M_{a,i,t} + e$$

Where $\mu_{a,i,t}$ is the maternal death rate for age a in country i for year t. $X_{a,i,t}$ is a vector of covariates that explain variation in maternal mortality rates across all countries. Substantial variation in the maternal mortality rate is not explained by these covariates, and the unexplained component, $M_{a,i,t}$ varies systematically over time and across countries. ? is the stochastic error in the maternal mortality rate due to sampling and to unmeasured factors that are not correlated in time and space.

Estimation of this general model can be divided into two steps. We call for convenience the estimation of $\beta X_{a,i,t}$ the linear model and estimation of $M_{a,i,t}$ the spatial-temporal local regression component.

Linear Model Estimation

There are three important steps in the development of the linear model: type of model, choice of covariates, and transformation of the covariates into the appropriate functional form. The data on maternal mortality from the various sources discussed in the main body of the paper can be expressed as either maternal mortality rates or counts of maternal deaths. We have tested both the use of count models and log death rate models. The advantage of count models is that due to small numbers in some vital registration data or in survey data, zero maternal deaths may be observed.

Because of the assumption of the poisson model that the rate of the event count is also the variance of the count, this model does not fit the maternal mortality data. The negative binomial, which allows for the rate of the event count to be overdispersed, is more appropriate. Moreover, since in maternal mortality the degree of overdispersion appears to be related to age, the most relevant count model is the generalized negative binomial, which we have implemented. As a second family of models, we estimated directly the relationship between the log of the maternal mortality rate and the explanatory variables. Because of zeros and many outliers, we tested a range of robust regression methods including Huber-White, Tukey, median regression and also OLS. All the robust regression methods yielded nearly identical estimates of the betas.

Based on the literature and the set of factors that might plausibly be related to maternal mortality, we considered the following covariates: total fertility rate, GDP per capita, HIV

seroprevalence, neonatal mortality, age-specific female education, skilled birth attendance and indicators for 5-year age groups 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49. We examined the relationship between each of these covariates and the log of the maternal mortality rate. This suggested that the appropriate transformations of the independent variables were the log of the total fertility, the log of the distributed lag of GDP per capita, and the inclusion of HIV-squared as well as HIV sero-prevalence in the model. Because of high co-linearity between skilled birth attendance, neonatal mortality and GDP per capita and the fact that SBA was only available for 1986-2008 and not for the entire interval, we did not include this variable in the final model. We also used predictive validity to compare the performance of models including SBA and excluding SBA and found that including SBA did not improve model fit over a version of the model that included neonatal mortality.

Webtable 2 provides the regression coefficients for three models: OLS, Generalized Negative Binomial and robust regression. The values of the betas on the covariates are quite similar across models. It is interesting to note that the count model yields similar results to the robust regression models with zero values dropped, because they cannot be transformed into log rates. Based on the similarity of results and out-of-sample predictive validity tests, we have more extensively evaluated the performance of the generalized negative binomial and robust regression method.

Spatial-Temporal Local Regression

Examination of the residuals from the first stage linear models shows clear patterns of serial auto-correlation as well as correlation across countries within regions. The purpose of spatial-temporal regression methods is to capture the information in these spatial and temporal

correlation patterns to improve prediction of the quantity of interest. Variants of these methods are widely used in the geospatial literature (Hengl, Heuvelink, and Stein 2004; Hudson and Wackernagel 1994; Knotters, Brus, and Voshaar 1995; Lado et al. 2008; Minasny and McBratney 2007). We capture this systemic pattern in the residuals by running a local fixed effects regression where the weights on the data for each country-year regression are a function of distance in time, space and age. Loess regression, used in many global health applications (Murray et al. 2007; Masanja et al. 2008), is an example of temporal local regression. We add to the temporal relatedness, spatial and age-group relatedness. Our time weights are similar to standard loess weights and take the form:

$$w_t = \left[1 - \left(\frac{|r_t - r_{est}|}{1 + \arg\max_t |r_t - r_{est}|}\right)^{\lambda}\right]^3$$

Spatial relatedness is only allowed between countries within a GBD region. The relative weight of data points from outside a country compared to the weight on observations from within a country is controlled by the parameter ζ which is the fraction of the total weight that is assigned to within country observations. Sub-national observations are counted as within country observations, but are given a weight compared to national observations that is only 0.2 times the national weight for the equivalent distance in time or age.

Because the determinants of maternal mortality that are not captured in the linear model but vary systematically across space and time are likely to affect more than one maternal age-group, we also estimate the local regression putting weights on adjacent age-groups. The form of the weights are a simple exponential decay such that the weight on the observation in the adjacent age-group is controlled by the the parameter omega in an exponential function. The final weight on all observations is the product of time weights, spatial weights and age weights.

Based on in-sample fit tests, we have chosen the time weighting parameter λ to be 0.5, ζ to be 0.8 and Ω to be 1.0. For small countries, we increase λ to equal 1.0 because of increased stochastic signal in the data; similarly, we increase λ to 2.0 for countries with no data available.

Predictive Validity

Given the range of options for the modeling strategy and the variation in in-sample fit, it is essential to objectively evaluate model performance. In-sample fit measures, such as the fraction of the variance explained by the predicted values, are extremely high with the addition of the spatial-temporal local regression component. But with this type of model which can track the data very closely, high in-sample fit does not necessarily mean improved predictions for years without data, or for the 21 countries with no data, or for backcasting or forecasting from the most recent observation to generate a complete time series for 1980-2008. For this reason, we have undertaken extensive predictive validity testing.

Four different types of predictive validity tests were undertaken: a) holding out a random sample of 20% of country-years of data; b) holding out all data from a random sample of 20% of countries; c) holding out the first 20% of years of data for all countries; d) holding out the last 20% of years for all countries. For each of these knock-out datasets, we estimate our model including the linear and spatial-temporal local regression components and compare predictions to the real data in the 20% of the sample held out. We repeat the 20% of countries and 20% of country-years tests 30 times to make sure our results are not an artifact of a given random sample of the data being withheld.

We examine four measures of predictive validity: root mean squared error, root median squared error, average relative error and median relative error. The RMSE and average relative

error are influenced by outliers while the root median squared error and median relative error are robust to the performance on outliers. Appendix A2, Table 3 provides for the generalized negative binomial and robust regression with and without the second stage spatial-temporal predictive validity measures for the four different types of tests. In all tests, the results are remarkably consistent. For the linear model alone, predictive validity is better for robust regression than the generalized negative binomial particularly for backcasting, forecasting and for predicting for countries with no data. Both models have median relative errors in excess of 40% and average relative errors that are at best 55% and extend as high as 94.5% for the negative binomial. Addition of the spatial-temporal component of the model substantially improves out-of-sample performance. In all metrics and all tests, the predictive validity analysis demonstrates that there is tremendous information content captured in the patterns of the residuals from the linear model over time and space. Median relative errors drop substantially to around 20% for forecasting, backcasting and to 16% for country-years. The most difficult test relevant to the 21 countries with no data shows that predictive validity is not as good with a median relative error of 36%. The average relative errors are higher, but still demonstrate substantial improvements over the linear model alone. The predictive validity tests confirm that the spatial-temporal component of the model is essential for improved performance.

In addition to the out-of-sample predictive validity tests above, we calculated in-sample performance. The absolute median relative error is just 12% in sample, while the average relative error is 25%. The root mean squared error and the root median squared error are 76.98 and 8.16, respectively.

Uncertainty Analysis

Depending on the analysis, uncertainty intervals may be computed for the expected value of the quantity of interest or for the observation or realization of the quantity of interest. In our case, we are interested in estimating the uncertainty in the expected value of the maternal death rate, MMR or maternal death numbers. Uncertainty in the expected value of an estimated quantity of interest can come from five sources. Most studies capture only one or two of these sources. In global health publications, there is marked variation across studies in practices about uncertainty; at the extreme some studies report no uncertainty intervals for descriptive measurements or use subjective intervals with no grounding in statistical theory such as reported by Hill et al for the 2005 maternal mortality estimates.

We outline the five potential sources of uncertainty in the expected value of the MMR or the number of maternal deaths. Not all of these sources can be propagated into the final uncertainty intervals of the expected value of the quantity of interest due to both data limitations and methodological challenges. The five sources are:

1. Uncertainty in the model parameters related to the uncertainty in the input dataset used in statistical estimation due to stochastic variance. Since each study, whether a vital registration data point or a survey data point, has stochastic measurement uncertainty associated with it, this means that there is greater uncertainty in the parameter estimates of the model than if there was no uncertainty in these measurements. In this study, we capture this source of uncertainty by simulating 100 draws from a binomial distribution for each study with the observed maternal cause fraction as π and the number of trials is the total number of deaths observed in the study for that maternal age-group. This

uncertainty is then propagated through each step of the study to generate an uncertainty distribution around the log maternal death rates used in the statistical model.

2. Uncertainty in the model parameters related to uncertainty in the input dataset that arises from non-sampling error. This non-sampling error could be due to biases that appear in different data systems due to survey implementation, misclassification, interviewer training and a myriad other problems. While in selected countries, with multiple observations, we observe that the variance at the same time is far greater than expected on the basis of sampling alone, we have found no generalized method for this dataset to estimate the non-sampling variance.

3. Uncertainty in the covariates used in the model. In some developing countries, there is likely to be considerable uncertainty in estimates of GDP per capita, educational attainment, neonatal mortality, HIV sero-prevalence and other potential covariates for maternal mortality. Uncertainty in independent variables, called errors in-variables in the econometric literature, also leads to biased estimation, which for causal modeling is an important but largely unresolved issue. As most producers of development data (UNAIDS being an important exception) do not report uncertainty intervals for their measurements, it is in practice not possible to capture this source of uncertainty in the estimation of the parameters of the model.

4. Uncertainty in model parameters related to estimation. Estimation of a statistical model yields uncertainty in the parameters of the model. Standard simulation methods have

been developed and widely applied to capture parameter uncertainty in a predicted quantity of interest. We include in this study, estimation uncertainty using simulation methods both the linear model and the spatial temporal model.

5. Uncertainty in the prediction of the expected value of the quantity of interest that is related to systematic variation not explained by the model. The size of this component of the model is related to how well the model explains the observed variation in the data. It can be large or small depending on the quantity being studied and the model that has been developed. This is the most challenging and perhaps important source of uncertainty to capture. We discuss the challenges and our approach to uncertainty estimation of this fundamental uncertainty below.

The main issue for category 5 is how to estimate the systematic variation not explained by the model. We can easily compute the variation in the dependent variable that is unexplained by the spatial-temporal regression model. The dependent variable, however, is not the expected value of the maternal death rate but the observation or realization of the maternal death rate in a study which includes both stochastic variance and non-sampling variance. Thus, the unexplained residual variance in the study observations is substantially larger than the systematic variance in the expected value of the maternal death rate that is unexplained by the model. The residual variance from the spatial-temporal regression model therefore includes three components: systematic variation, stochastic variation and non-sampling variation.

If one is willing to assume that each of these components in a large dataset is normally distributed, it is possible to estimate the systematic variance by subtracting an estimate of the

stochastic and non-sampling variances from the total residual variance. The remaining variance is then the systematic unexplained variance in the expected value of the maternal death rate. However, while the stochastic variance can be identified using simulation methods, it is not possible to estimate the contribution of non-sampling variance to the residual variance. Rather than underestimate uncertainty by not capturing systematic variance unexplained by the model, we have chosen to include both impact of non-sampling variance and systematic variation in the expected value not captured by the model. It is important to note that this quantity is a marked overestimate of the systematic variation not explained by the model because non-sampling variance in the studies of maternal mortality appears to be large. Comparison of multiple national sources of data for India at a given time, demonstrates huge variance which is not explained by stochastic variance. We have, however, not found an effective method for these data sources to decompose the remaining variance into non-sampling variance and systematic variance.

Because we observe that stochastic variance will vary by type of data collection mechanism, we have undertaken the simulations and computations of the variances separately for countries with VR data alone and all other countries. To avoid the impact of outliers on the estimation of the standard deviation of the residuals and the stochastic variance, we use robust estimators of the standard deviation. For the 21 countries with no data from 1980-2008, we use the observed relationship from the predictive validity studies; this demonstrated that the standard deviation of the residuals for countries without any data is 1.7 times larger than for countries with data. We therefore scale the estimated standard deviation of the non-sampling variance plus systematic variance by this constant.

In summary, we propagate uncertainty from four sources into our final estimates for each country and year: sampling uncertainty in the underlying studies, parameter uncertainty in the

linear model, parameter uncertainty in the spatial temporal local regressions and an estimate of the fundamental uncertainty unexplained by the estimation model. Sampling uncertainty is generated through randomly sampling from the binomial distribution using the observed fraction of deaths due to maternal causes as π and the total number of deaths as the number of trials. We generate 100 datasets by drawing from the binomial distribution of each observation. For each dataset, we compute the linear model and draw from the variance-covariance matrix of the betas of the regression 5 times. For each of the 500 draws of the sampling uncertainty and the parameter uncertainty, we then estimate the complete set of local regressions. For each variance-covariance matrix of each of the local regressions, we sample 5 times.

We estimate the systematic component of the unexplained variance in two steps. First, we compute a robust estimate of the stochastic uncertainty using the bootstrap samples described above. Second, we subtract this estimate of stochastic variance from the total observed variance of the residuals. This yields an estimate of the combination of variance due to non-sampling error and systematic variation in the expected value of the maternal death rate. Although this quantity is an over-estimate of the systematic variance, we nevertheless use it for the final stage of the uncertainty analysis.

This procedure generates 2,500 predictions of each MMR and number of maternal deaths. We use the full distribution of these values to compute all quantities of interest such as global, regional or national deaths and MMRs and rates of change.

References

Hengl, T, G Heuvelink, and A Stein. 2004. "A Generic Framework for Spatial Prediction of Soil Variables Based on Regression-Kriging." *Geoderma* 120 (1-2): 75–93.

Hudson, G, and H Wackernagel. 1994. "Mapping Temperature Using Kriging with External Drift: Theory and an Example From Scotland." *International Journal of Climatology*.

Knotters, M, D J Brus, and J H Oude Voshaar. 1995. “A Comparison of Kriging, Co-Kriging and Kriging Combined with Regression for Spatial Interpolation of Horizon Depth with Censored Observations.” *Geoderma* 67 (3-4): 227–246.

Lado, L R, D Polya, L Winkel, M Berg, and A Hegan. 2008. “Modelling Arsenic Hazard in Cambodia: a Geostatistical Approach Using Ancillary Data.” *Applied Geochemistry*.

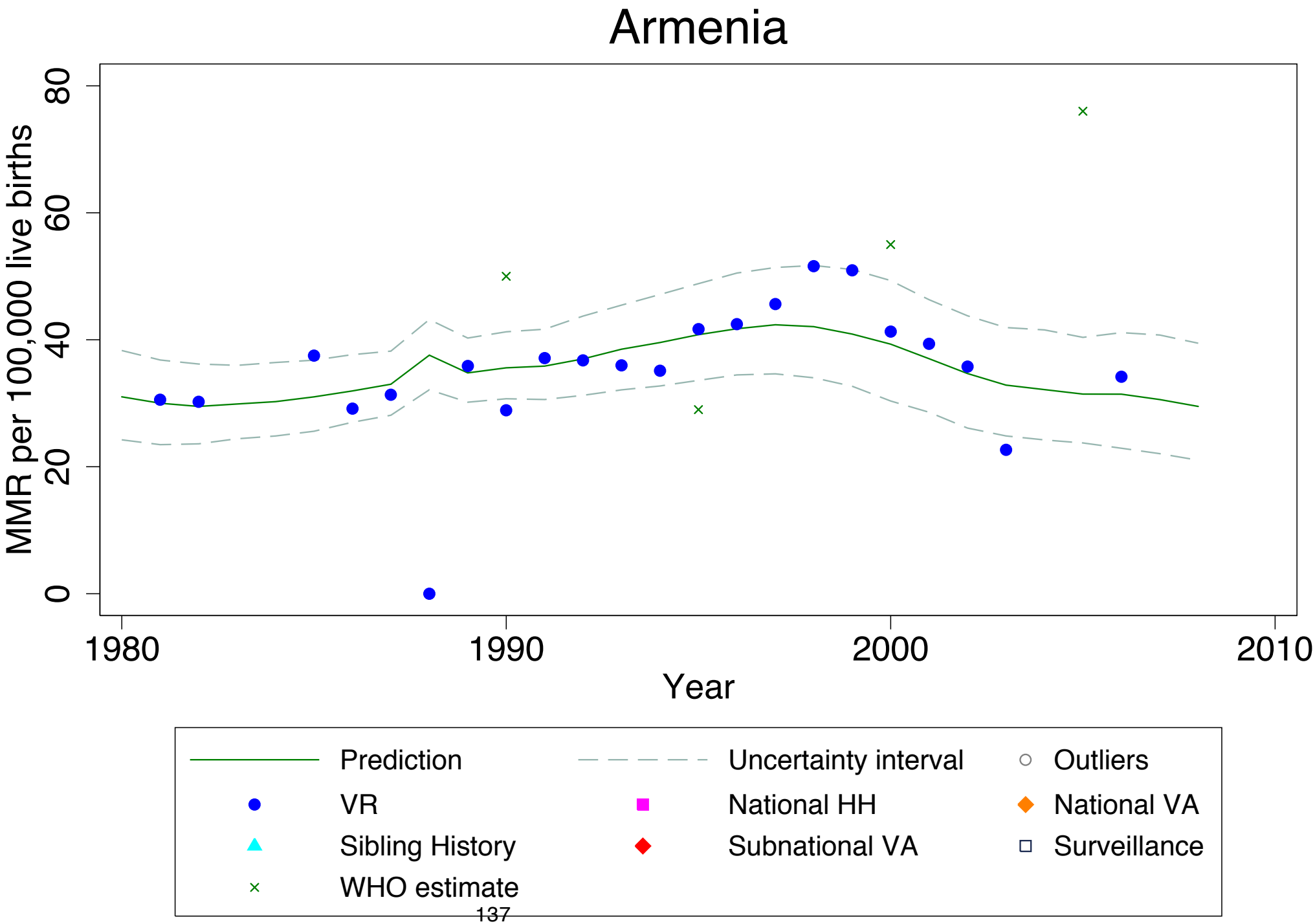
Masanja, Honorati, Don de Savigny, Paul Smithson, Joanna Schellenberg, Theopista John, Conrad Mbuya, Gabriel Upunda, et al. 2008. “Child Survival Gains in Tanzania: Analysis of Data From Demographic and Health Surveys..” *Lancet* 371 (9620) (April 12): 1276–1283. doi:10.1016/S0140-6736(08)60562-0.

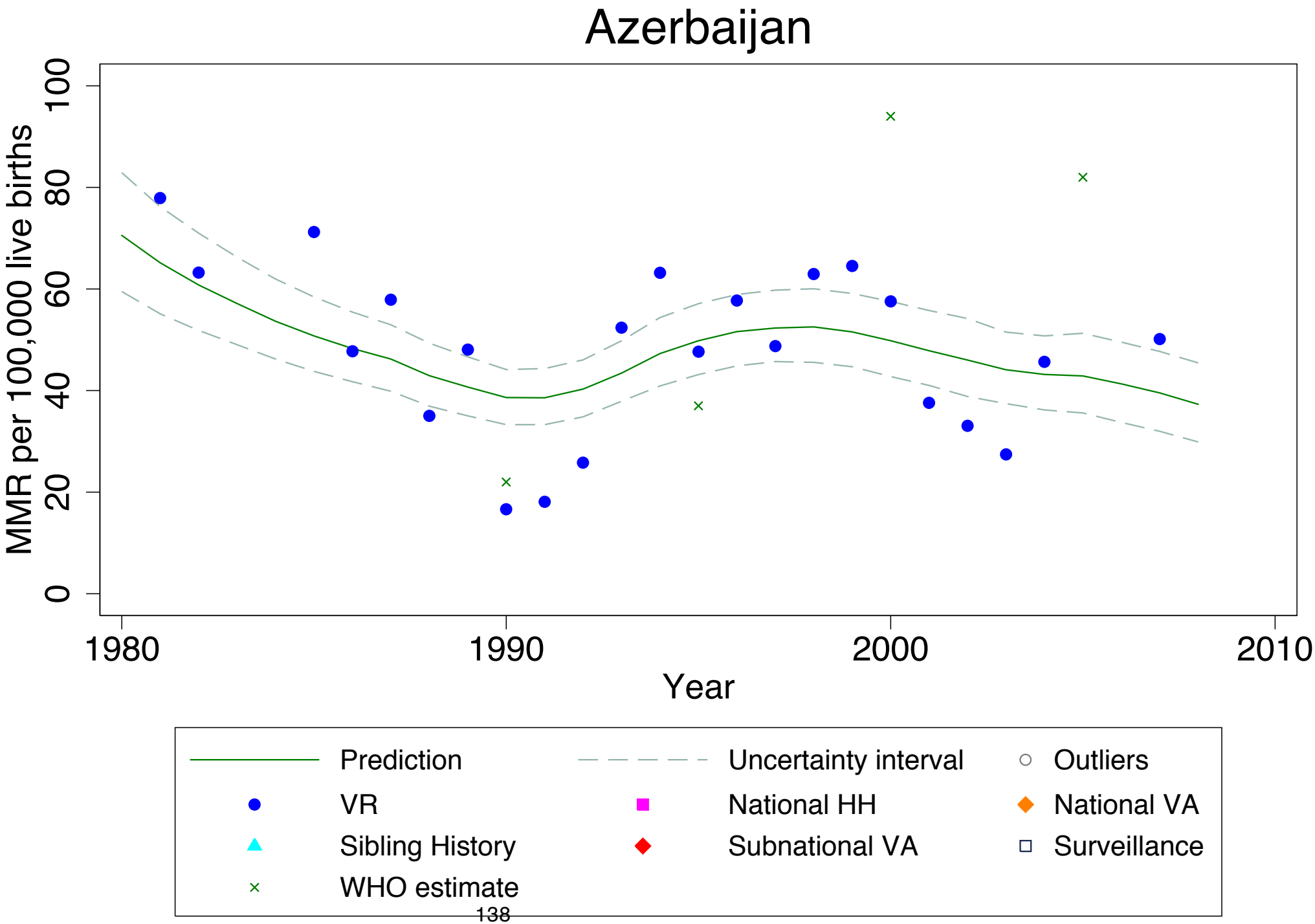
Minasny, B, and A B McBratney. 2007. “Spatial Prediction of Soil Properties Using EBLUP with the Matérn Covariance Function.” *Geoderma* 140 (4): 324–326.

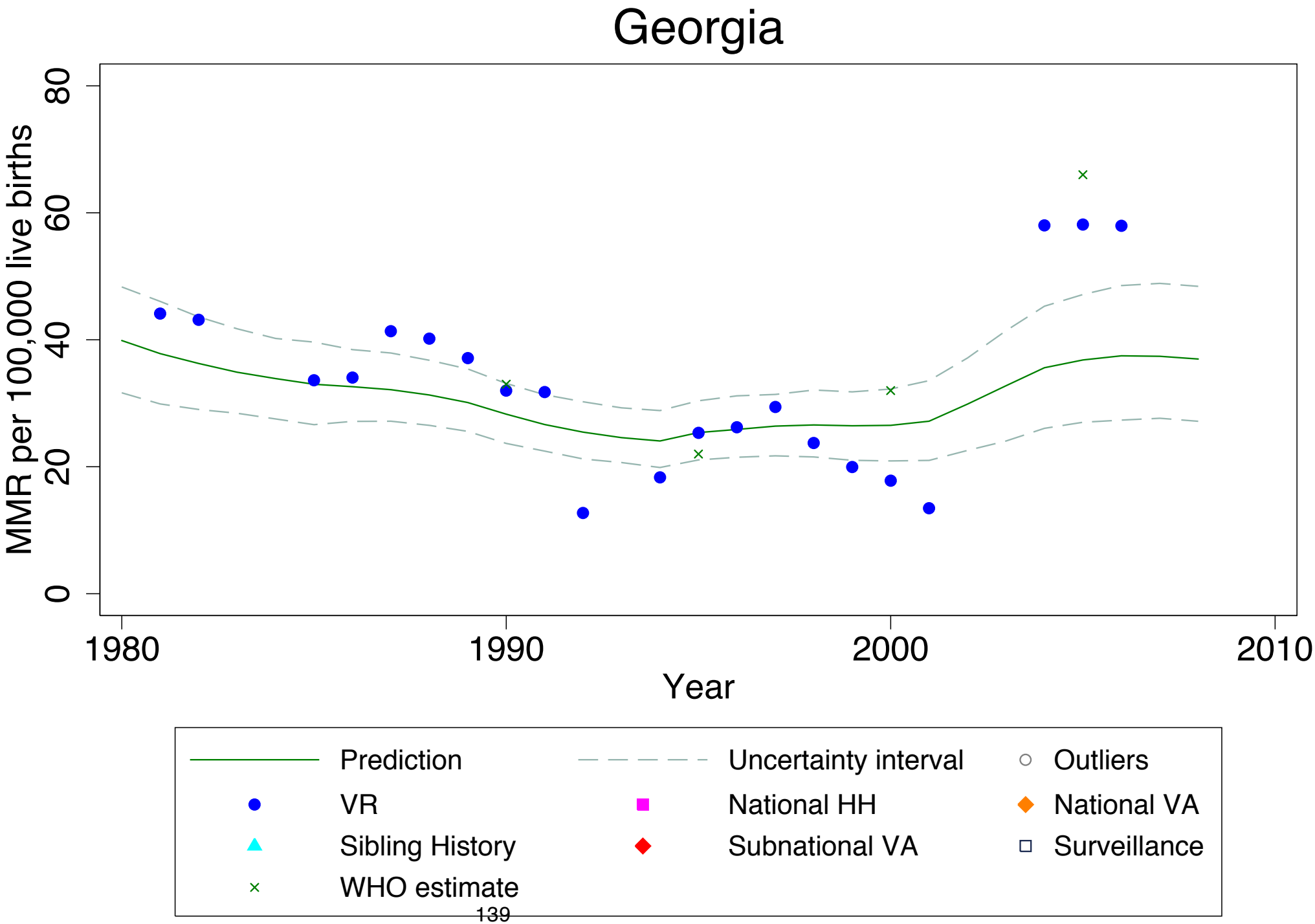
Murray, C J, T Laakso, K Shibuya, K Hill, and A D Lopez. 2007. “Can We Achieve Millennium Development Goal 4? New Analysis of Country Trends and Forecasts of Under-5 Mortality to 2015.” *Lancet* 370 (9592) (September 1): 1040–1054.

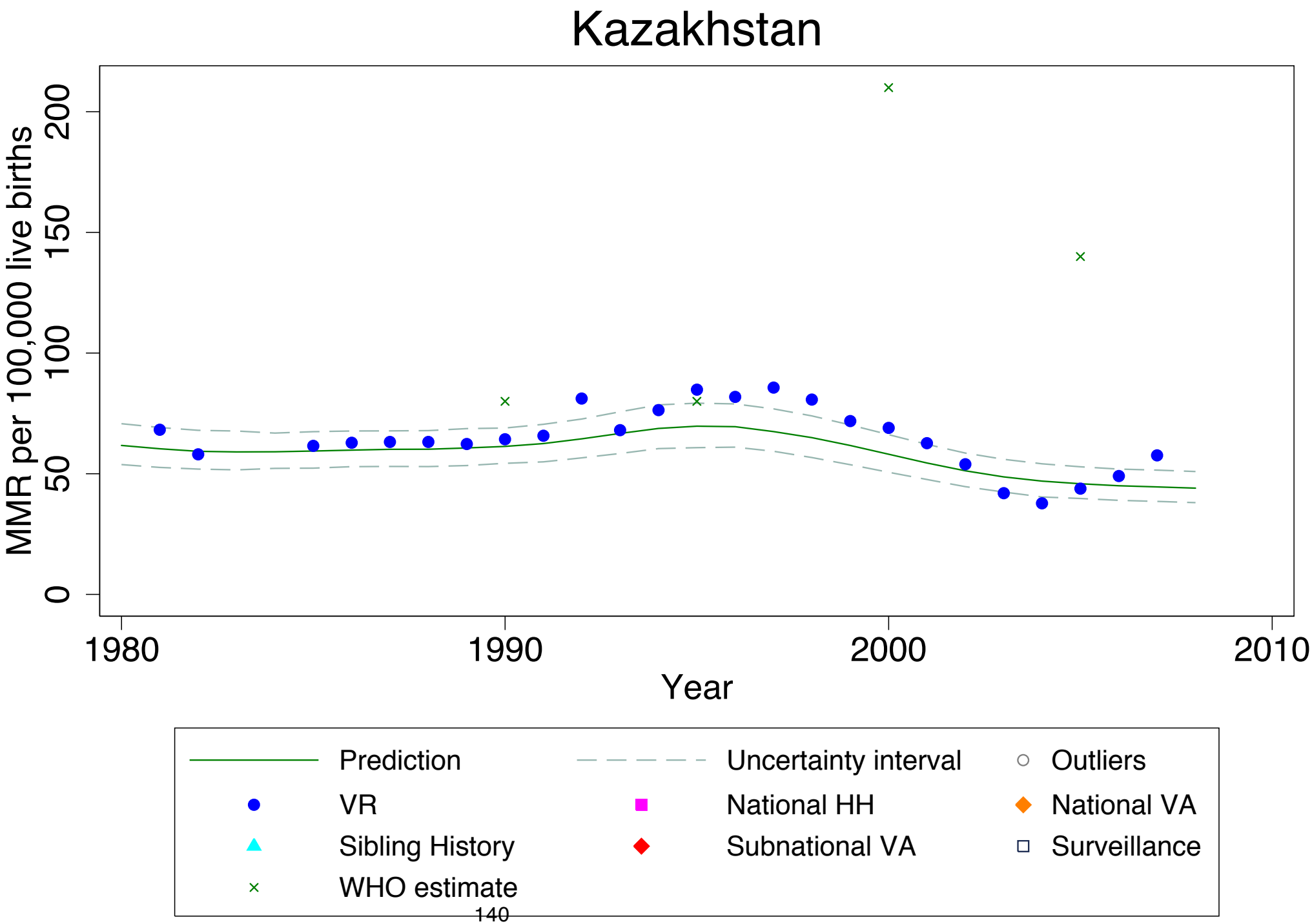
Rajaratnam, J K, J R Marcus, A Levin-Rector, A N Chalupka, H Wang, L Dwyer, M Costa, A D Lopez, and C J Murray. 2010. “Worldwide Mortality in Men and Women Aged 15-59 Years From 1970 to 2010: a Systematic Analysis.” *Lancet* 375 (9727) (May 1): 1704–1720.

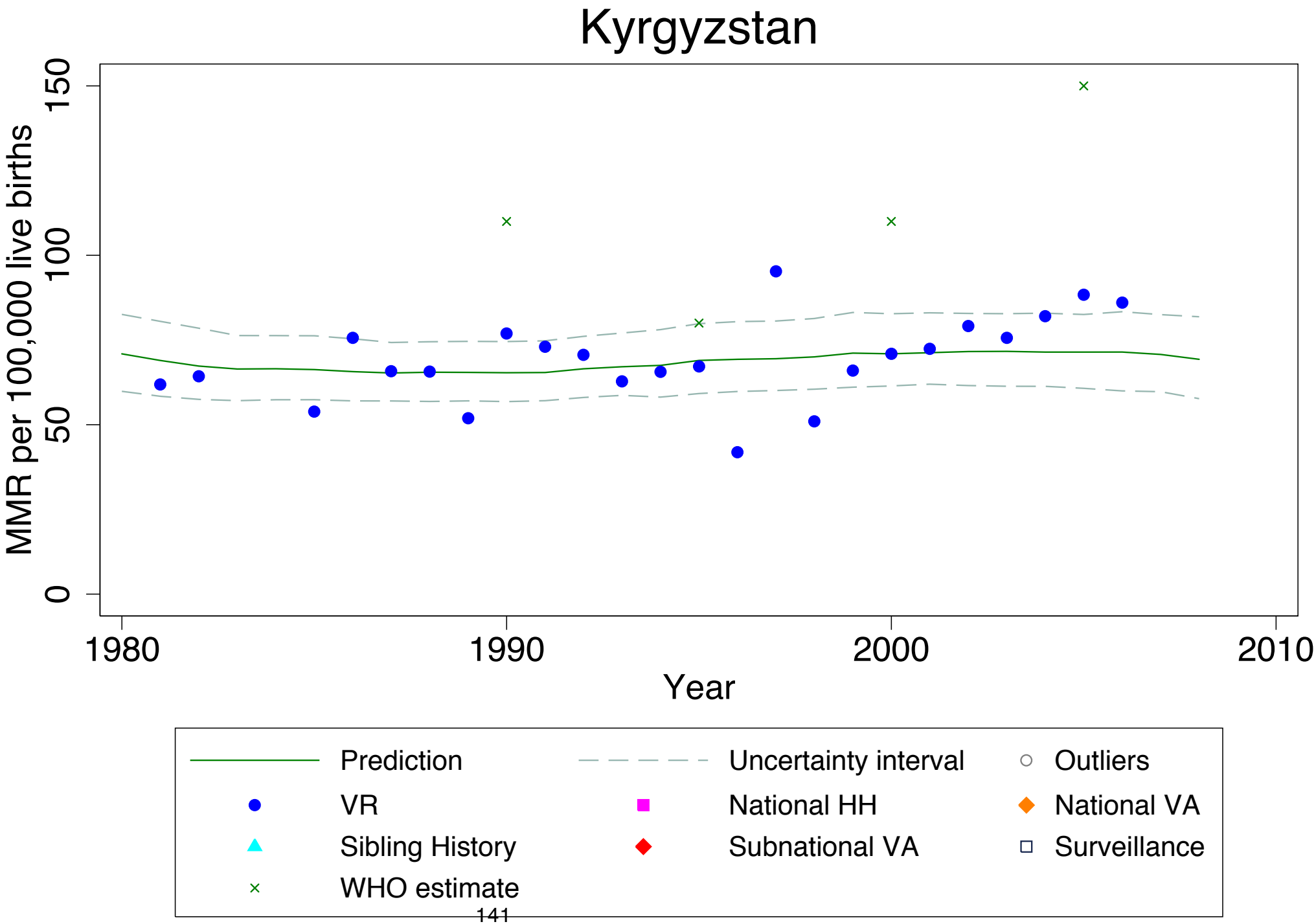
Webfigure 1. Predicted MMR per 100,000 live births with uncertainty by country

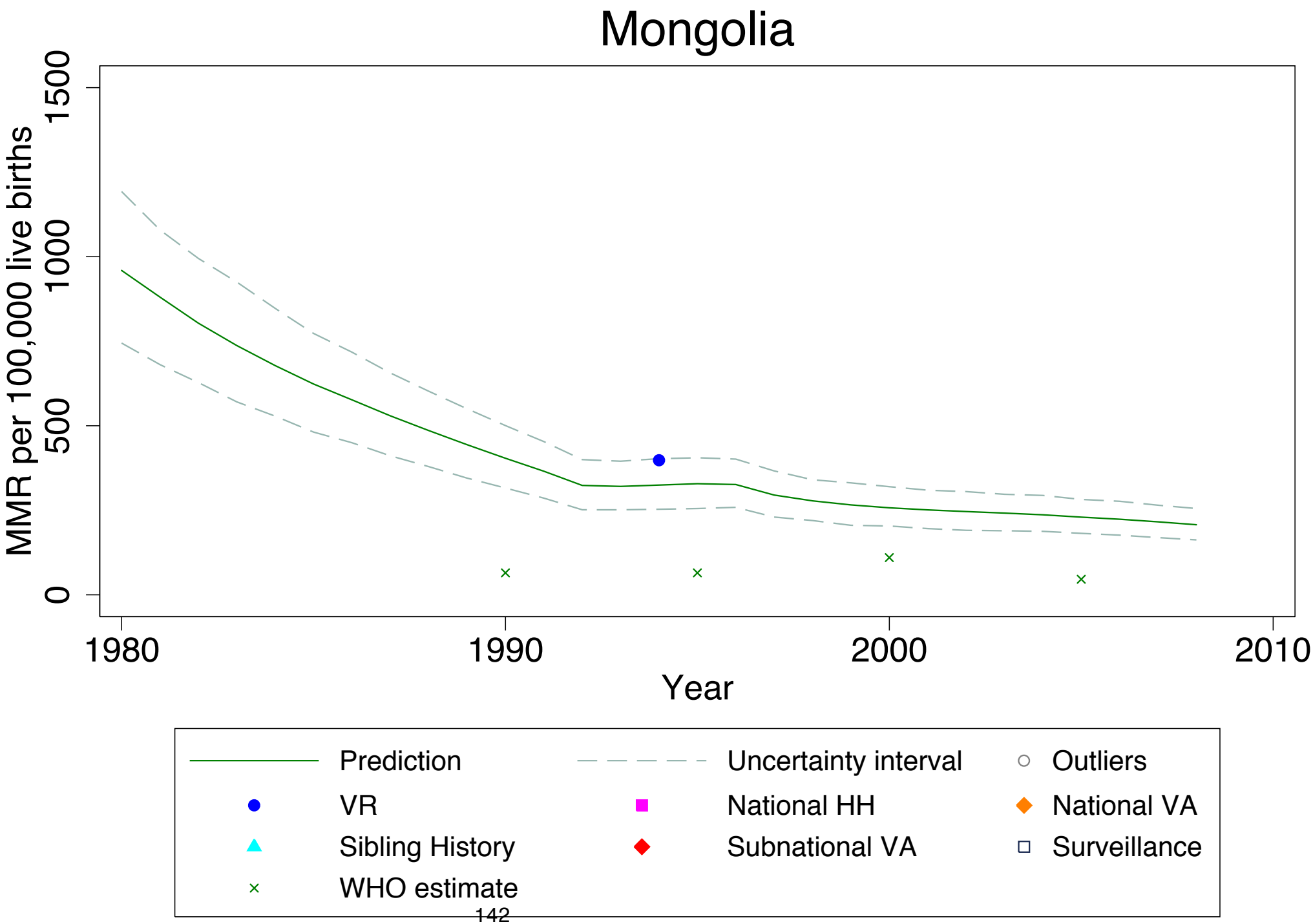

Armenia
MMR per 100,000 live births
0
20
40
60
80
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

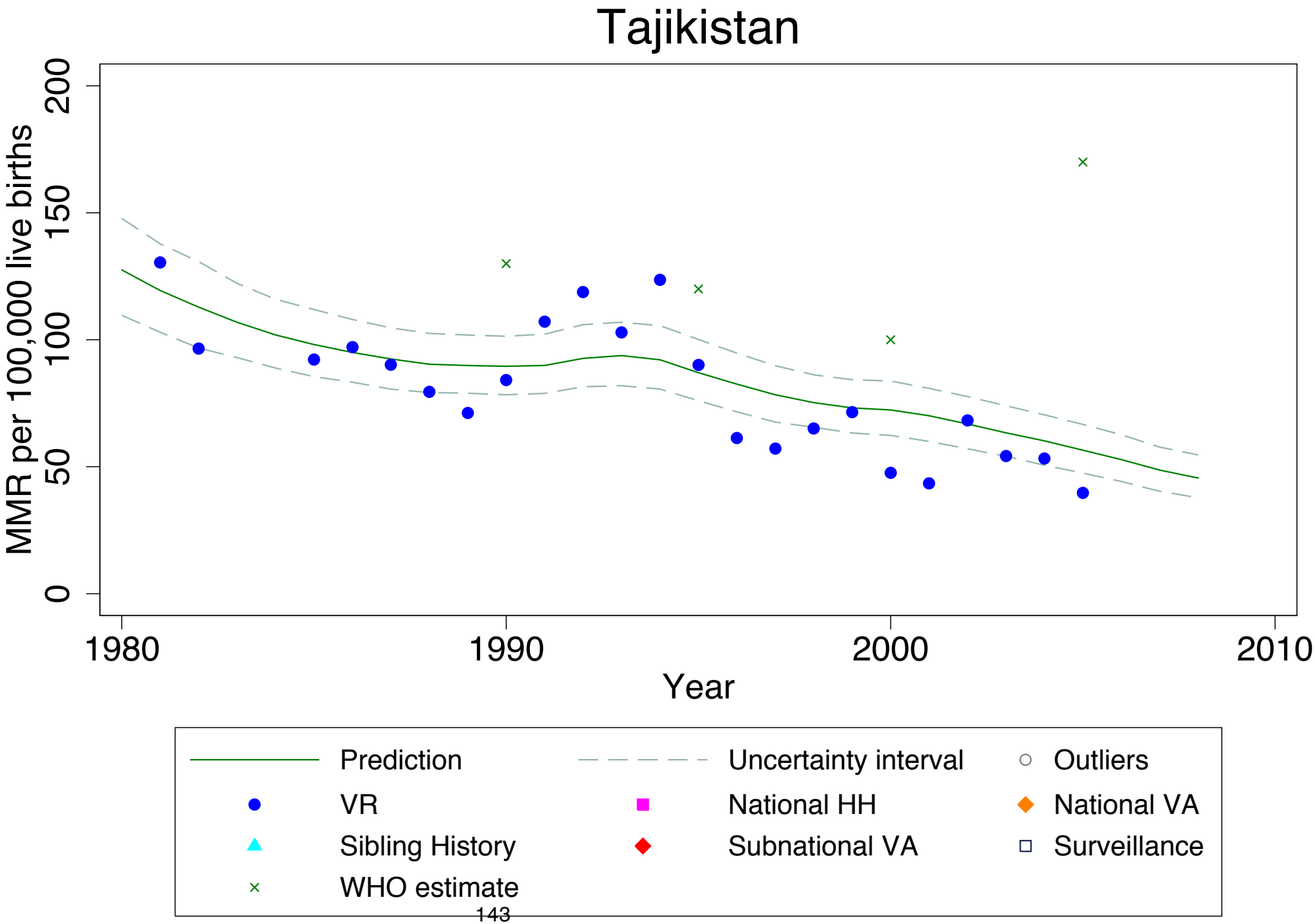

Azerbaijan
MMR per 100,000 live births
0
20
40
60
80
100
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

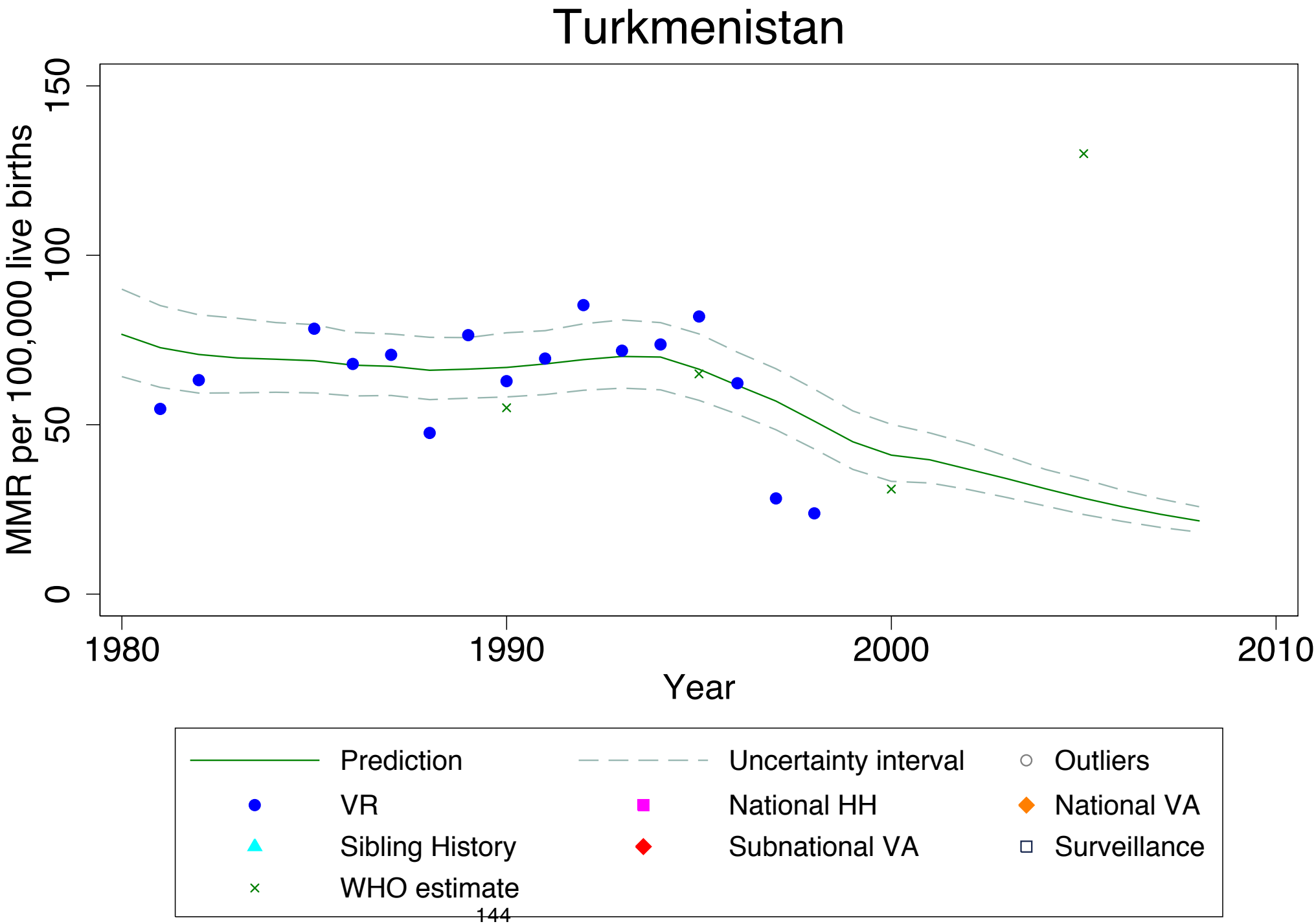

Georgia
MMR per 100,000 live births
0
20
40
60
80
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Kazakhstan
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Kyrgyzstan
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Mongolia
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Tajikistan
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Turkmenistan
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
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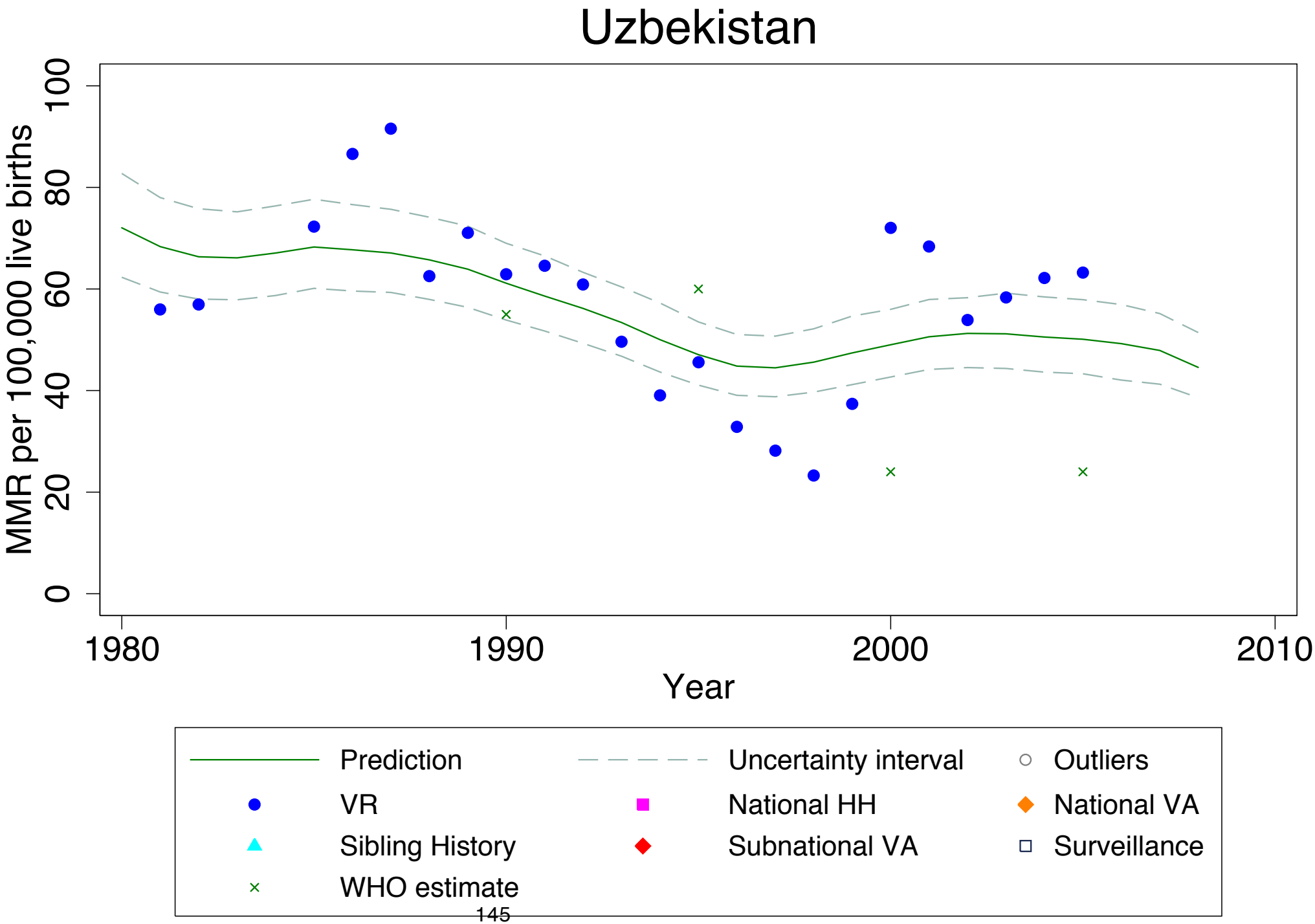
Uzbekistan
MMR per 100,000 live births
0
20
40
60
80
100
1980
1990
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2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
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Sibling History
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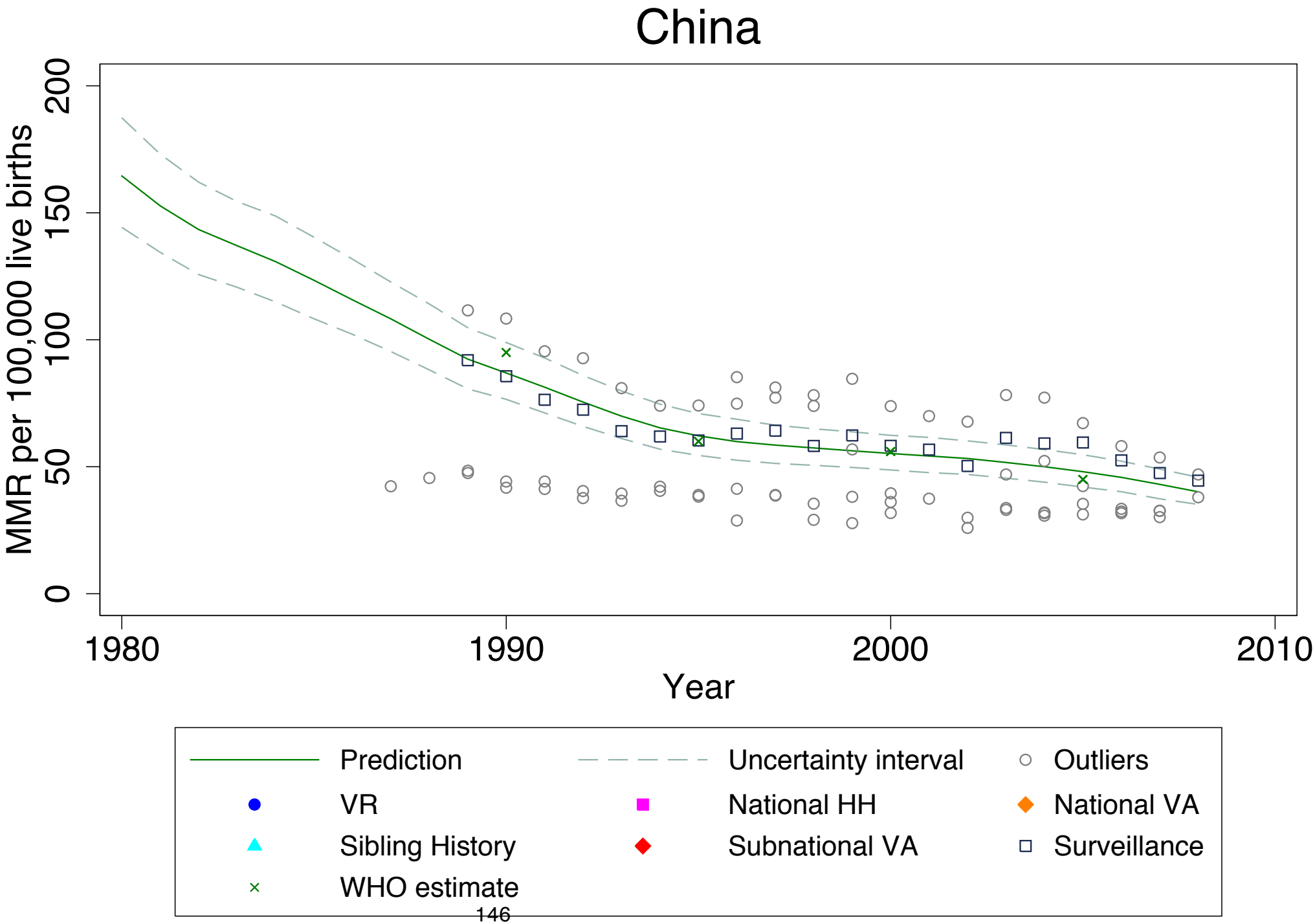
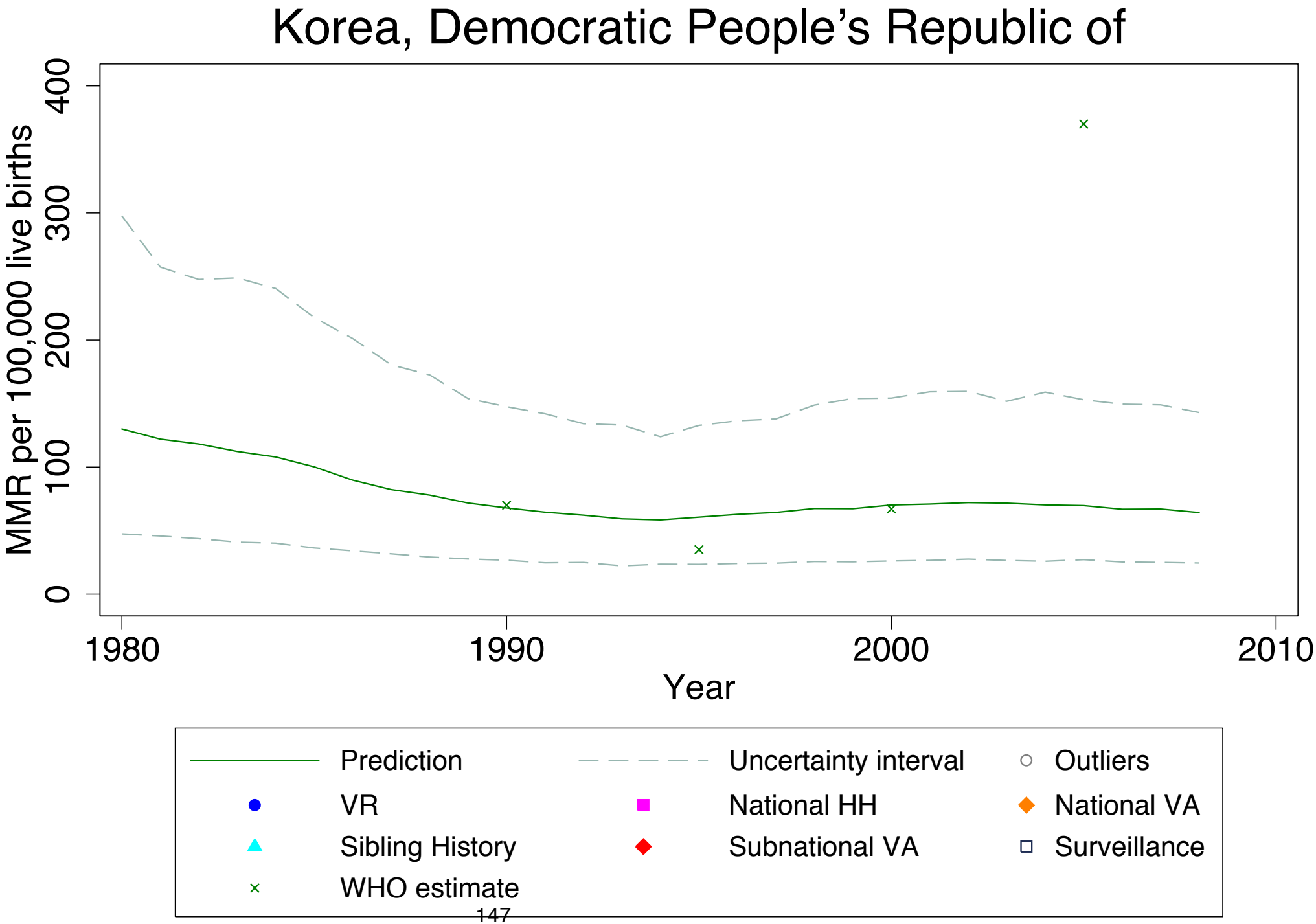
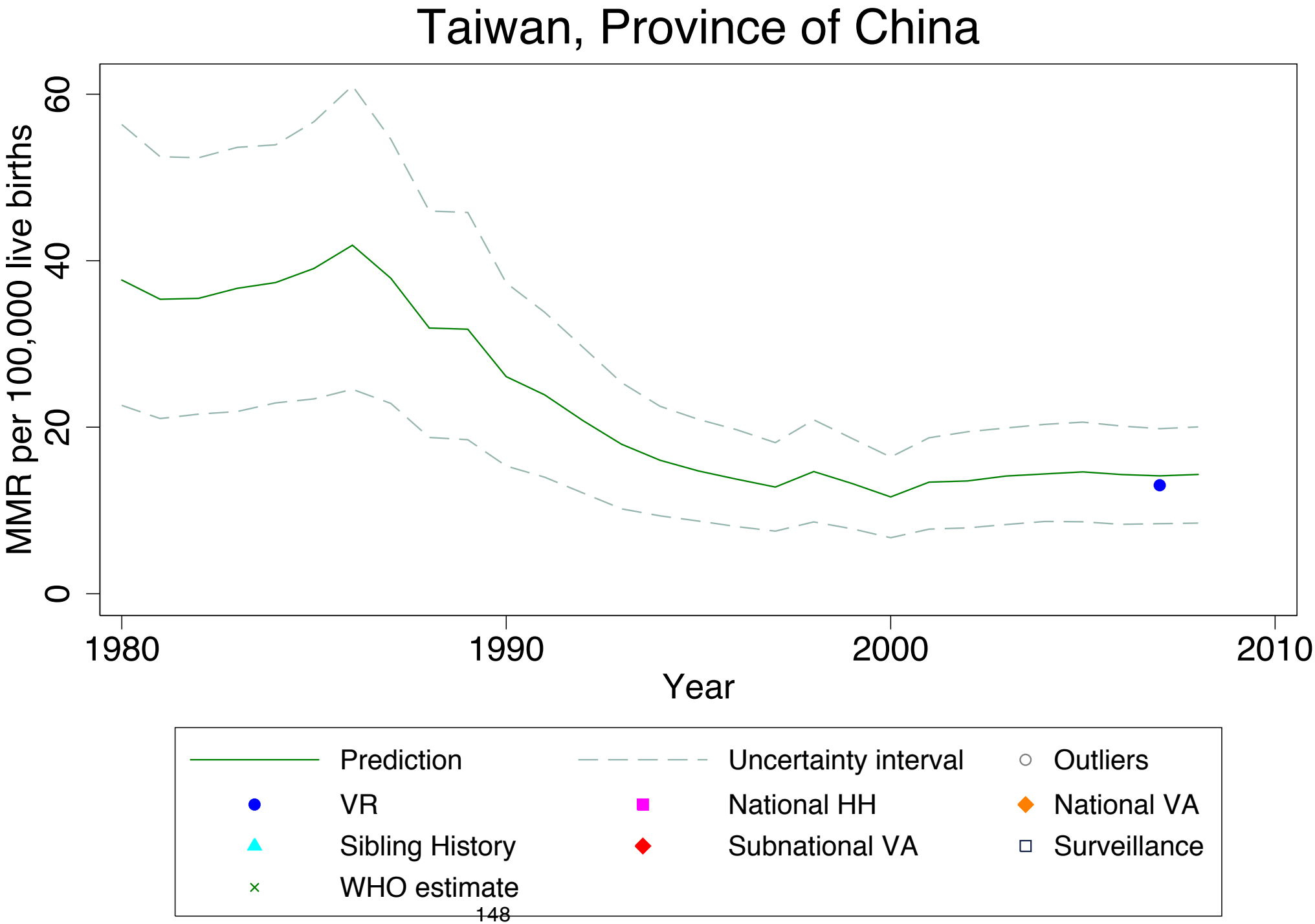
Surveillance
WHO estimate


China
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Korea, Democratic People's Republic of
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Taiwan, Province of China
MMR per 100,000 live births
0
20
40
60
1980
1990
2000
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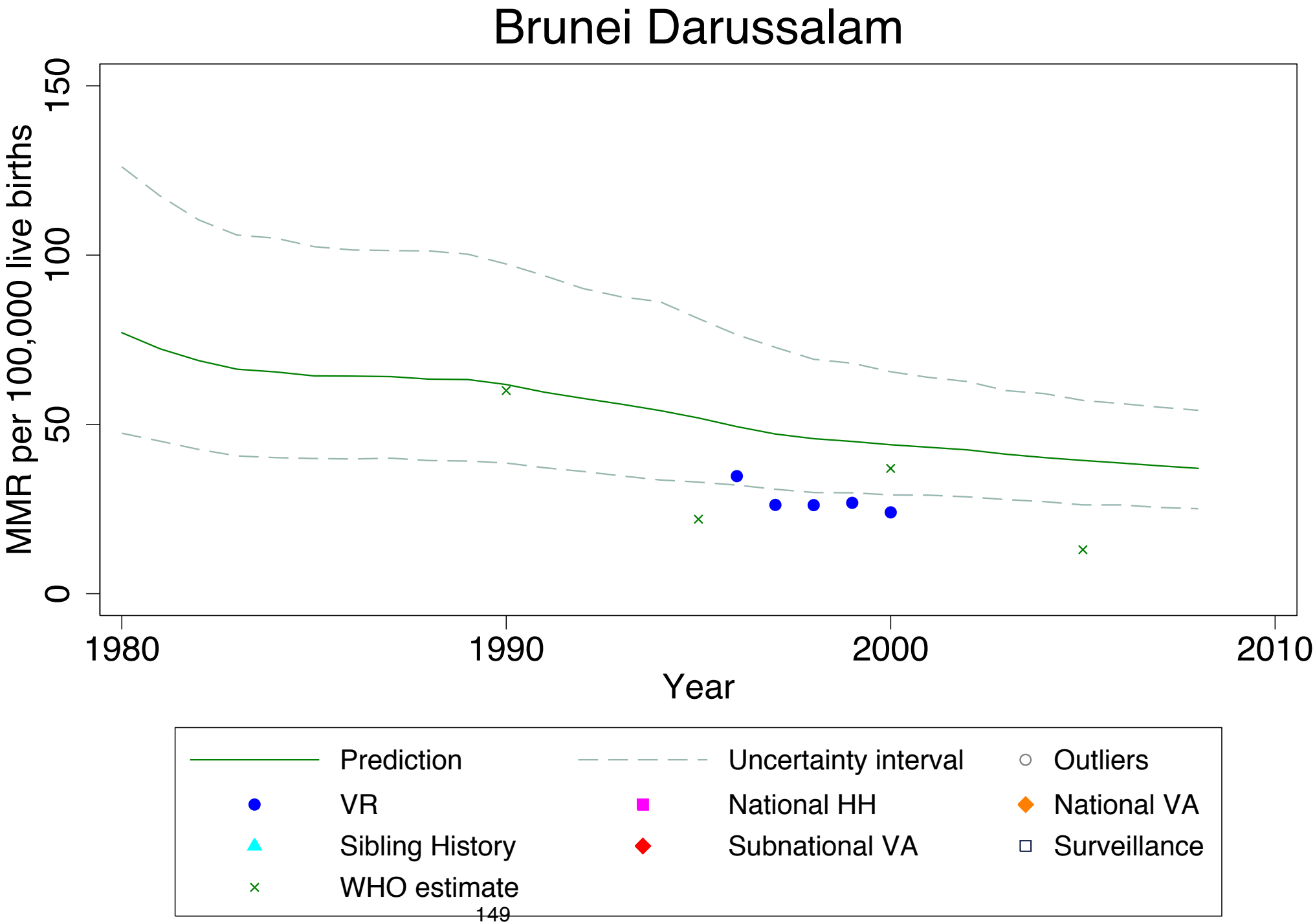
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Brunei Darussalam
MMR per 100,000 live births
0
50
100
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1990
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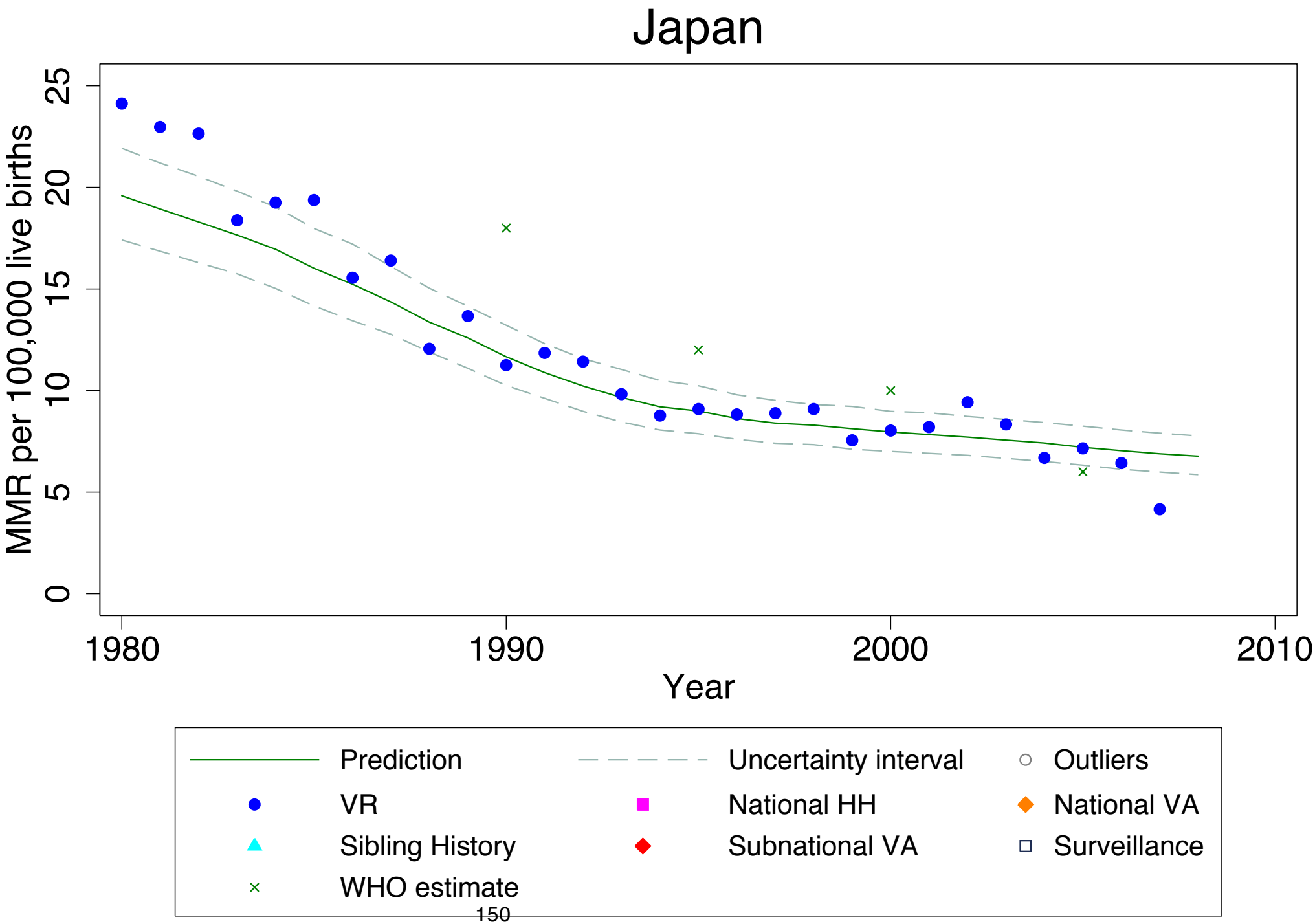
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Japan
MMR per 100,000 live births
0
5
10
15
20
25
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
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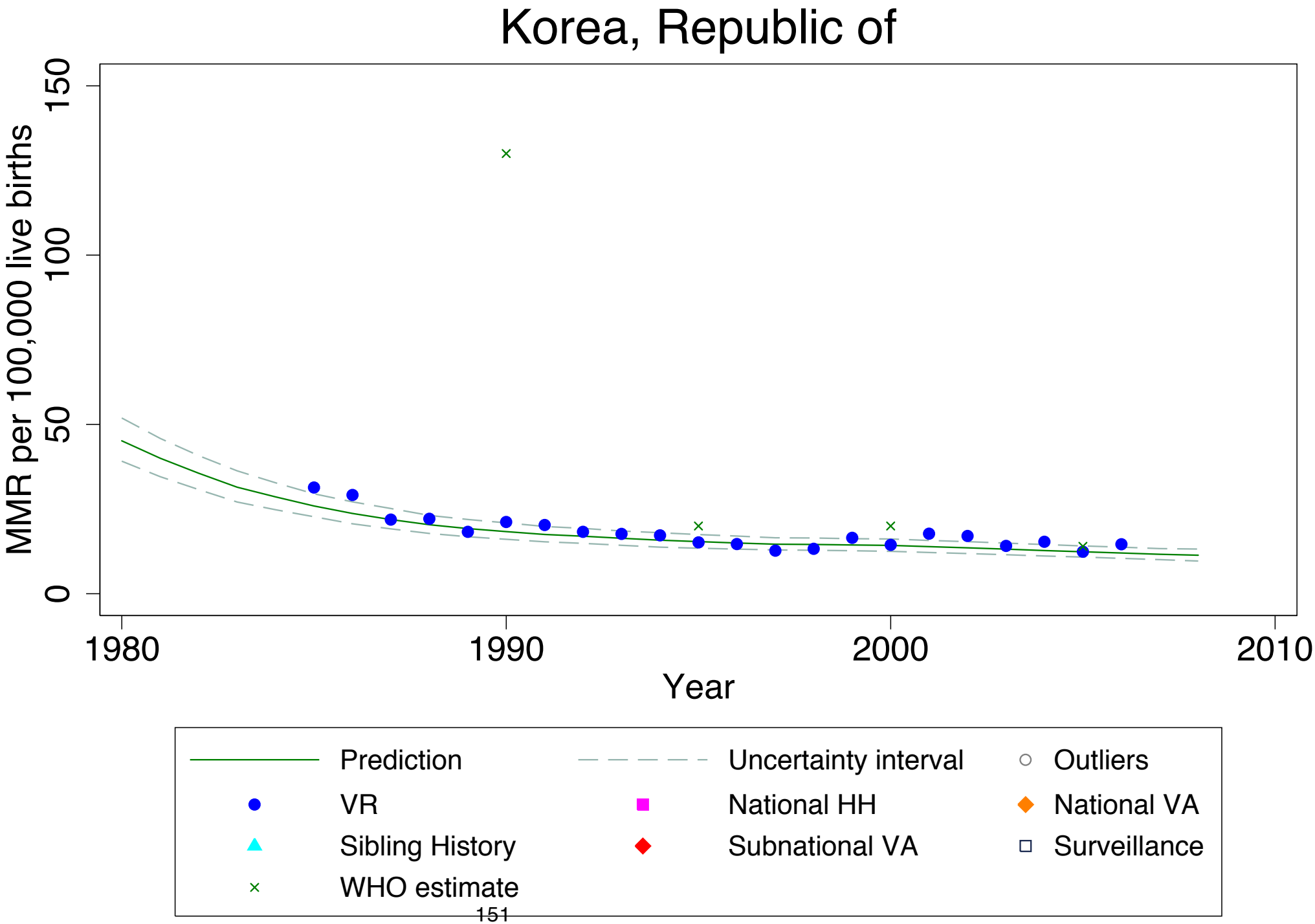
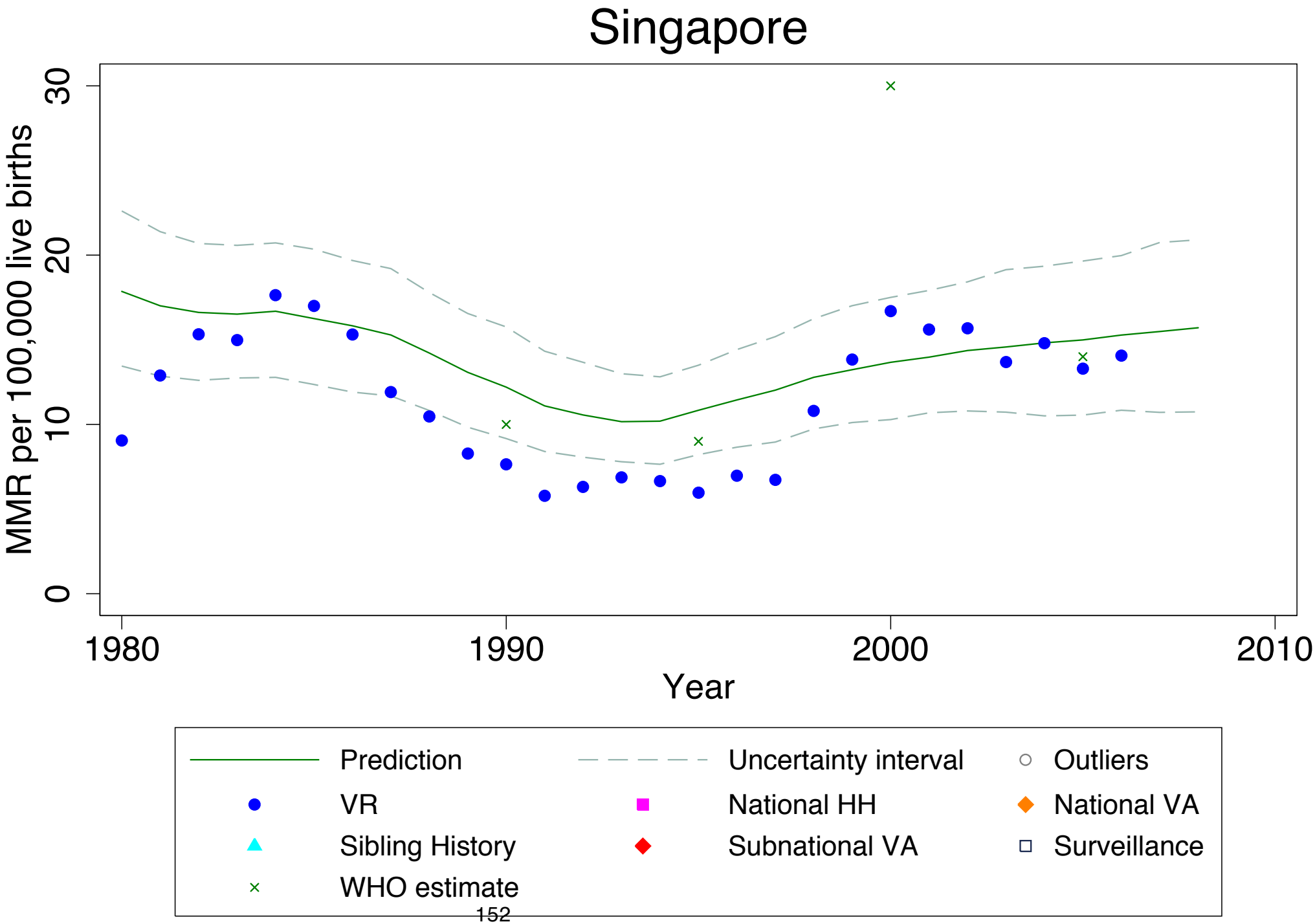
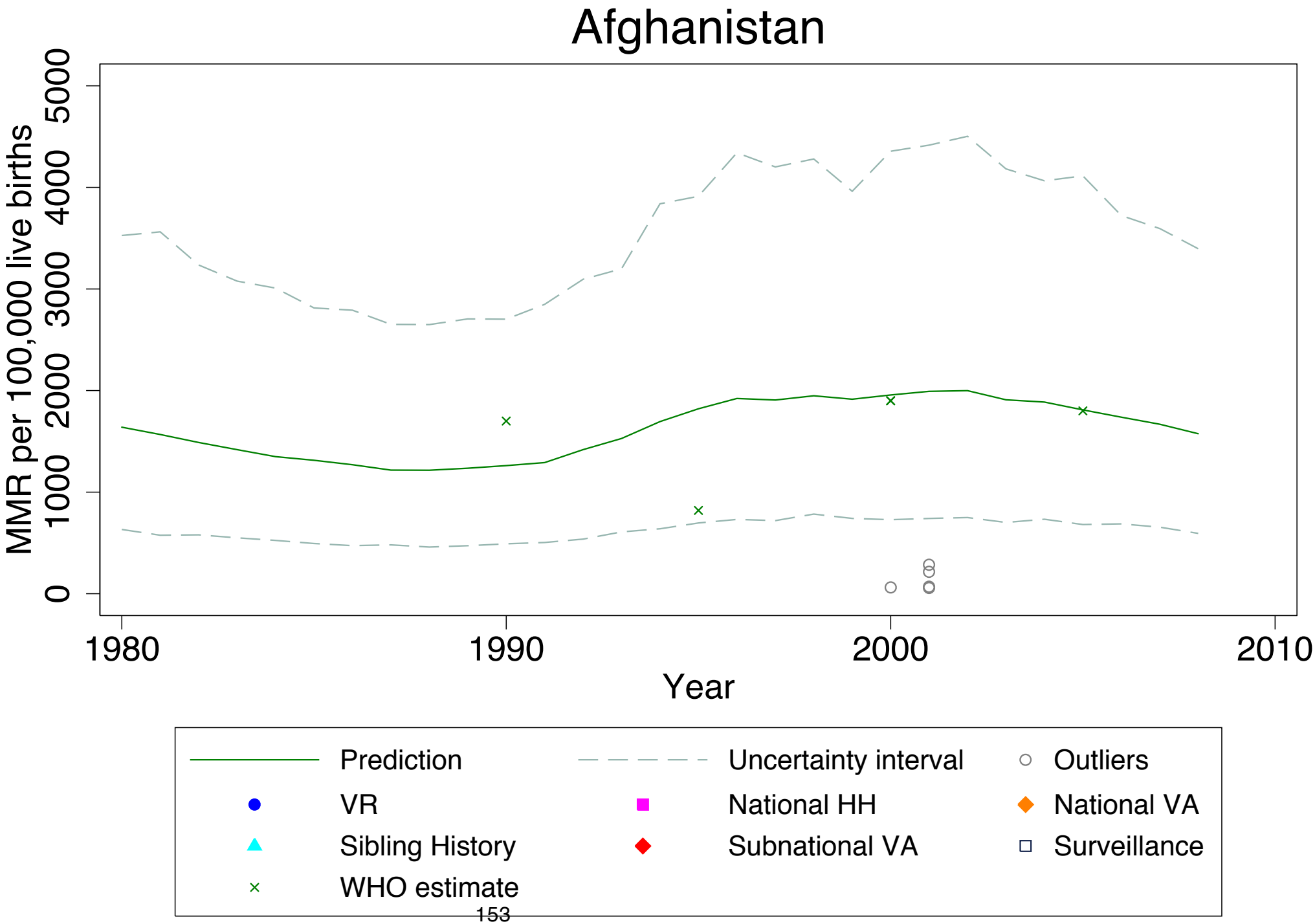
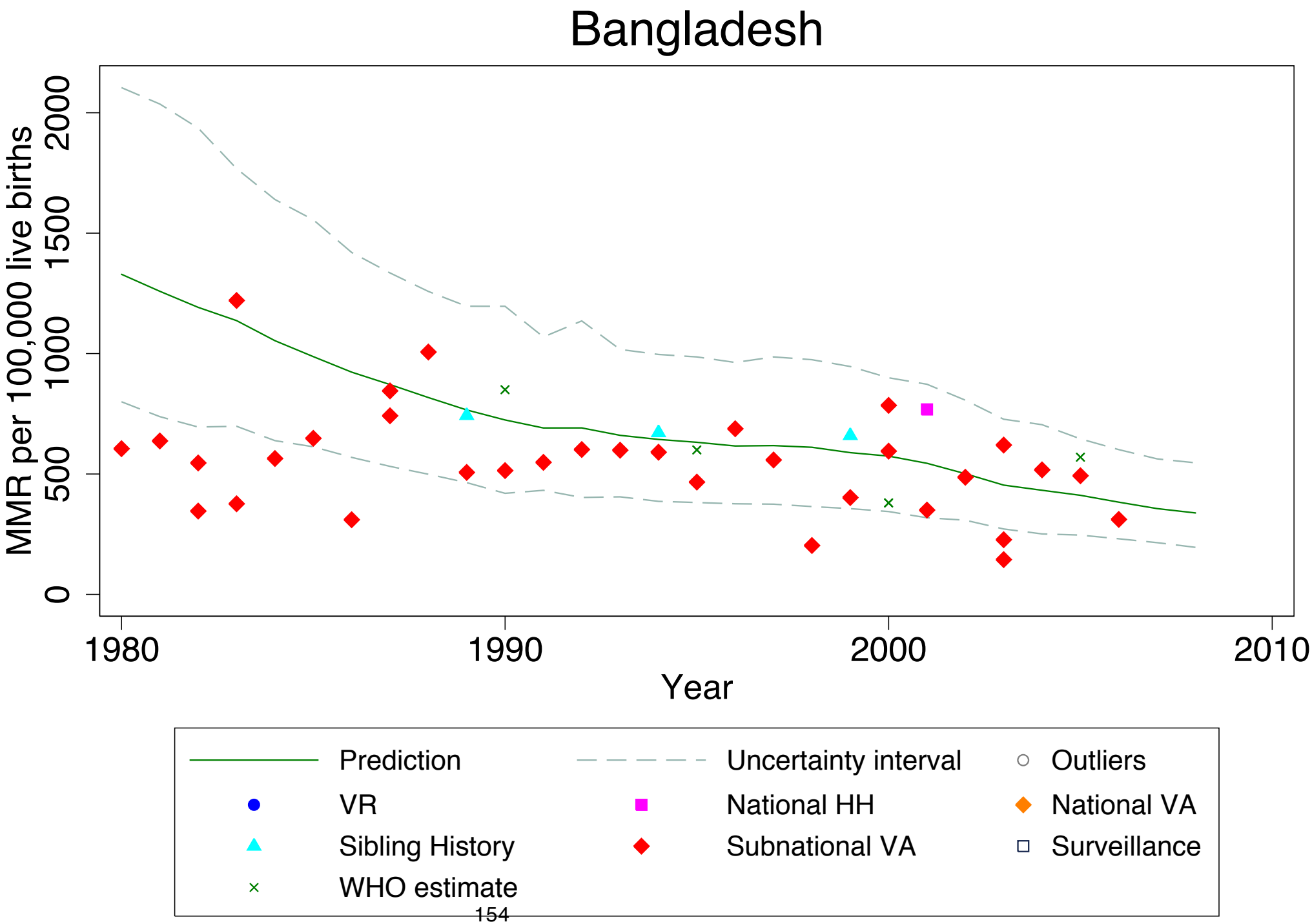
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Korea, Republic of
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Singapore
MMR per 100,000 live births
0
10
20
30
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Afghanistan
MMR per 100,000 live births
0
1000
2000
3000
4000
5000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Bangladesh
MMR per 100,000 live births
0
500
1000
1500
2000
1980
1990
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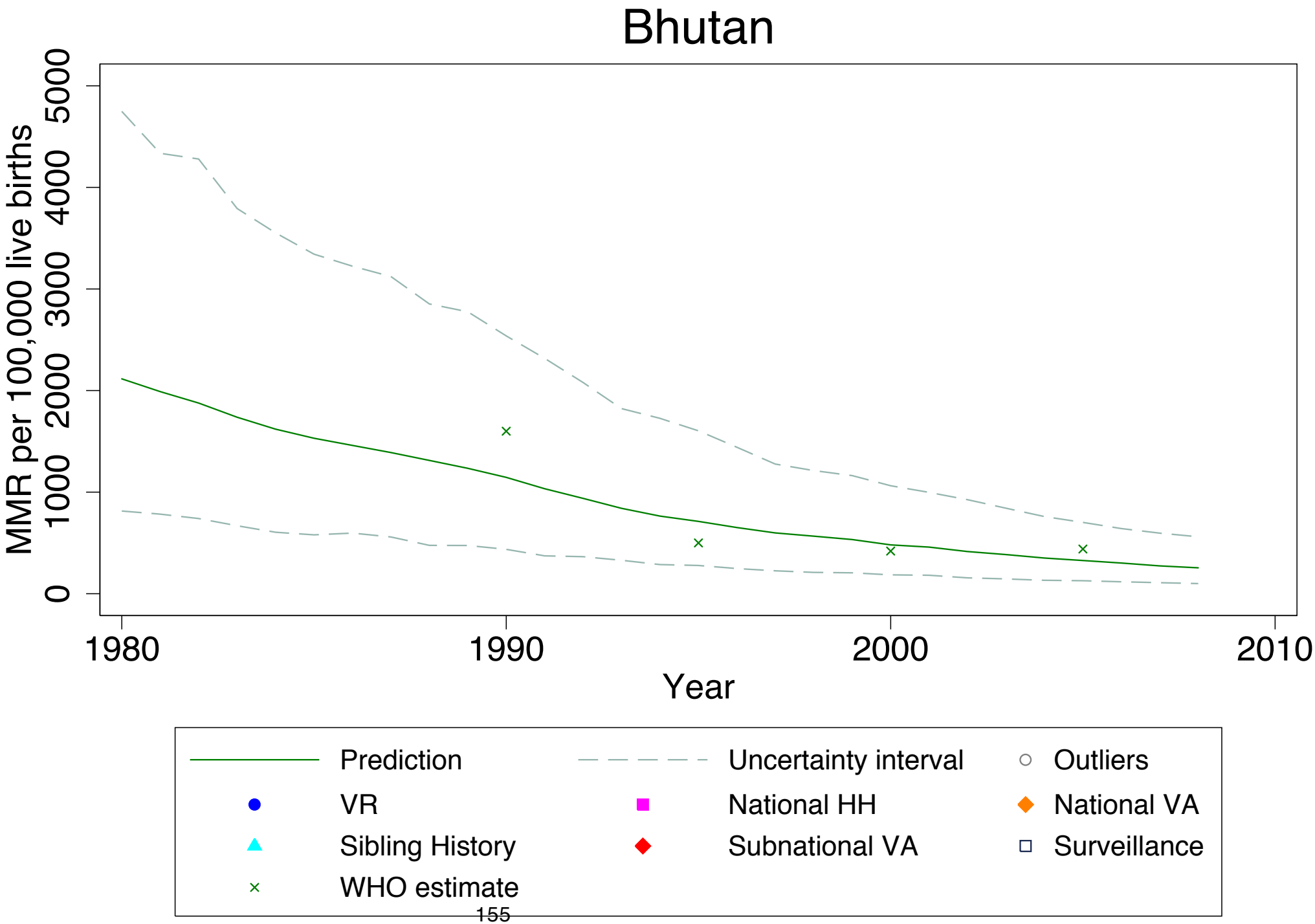
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Bhutan
MMR per 100,000 live births
0
1000
2000
3000
4000
5000
1980
1990
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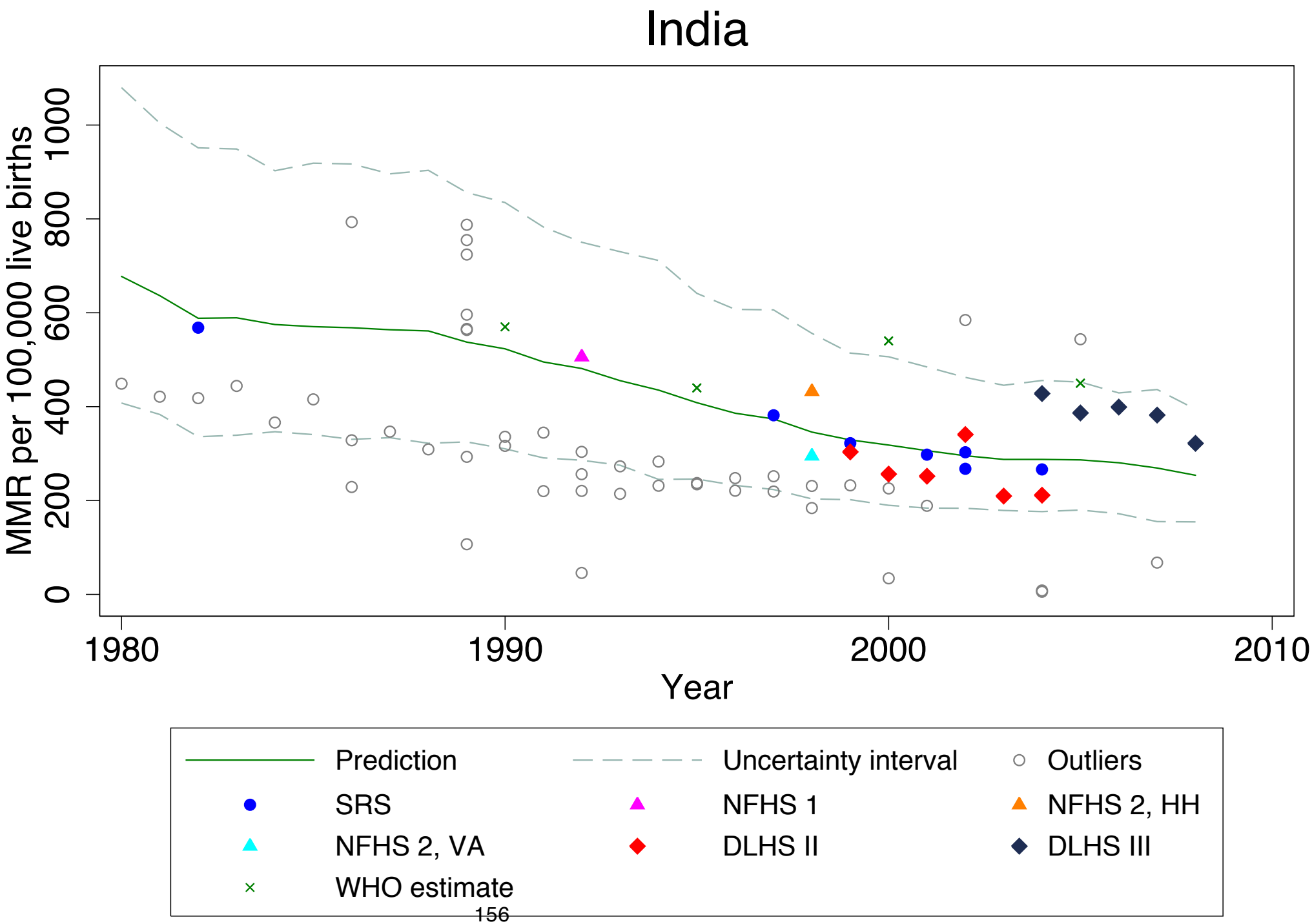
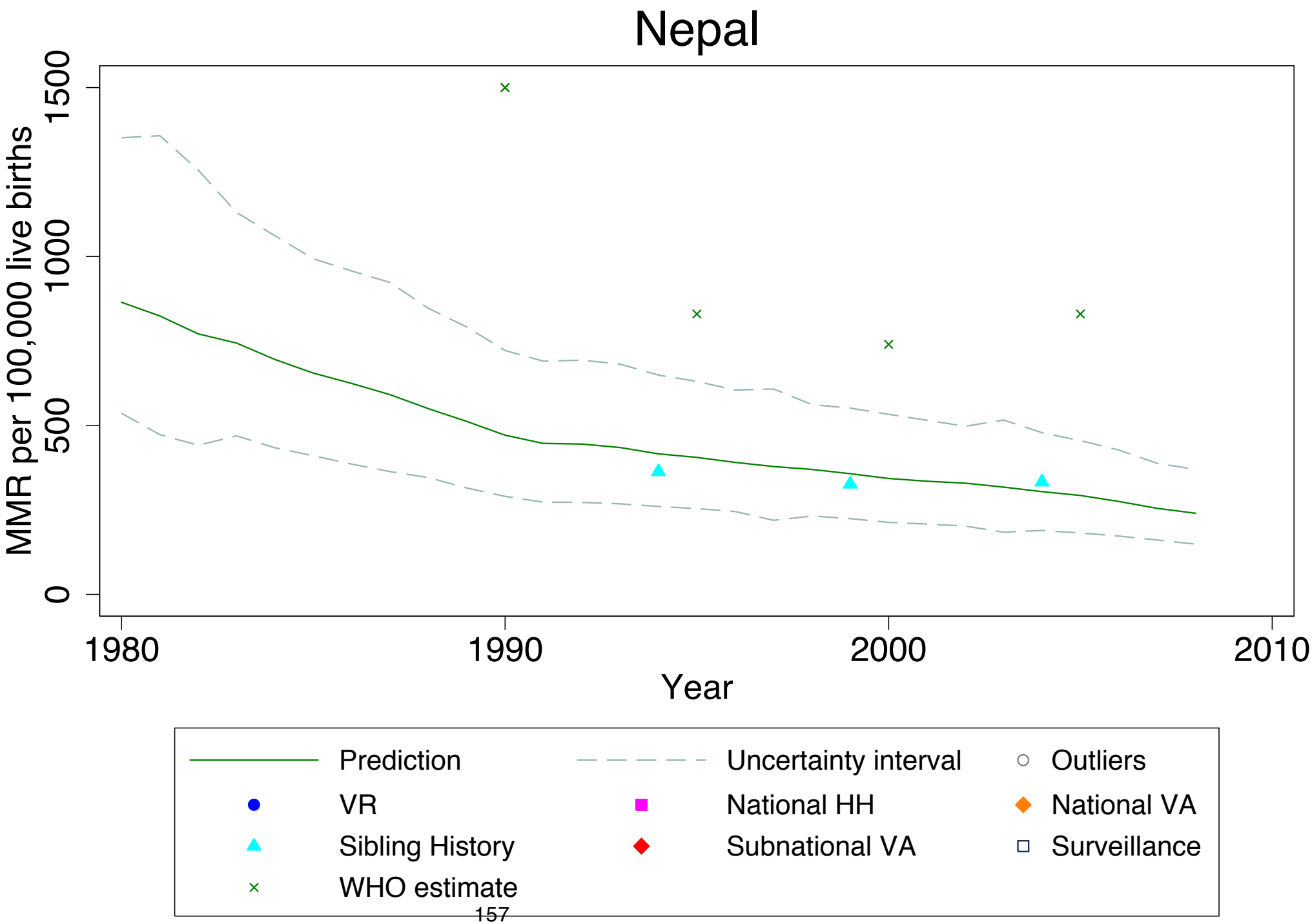
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


India
MMR per 100,000 live births
0
200
400
600
800
1000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
SRS
NFHS 1
NFHS 2, HH
NFHS 2, VA
DLHS II
DLHS III
WHO estimate


Nepal
MMR per 100,000 live births
0
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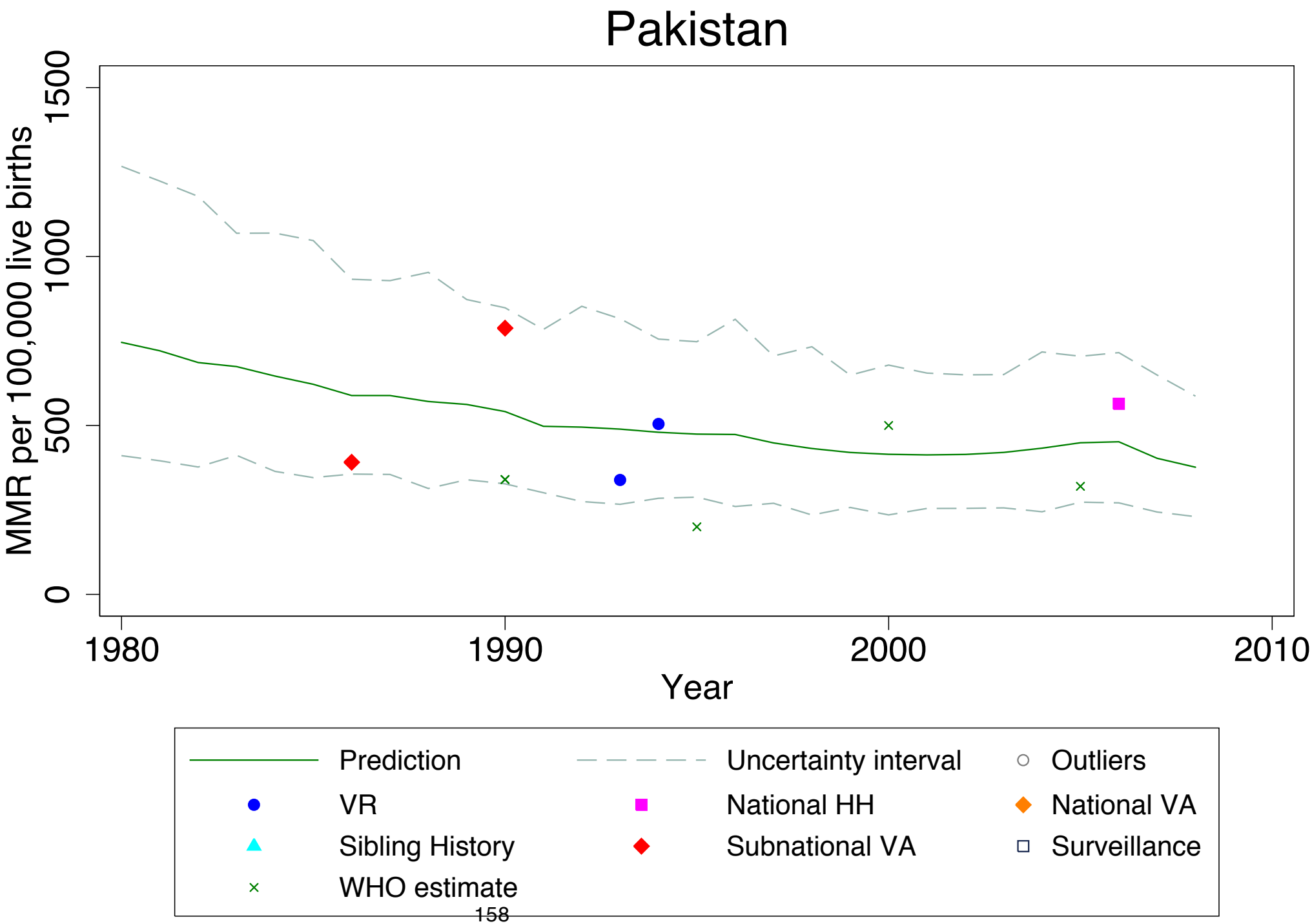
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Pakistan
MMR per 100,000 live births
0
500
1000
1500
1980
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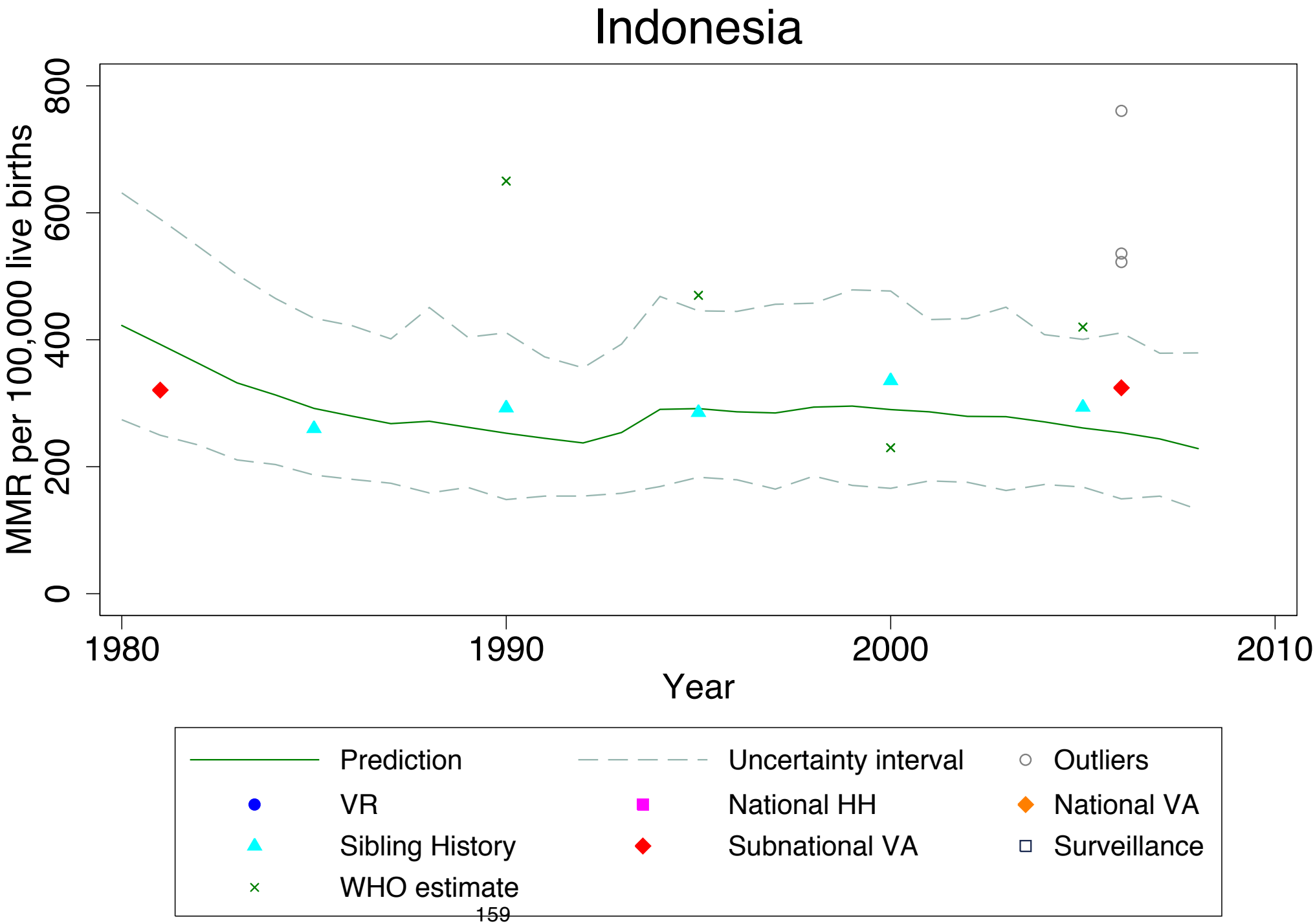
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Indonesia
MMR per 100,000 live births
0
200
400
600
800
1980
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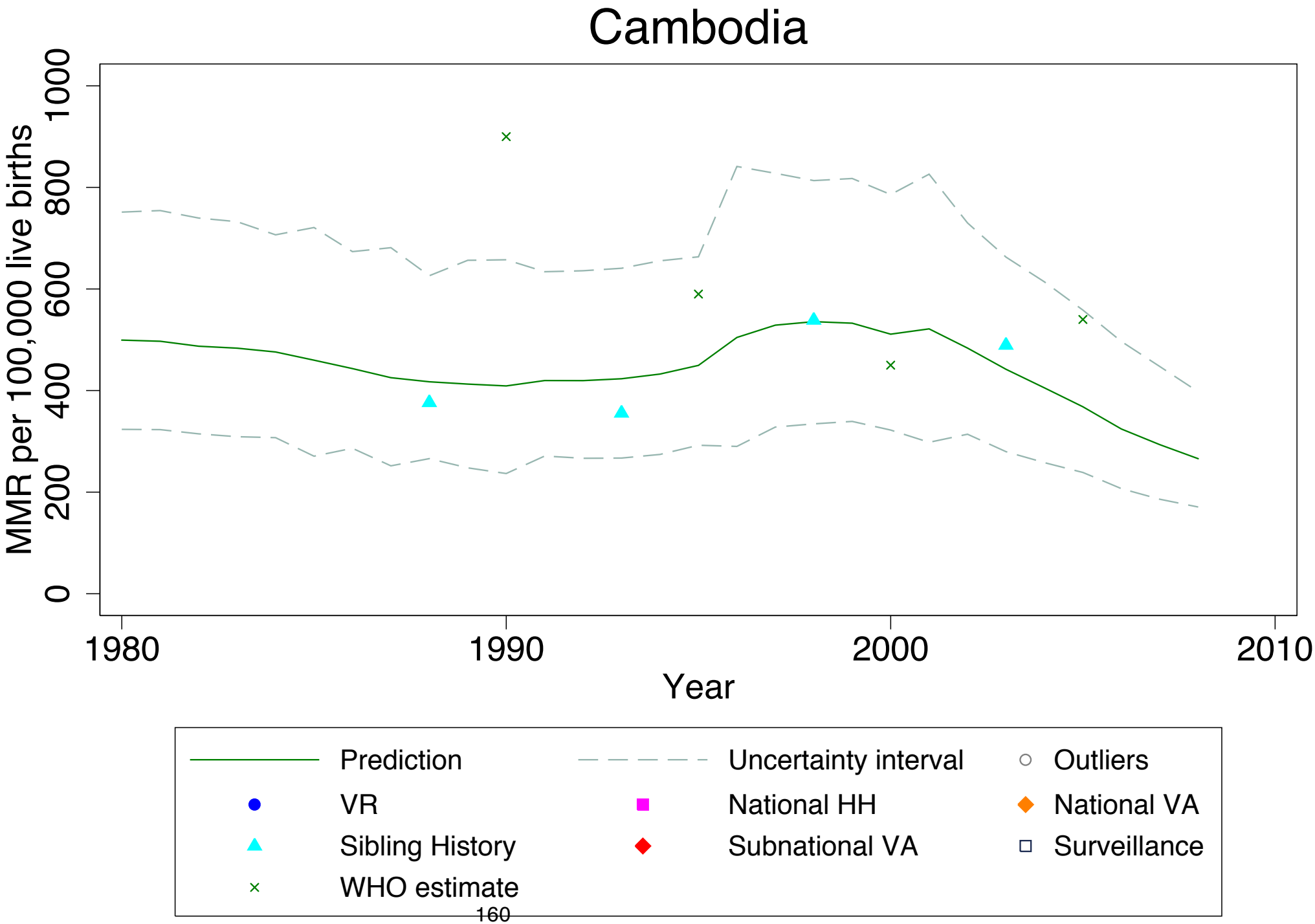
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Cambodia
MMR per 100,000 live births
0
200
400
600
800
1000
1980
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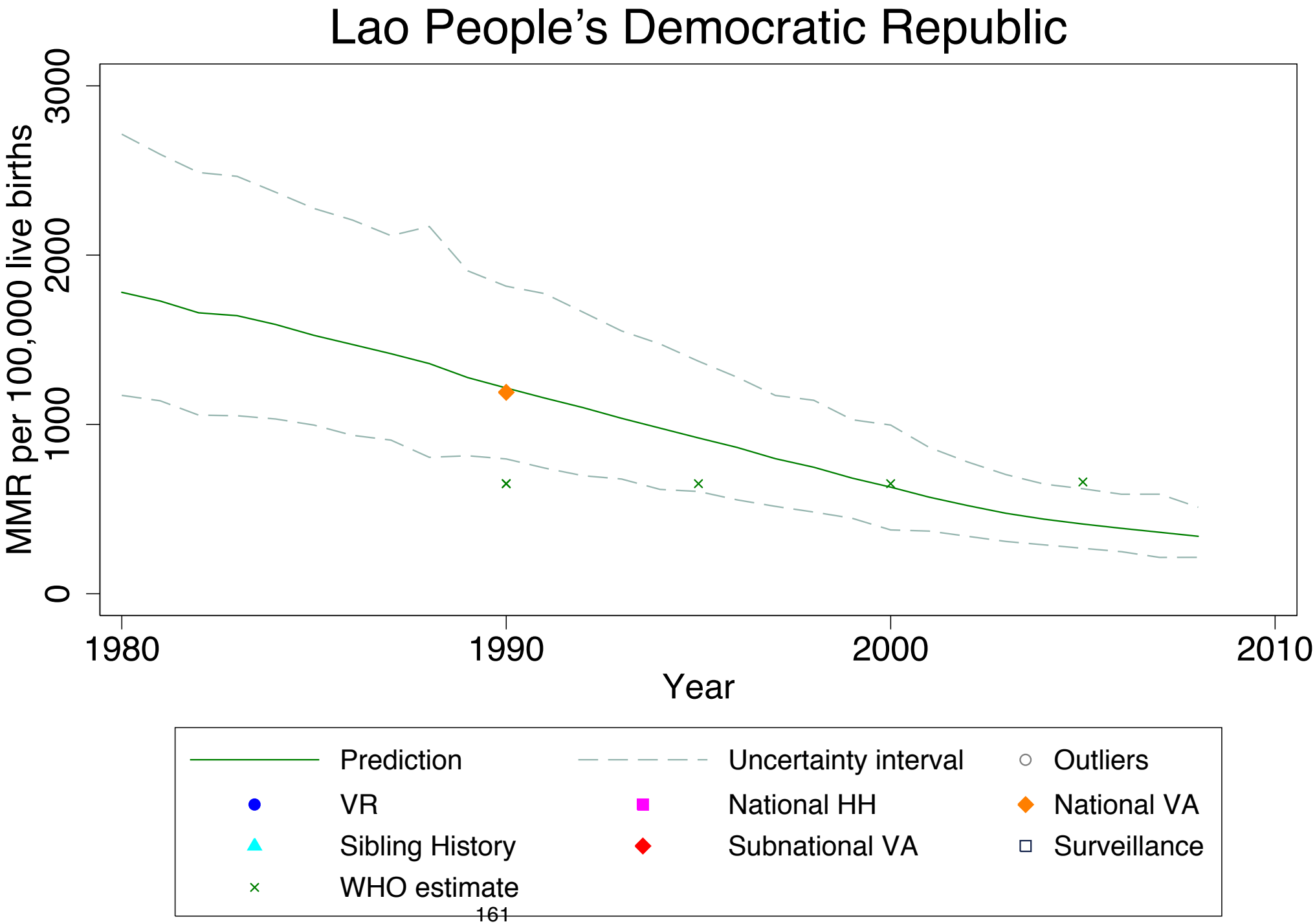
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Lao People's Democratic Republic
MMR per 100,000 live births
0
1000
2000
3000
1980
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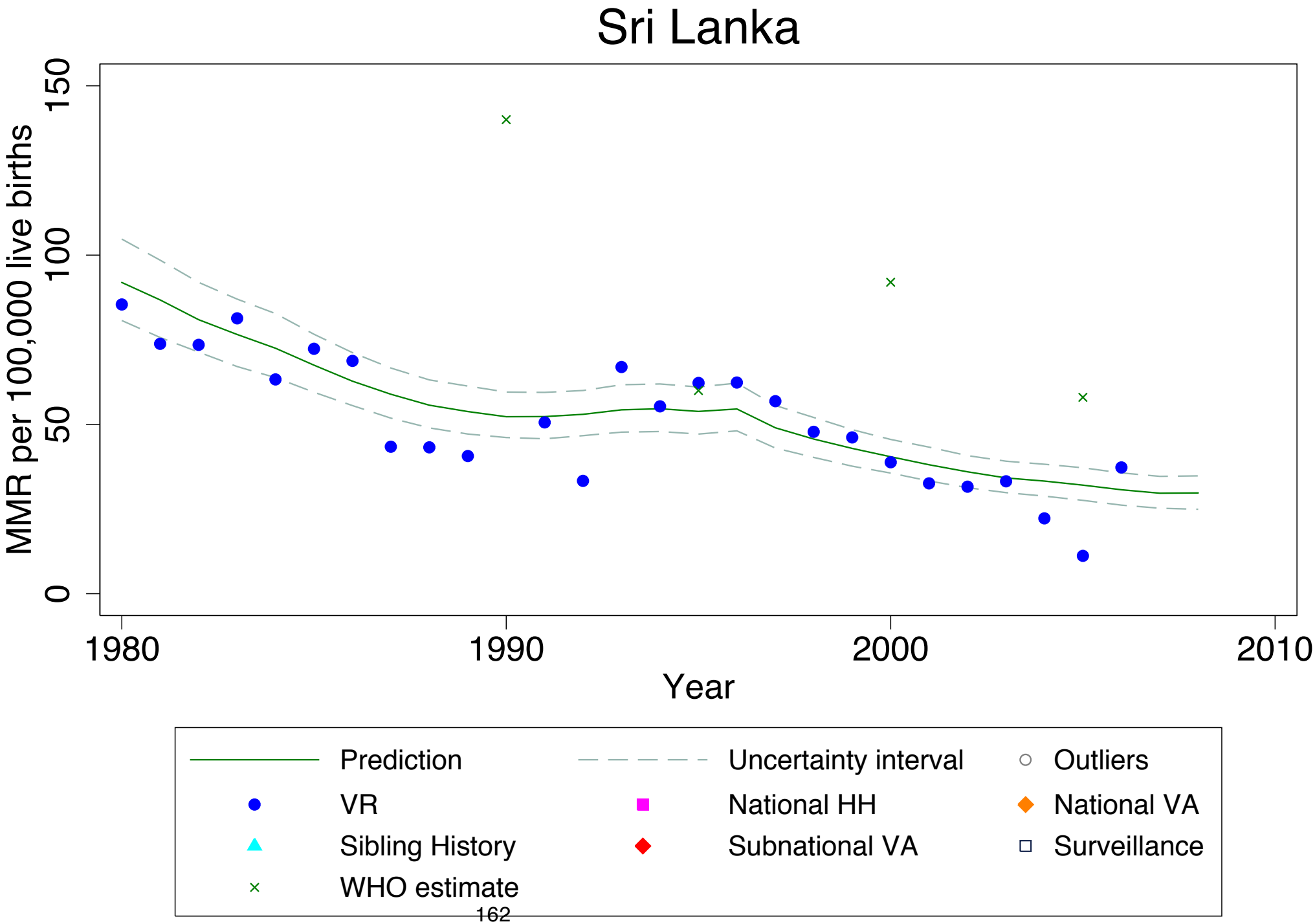
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Sri Lanka
MMR per 100,000 live births
0
50
100
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1980
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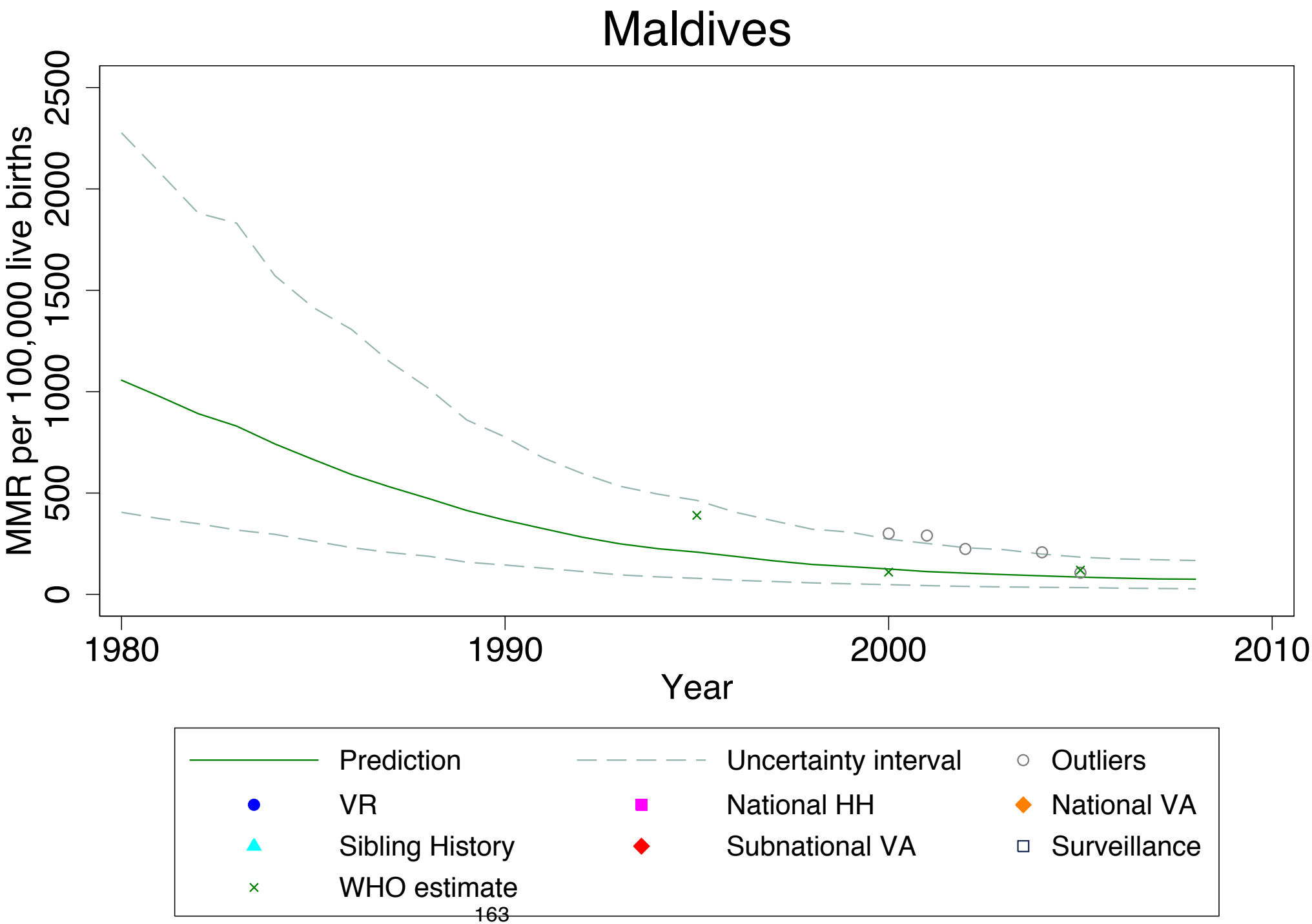
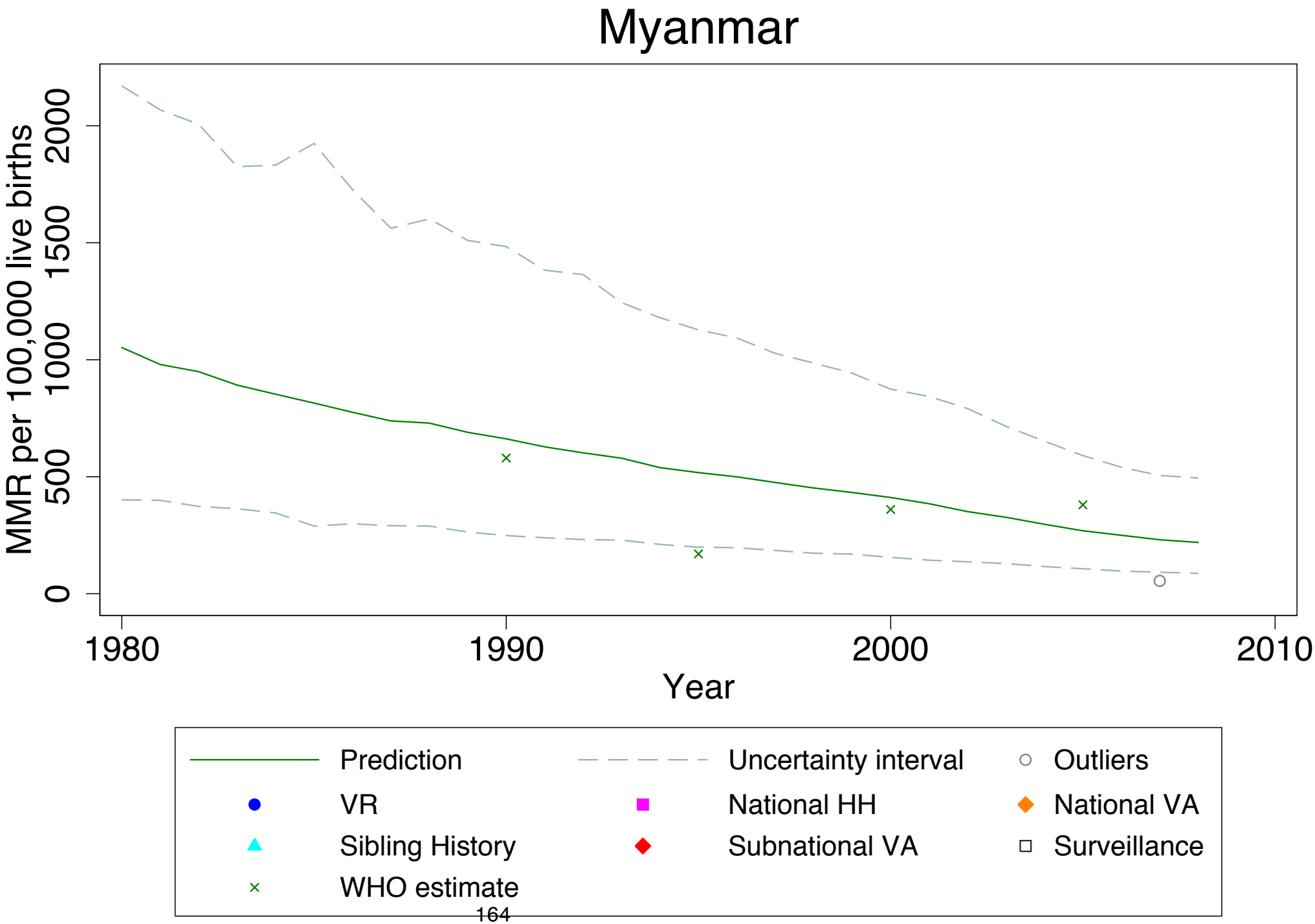
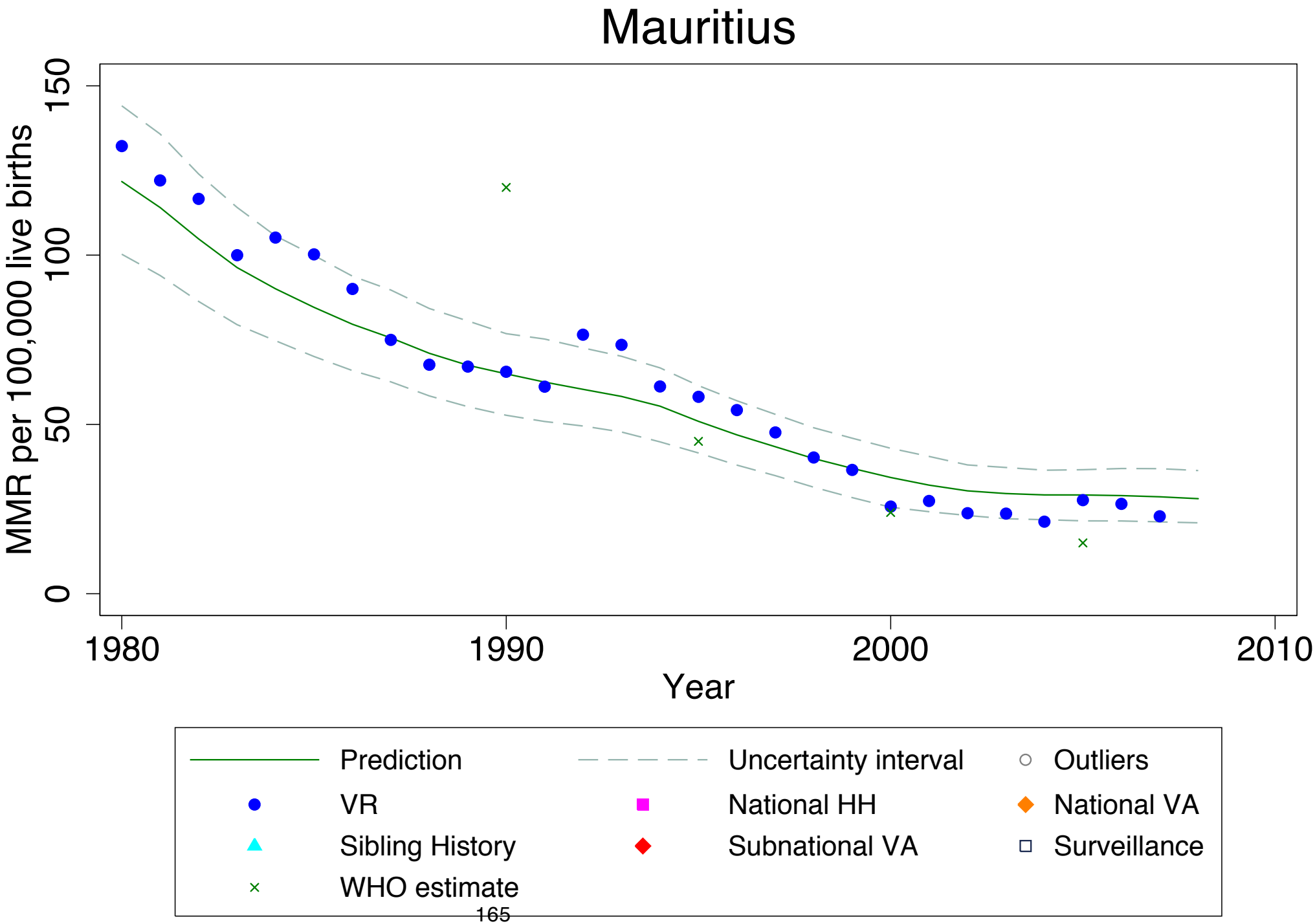
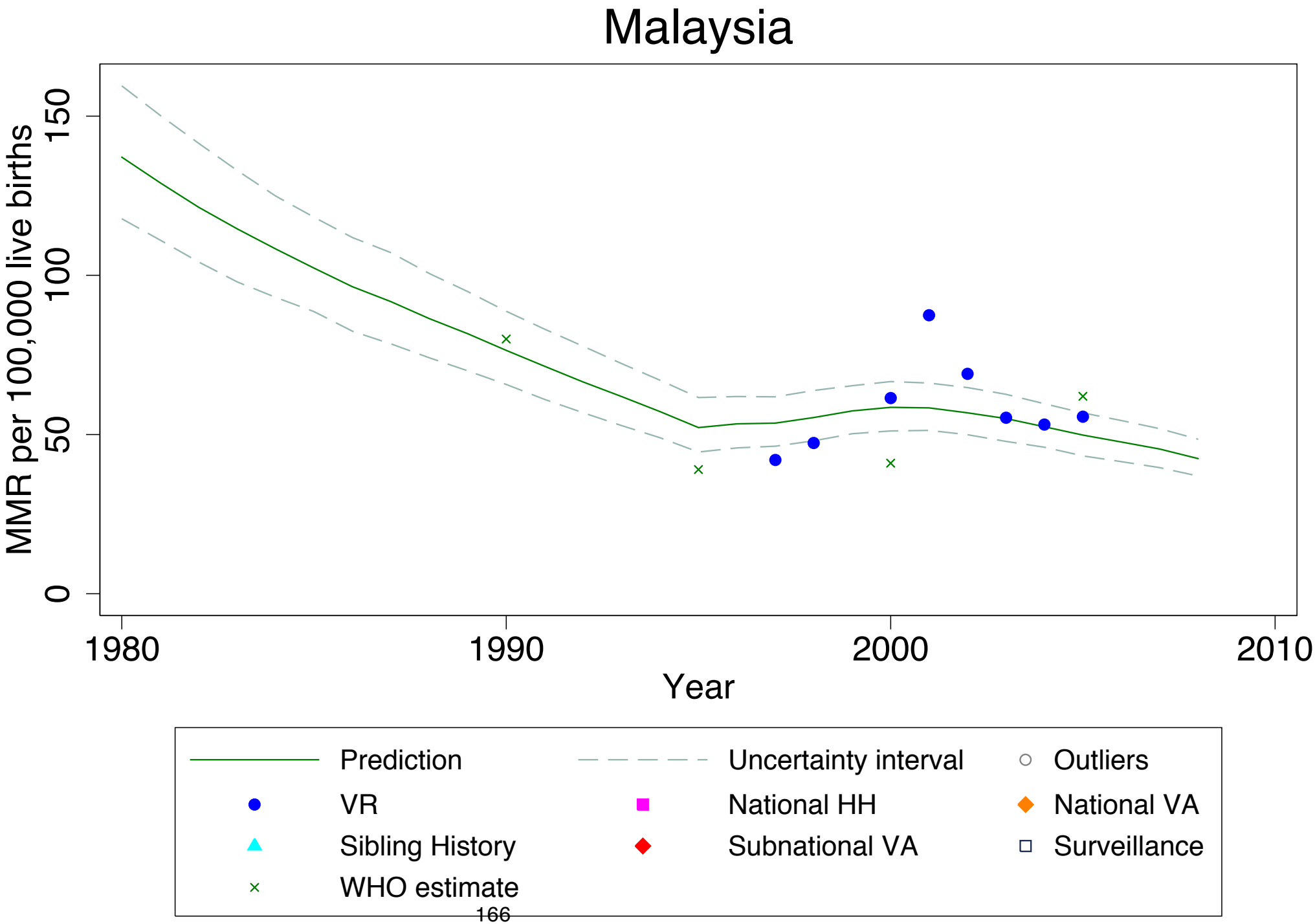
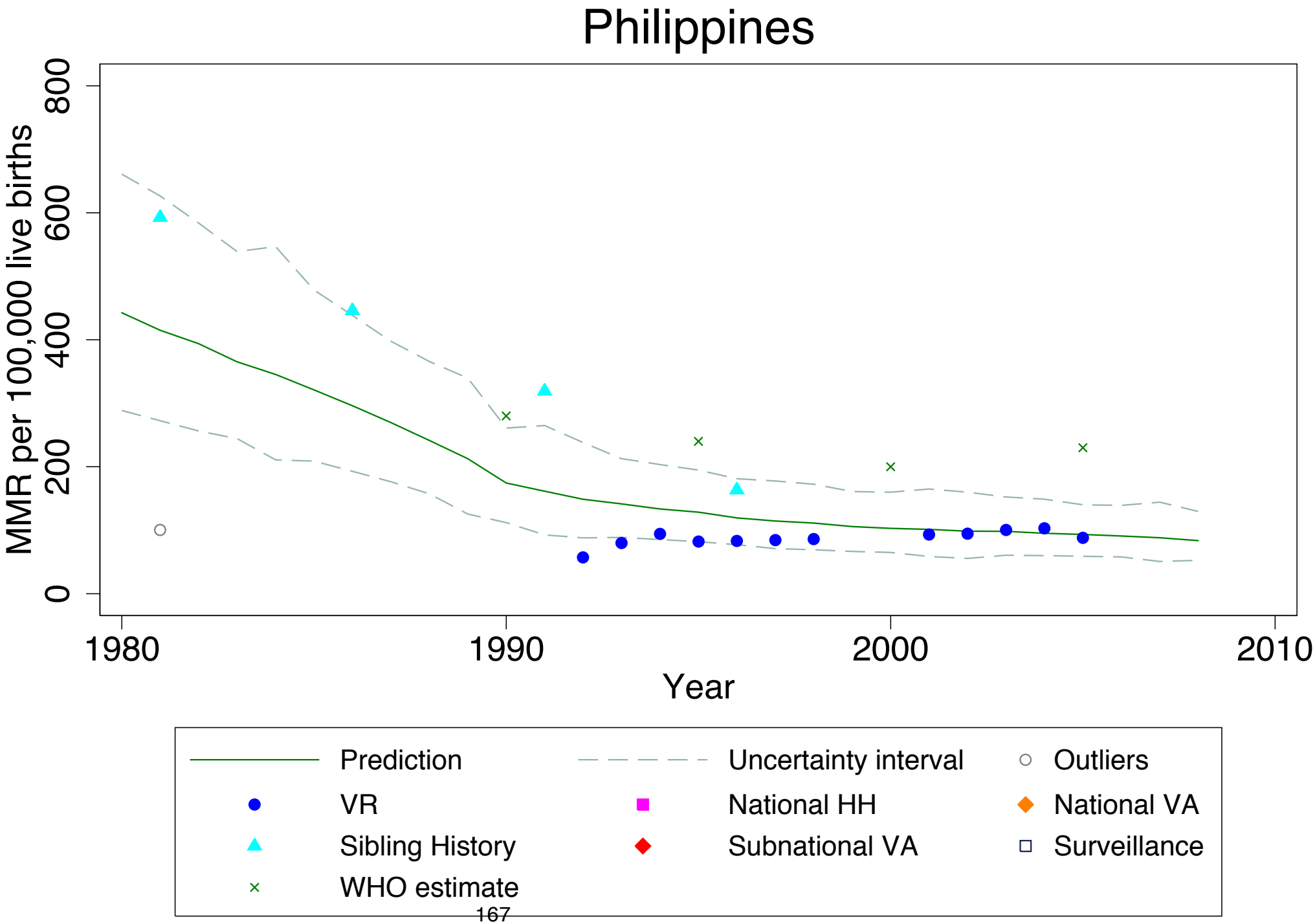
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

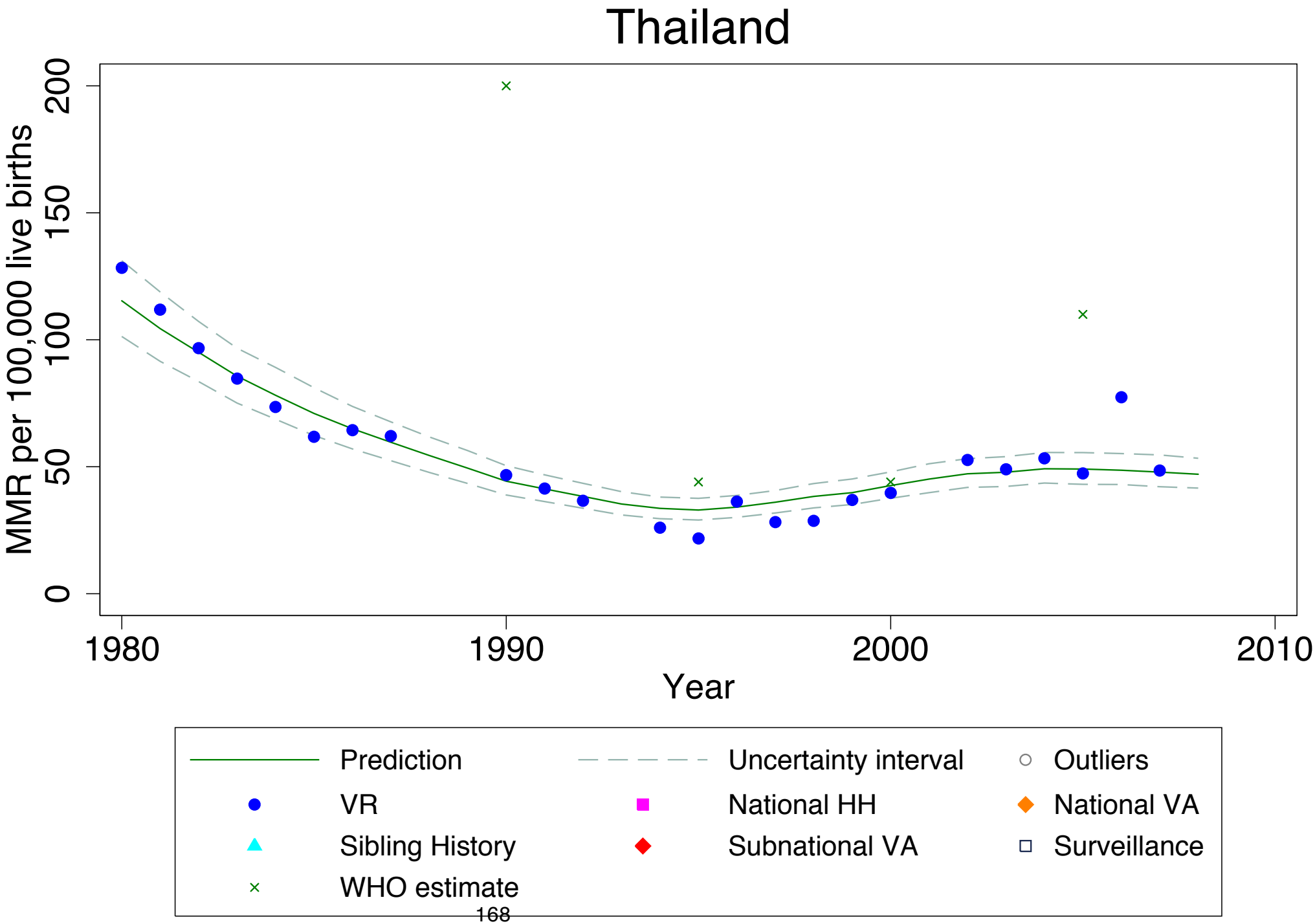

Maldives
MMR per 100,000 live births
0
500
1000
1500
2000
2500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

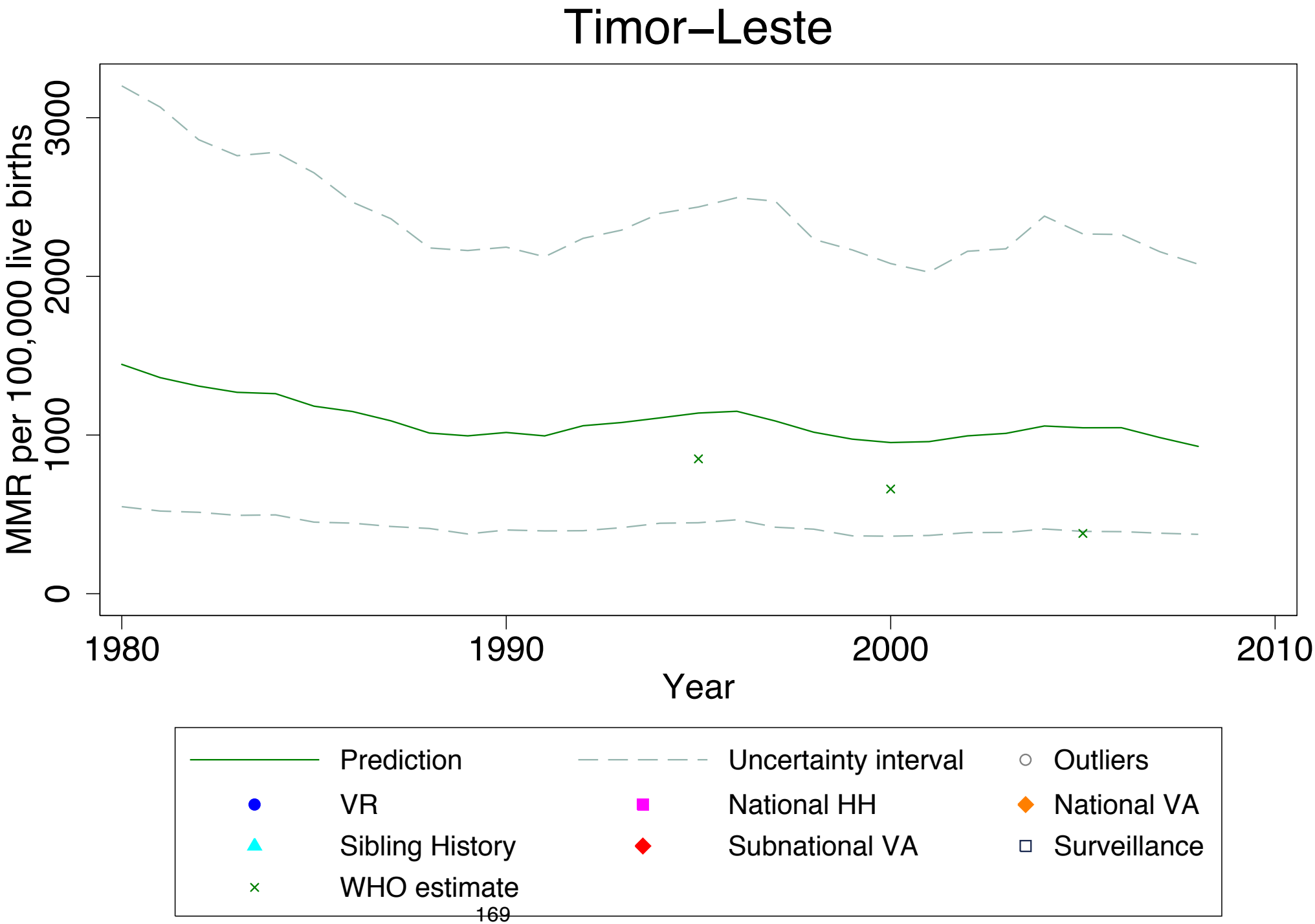

Myanmar
MMR per 100,000 live births
0
500
1000
1500
2000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

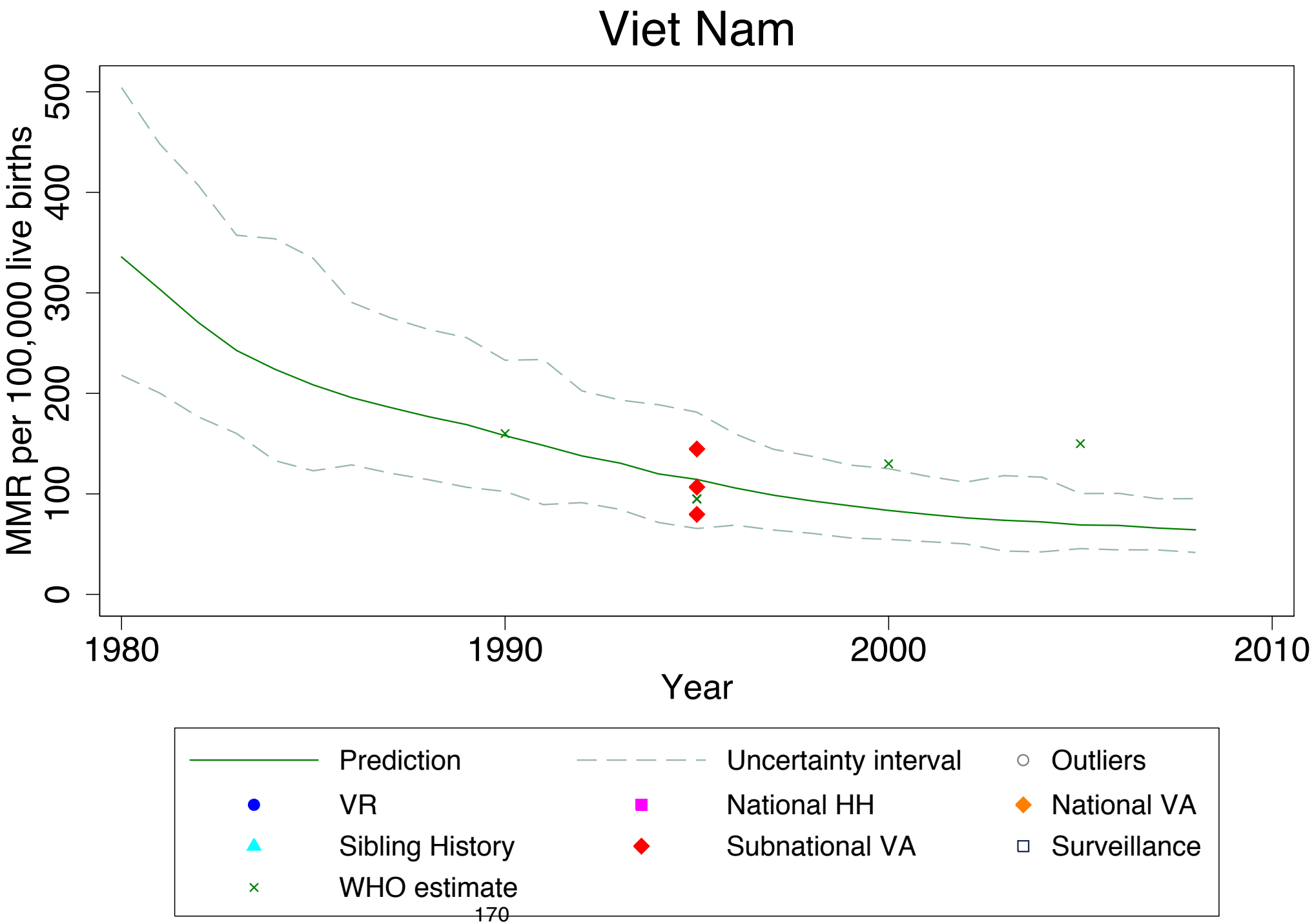

Mauritius
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

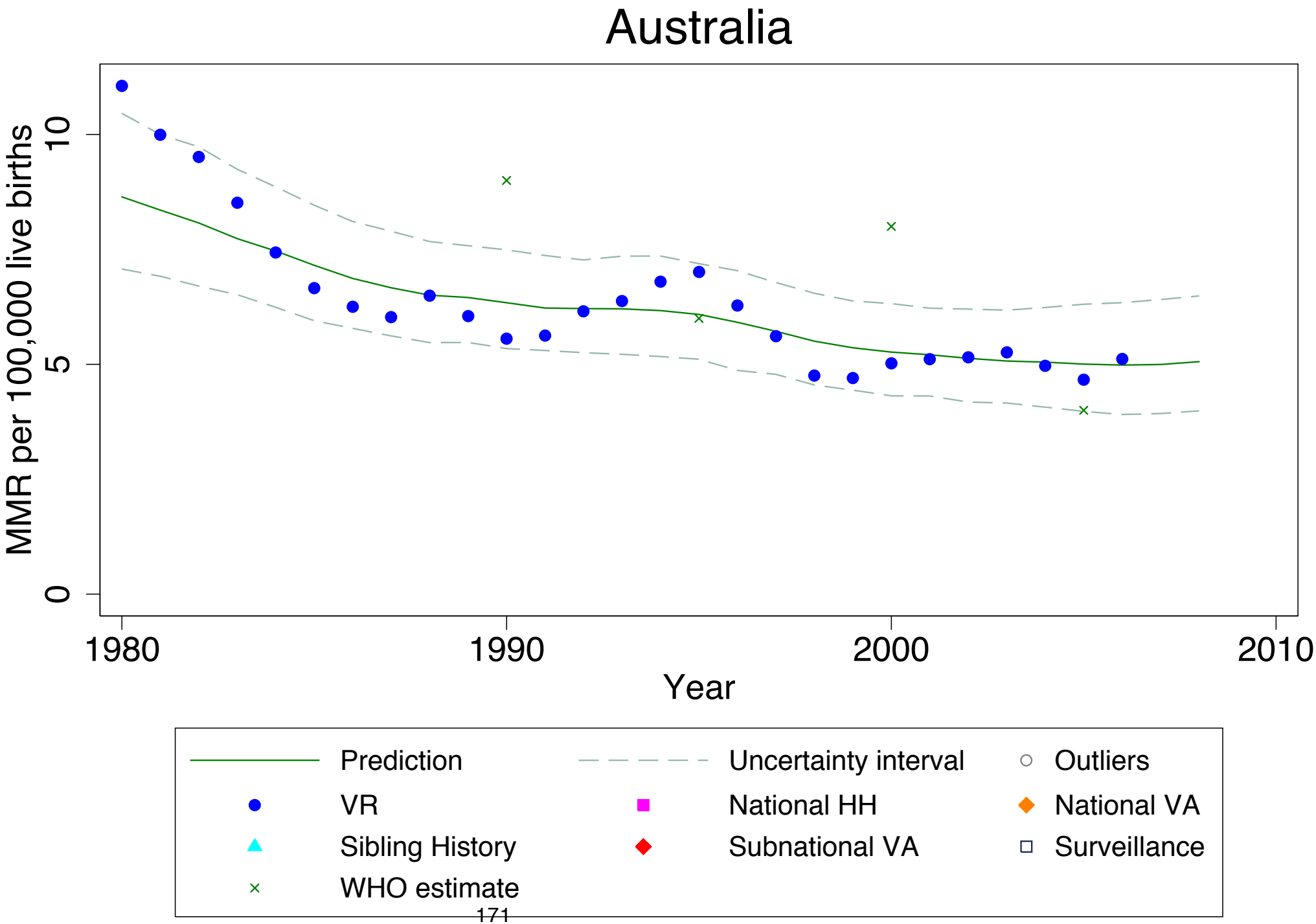

Malaysia
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

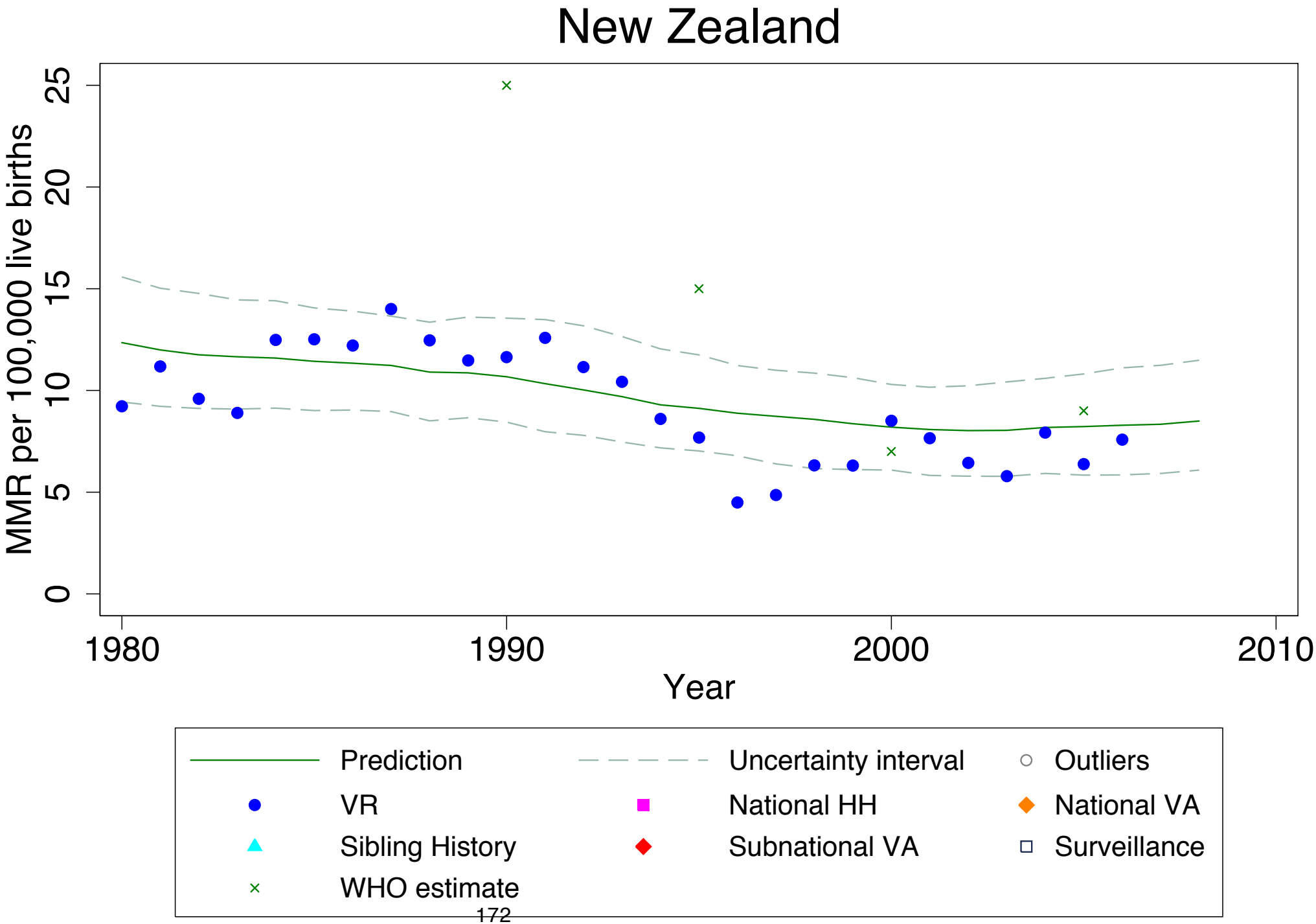

Philippines
MMR per 100,000 live births
0
200
400
600
800
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

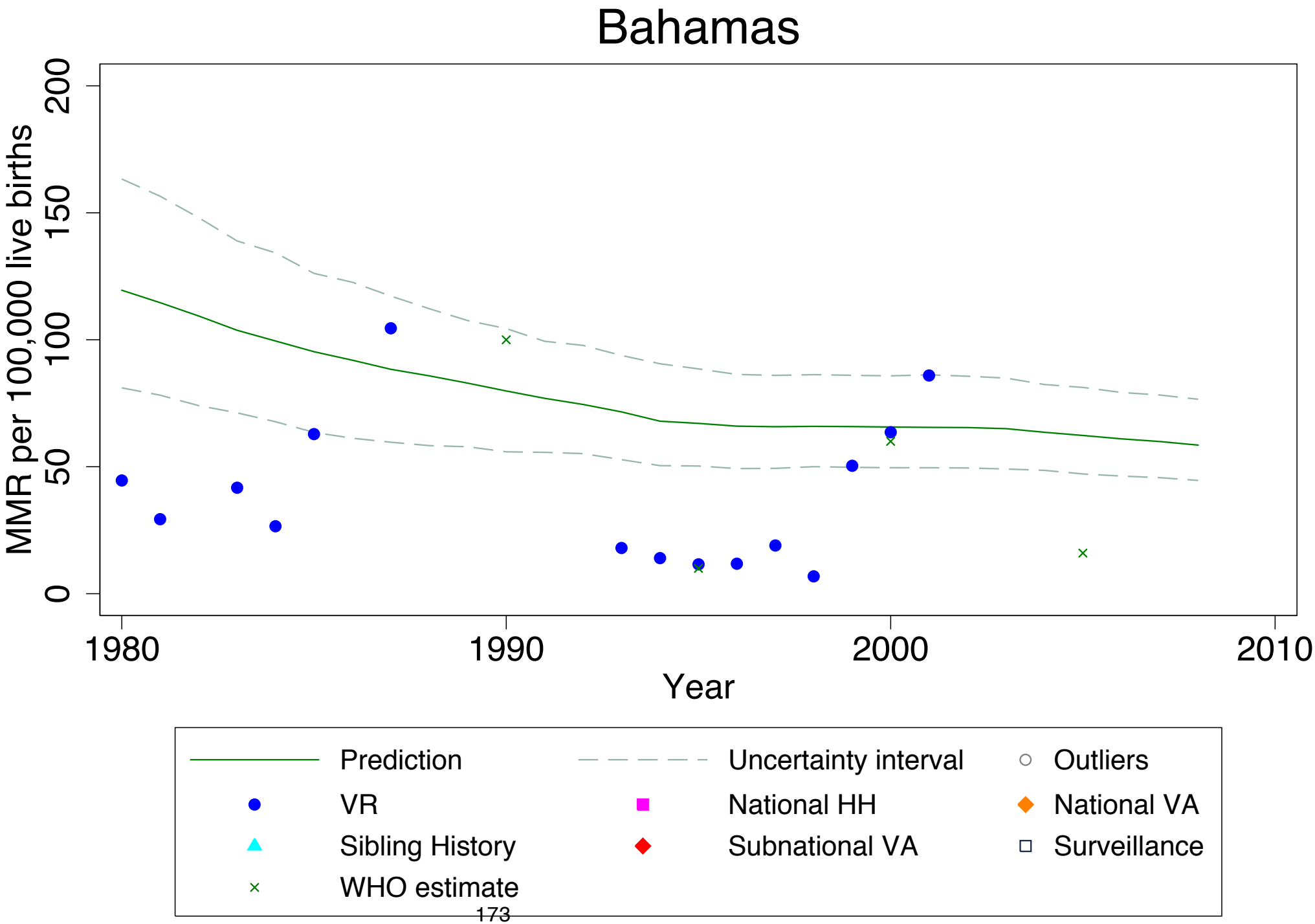

Thailand
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

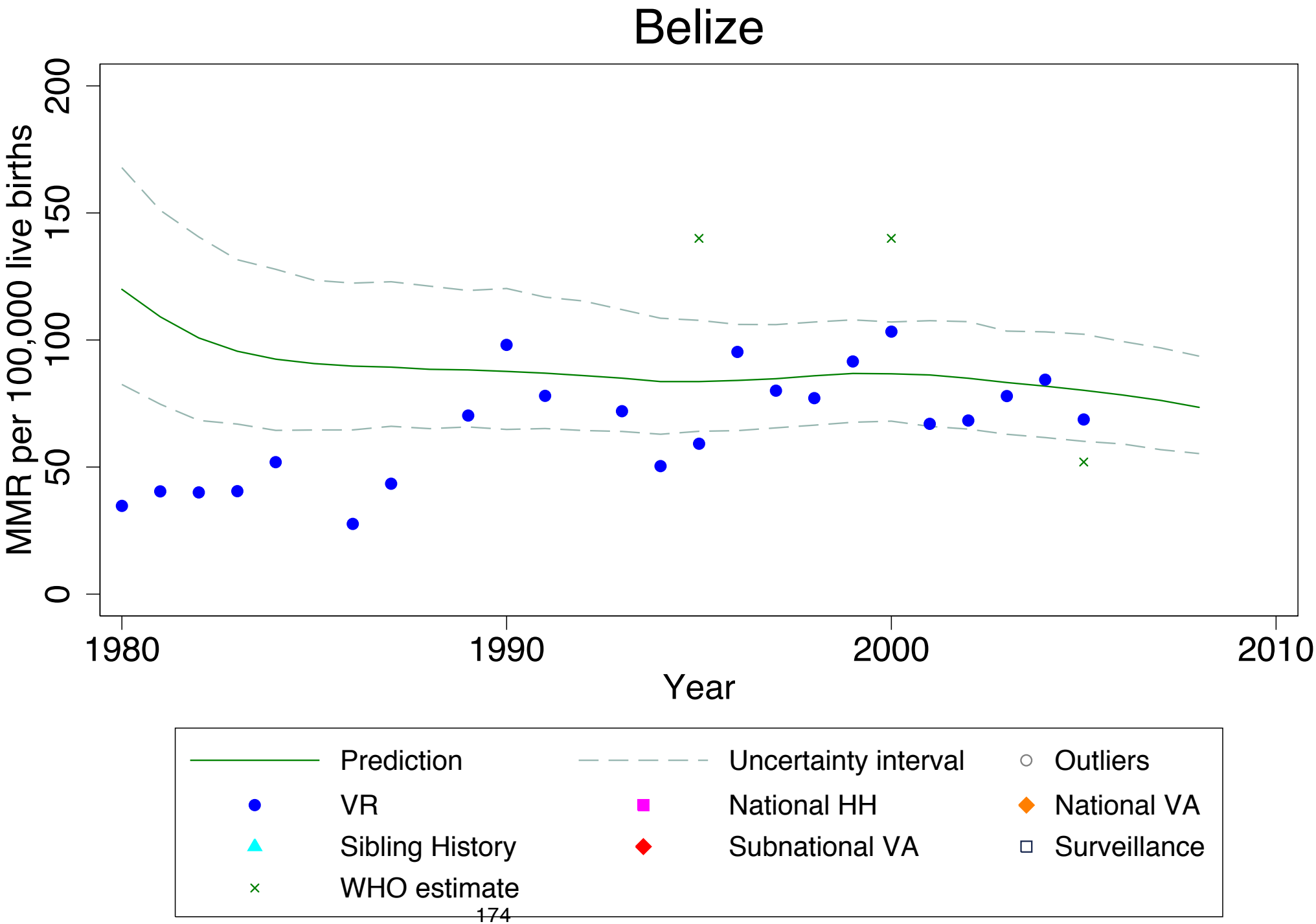

Timor−Leste
MMR per 100,000 live births
0
1000
2000
3000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

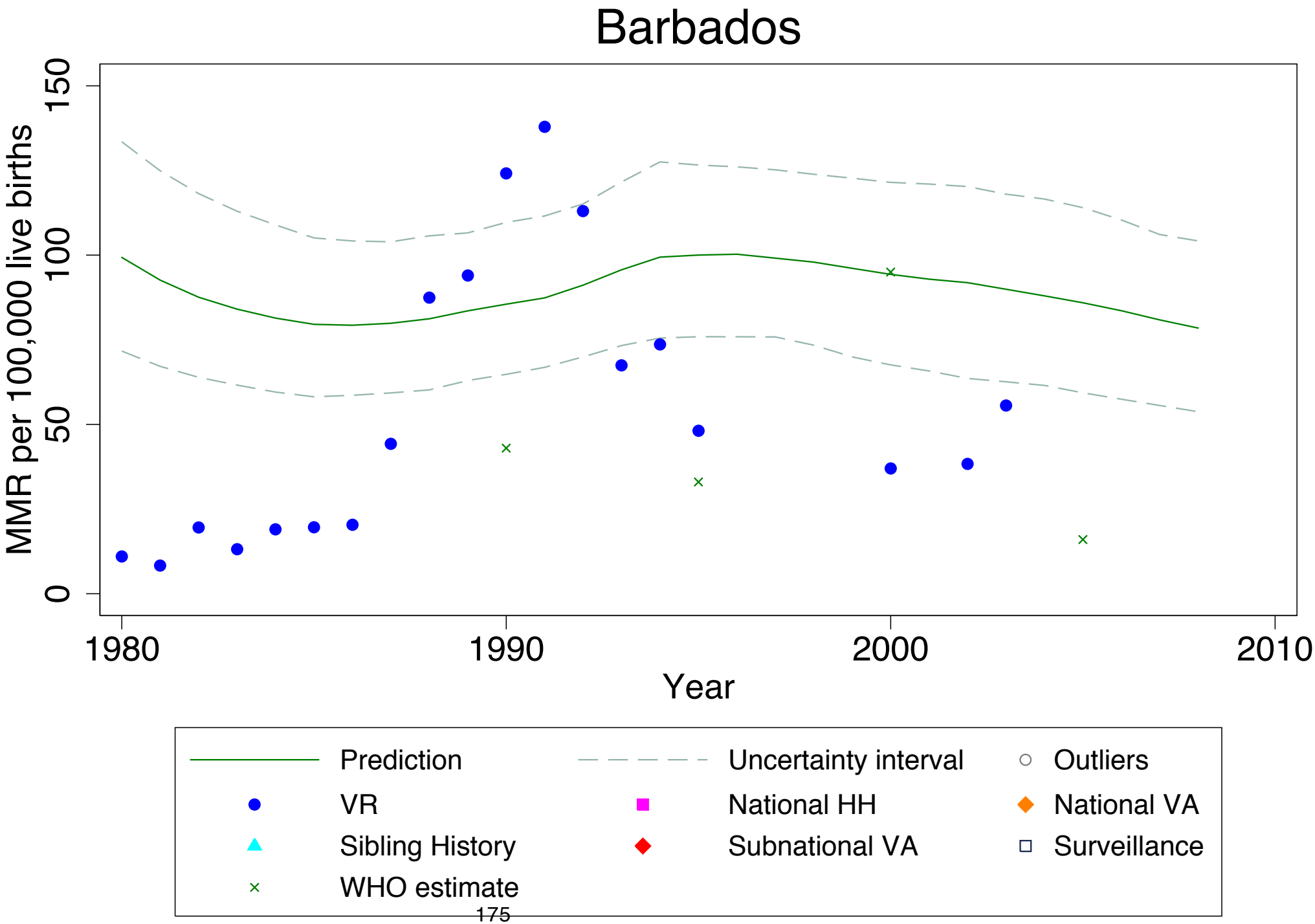

Viet Nam
MMR per 100,000 live births
0
100
200
300
400
500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

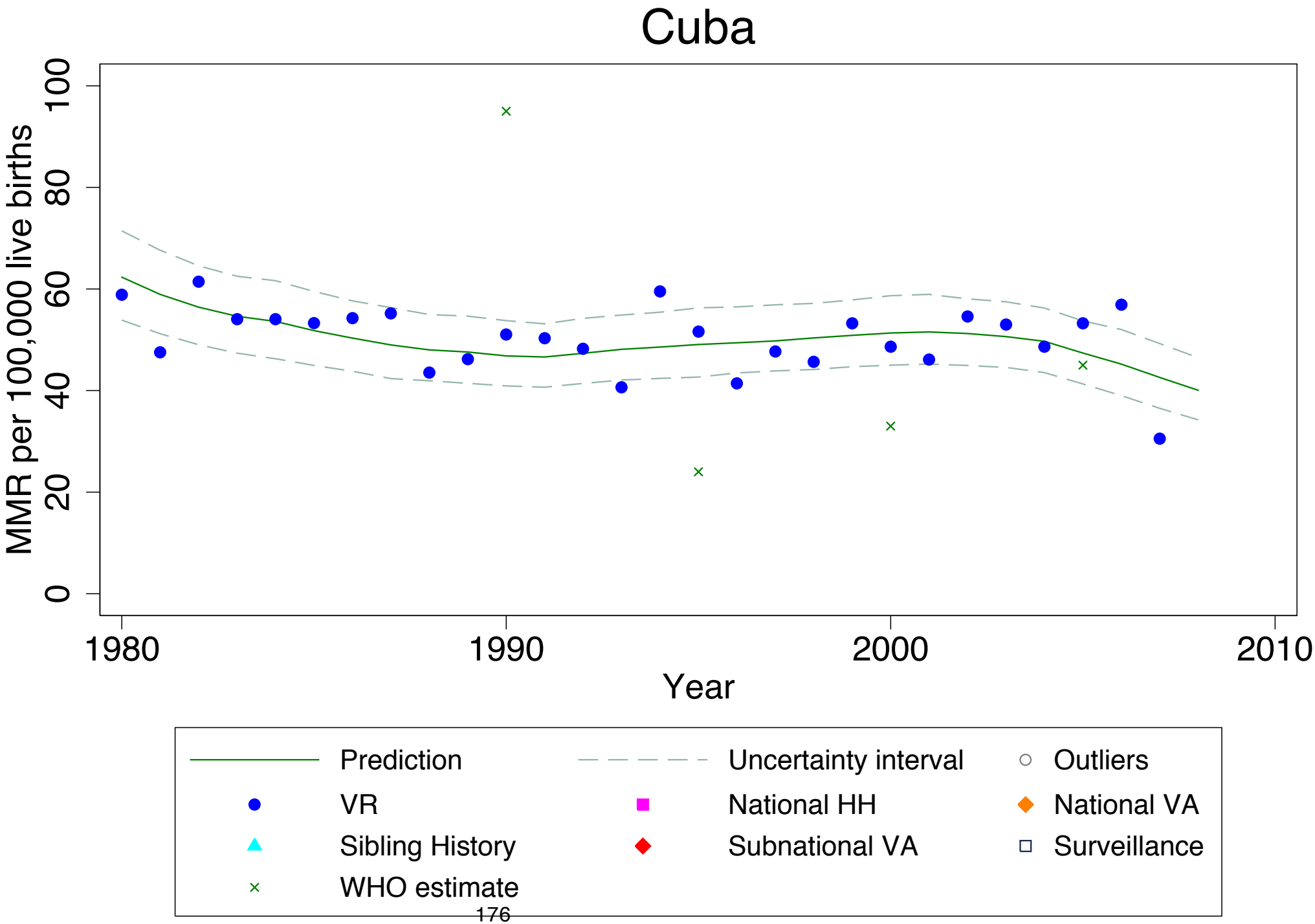

Australia
MMR per 100,000 live births
0
5
10
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

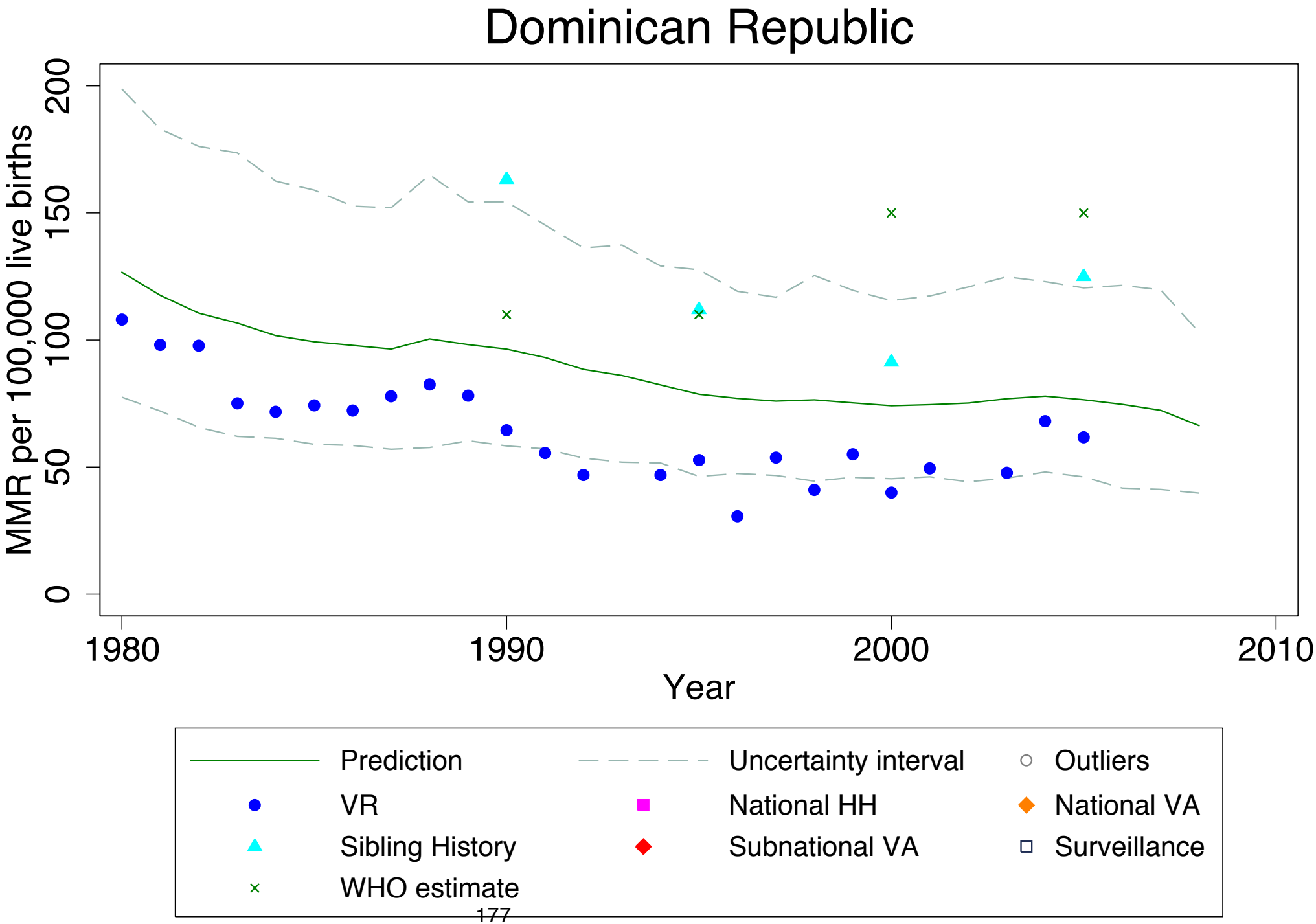

New Zealand
MMR per 100,000 live births
0
5
10
15
20
25
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

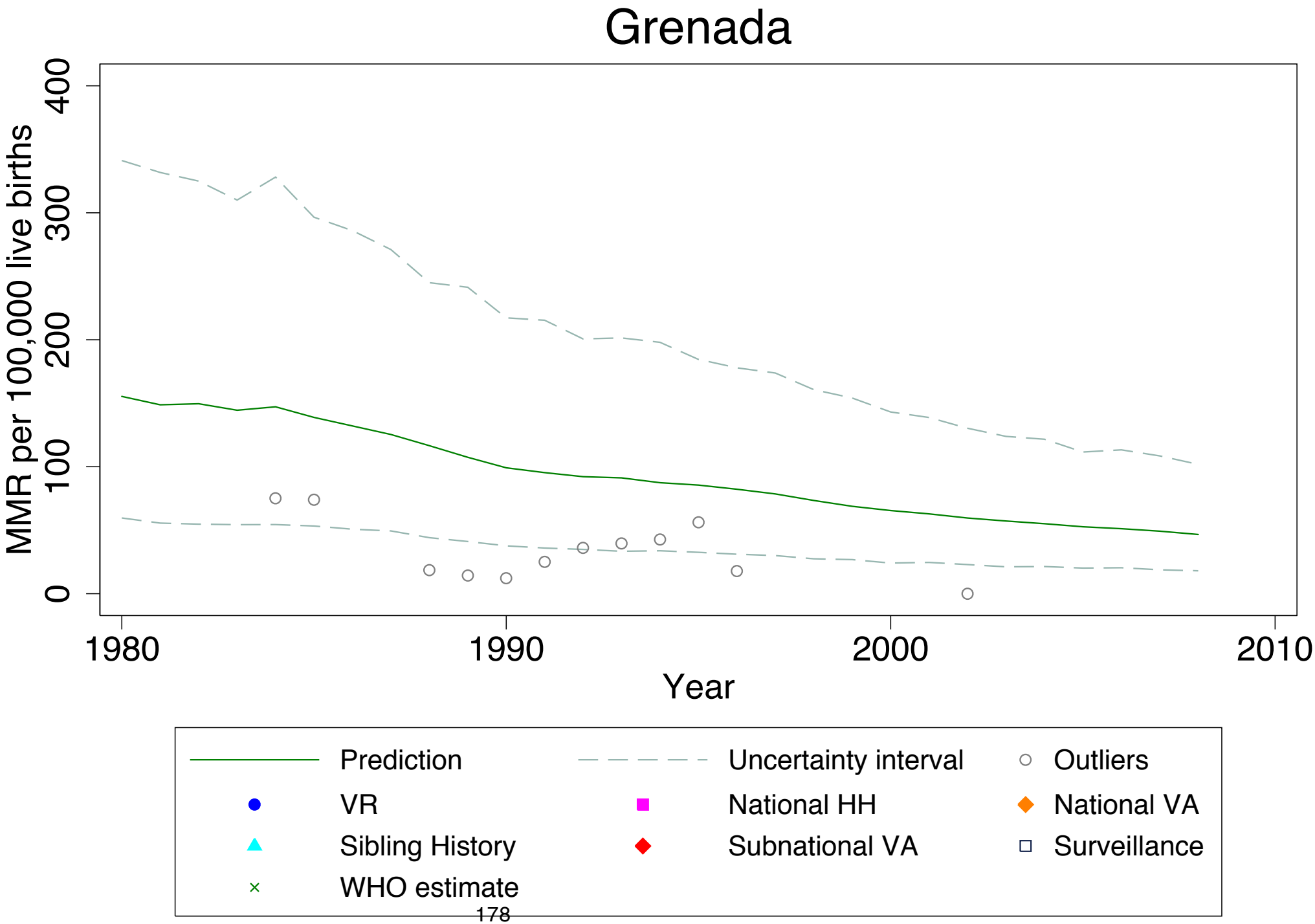

Bahamas
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

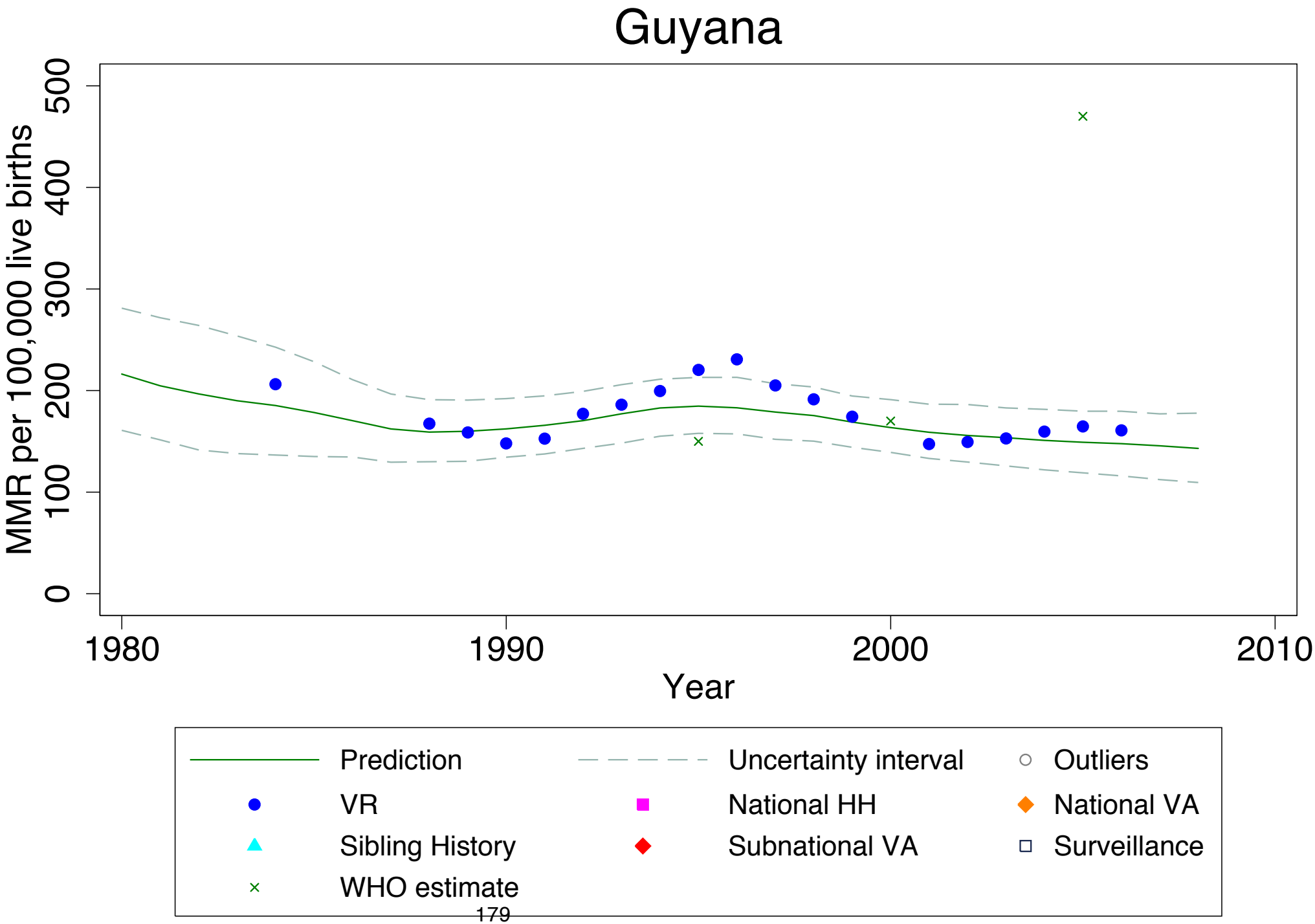

Belize
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

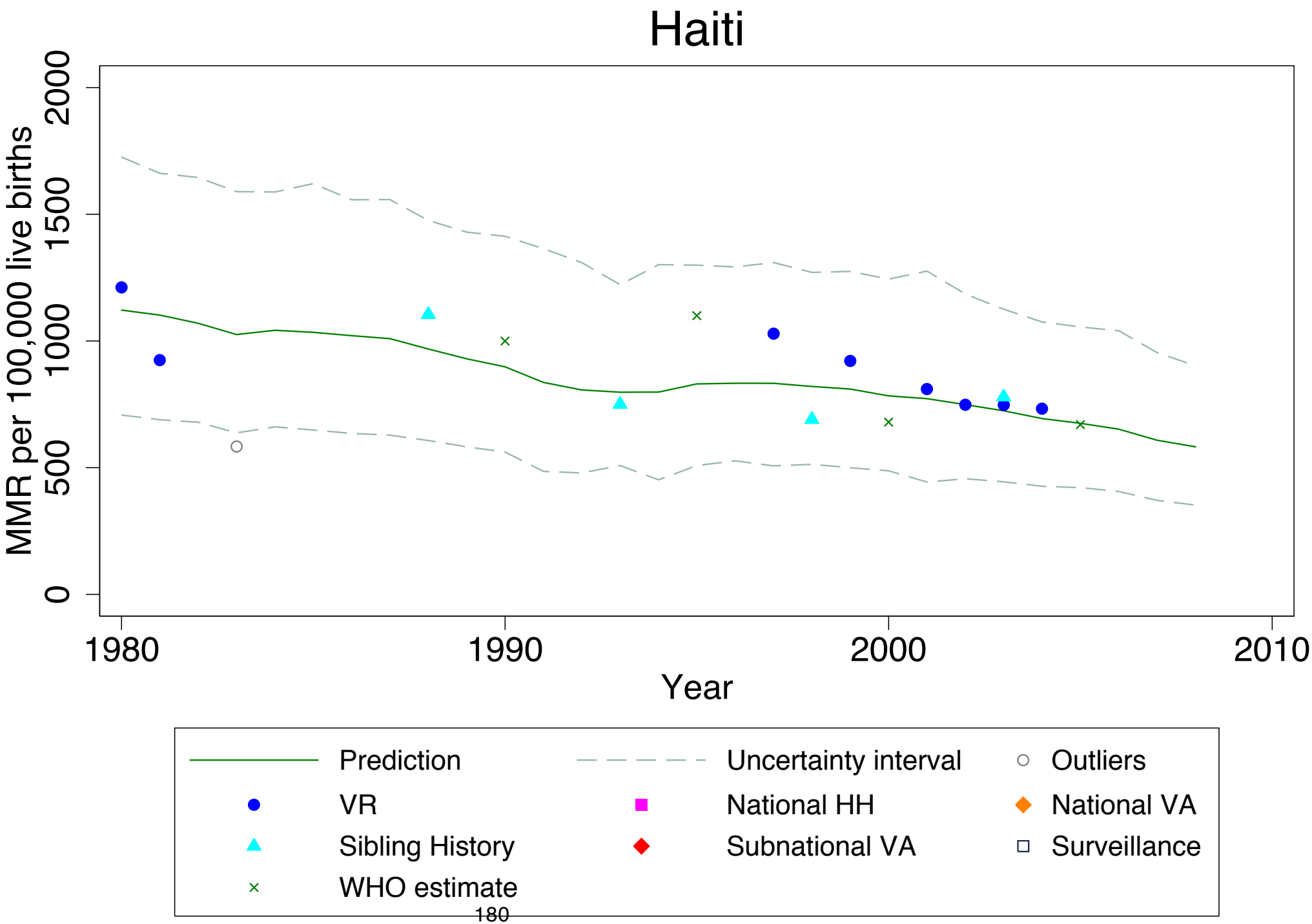

Barbados
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

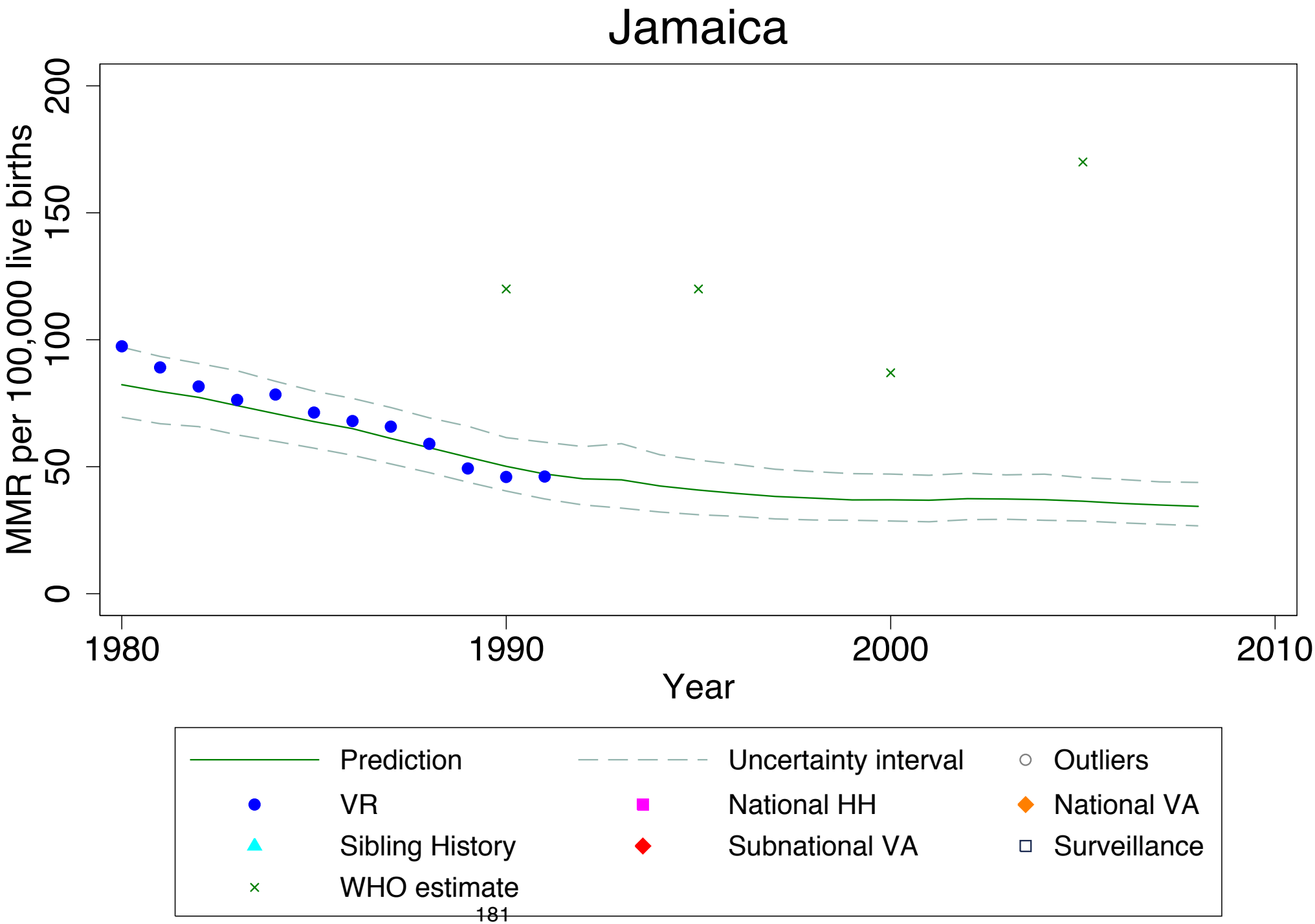

Cuba
MMR per 100,000 live births
0
20
40
60
80
100
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

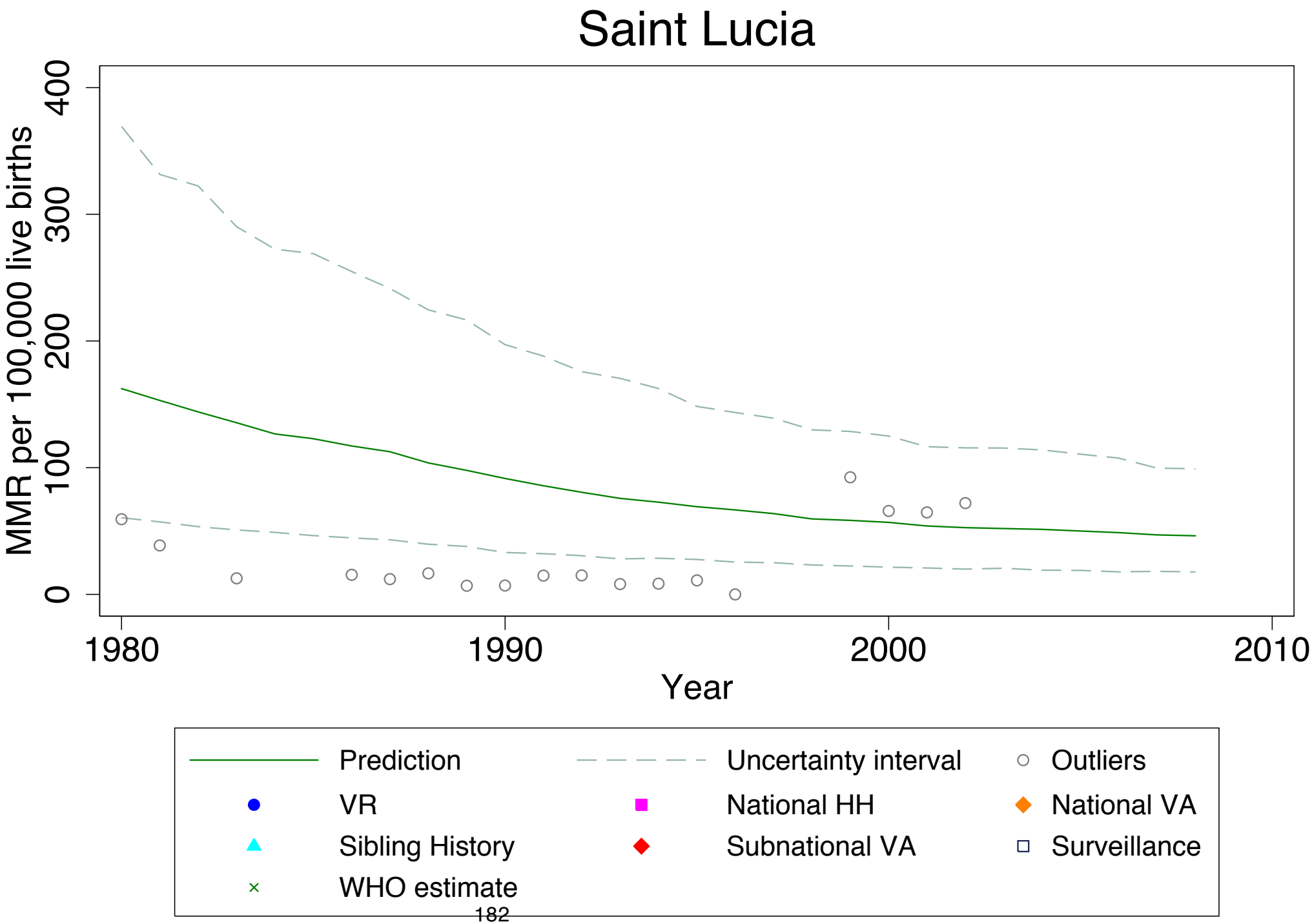

Dominican Republic
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

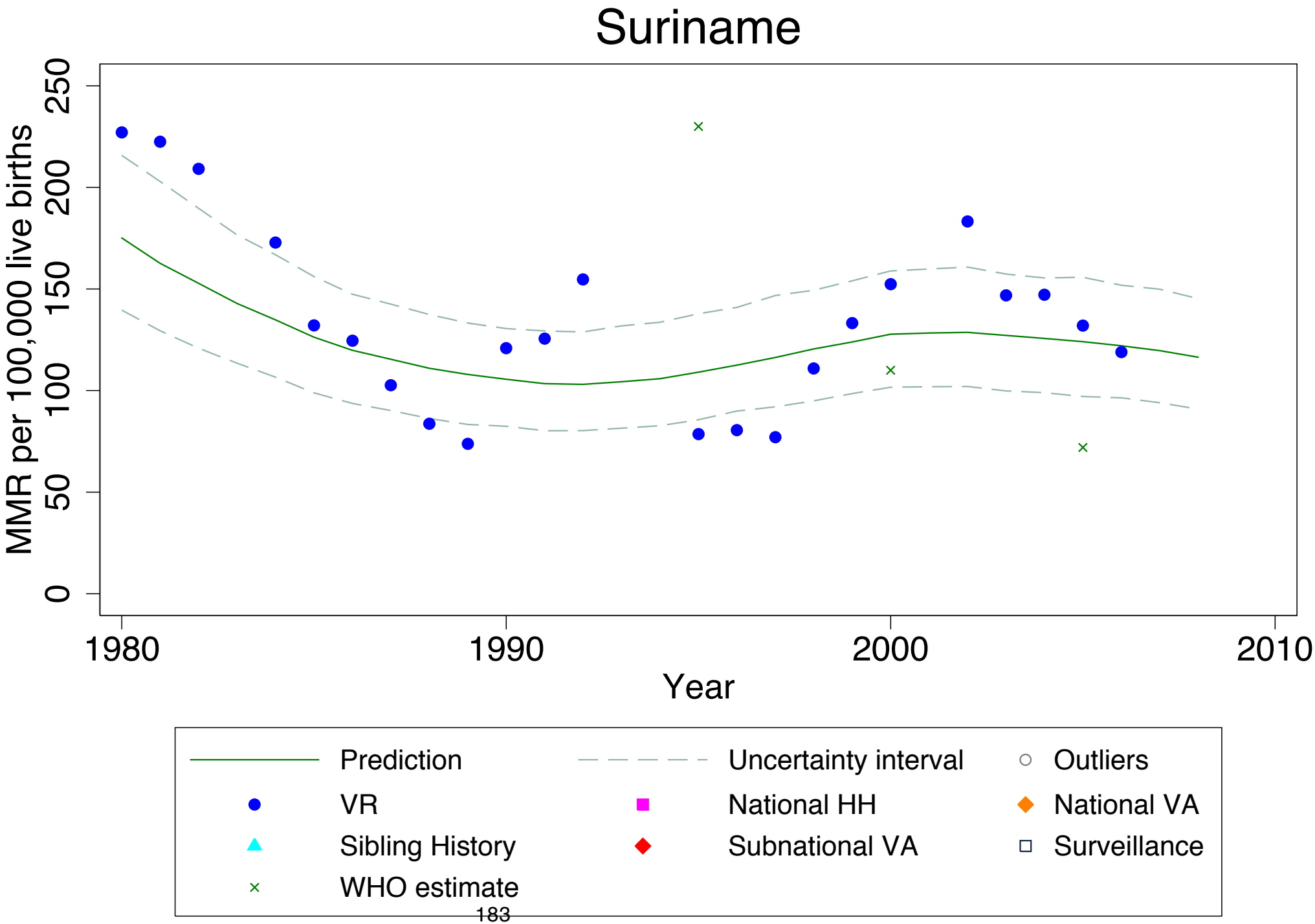

Grenada
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

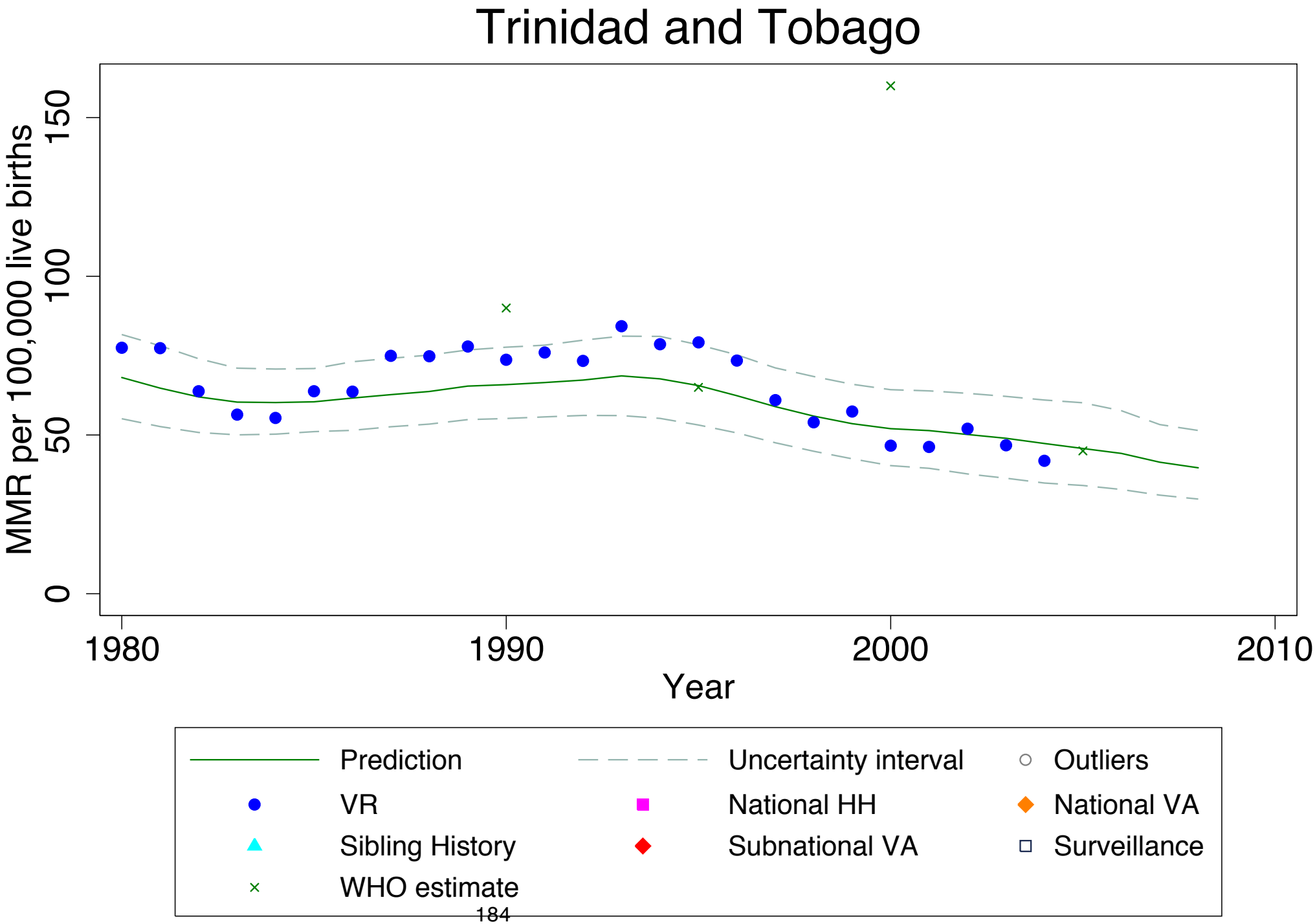

Guyana
MMR per 100,000 live births
0
100
200
300
400
500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

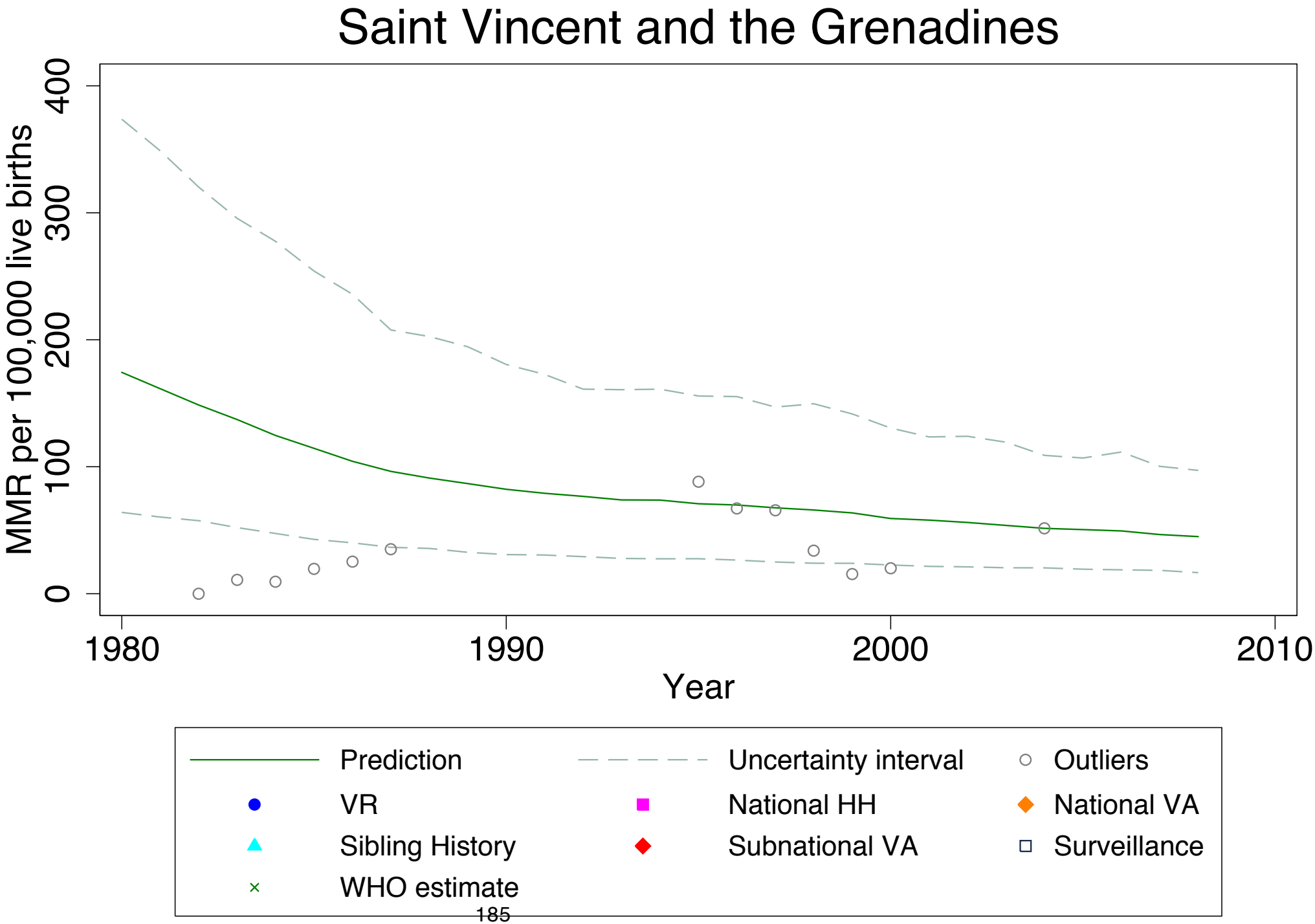

Haiti
MMR per 100,000 live births
0
500
1000
1500
2000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

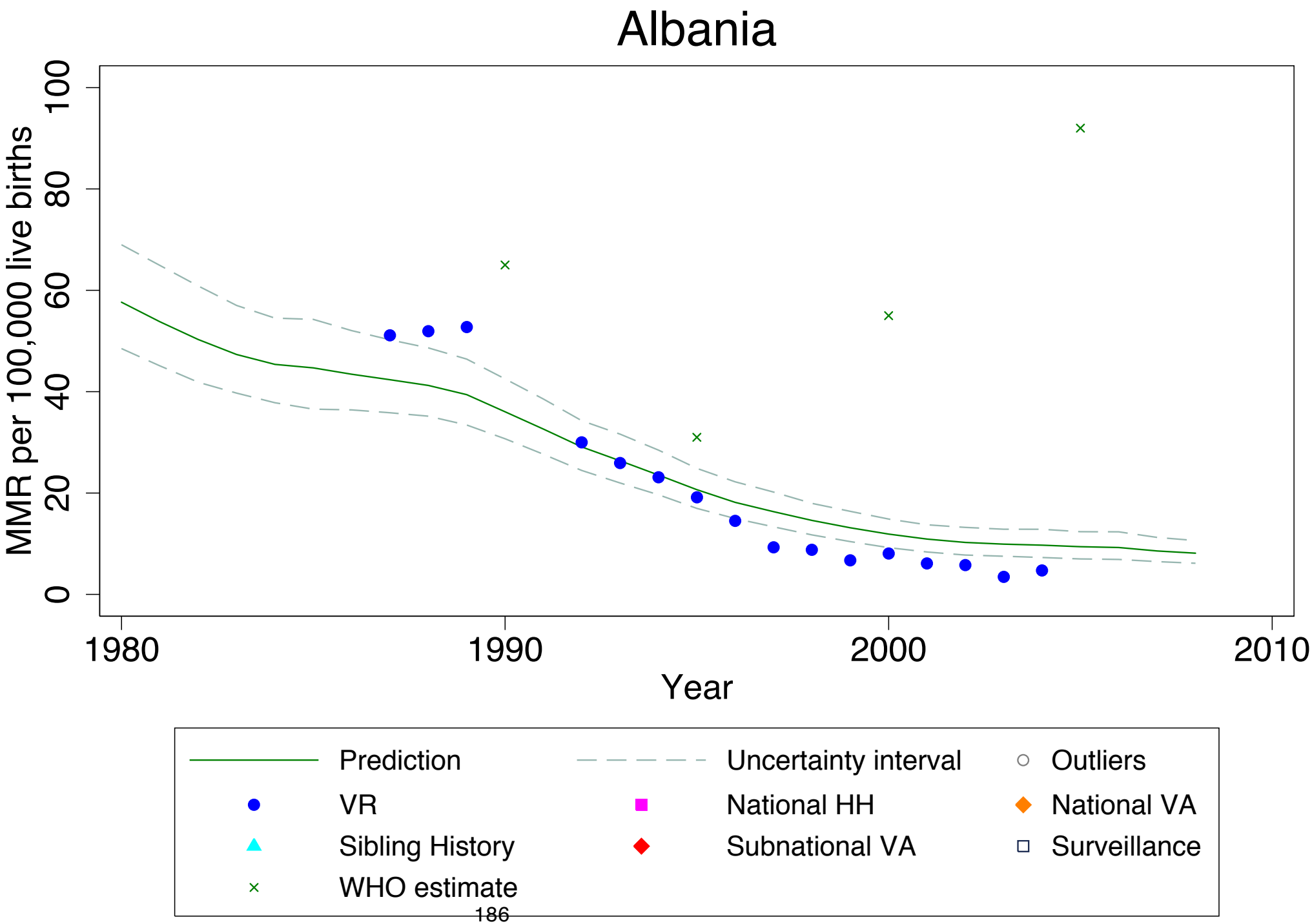

Jamaica
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

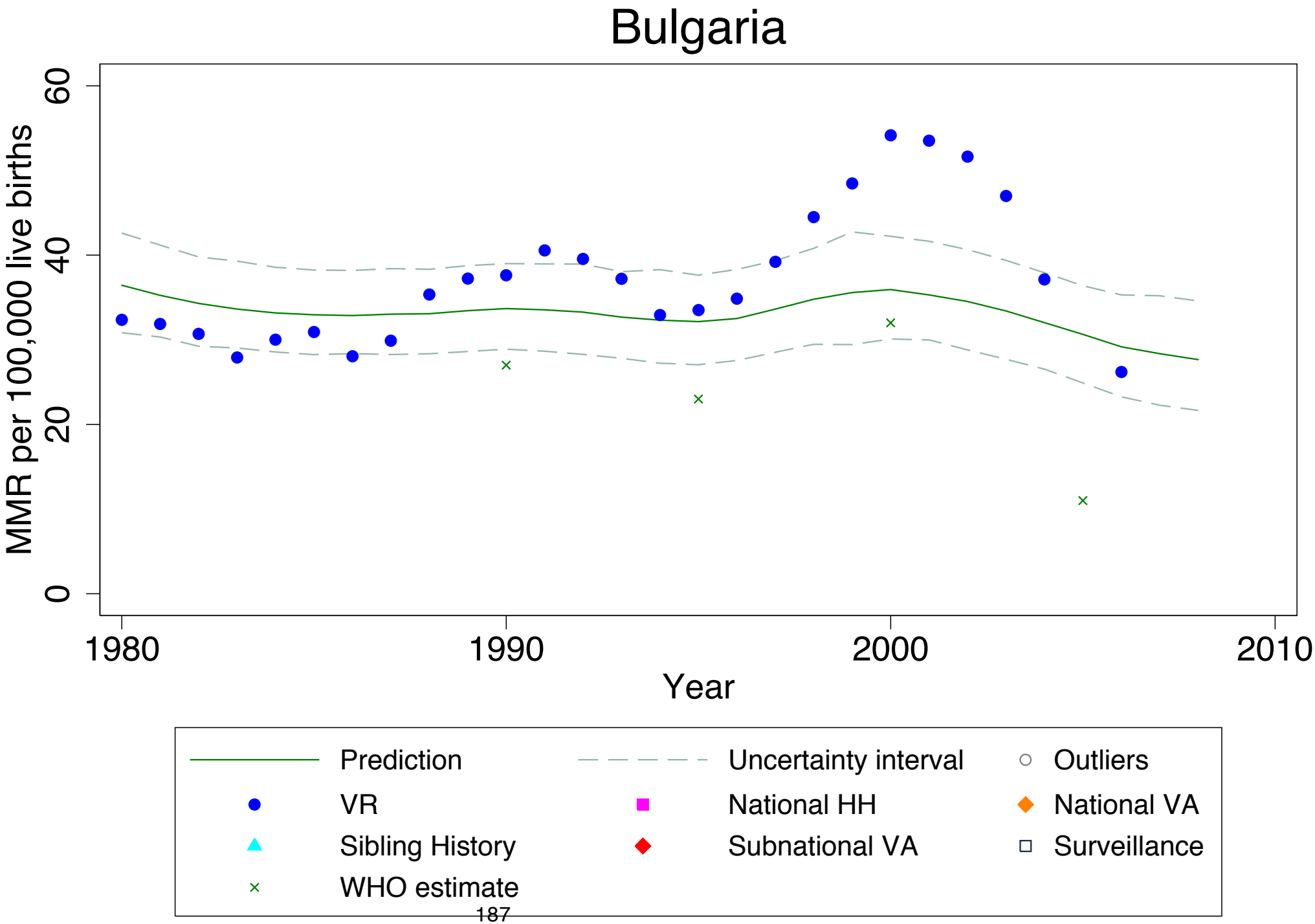

Saint Lucia
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

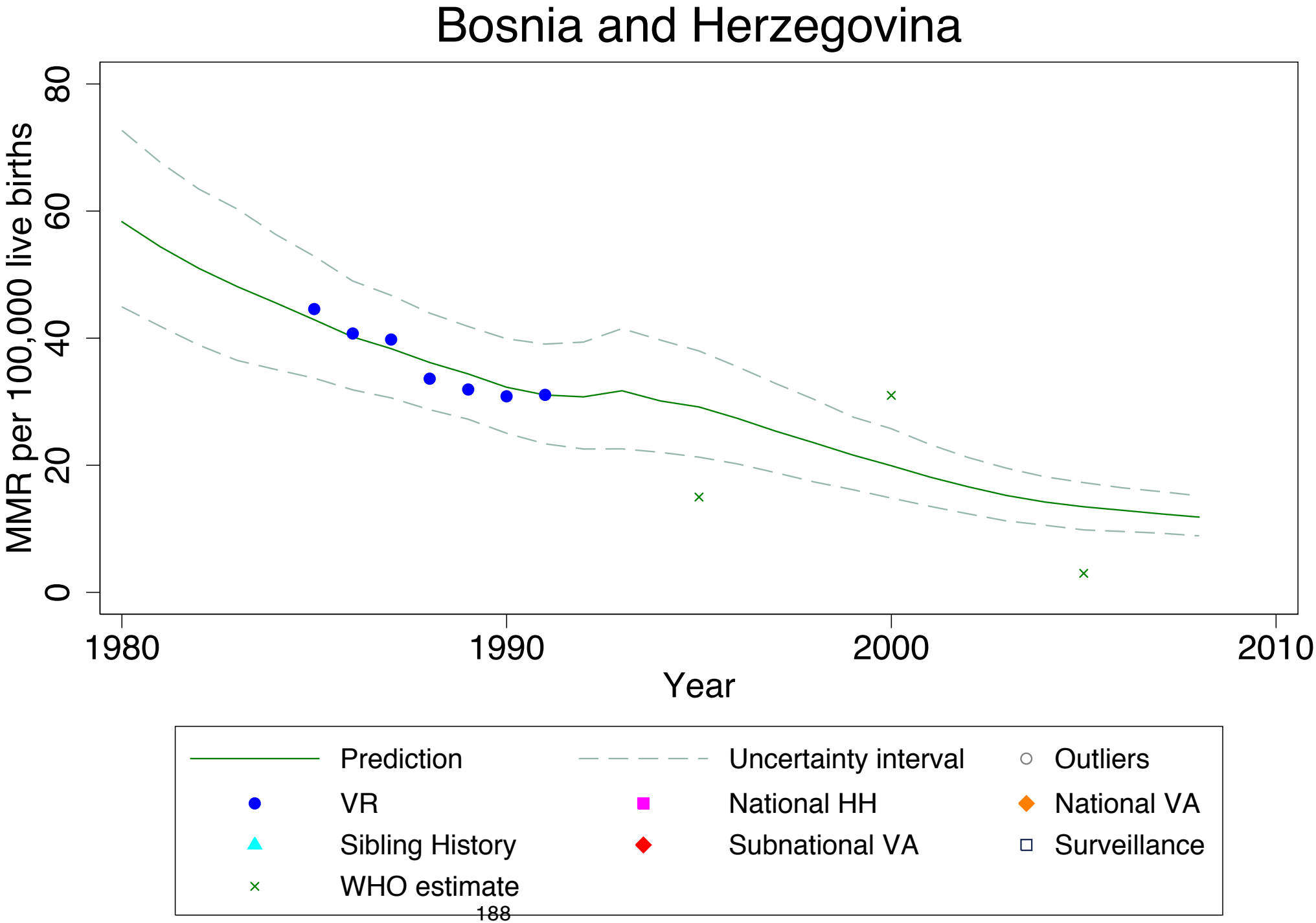

Suriname
MMR per 100,000 live births
0
50
100
150
200
250
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

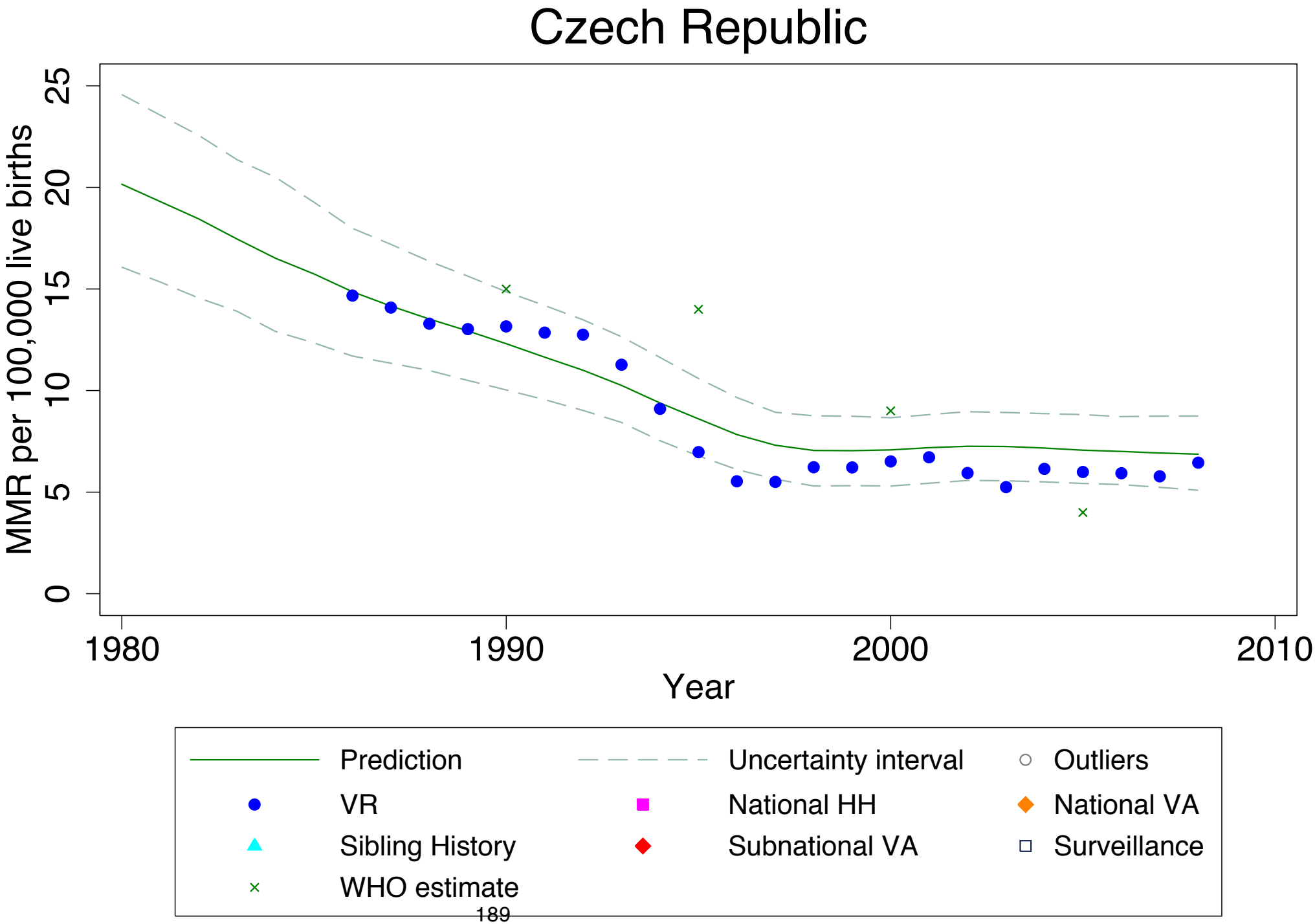

Trinidad and Tobago
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

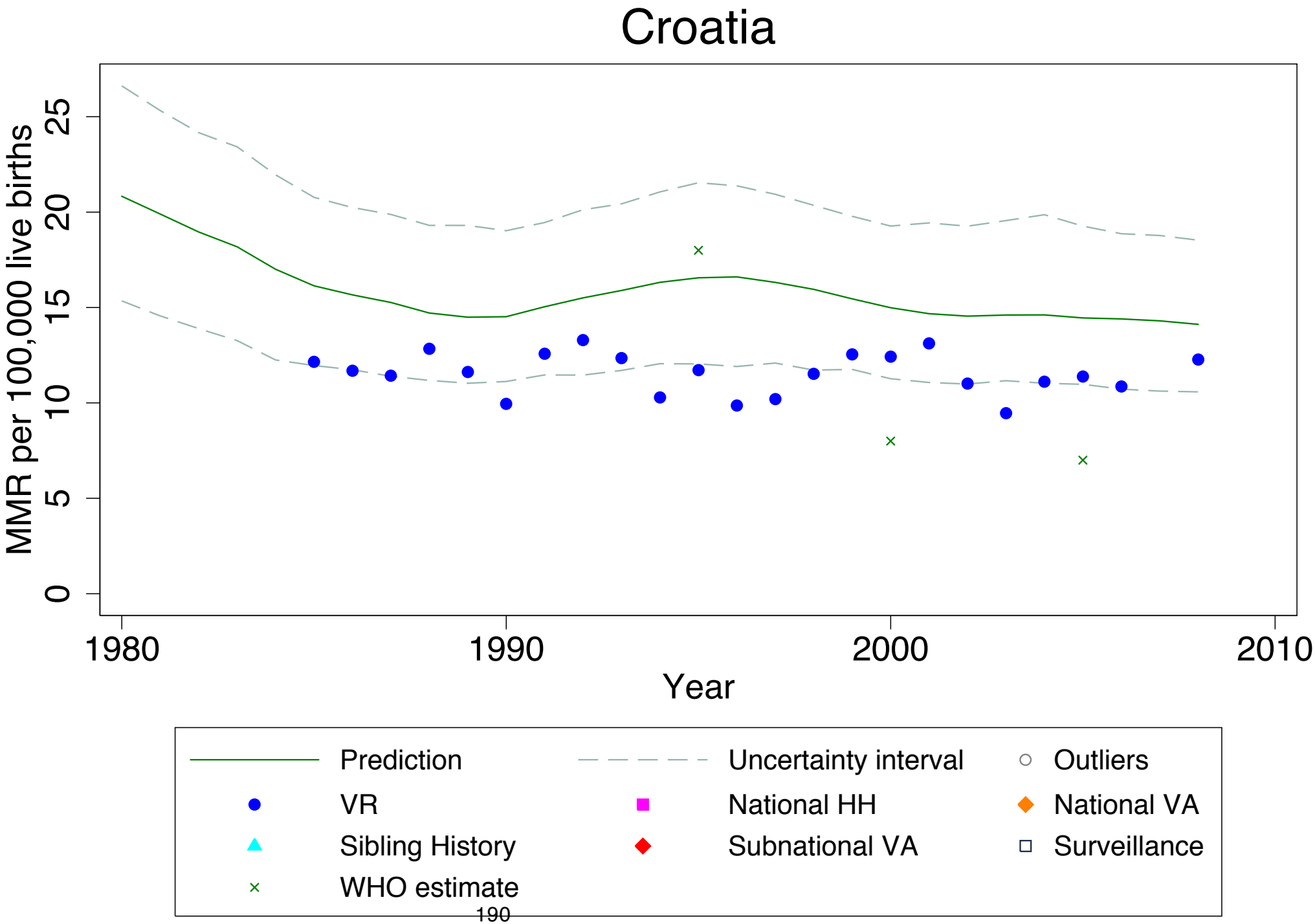

Saint Vincent and the Grenadines
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

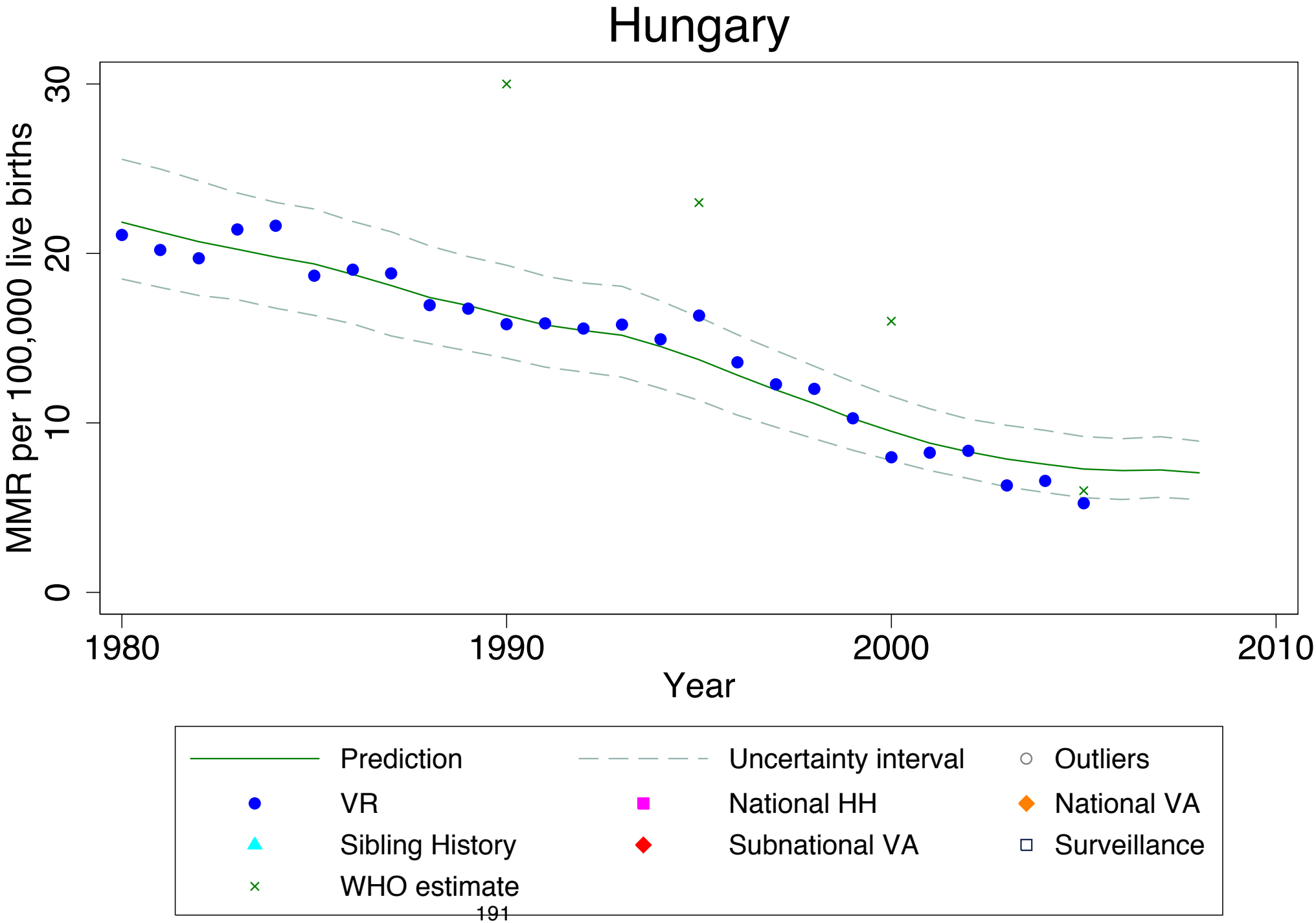

Albania
MMR per 100,000 live births
0
20
40
60
80
100
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

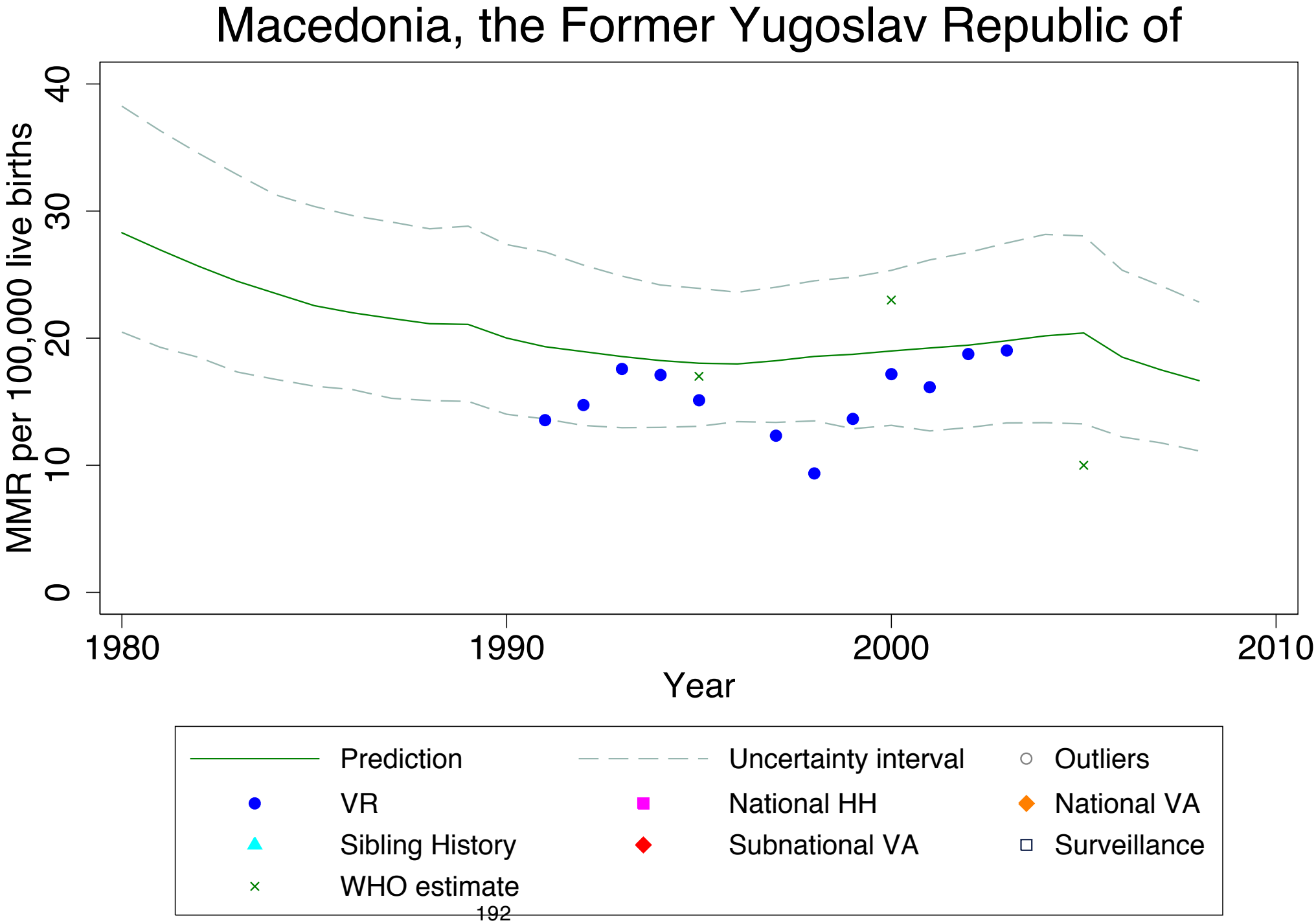

Bulgaria
MMR per 100,000 live births
0
20
40
60
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

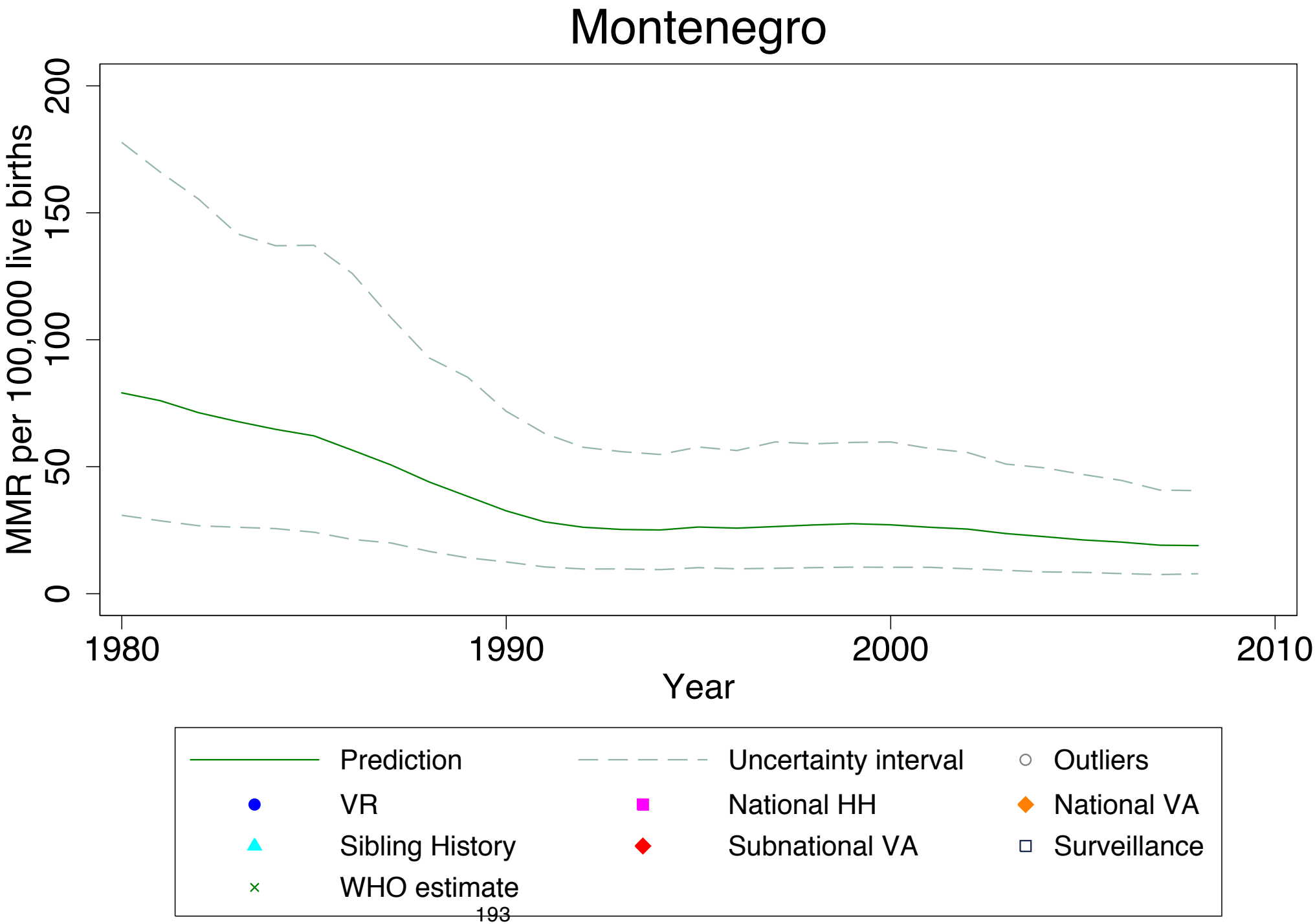

Bosnia and Herzegovina
MMR per 100,000 live births
0
20
40
60
80
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

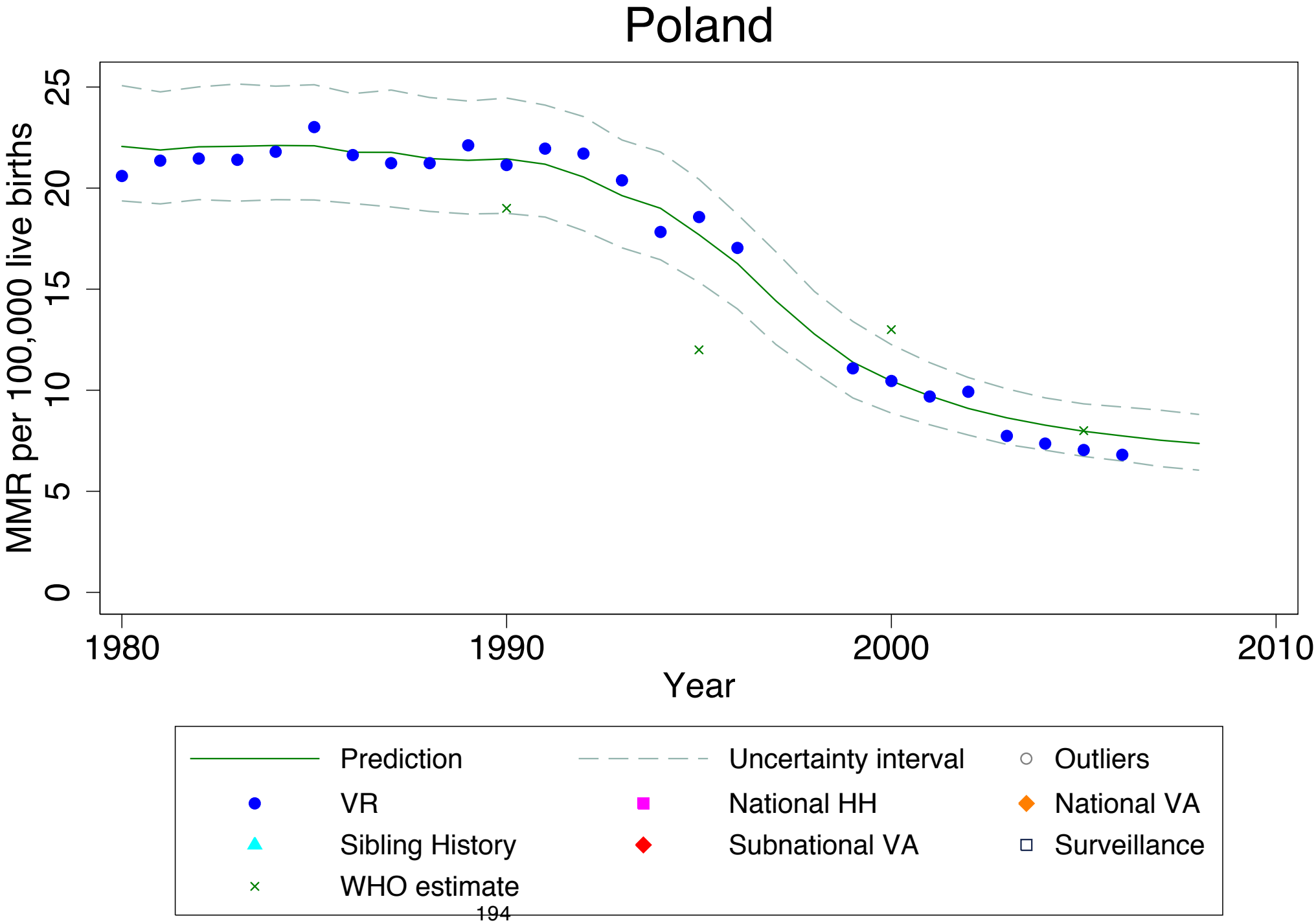

Czech Republic
MMR per 100,000 live births
0
5
10
15
20
25
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

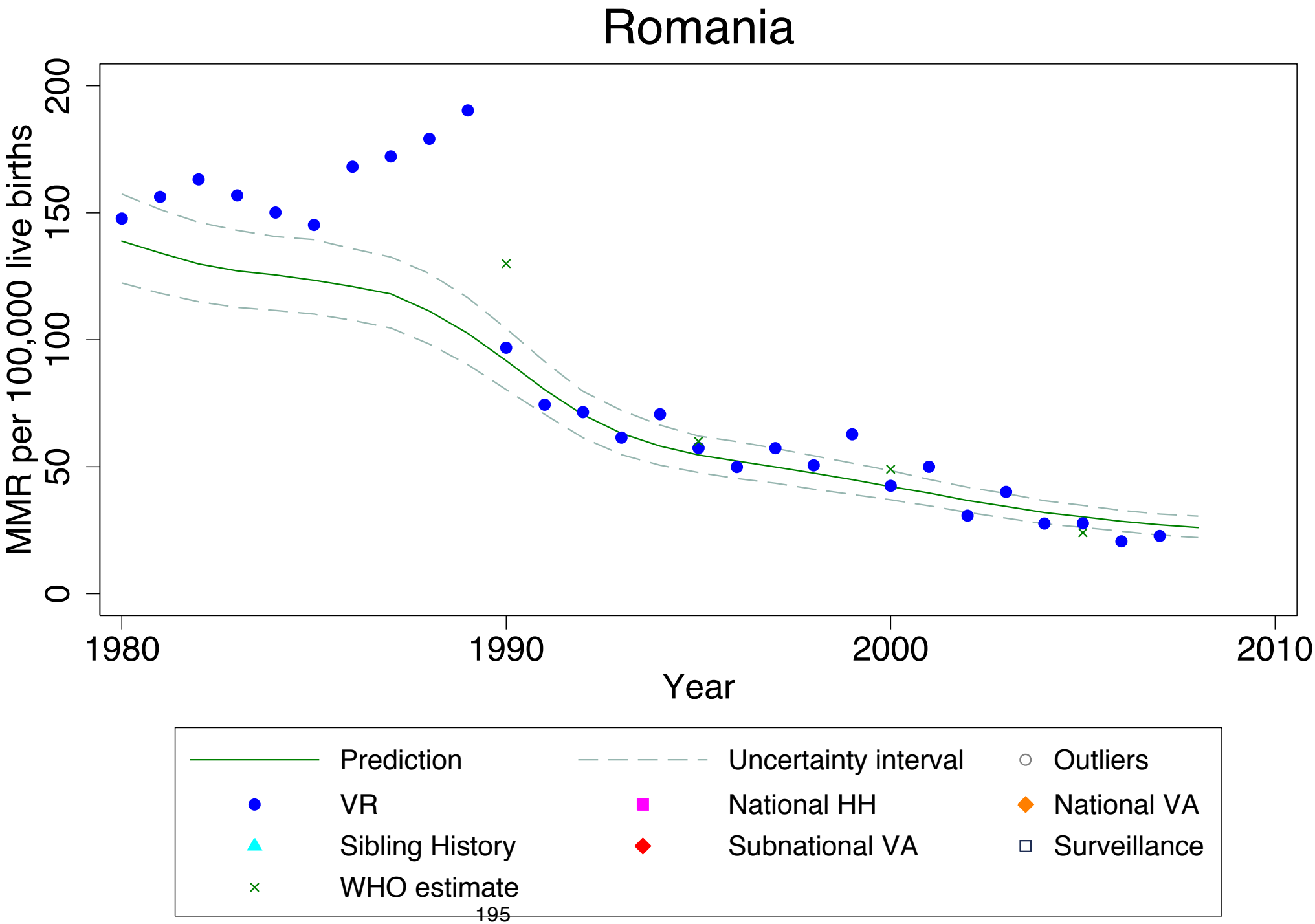

Croatia
MMR per 100,000 live births
0
5
10
15
20
25
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

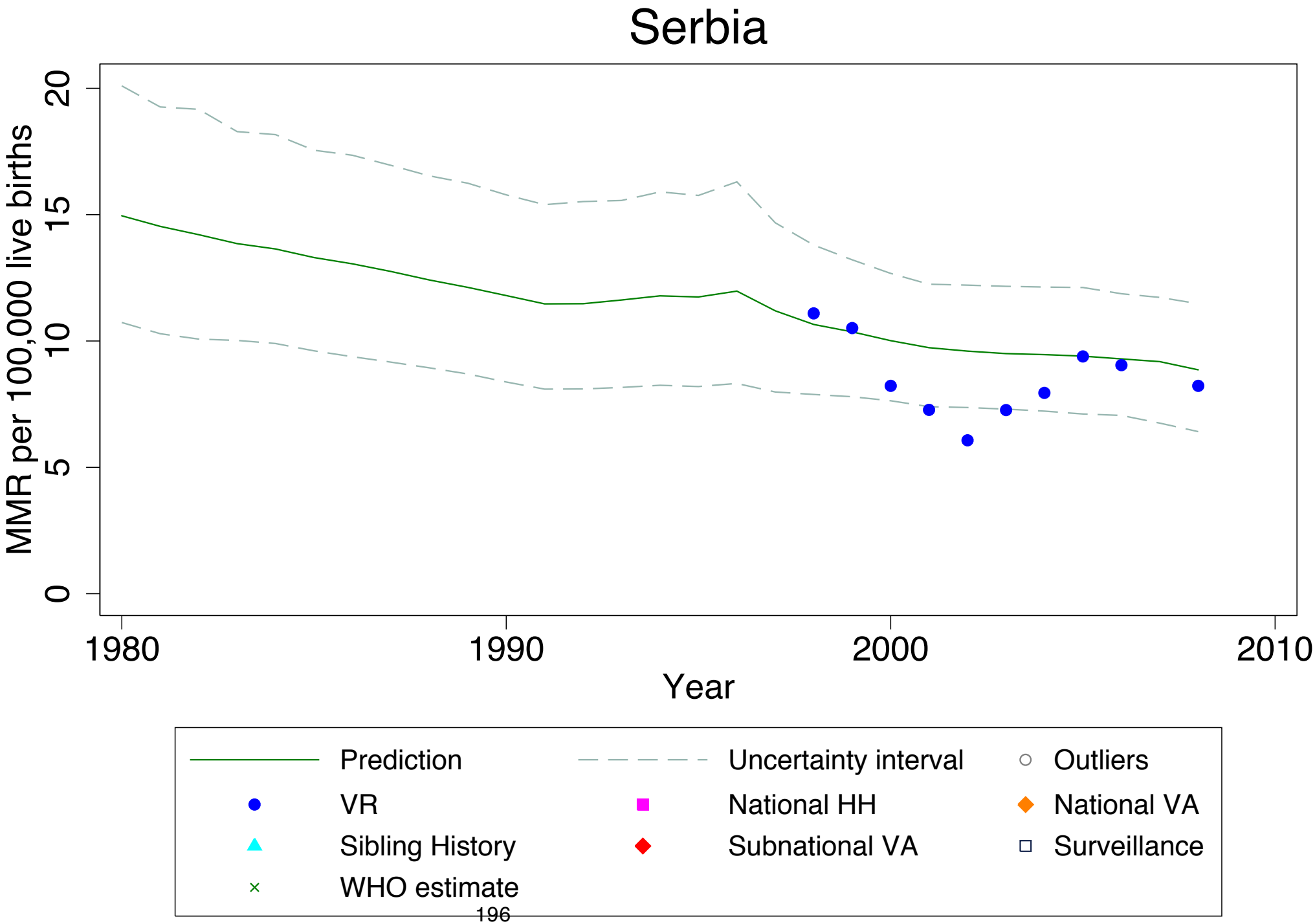

Hungary
MMR per 100,000 live births
0
10
20
30
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

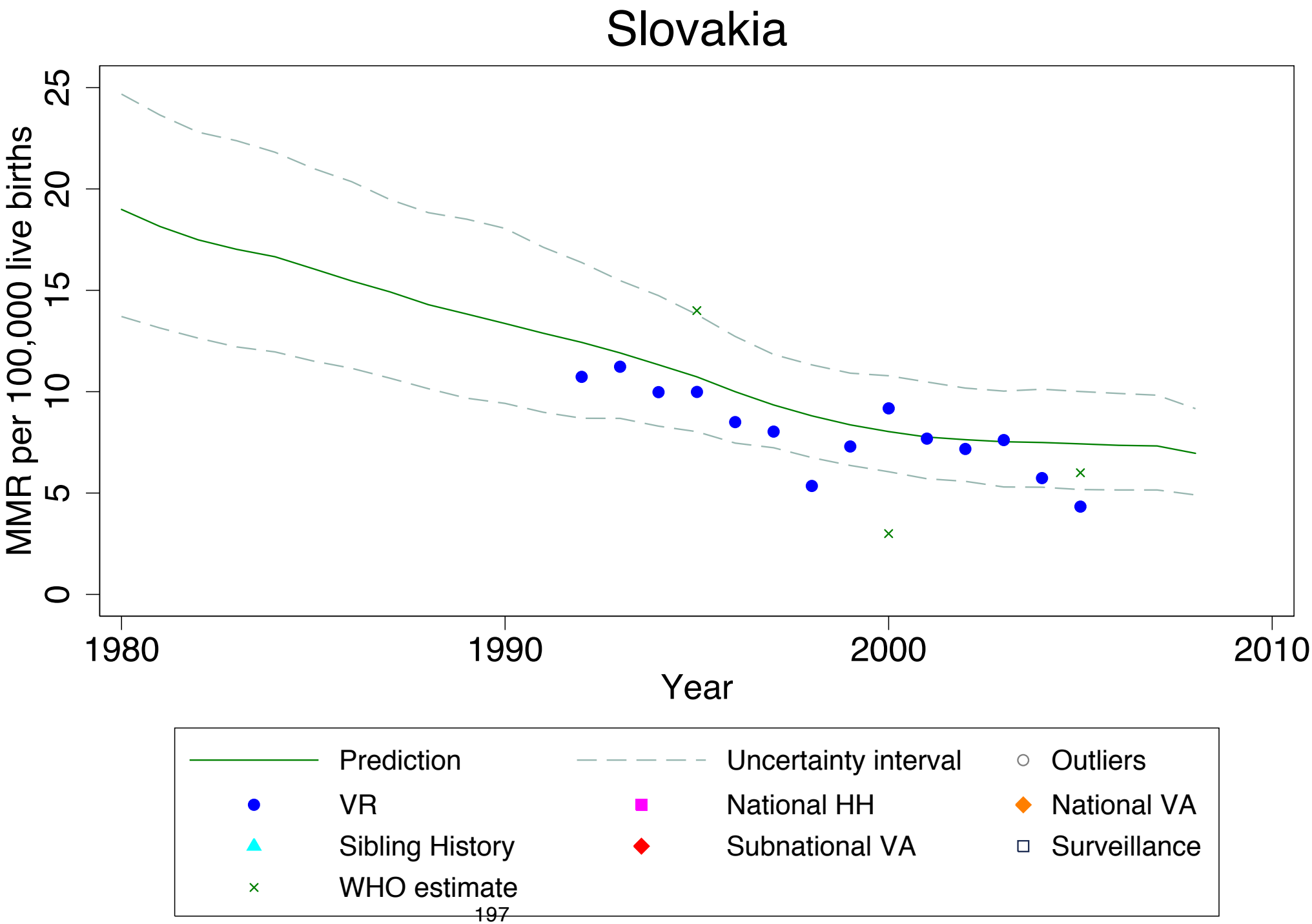

Macedonia, the Former Yugoslav Republic of
MMR per 100,000 live births
0
10
20
30
40
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

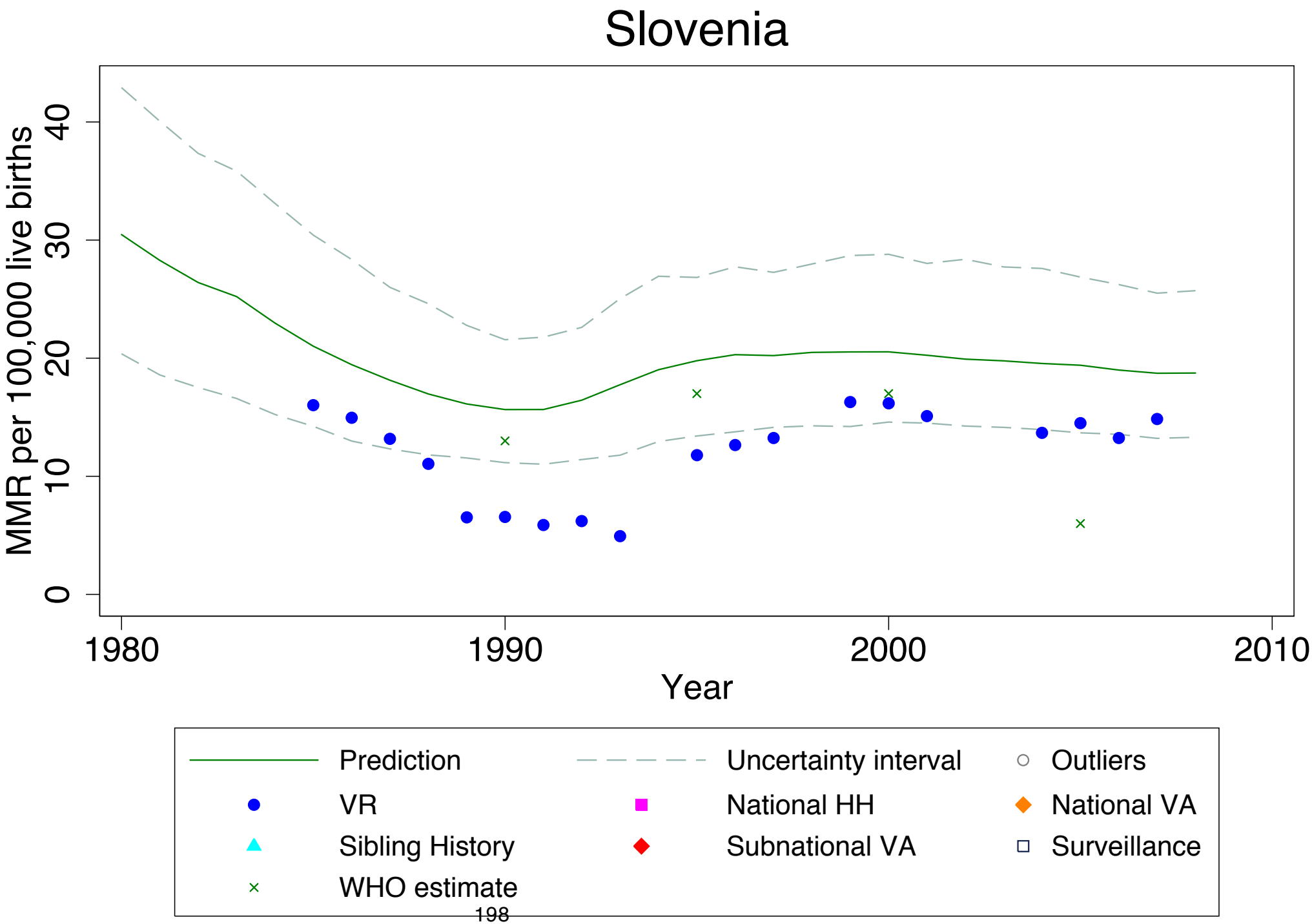

Montenegro
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Poland
MMR per 100,000 live births
0
5
10
15
20
25
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Romania
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Serbia
MMR per 100,000 live births
0
5
10
15
20
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Slovakia
MMR per 100,000 live births
0
5
10
15
20
25
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Slovenia
MMR per 100,000 live births
0
10
20
30
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1980
1990
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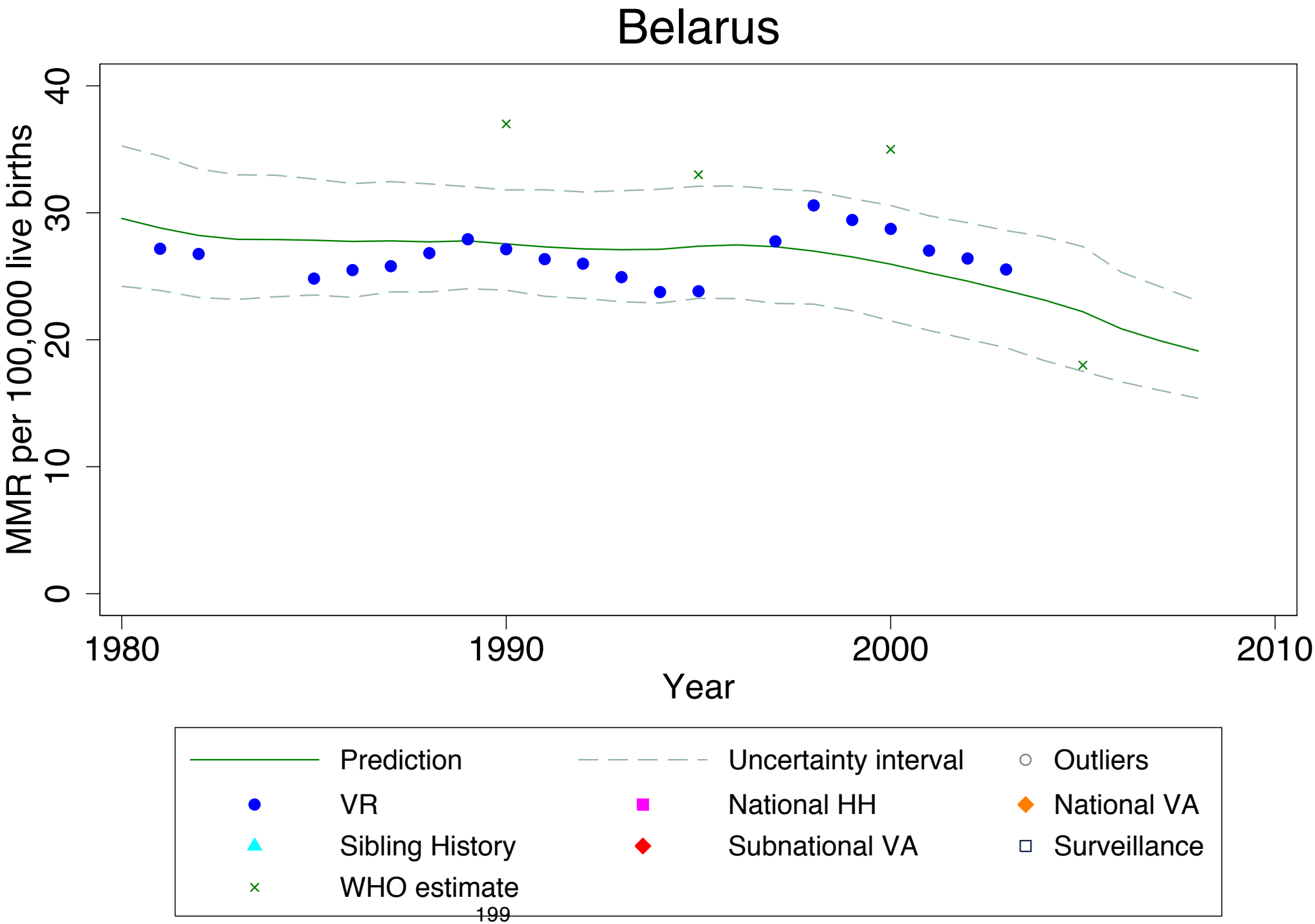
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Belarus
MMR per 100,000 live births
0
10
20
30
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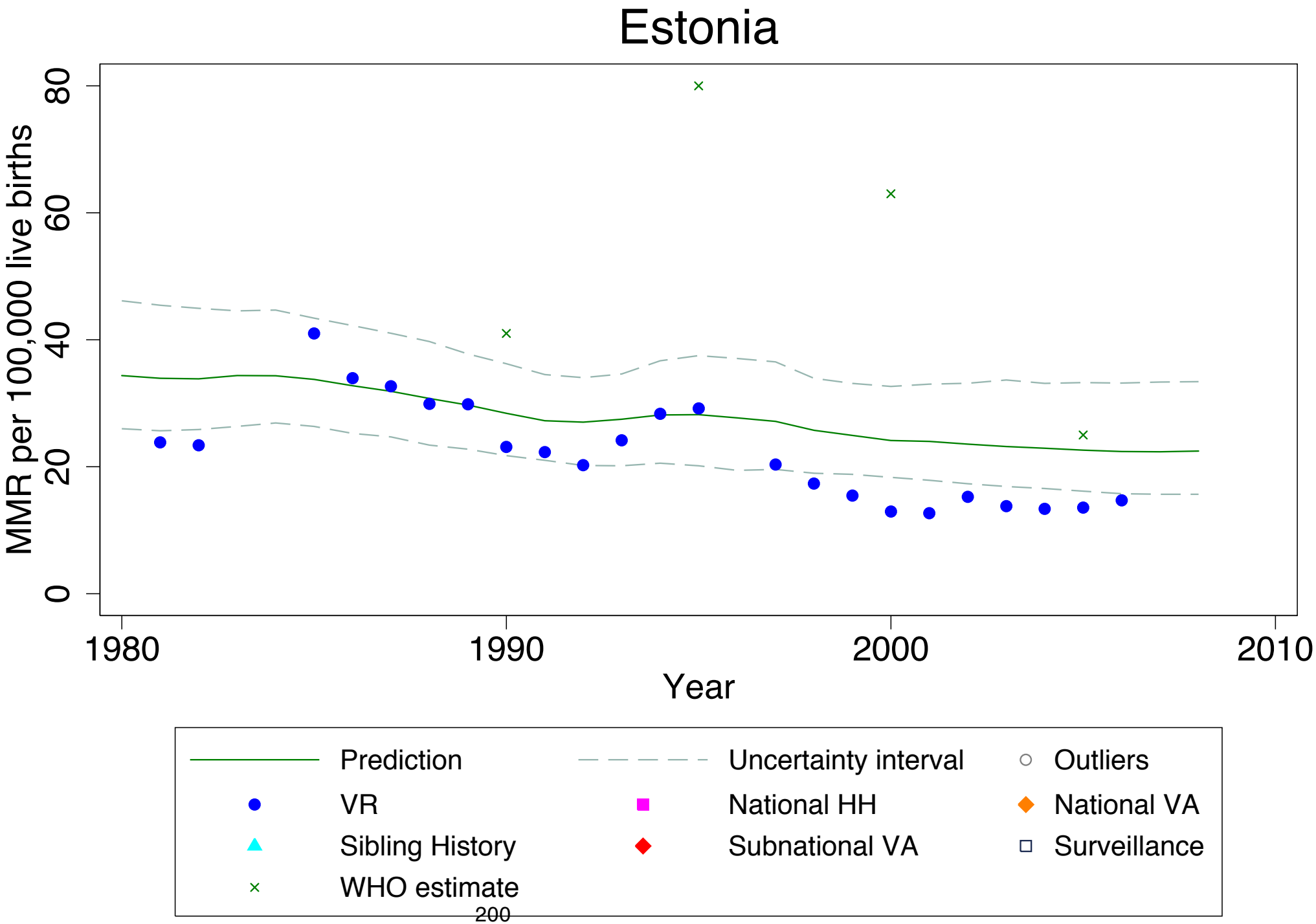
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Estonia
MMR per 100,000 live births
0
20
40
60
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1980
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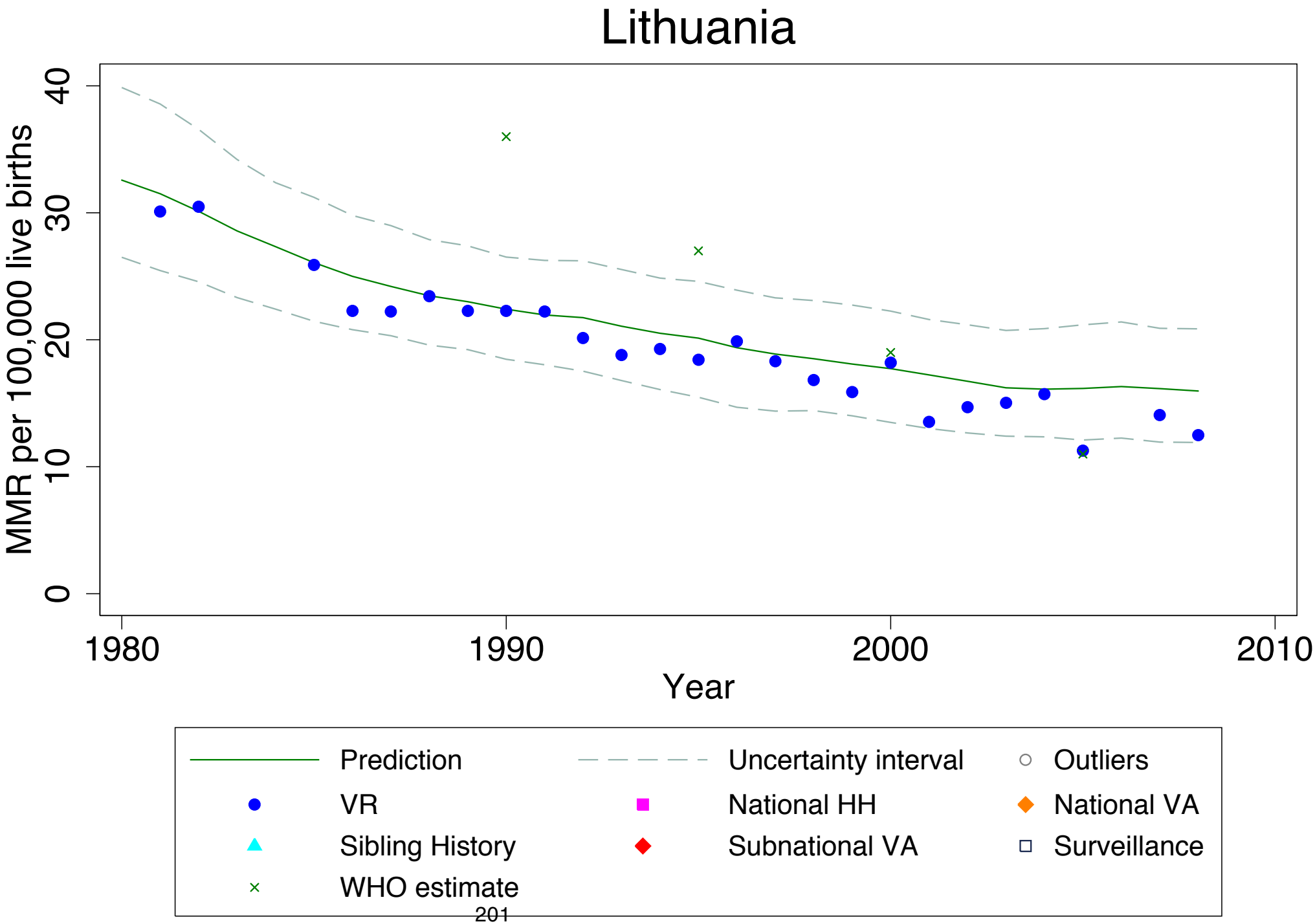
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Lithuania
MMR per 100,000 live births
0
10
20
30
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1980
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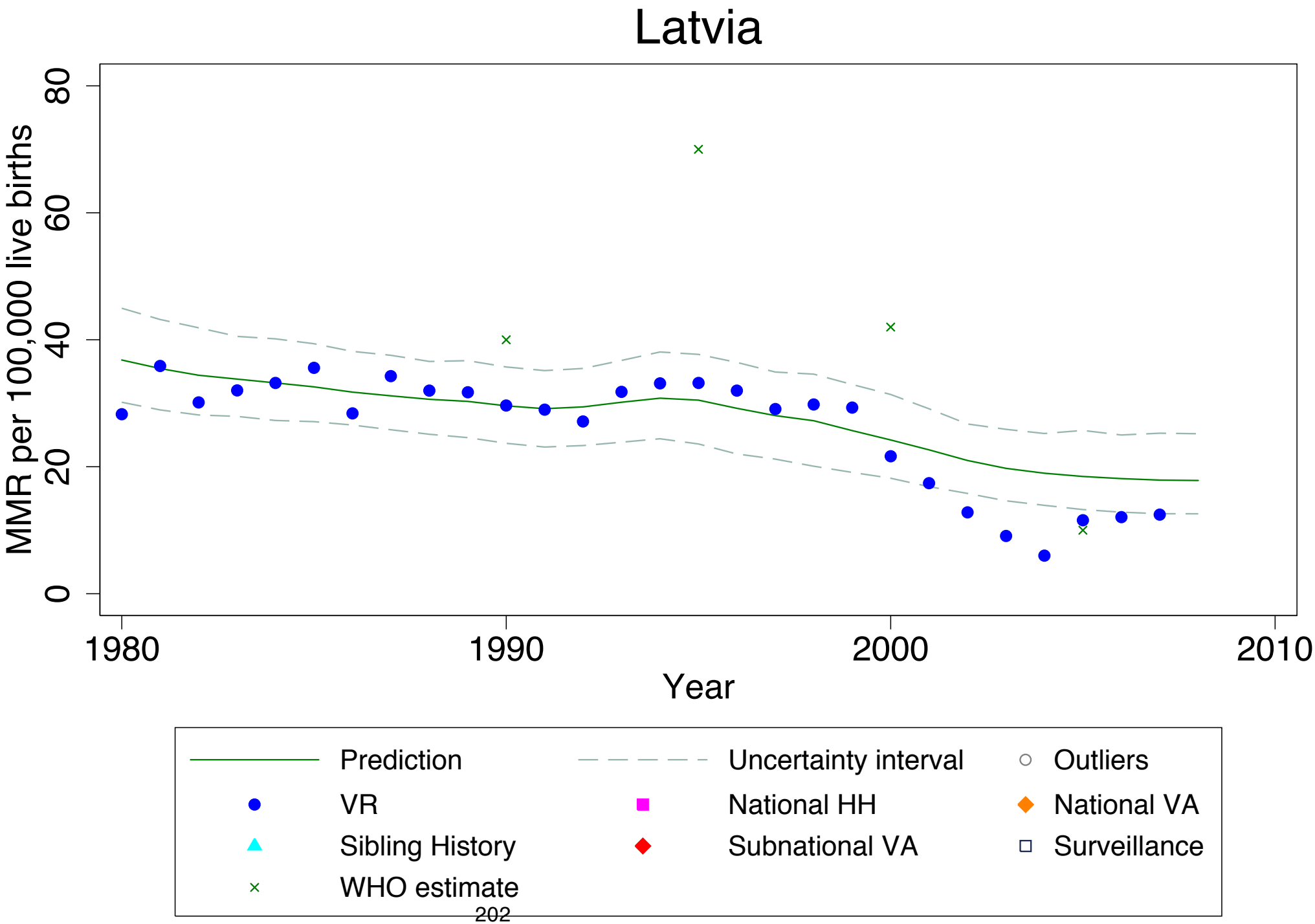
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Latvia
MMR per 100,000 live births
0
20
40
60
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1980
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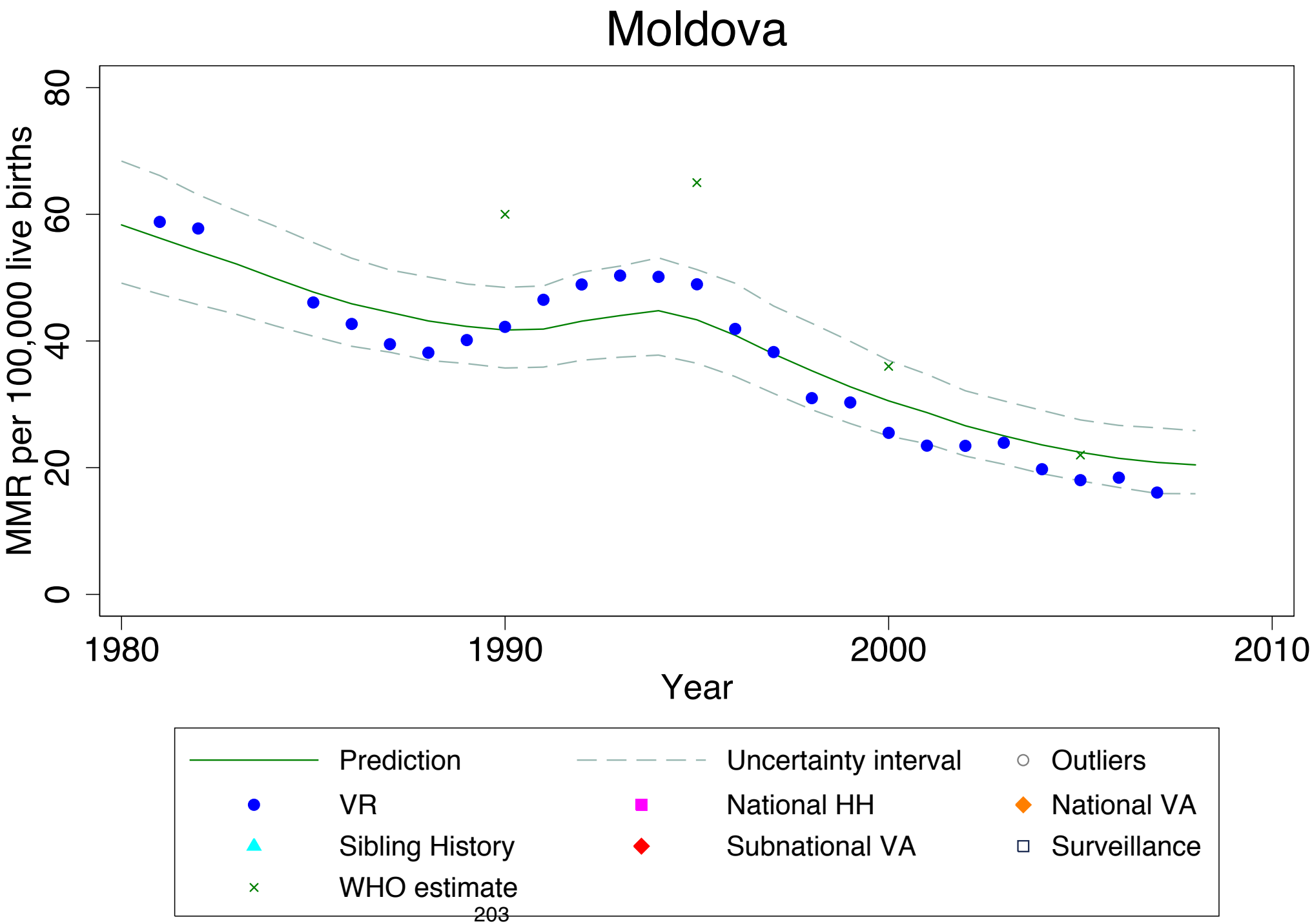
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Moldova
MMR per 100,000 live births
0
20
40
60
80
1980
1990
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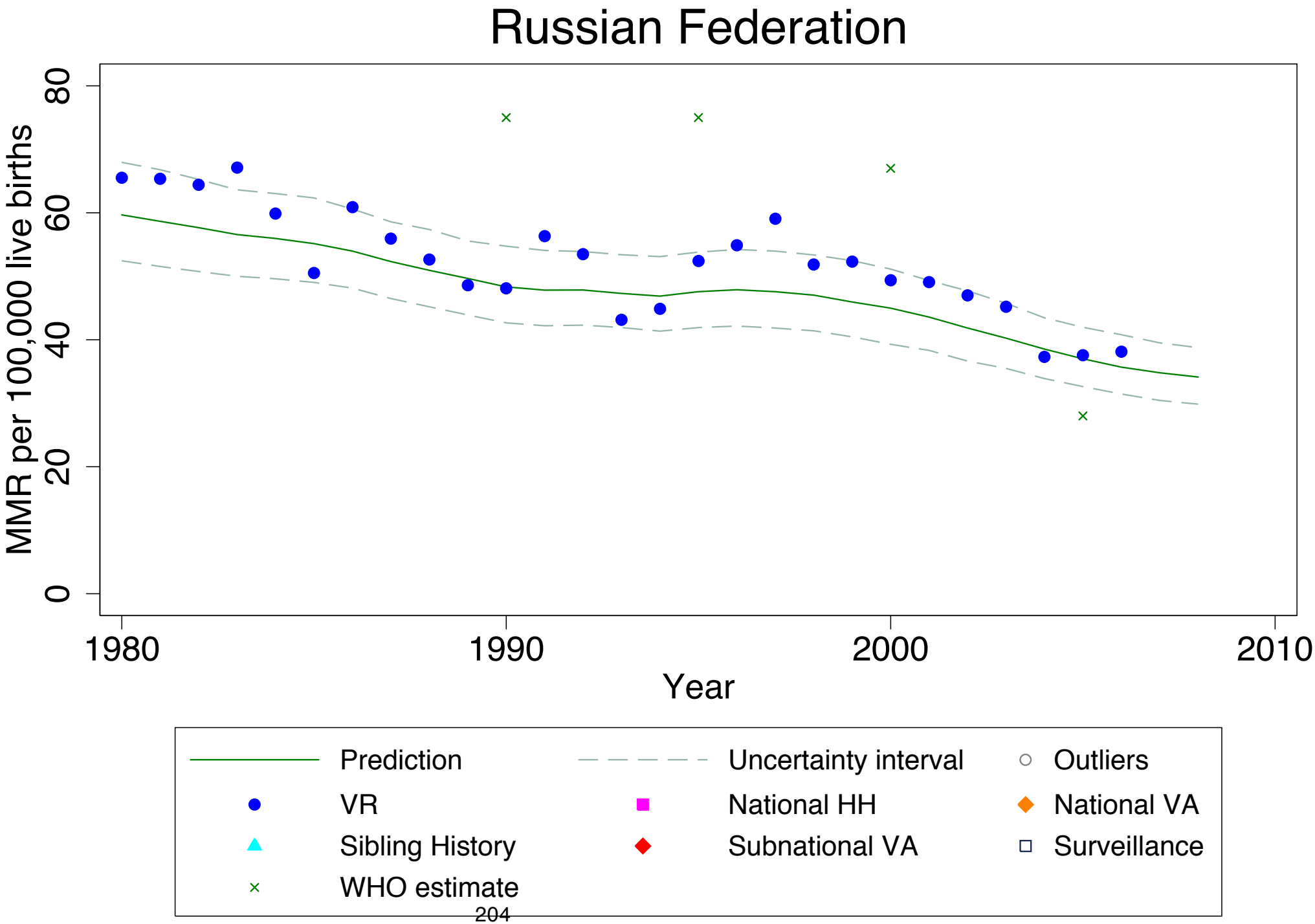
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Russian Federation
MMR per 100,000 live births
0
20
40
60
80
1980
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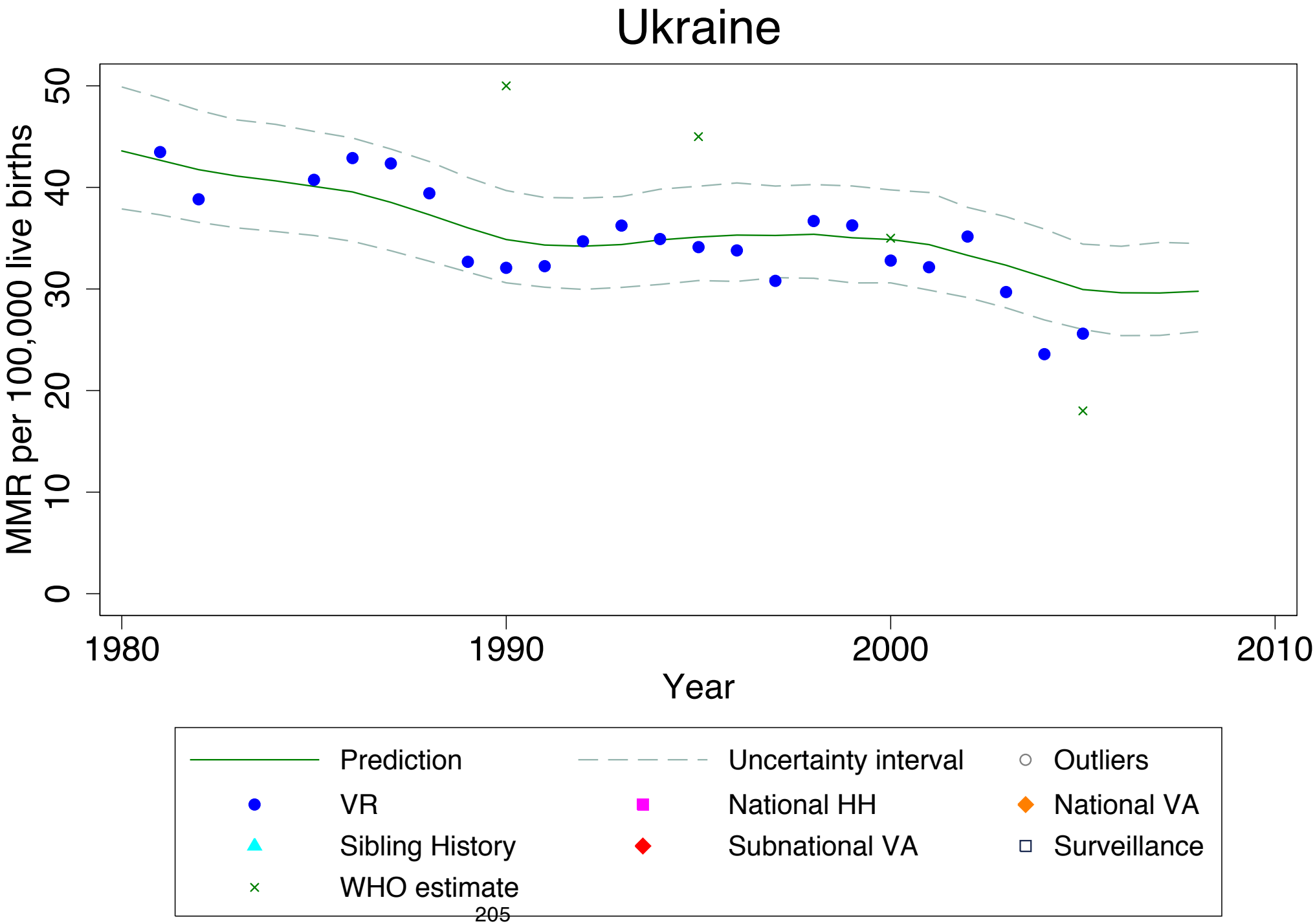
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Ukraine
MMR per 100,000 live births
0
10
20
30
40
50
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1990
2000
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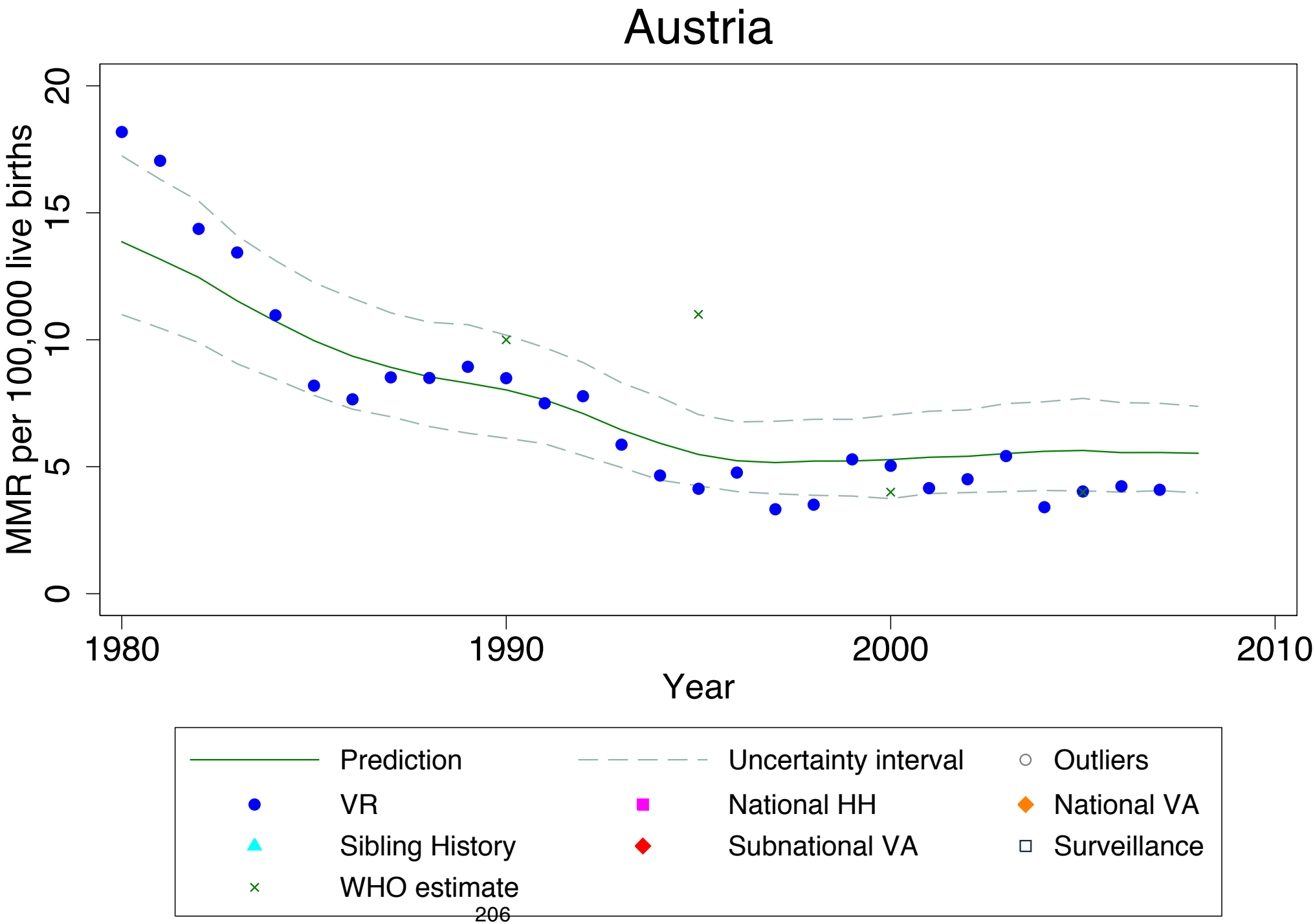
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Austria
MMR per 100,000 live births
0
5
10
15
20
1980
1990
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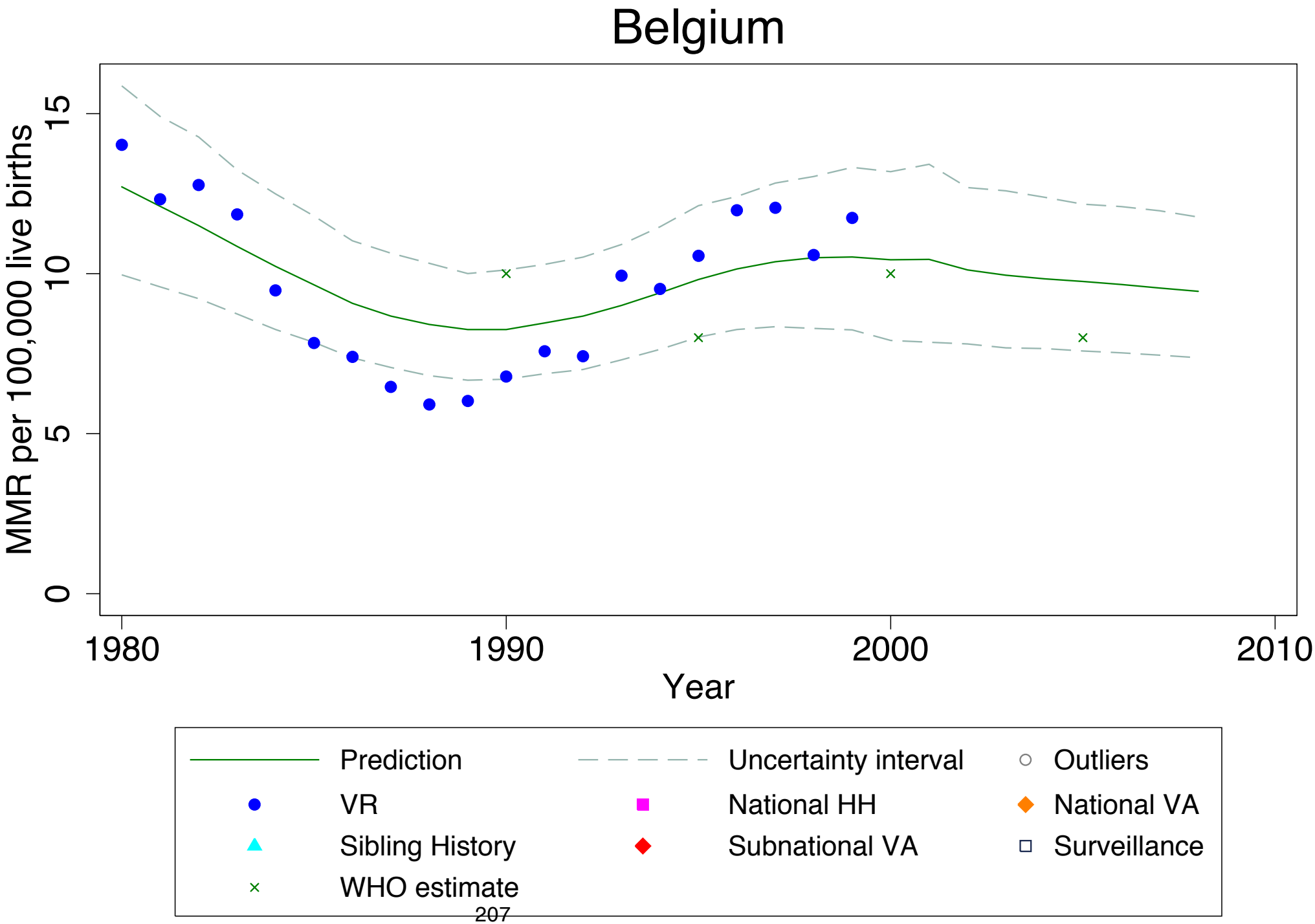
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Belgium
MMR per 100,000 live births
0
5
10
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1980
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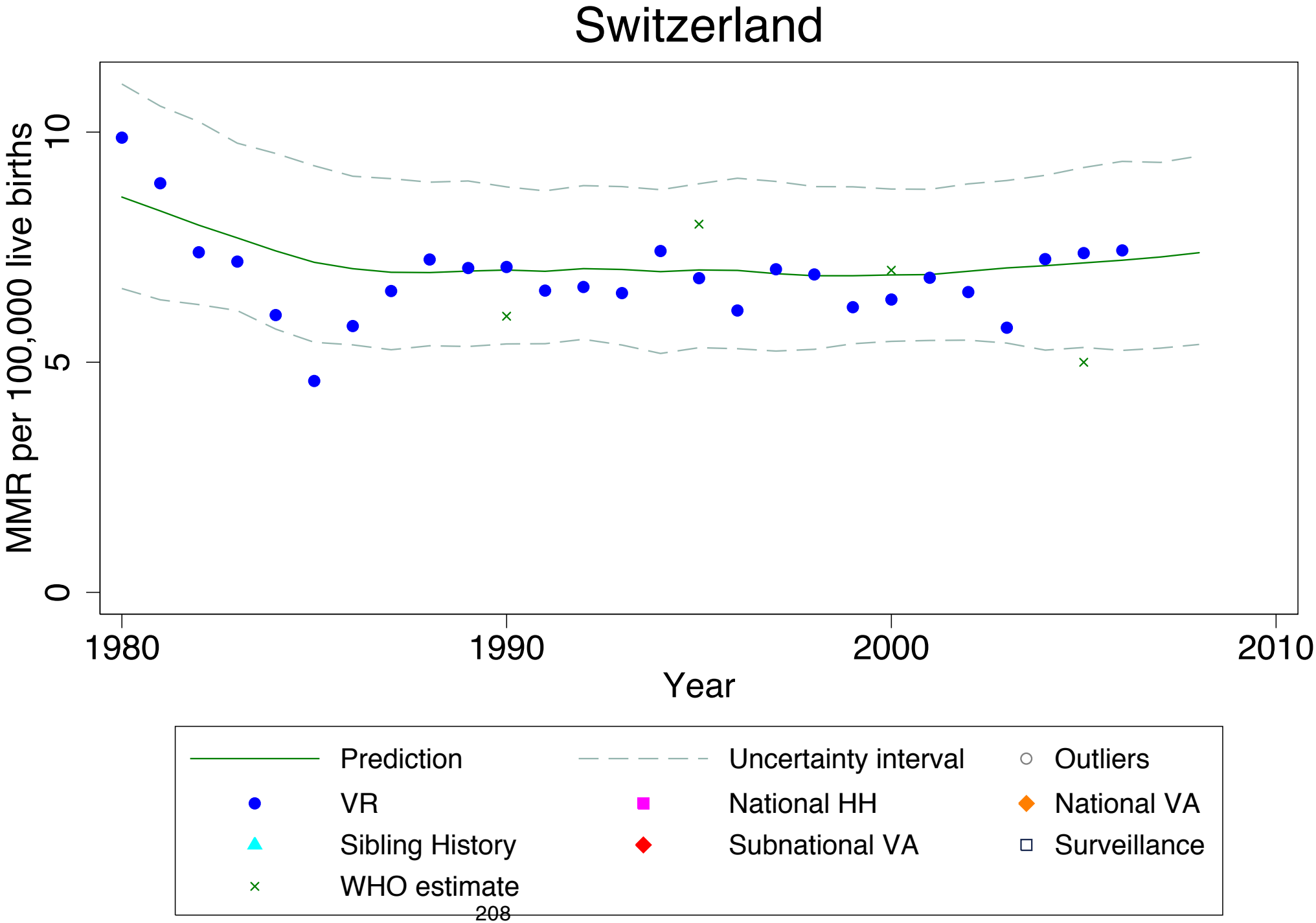
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Switzerland
MMR per 100,000 live births
0
5
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1980
1990
2000
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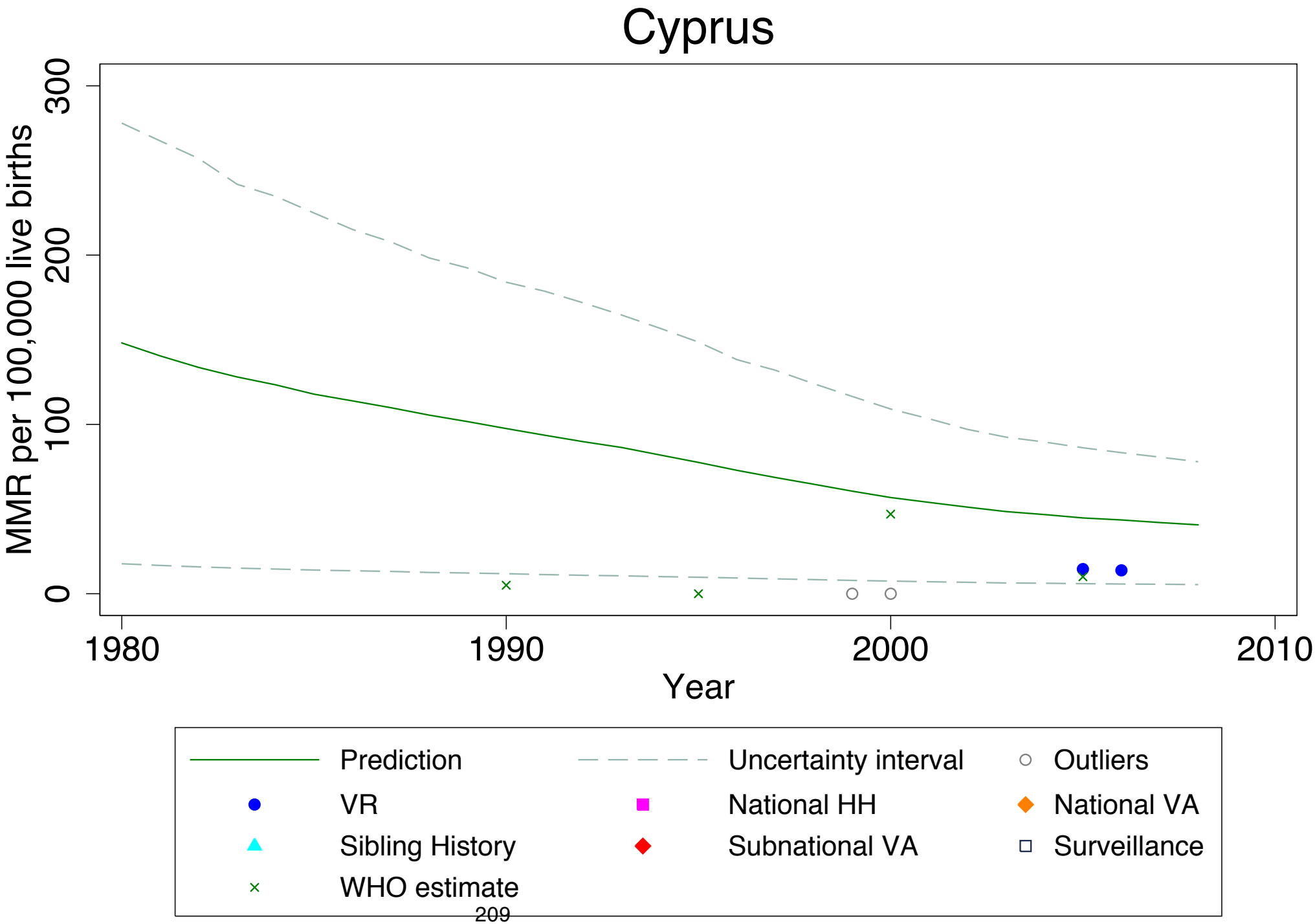
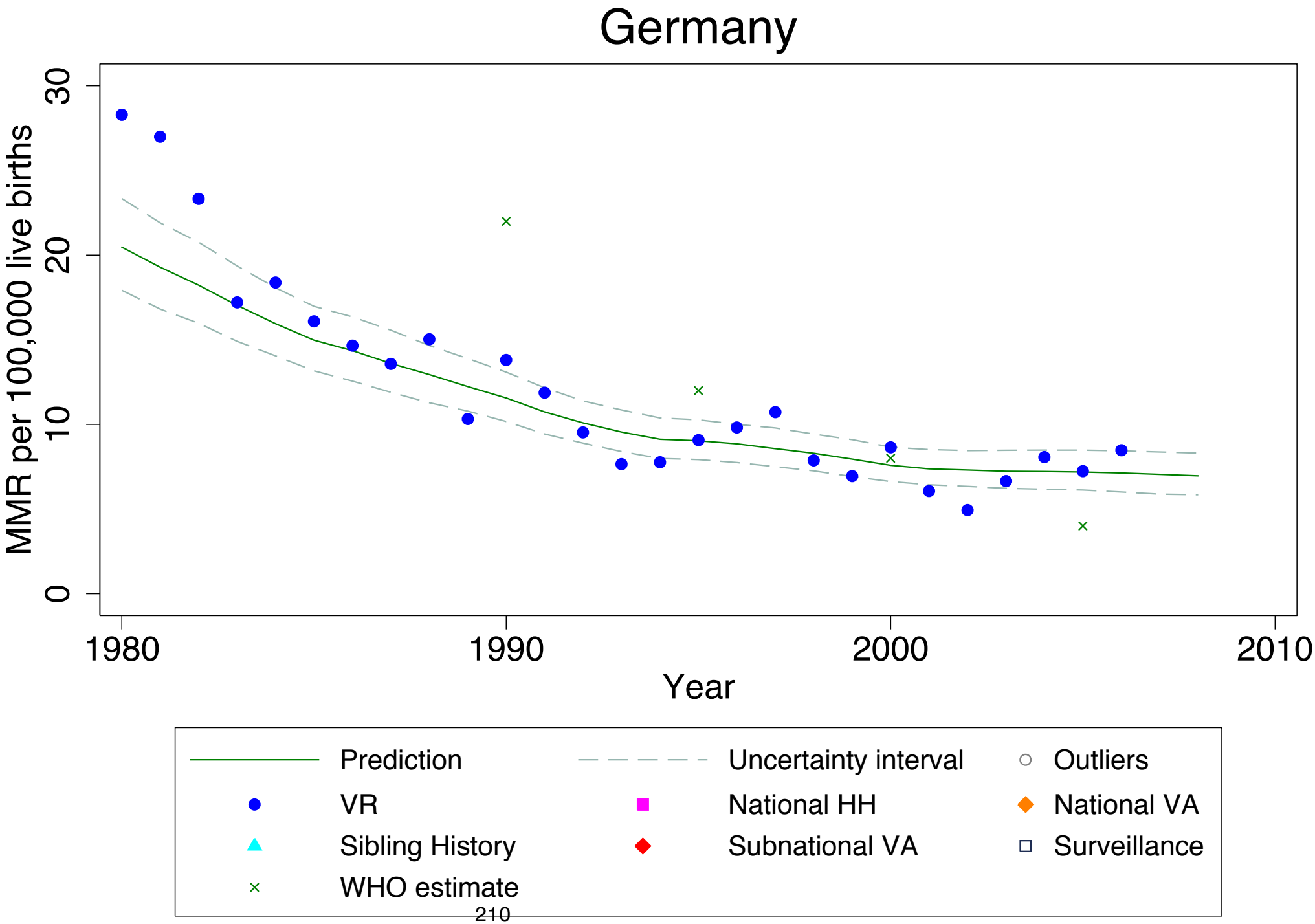
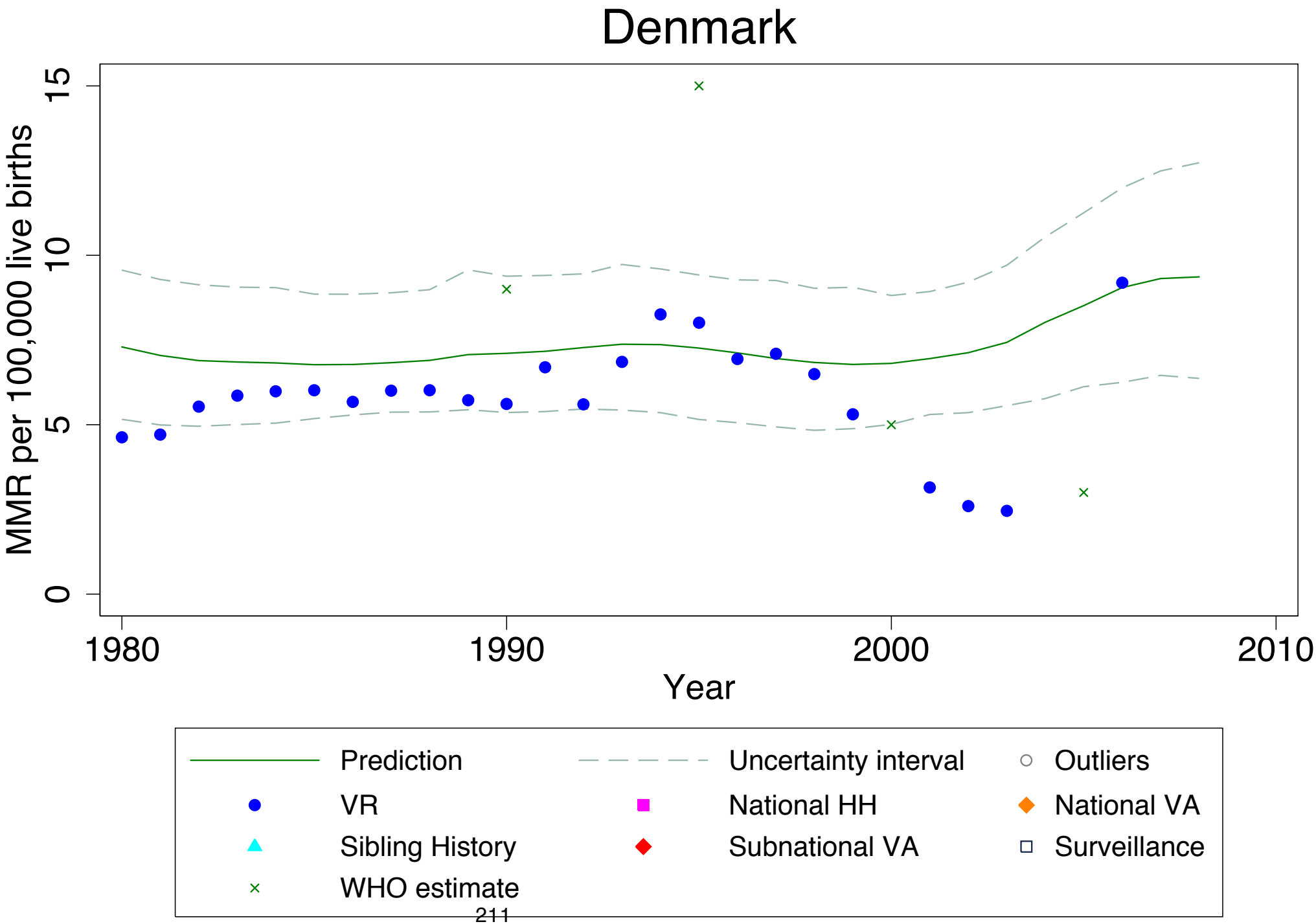
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Cyprus
MMR per 100,000 live births
0
100
200
300
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Germany
MMR per 100,000 live births
0
10
20
30
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Denmark
MMR per 100,000 live births
0
5
10
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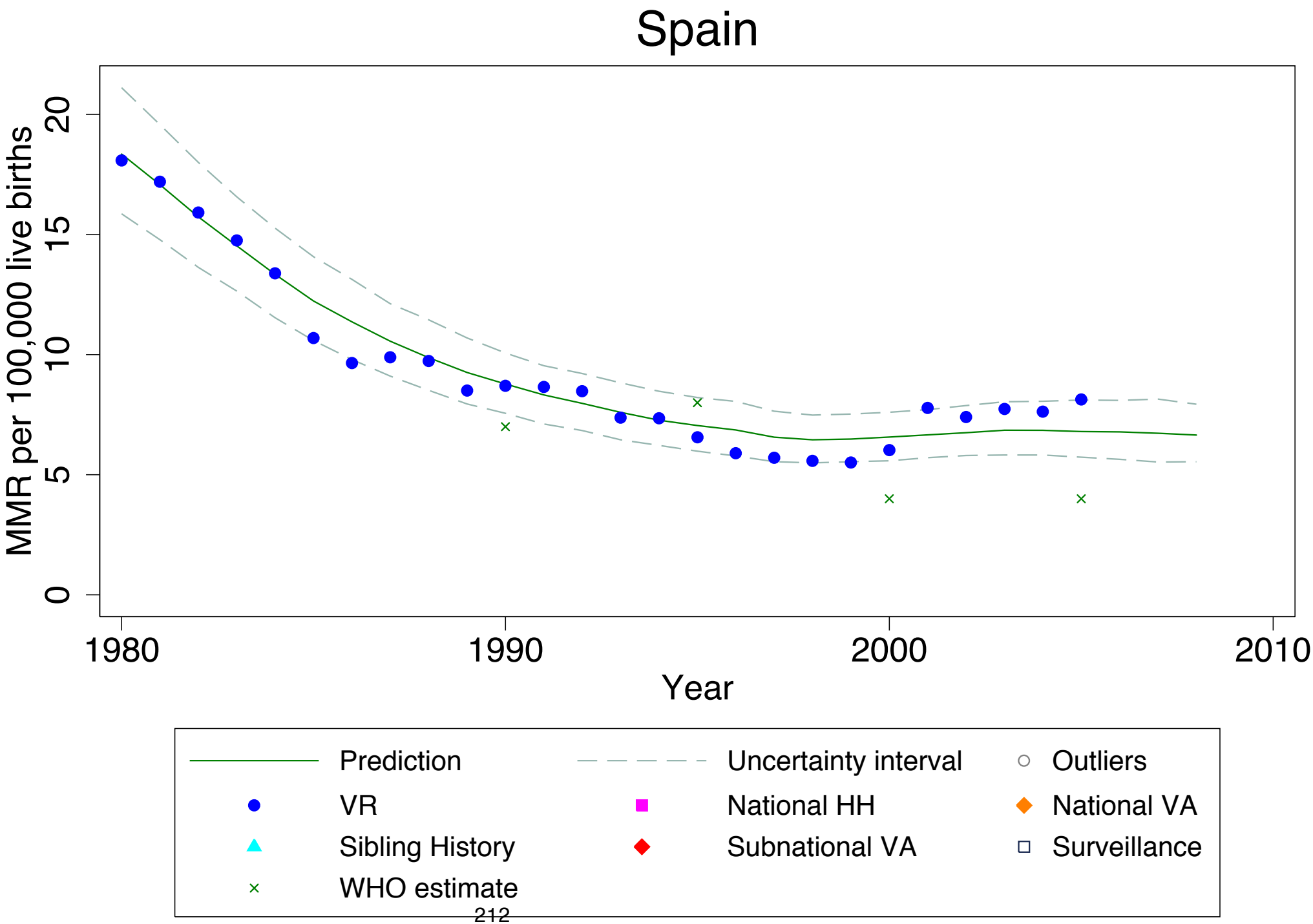
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Spain
MMR per 100,000 live births
0
5
10
15
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Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
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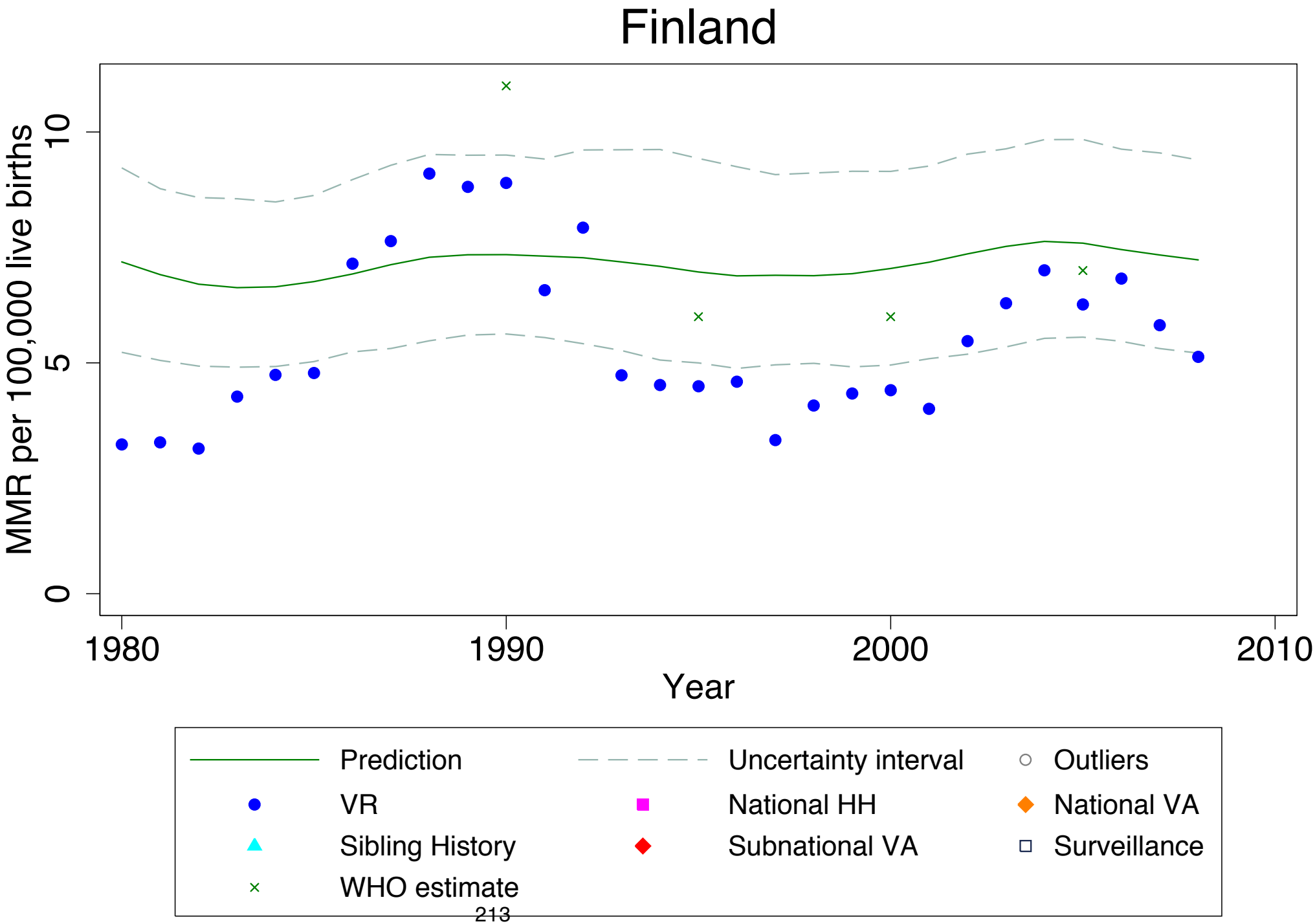
Subnational VA
Surveillance
WHO estimate


Finland
MMR per 100,000 live births
0
5
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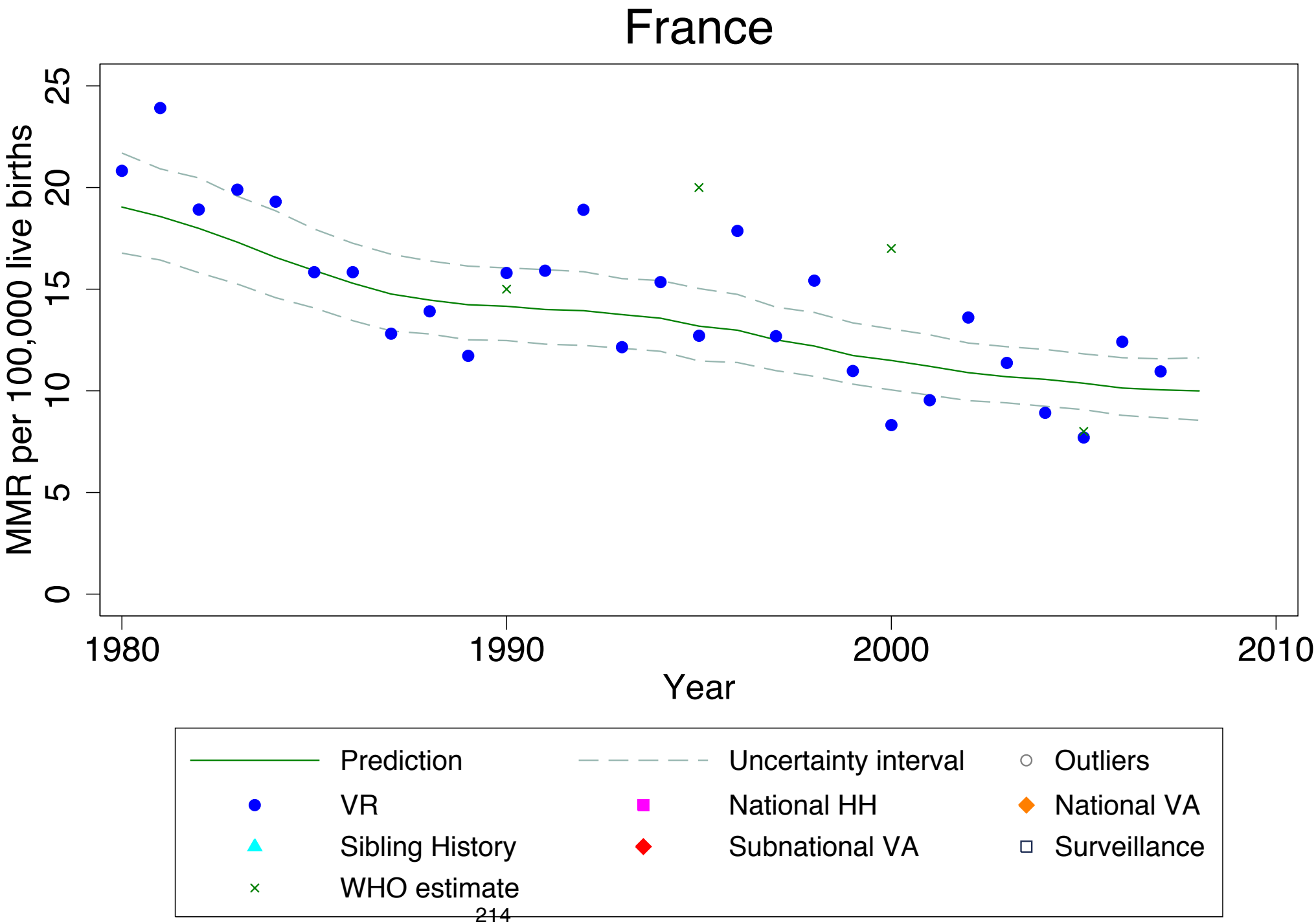
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


France
MMR per 100,000 live births
0
5
10
15
20
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Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
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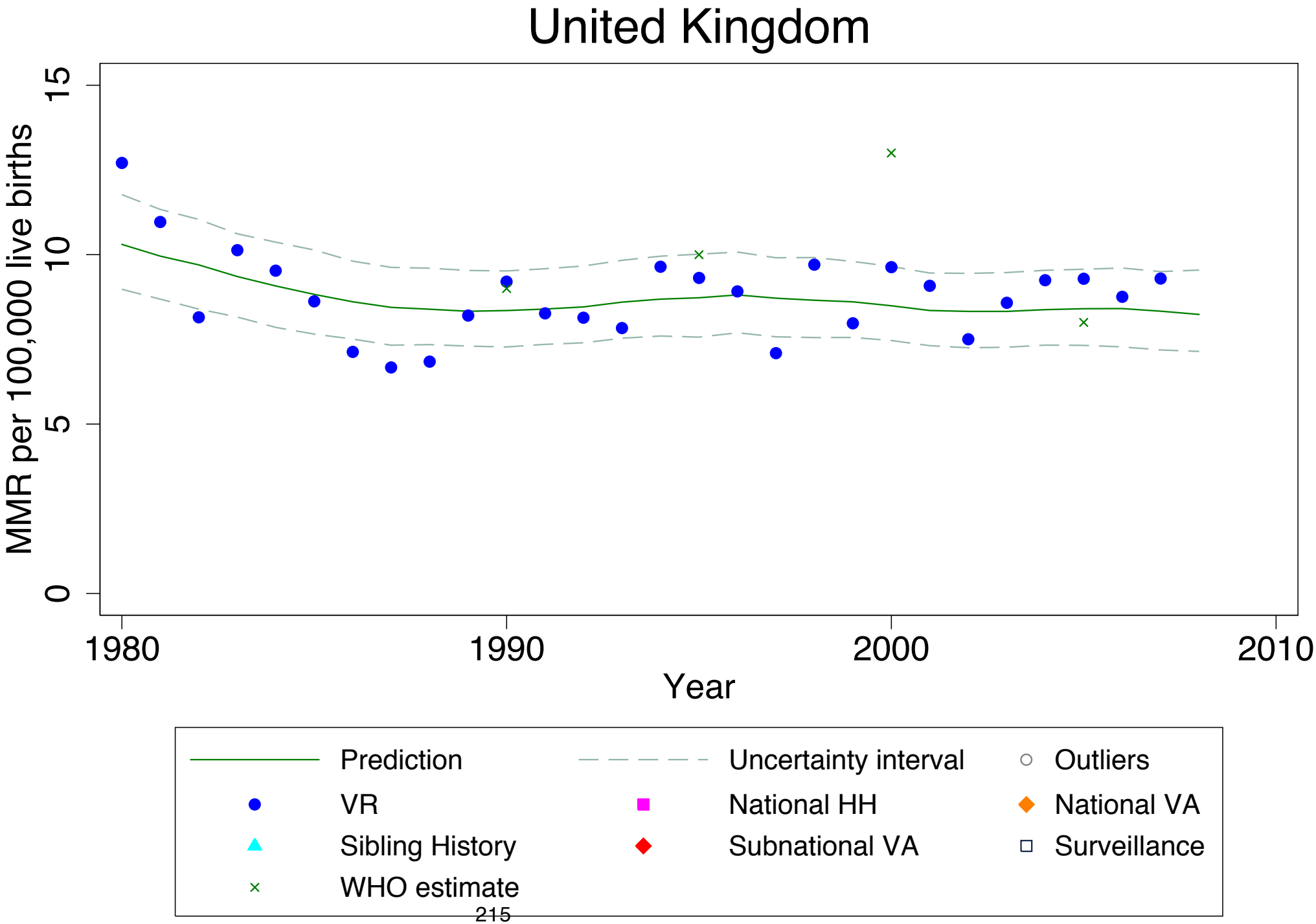
Subnational VA
Surveillance
WHO estimate


United Kingdom
MMR per 100,000 live births
0
5
10
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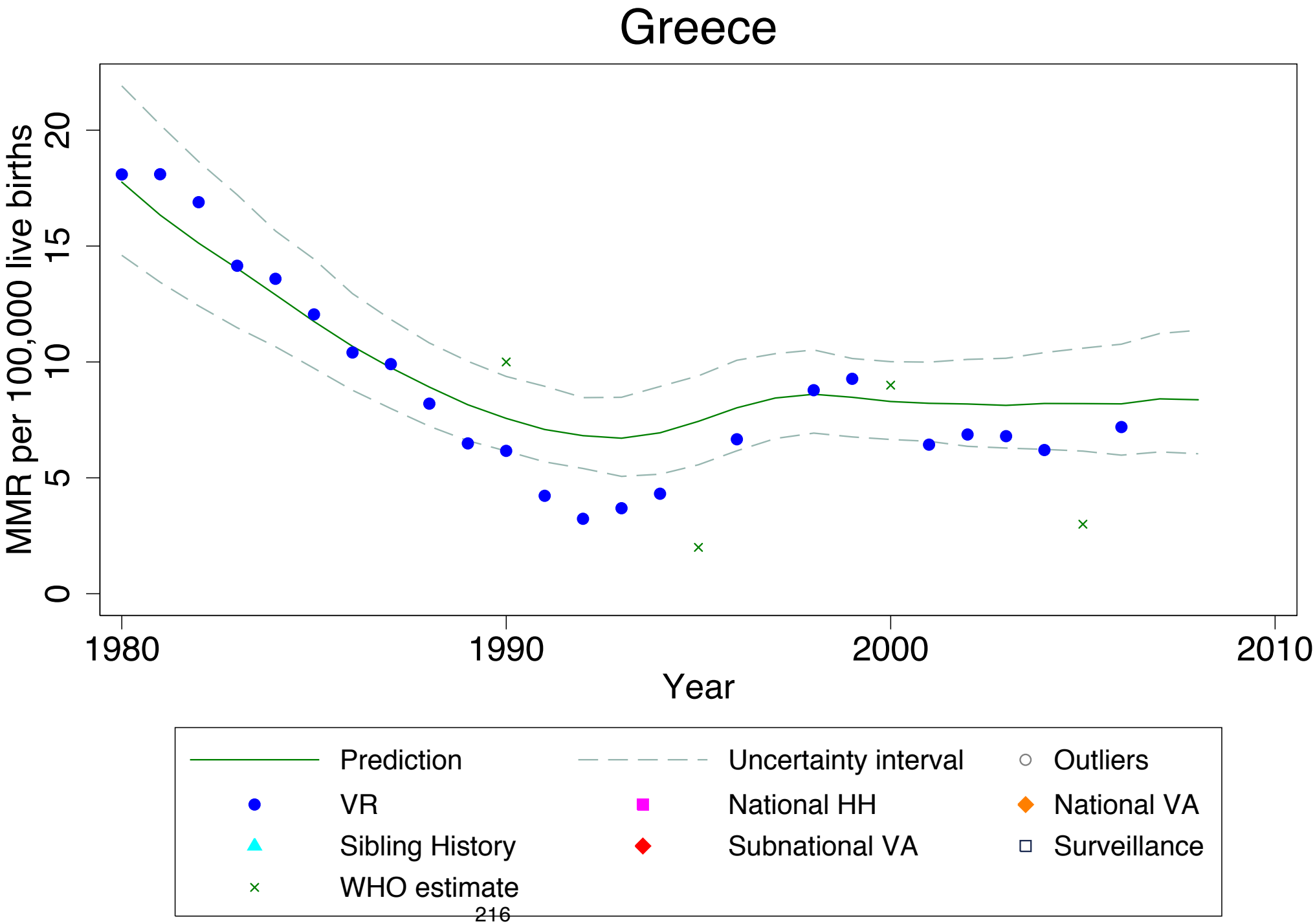
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Greece
MMR per 100,000 live births
0
5
10
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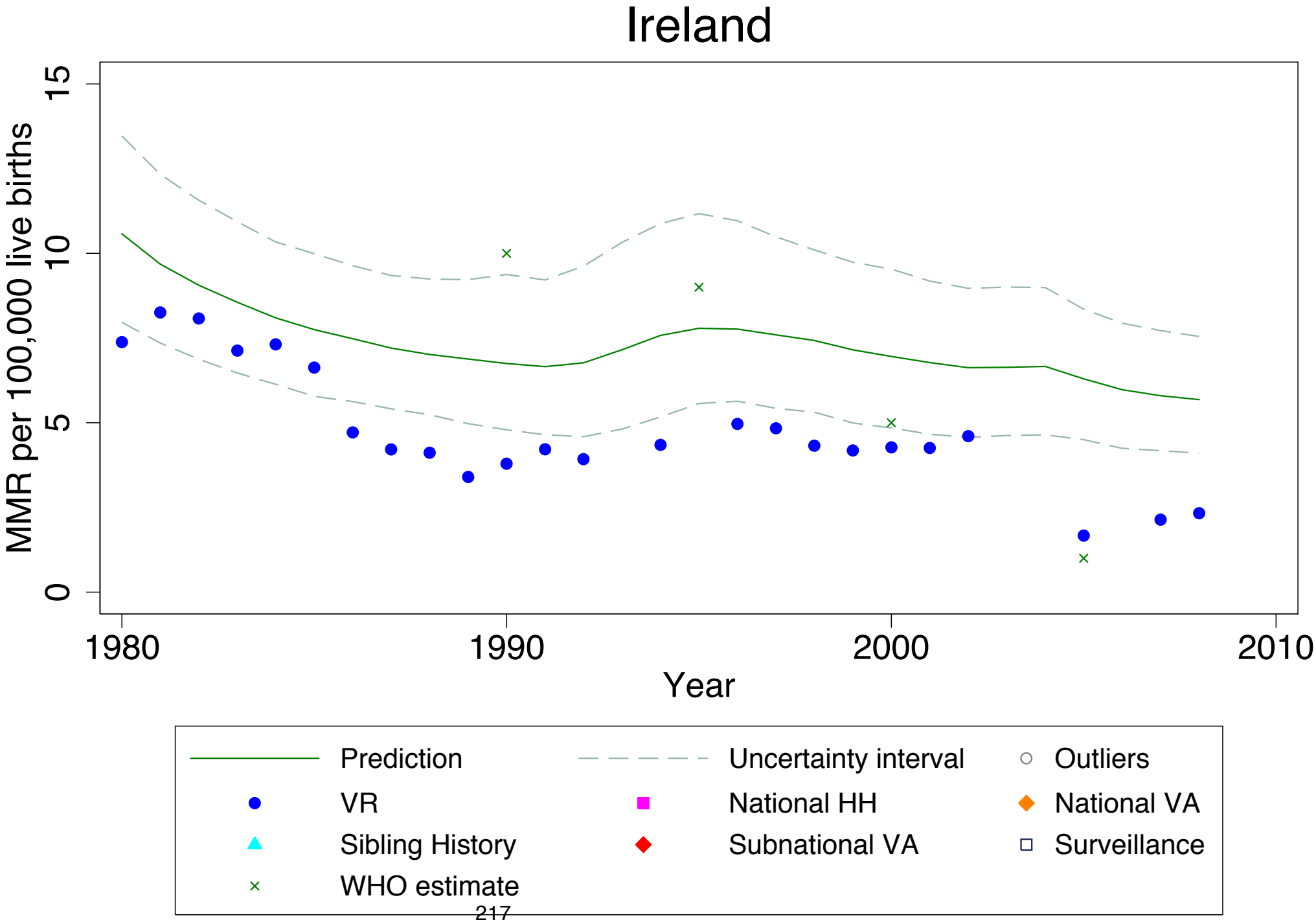
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Ireland
MMR per 100,000 live births
0
5
10
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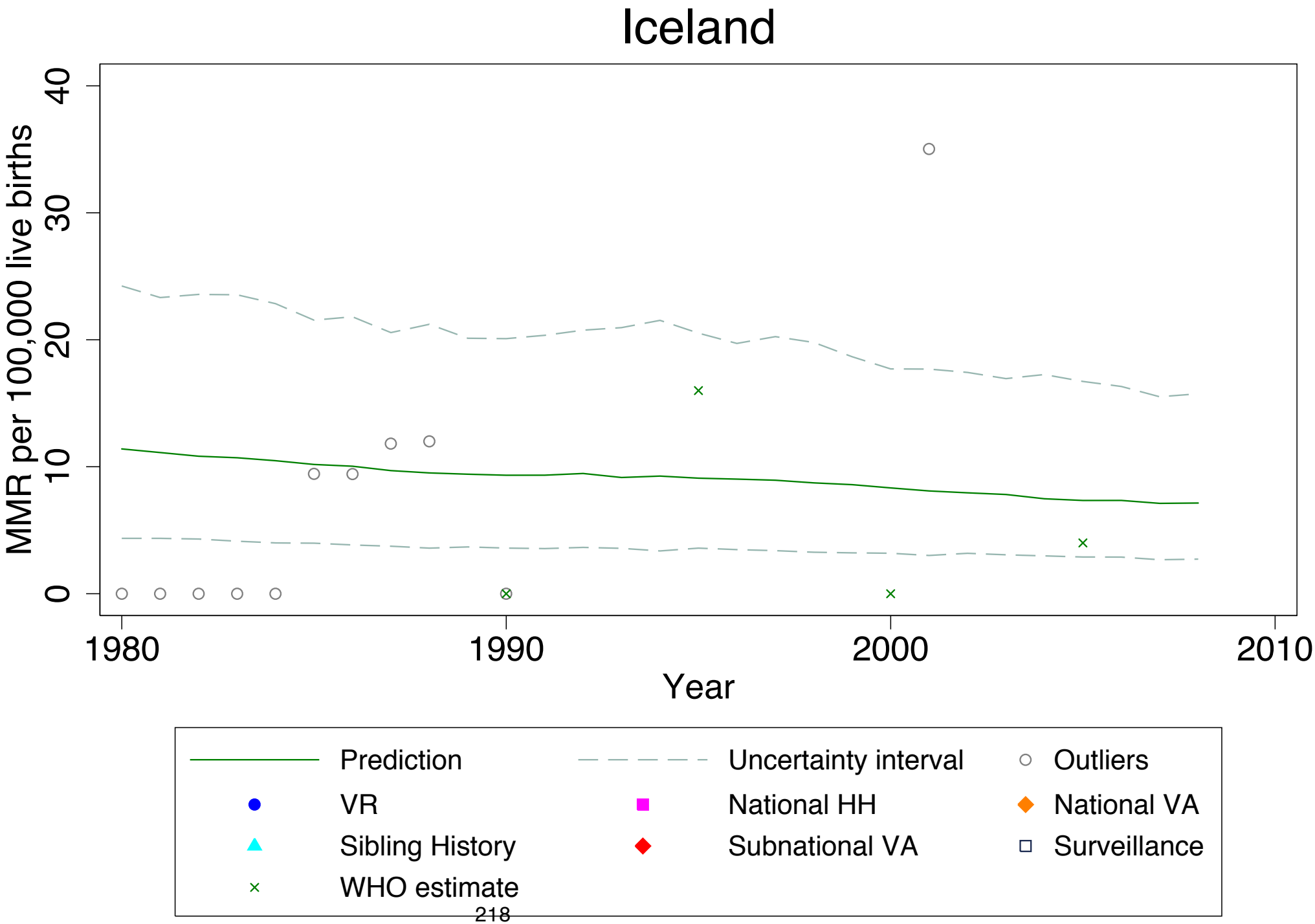
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Iceland
MMR per 100,000 live births
0
10
20
30
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1980
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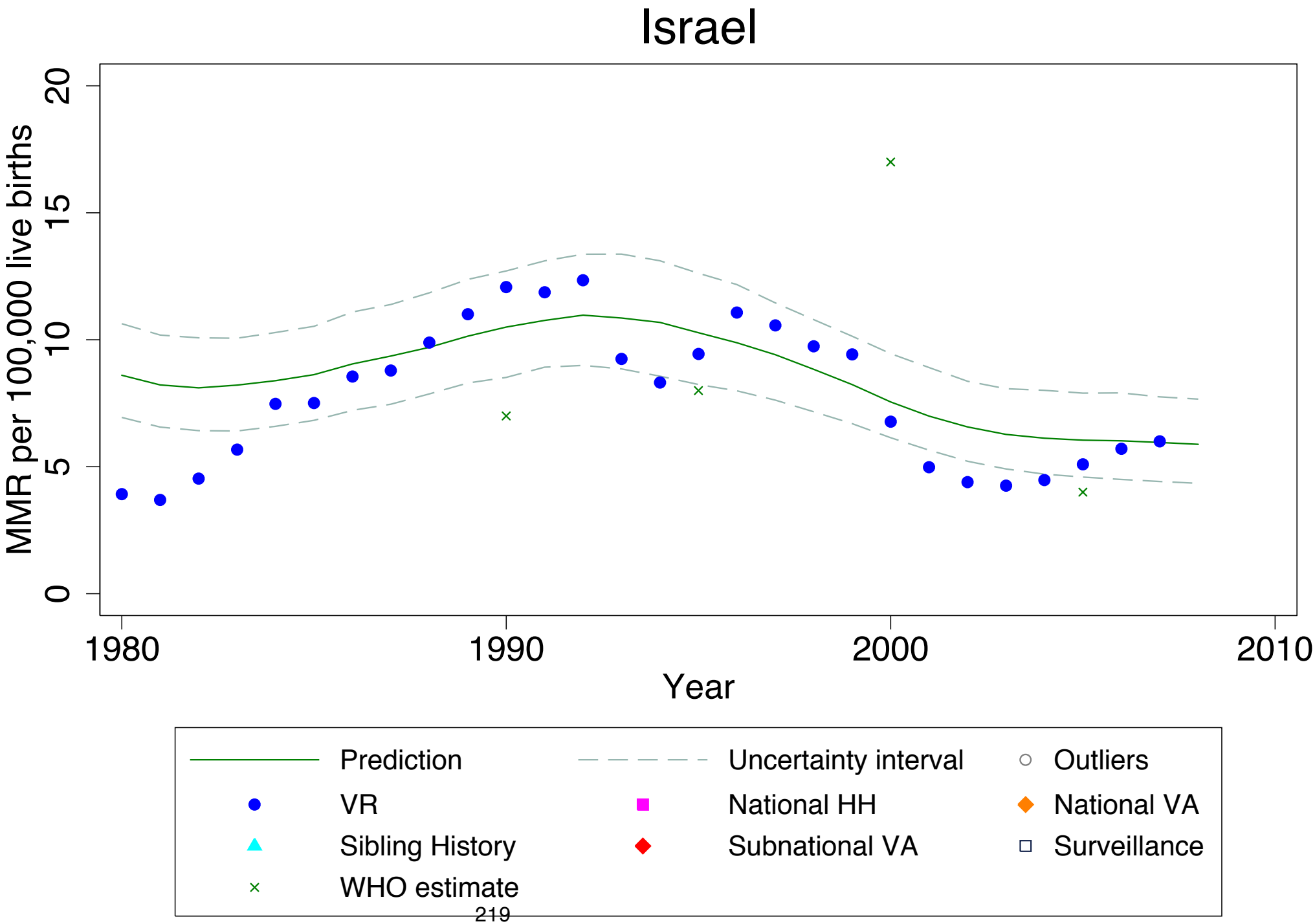
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Israel
MMR per 100,000 live births
0
5
10
15
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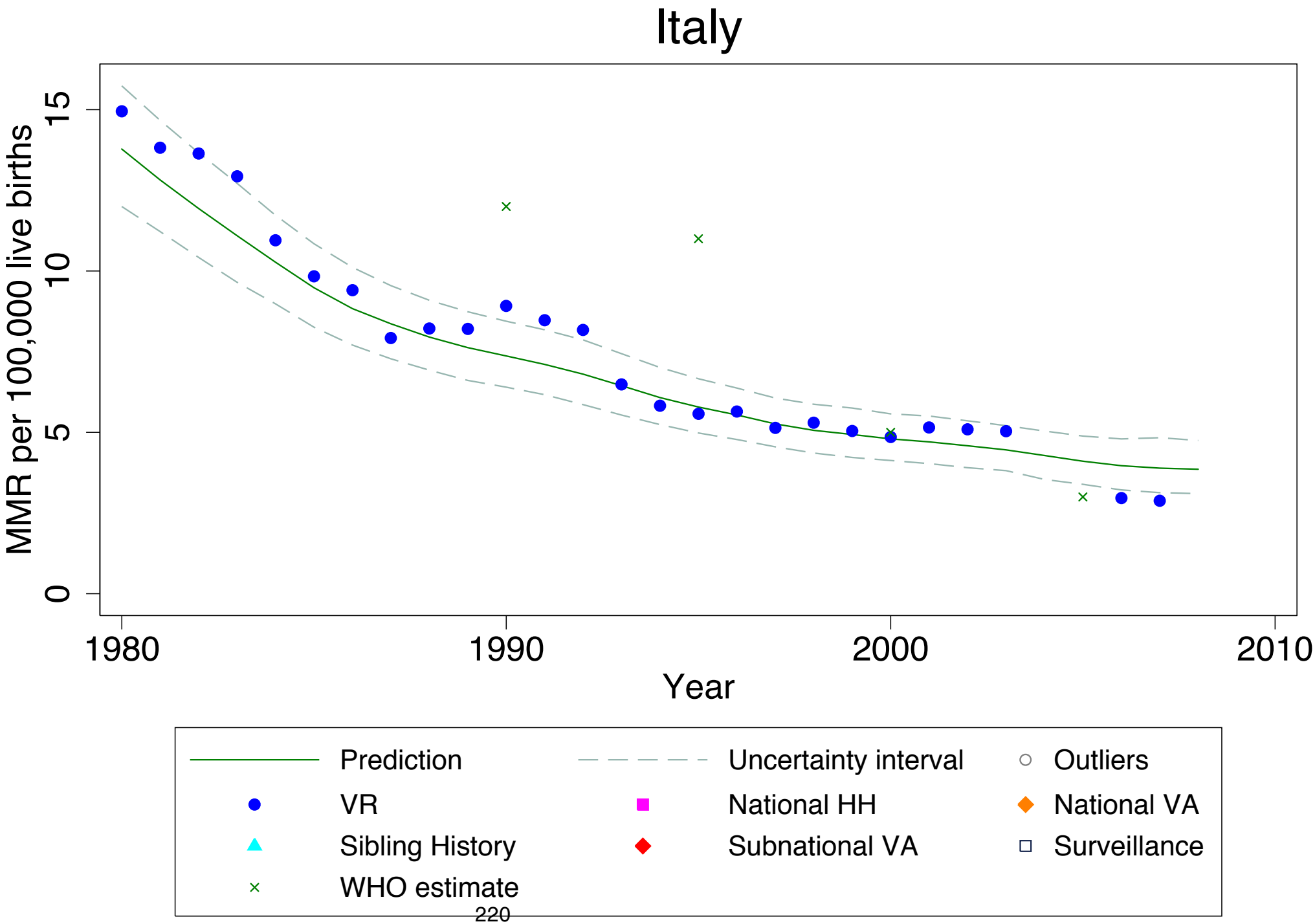
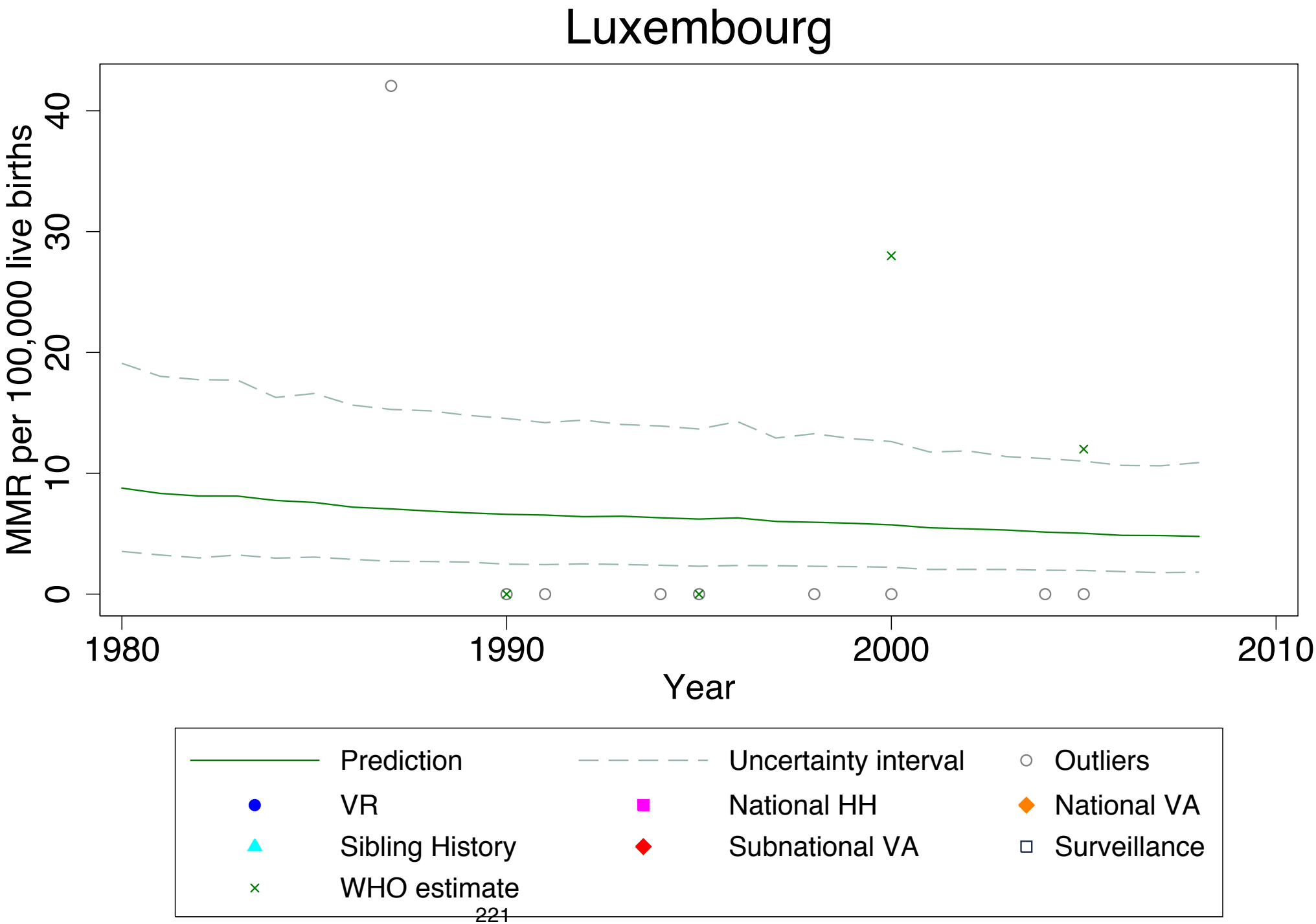
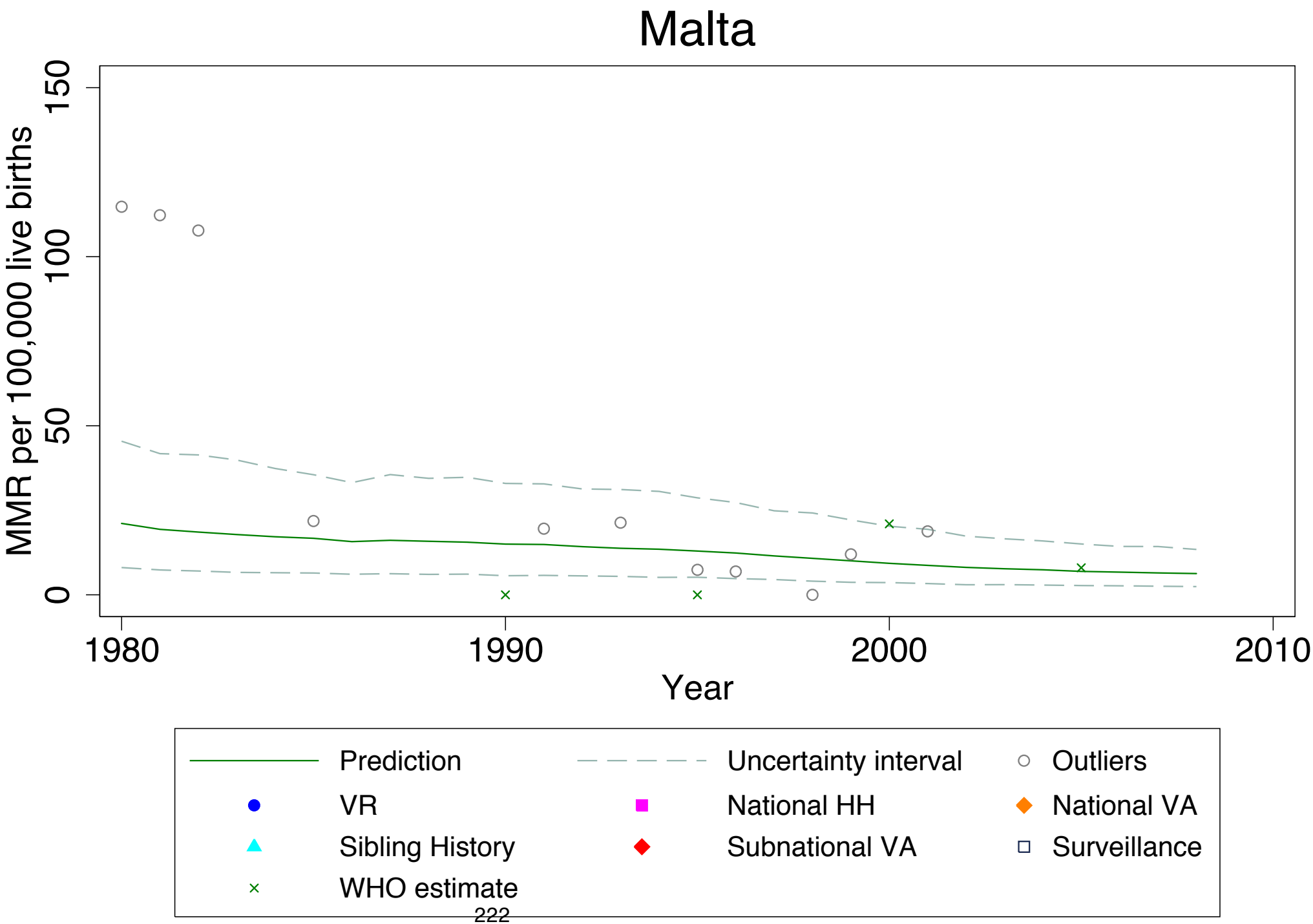
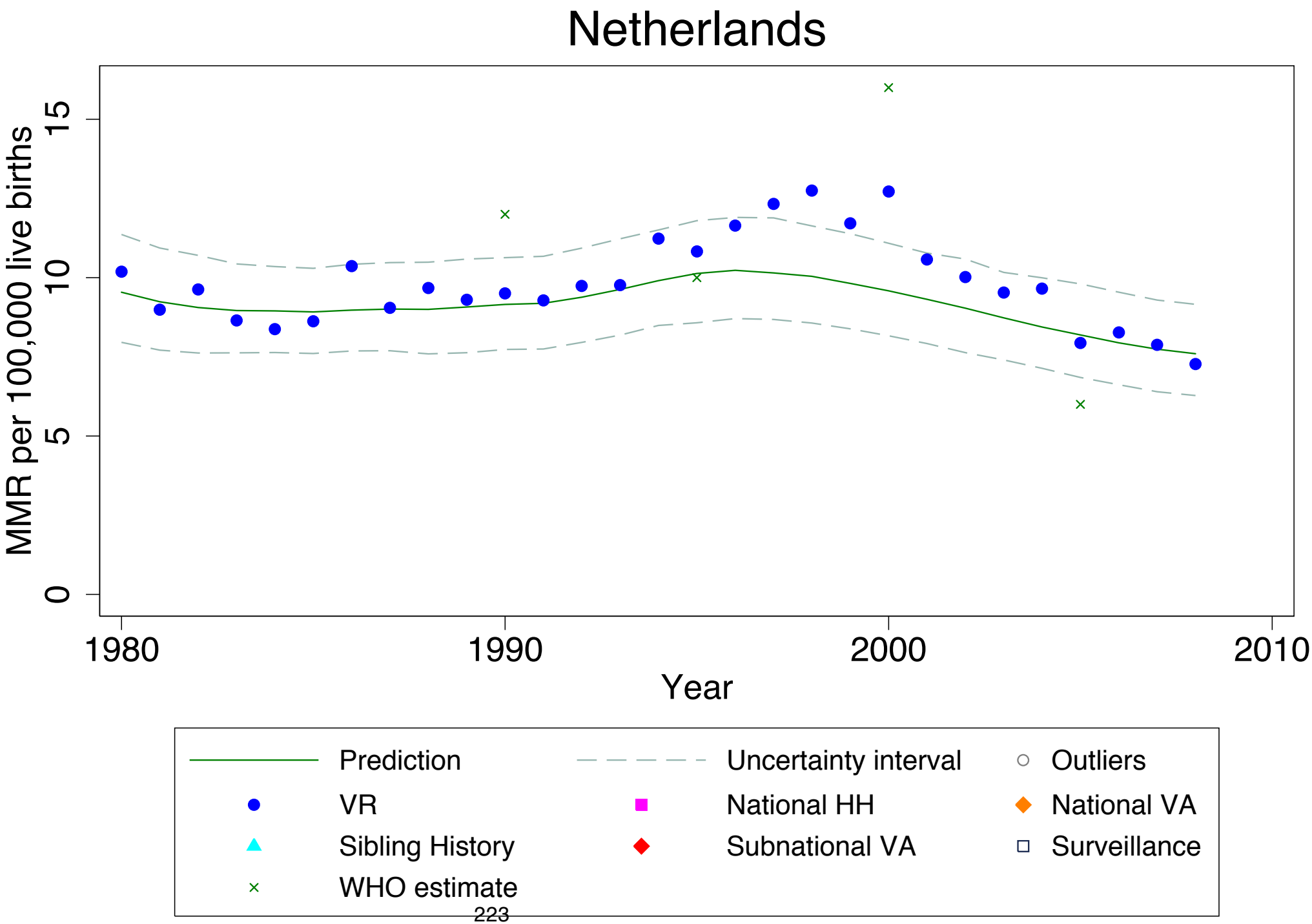
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Italy
MMR per 100,000 live births
0
5
10
15
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Luxembourg
MMR per 100,000 live births
0
10
20
30
40
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Malta
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Netherlands
MMR per 100,000 live births
0
5
10
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1980
1990
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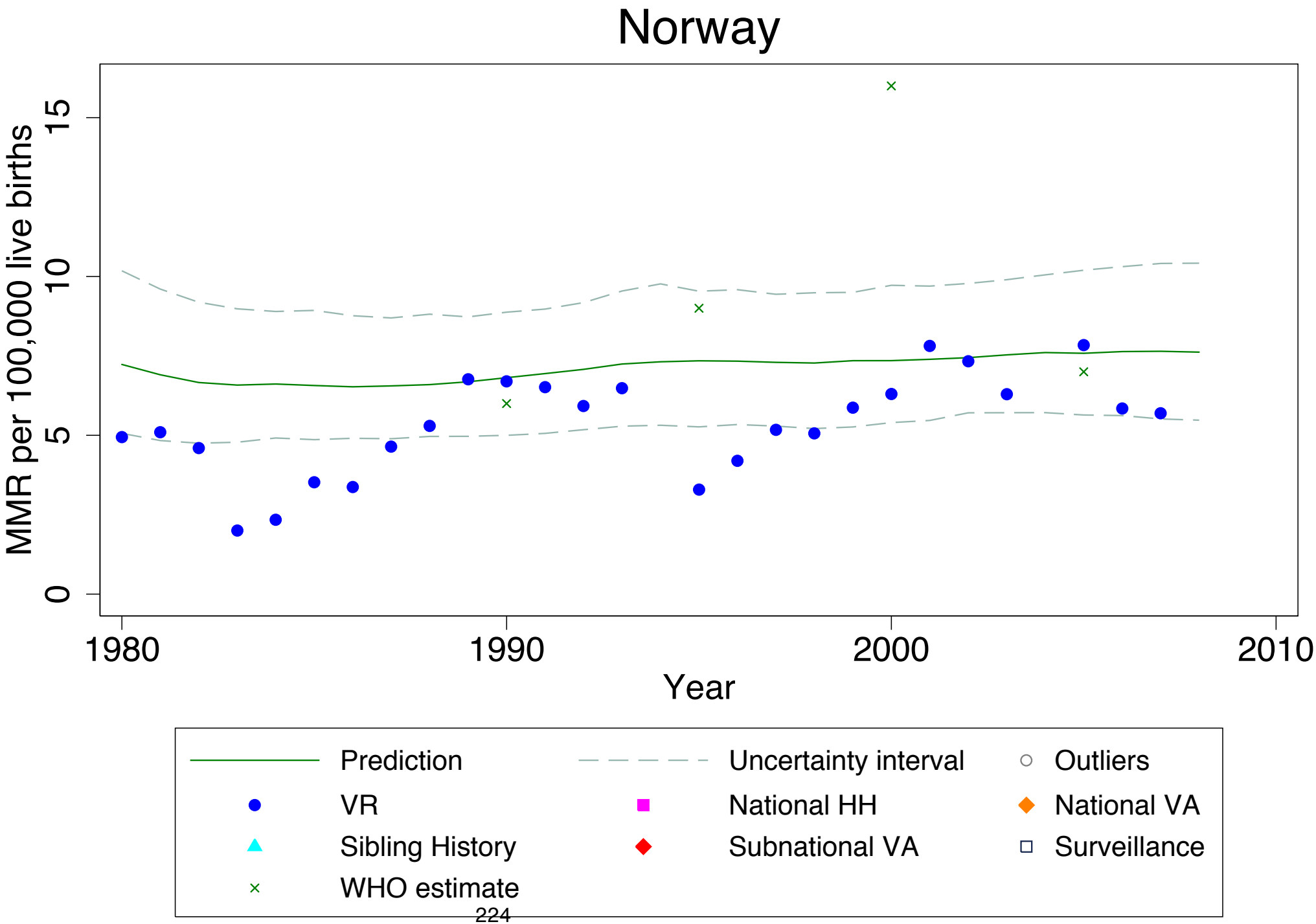
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Norway
MMR per 100,000 live births
0
5
10
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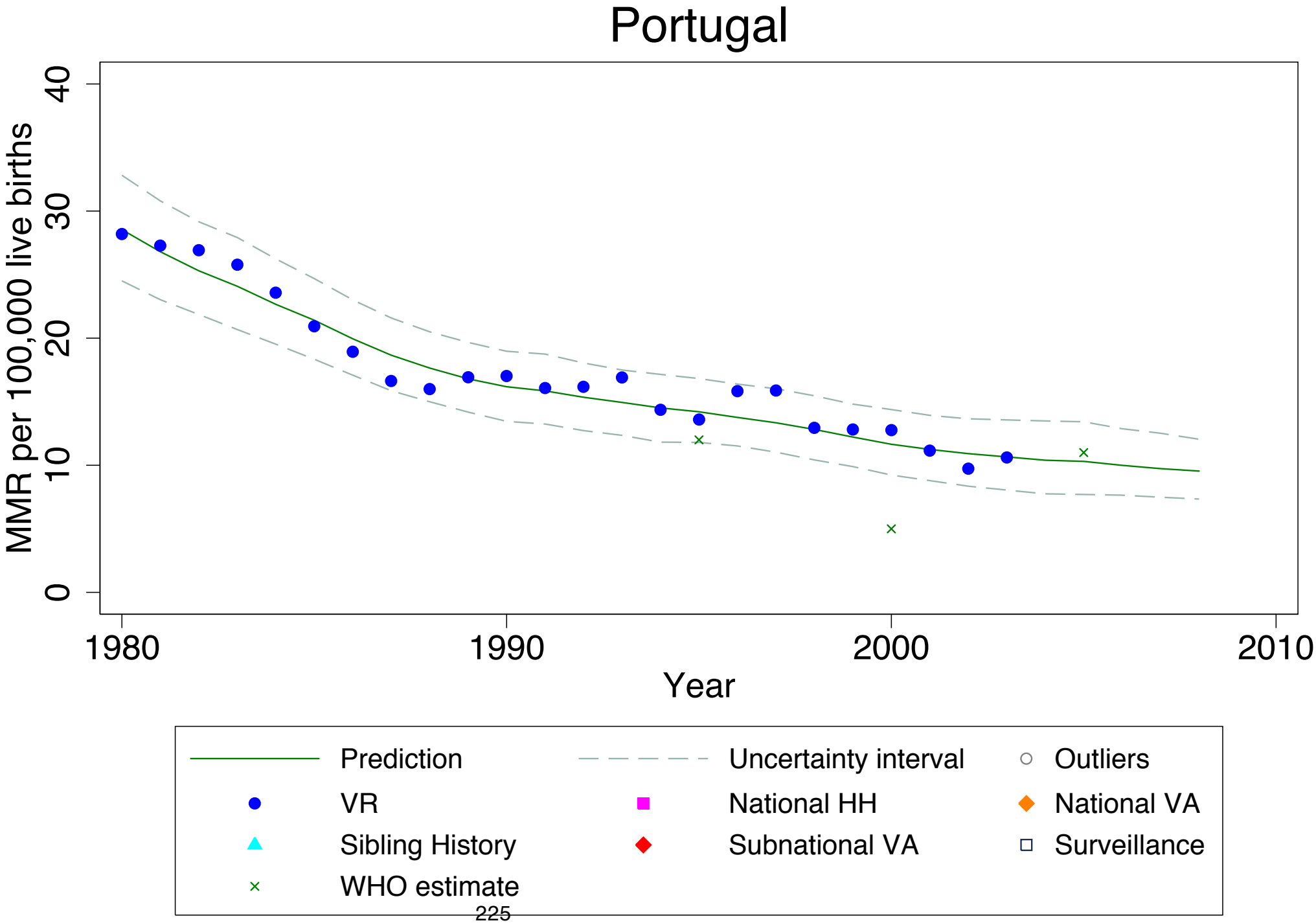
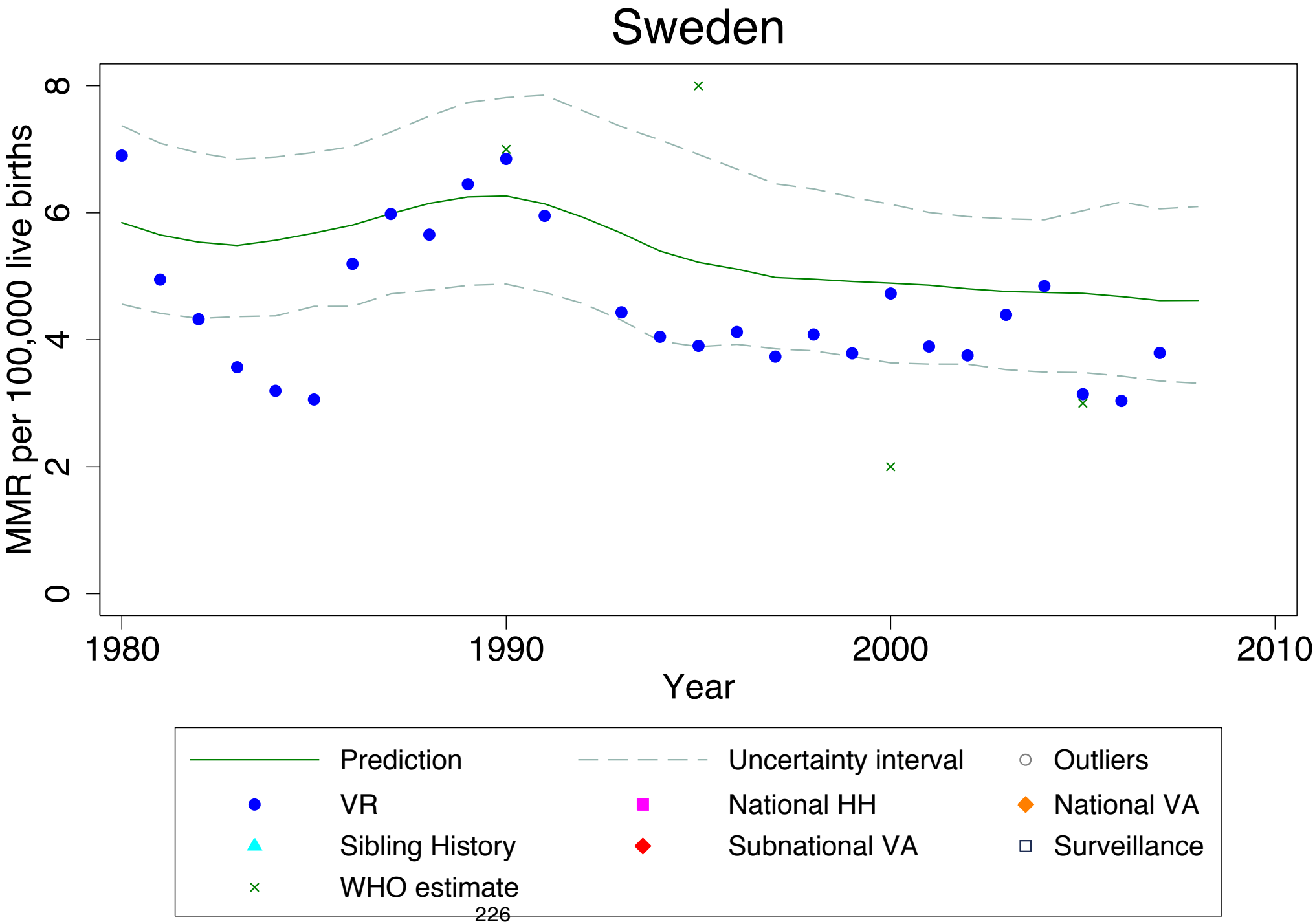
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Portugal
MMR per 100,000 live births
0
10
20
30
40
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Sweden
MMR per 100,000 live births
0
2
4
6
8
1980
1990
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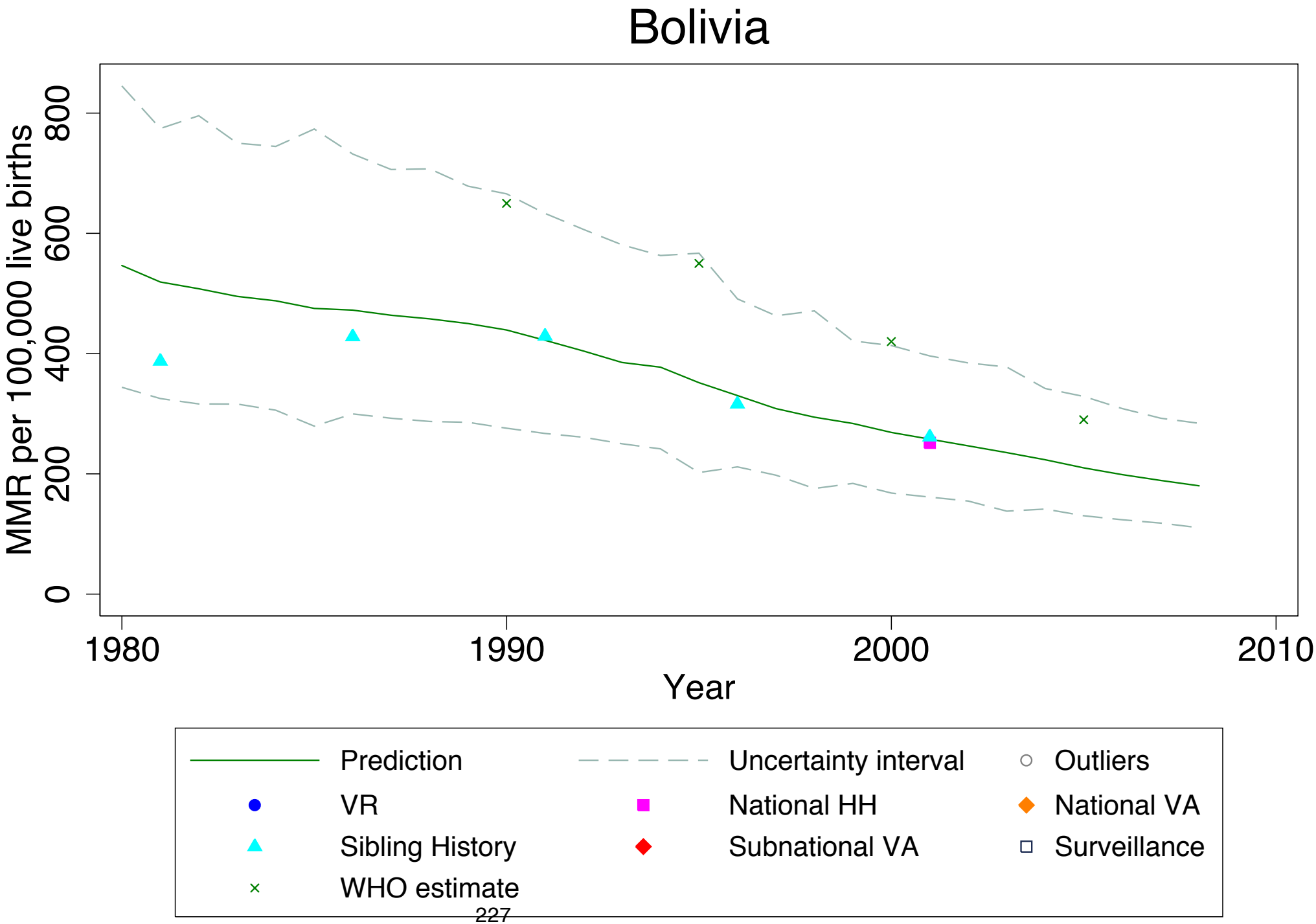
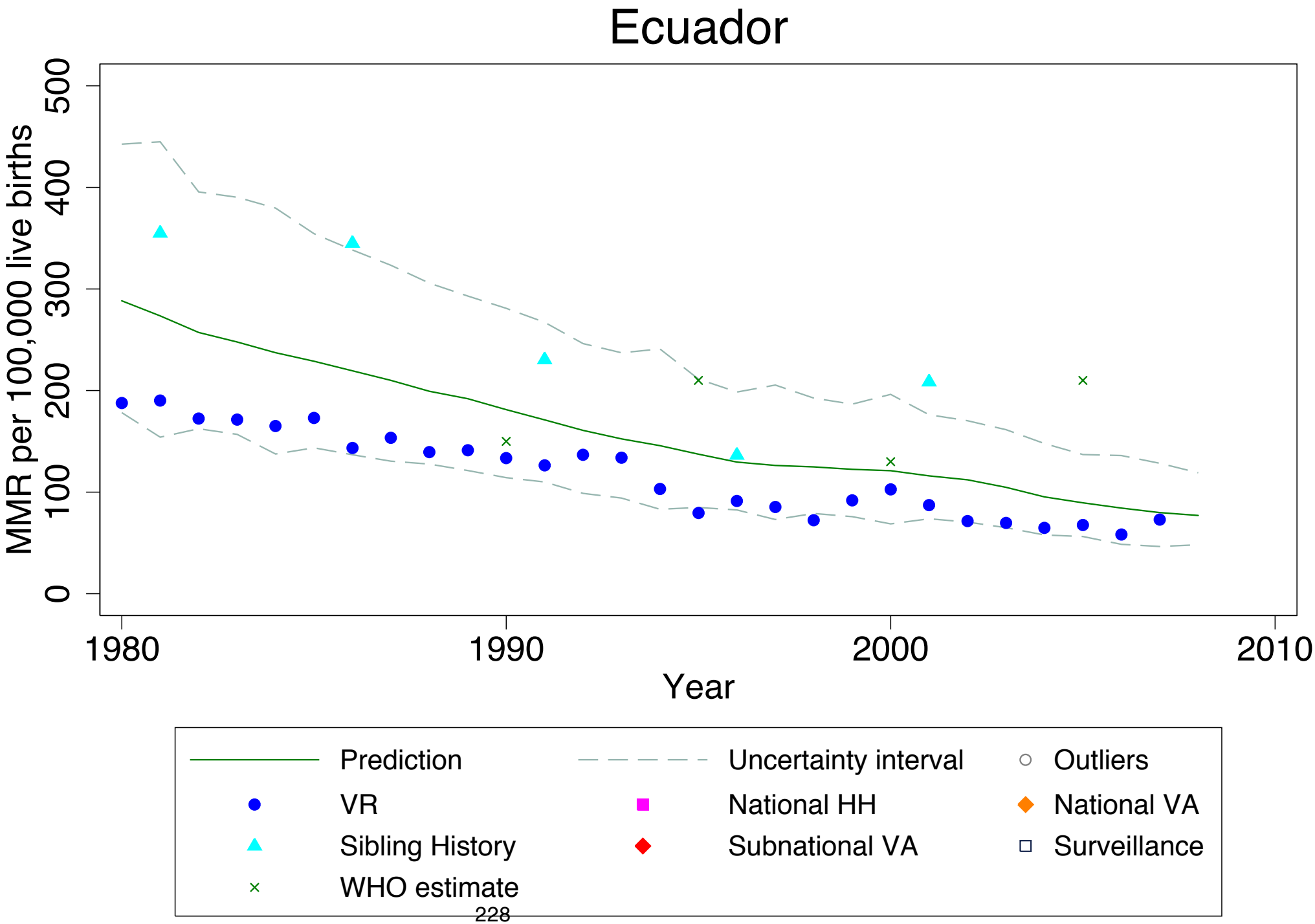
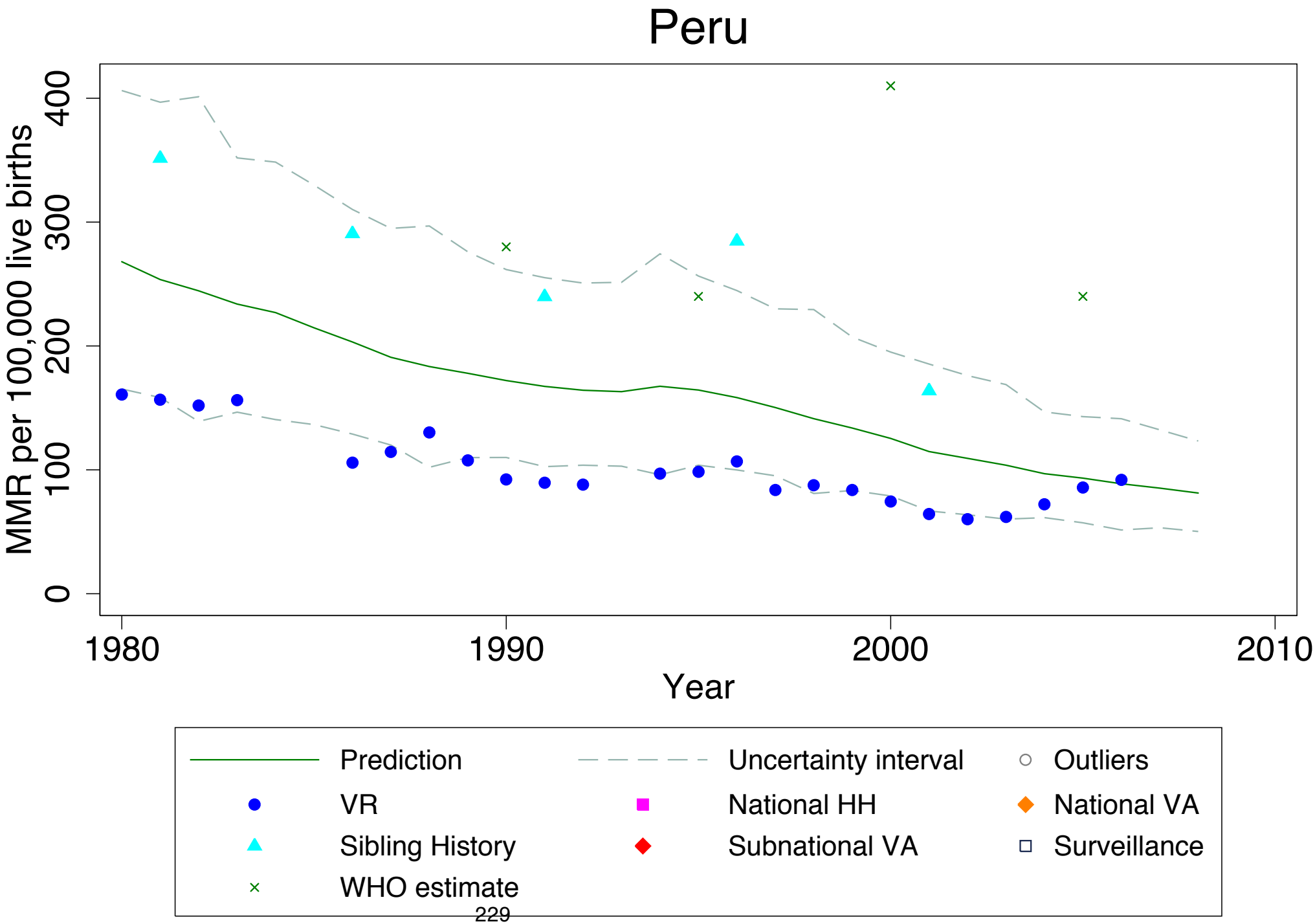
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Bolivia
MMR per 100,000 live births
0
200
400
600
800
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Ecuador
MMR per 100,000 live births
0
100
200
300
400
500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Peru
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
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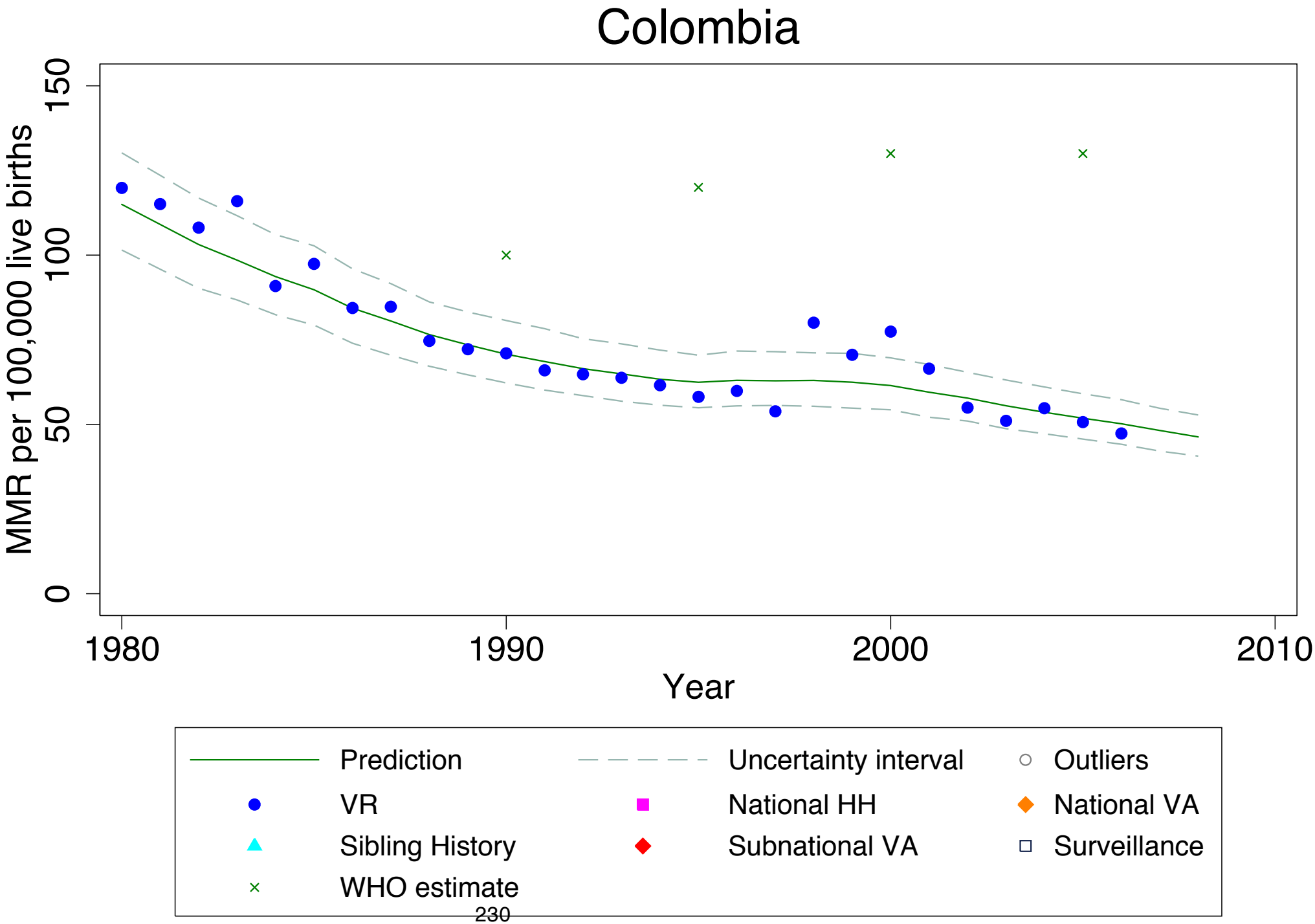
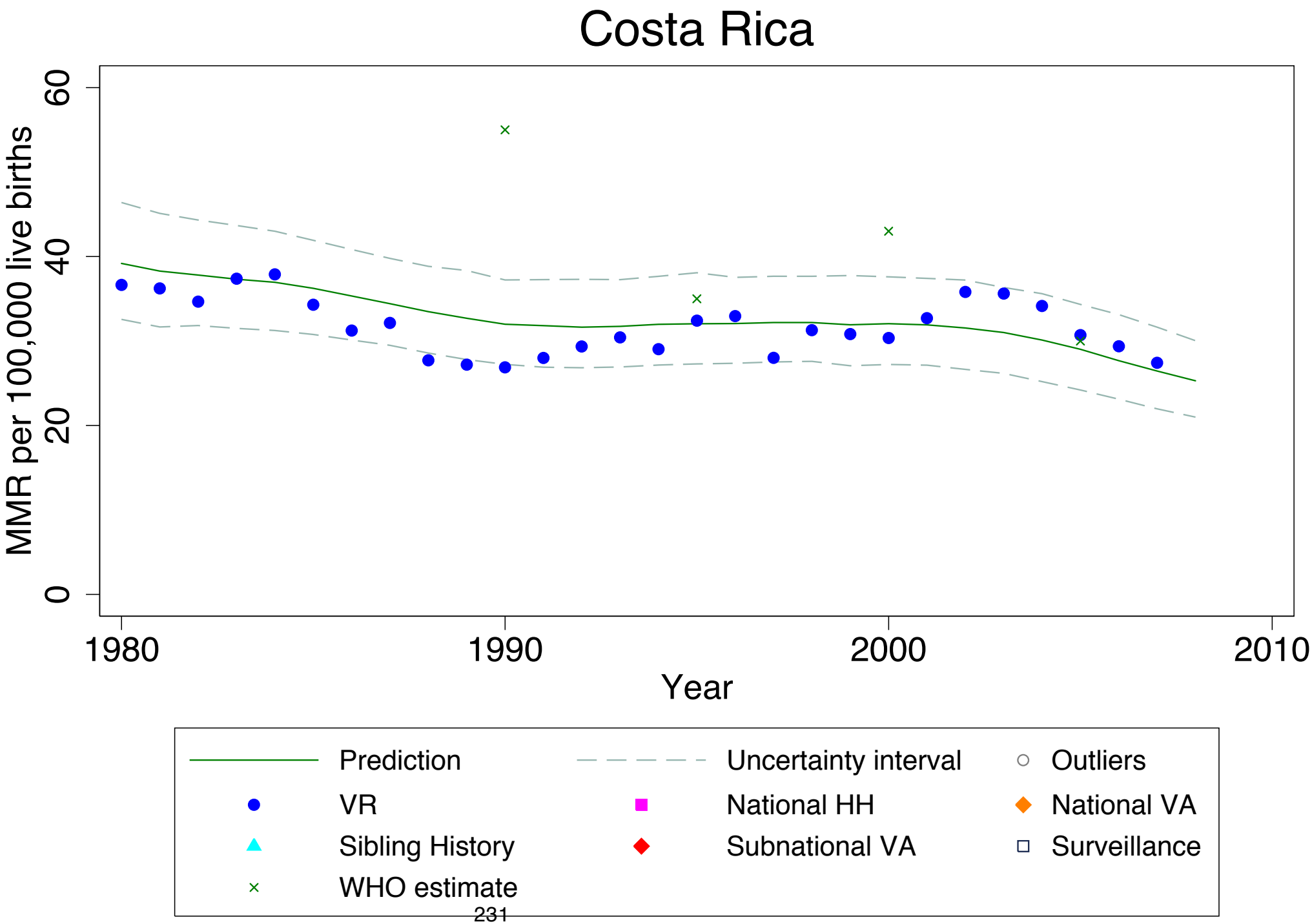
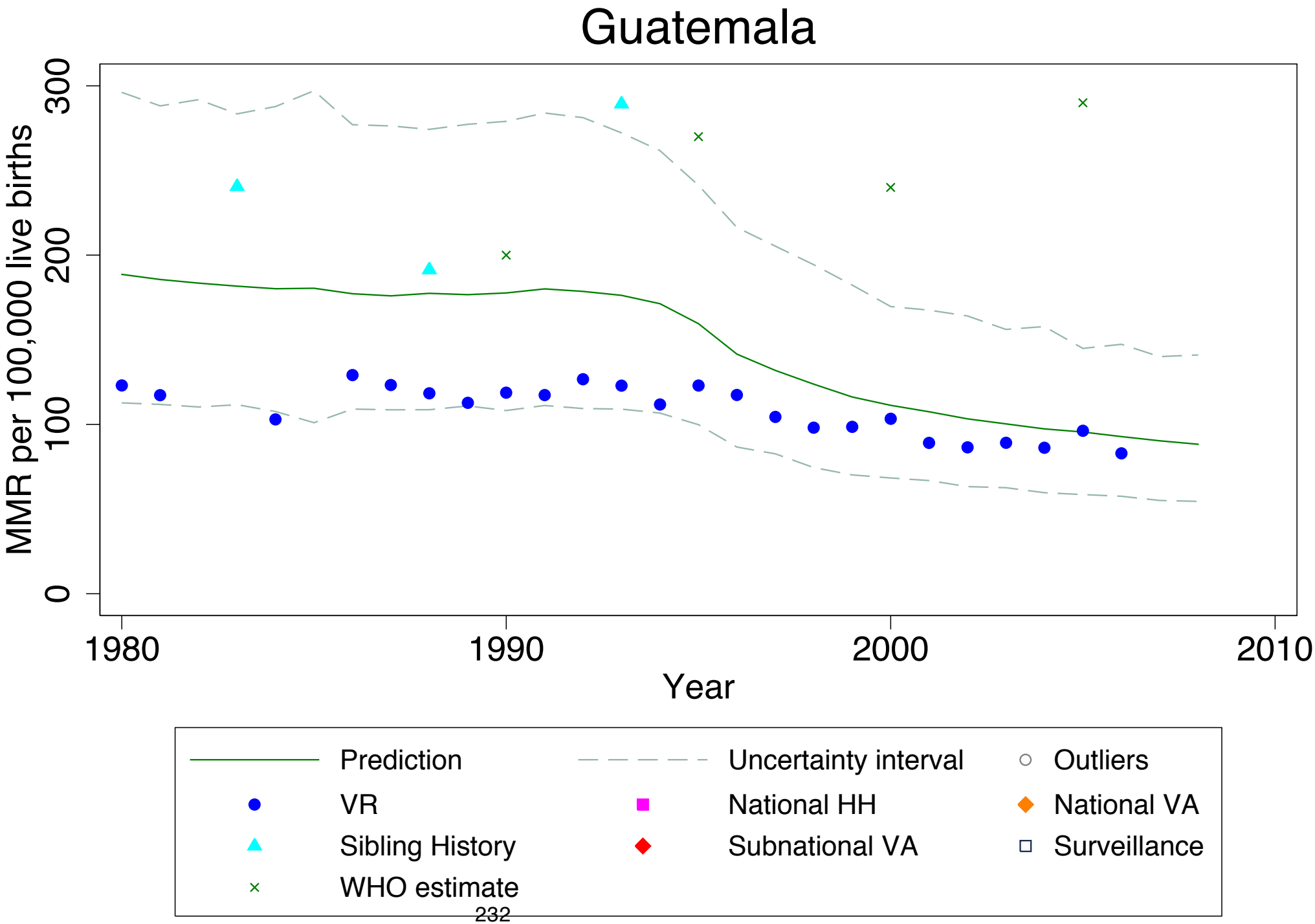
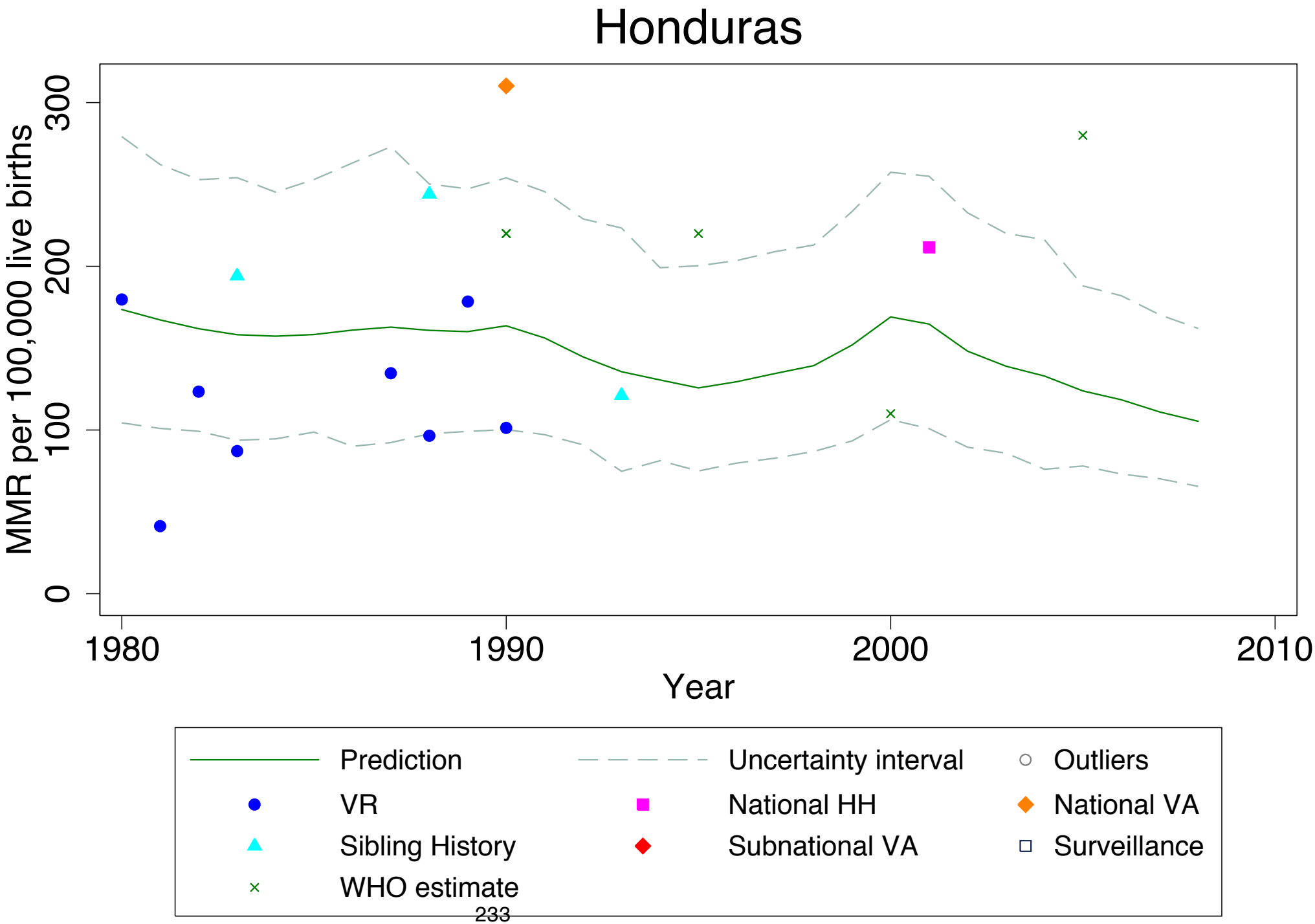
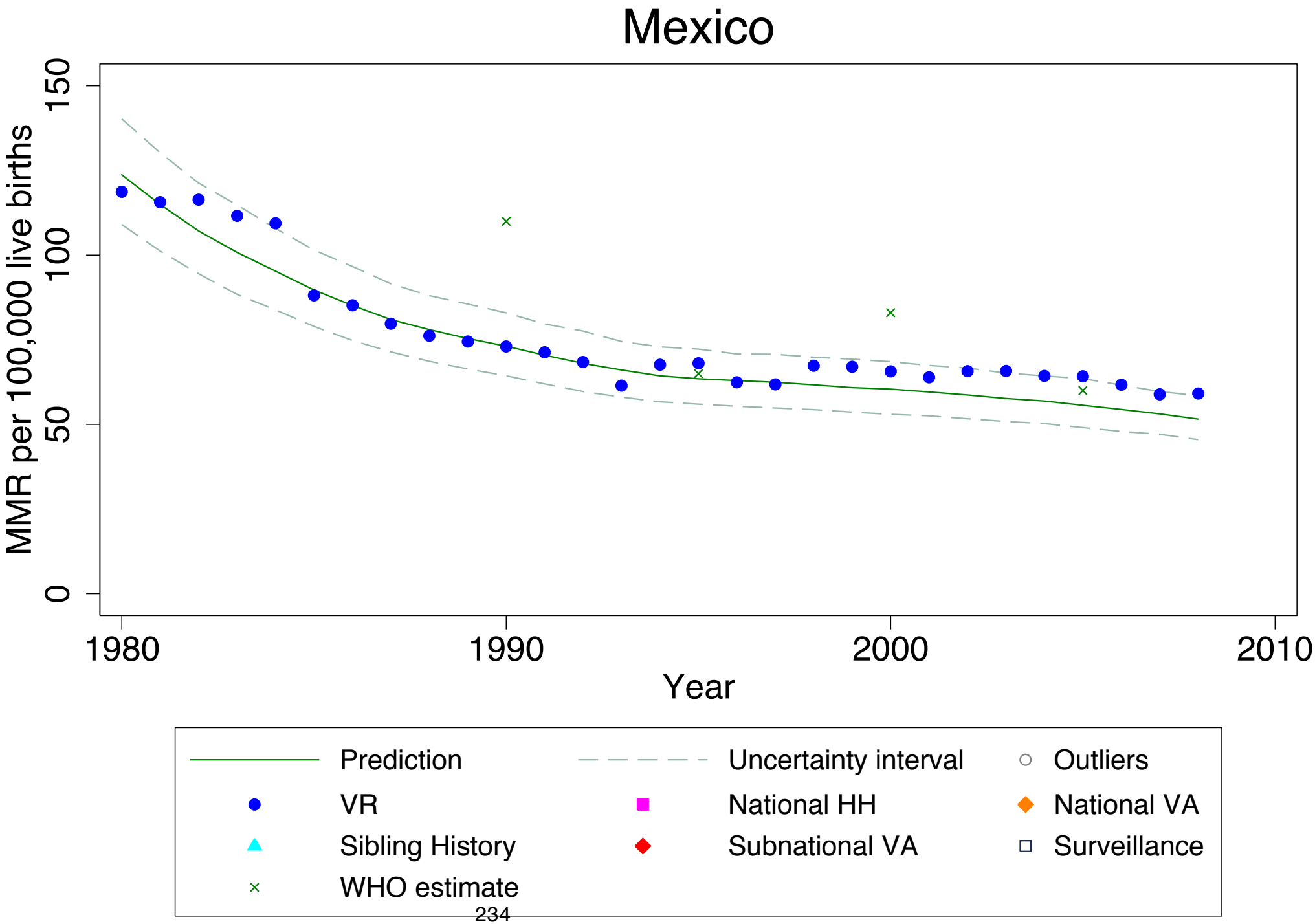
Surveillance
WHO estimate

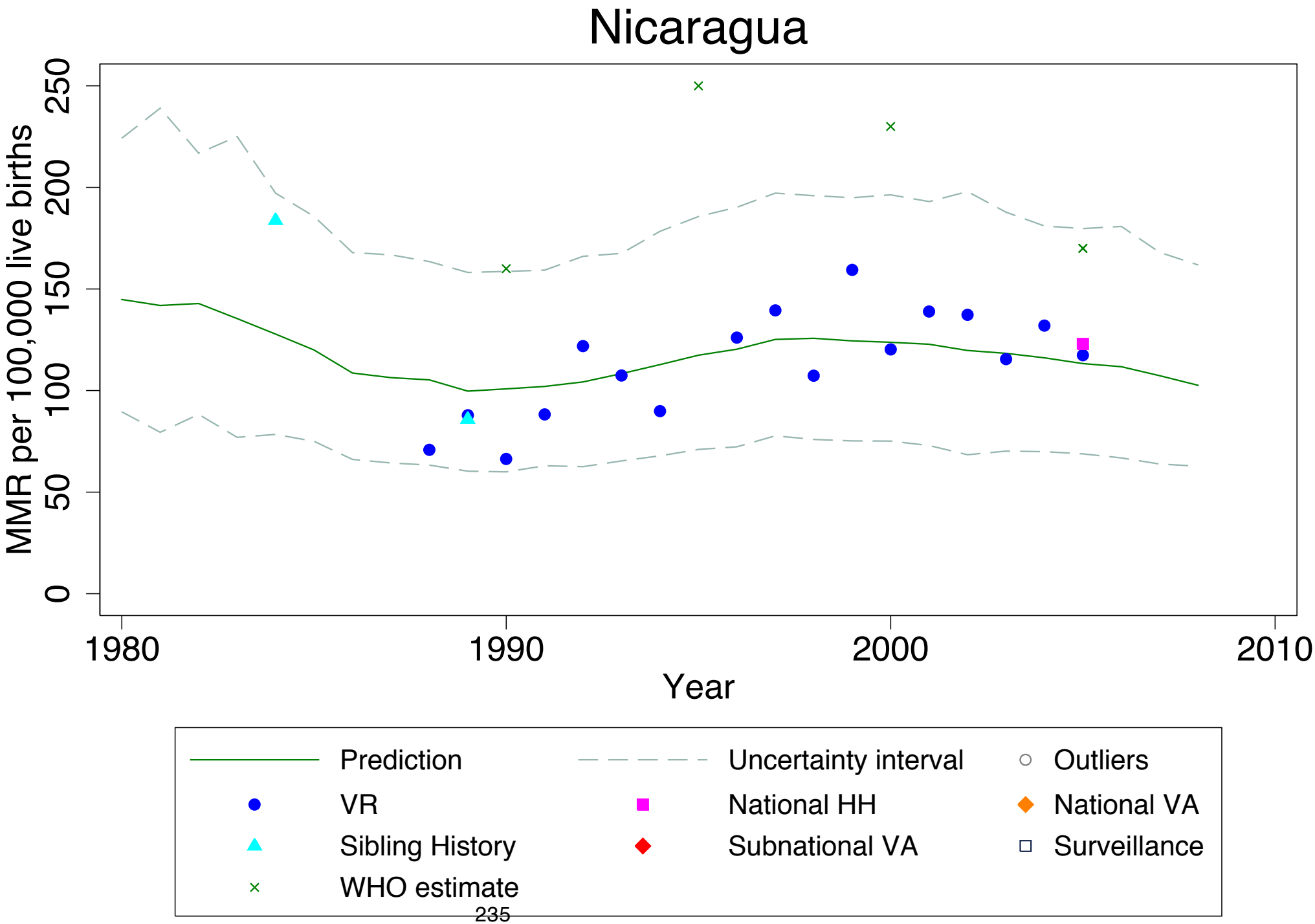

Colombia
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

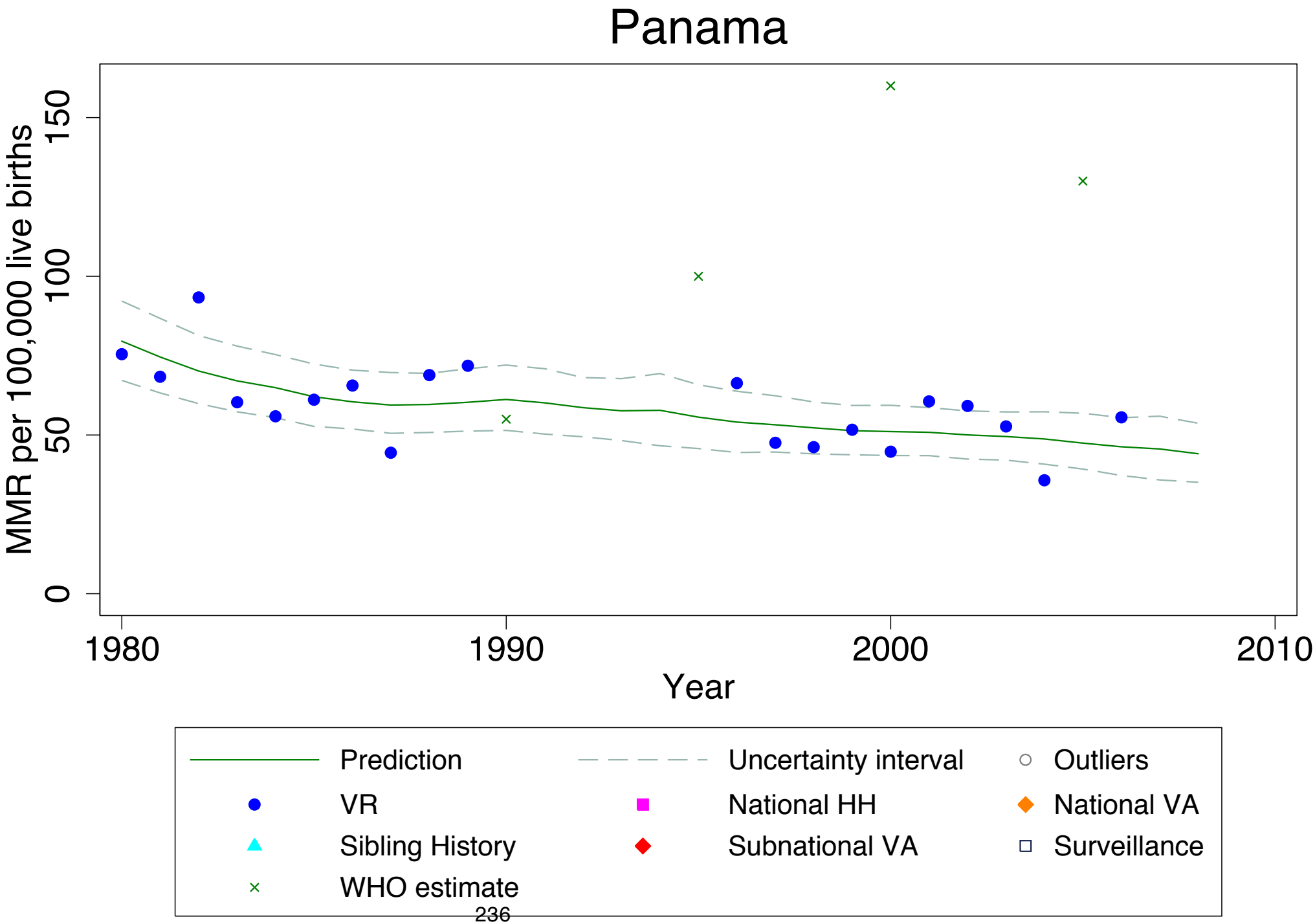

Costa Rica
MMR per 100,000 live births
0
20
40
60
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

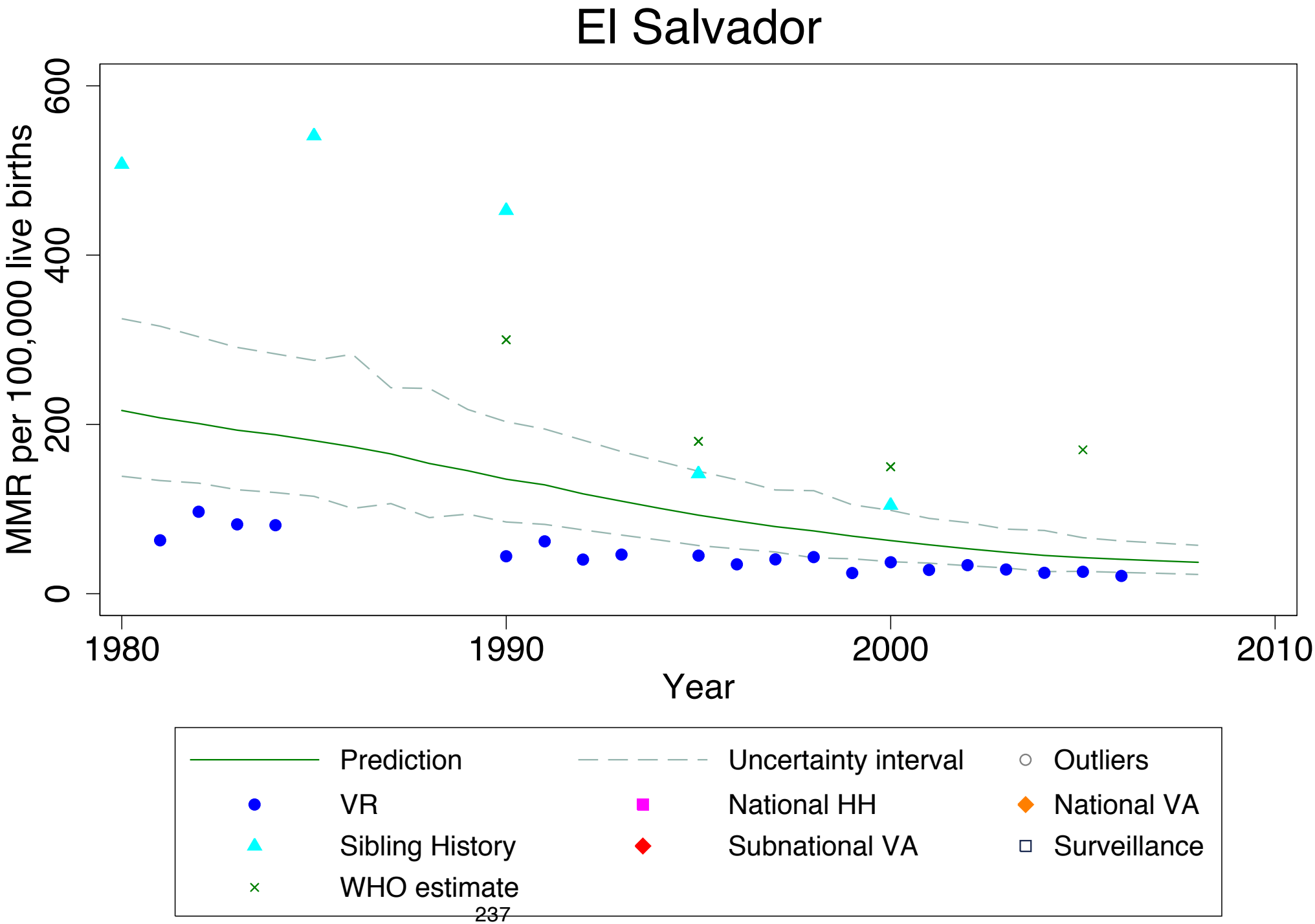

Guatemala
MMR per 100,000 live births
0
100
200
300
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

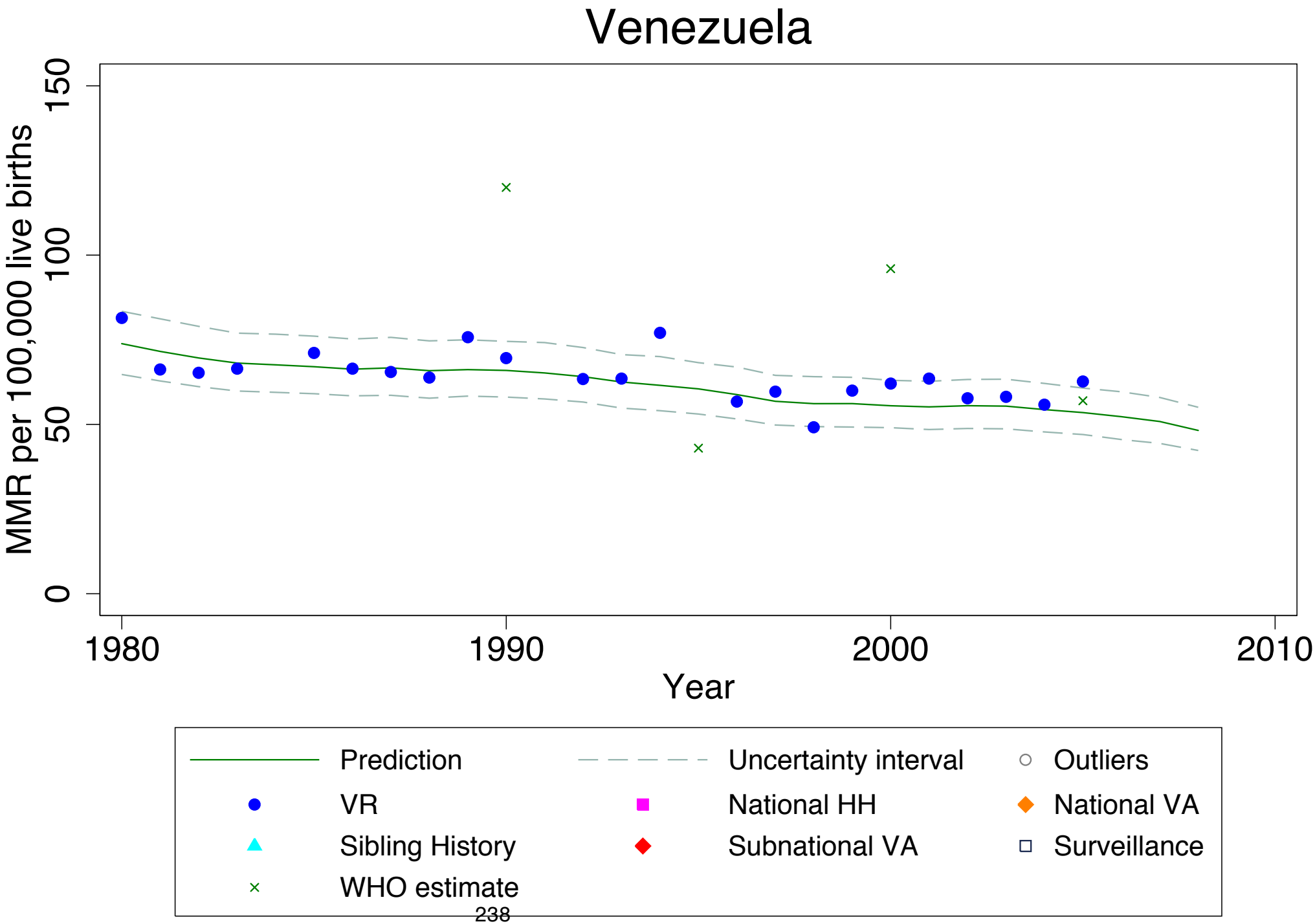

Honduras
MMR per 100,000 live births
0
100
200
300
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

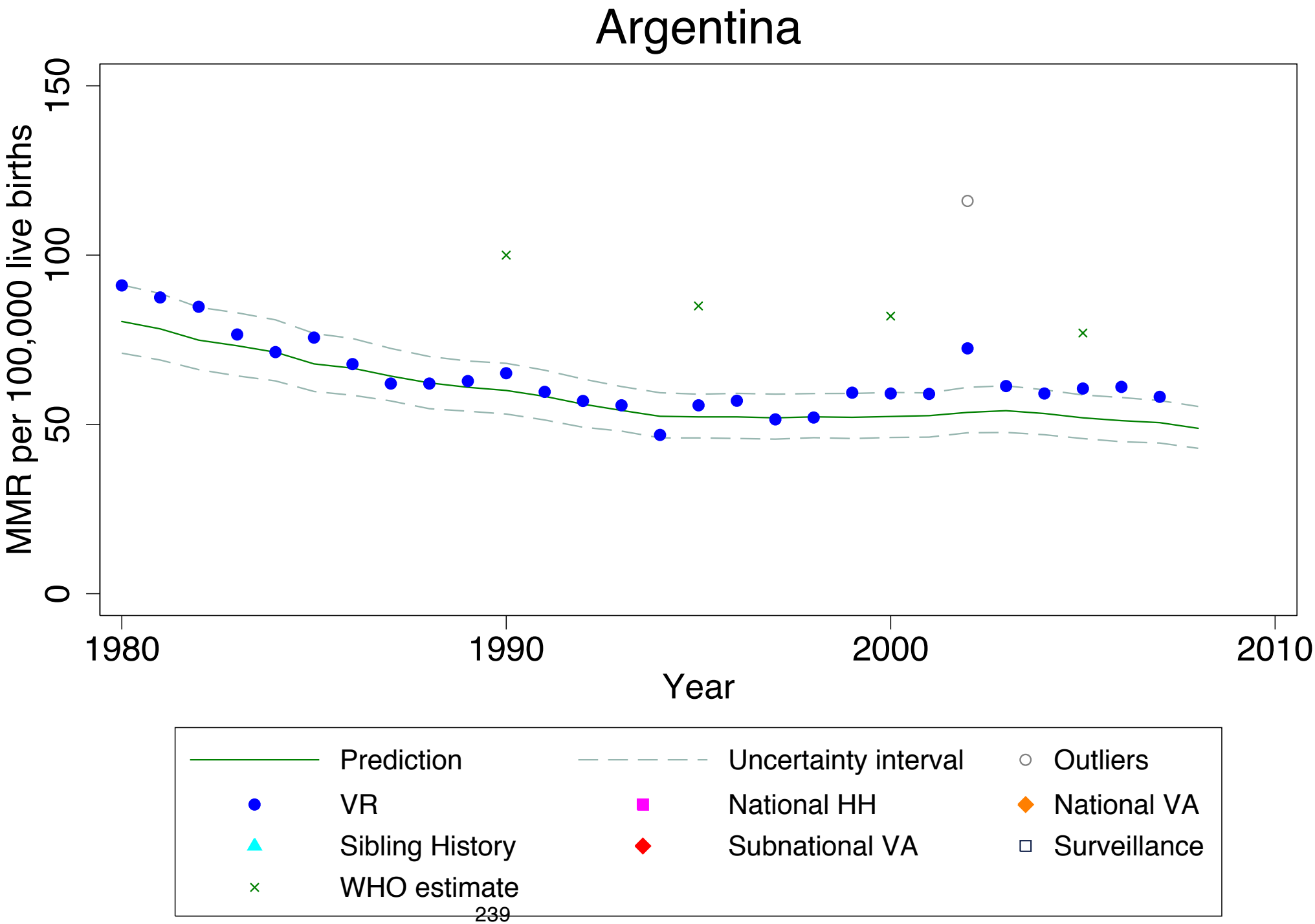

Mexico
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

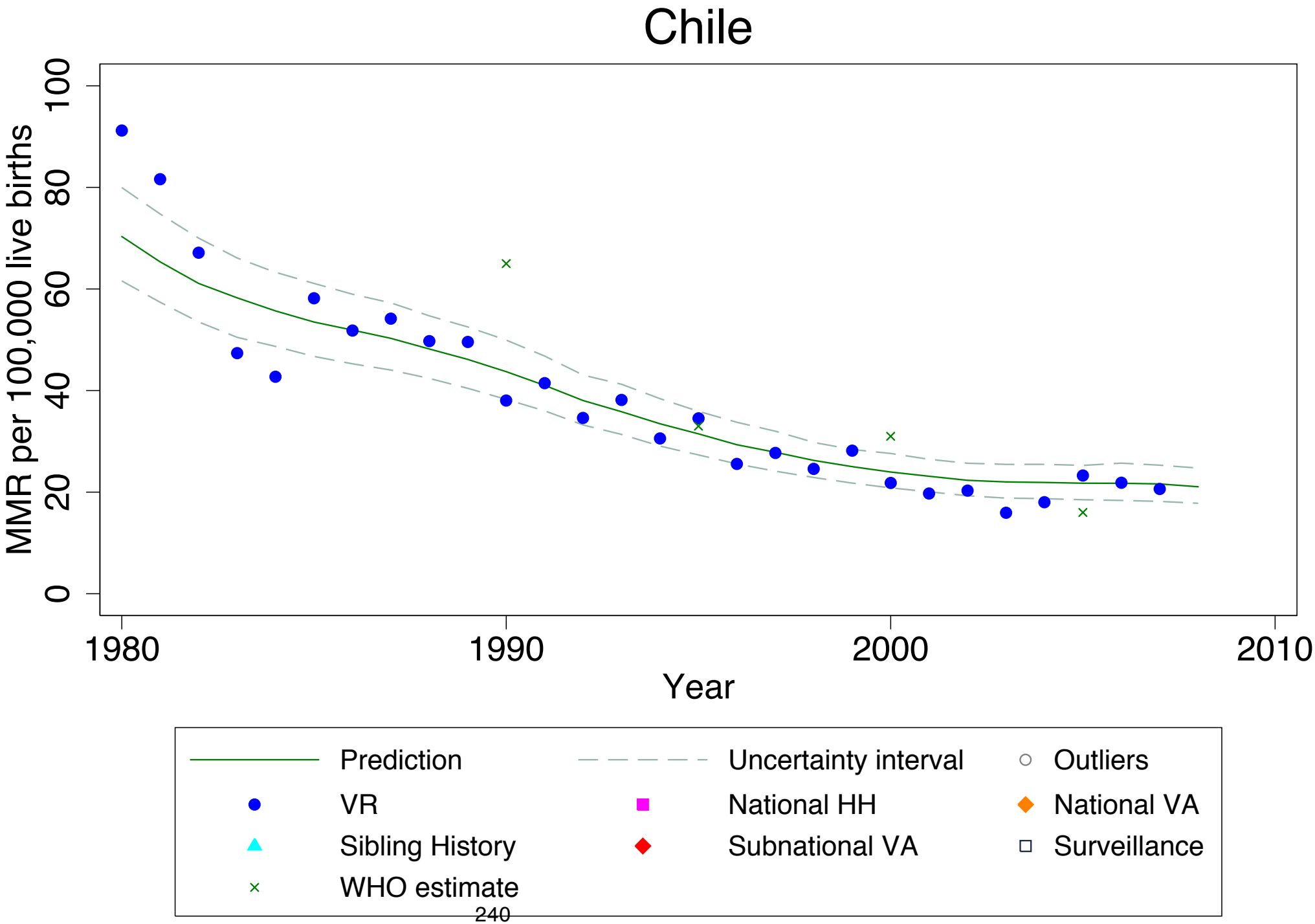

Nicaragua
MMR per 100,000 live births
0
50
100
150
200
250
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

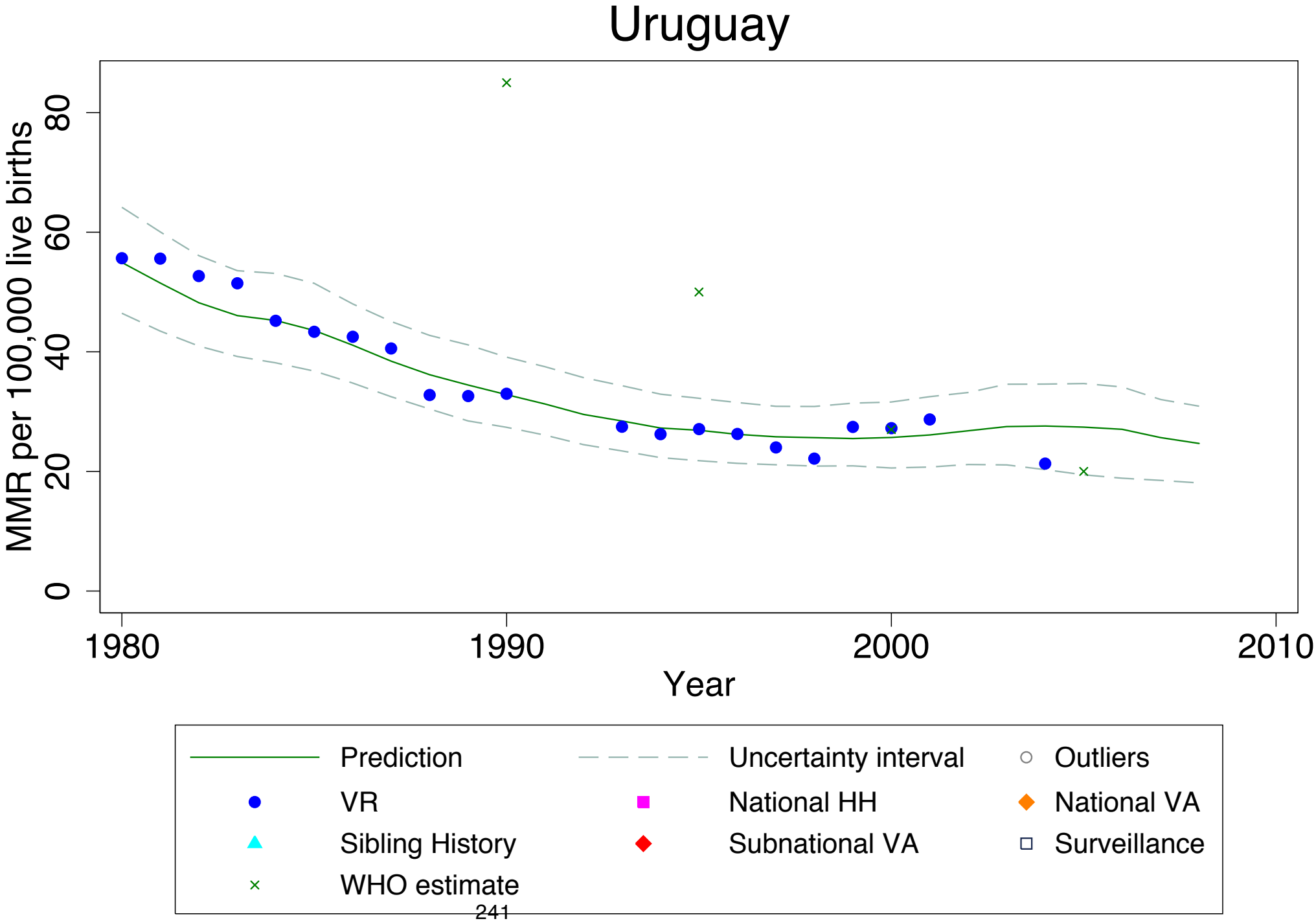

Panama
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

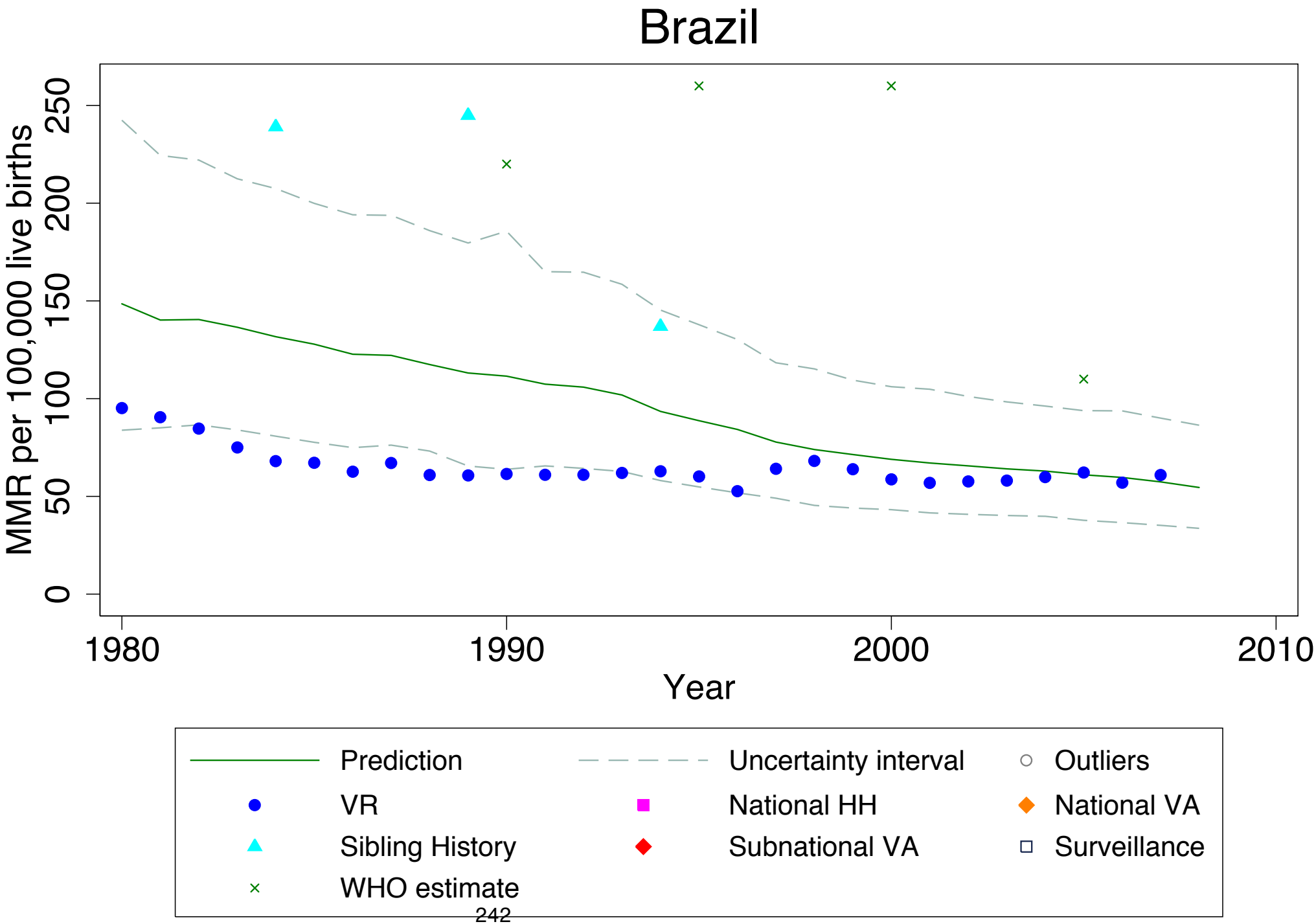

El Salvador
MMR per 100,000 live births
0
200
400
600
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

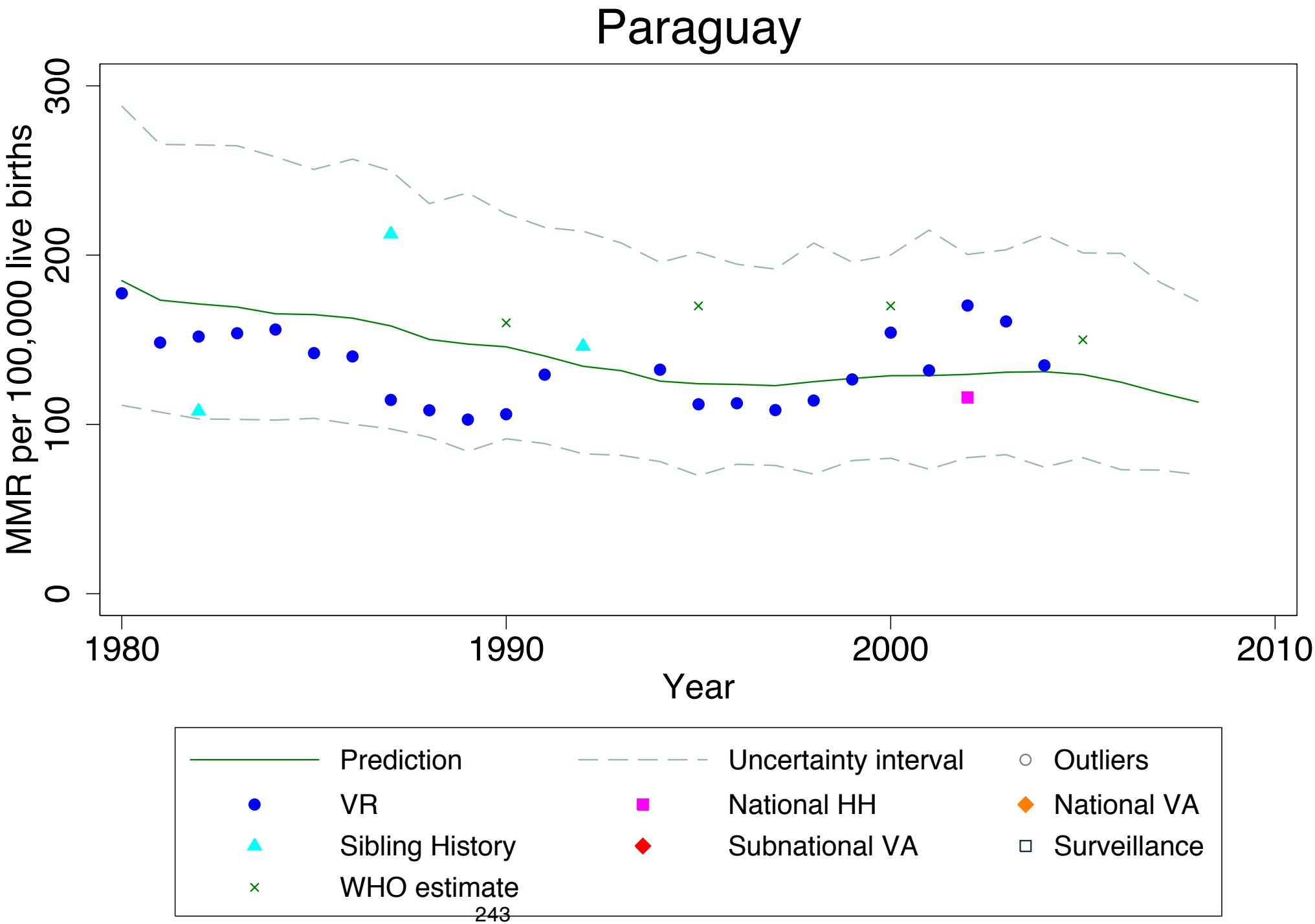

Venezuela
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

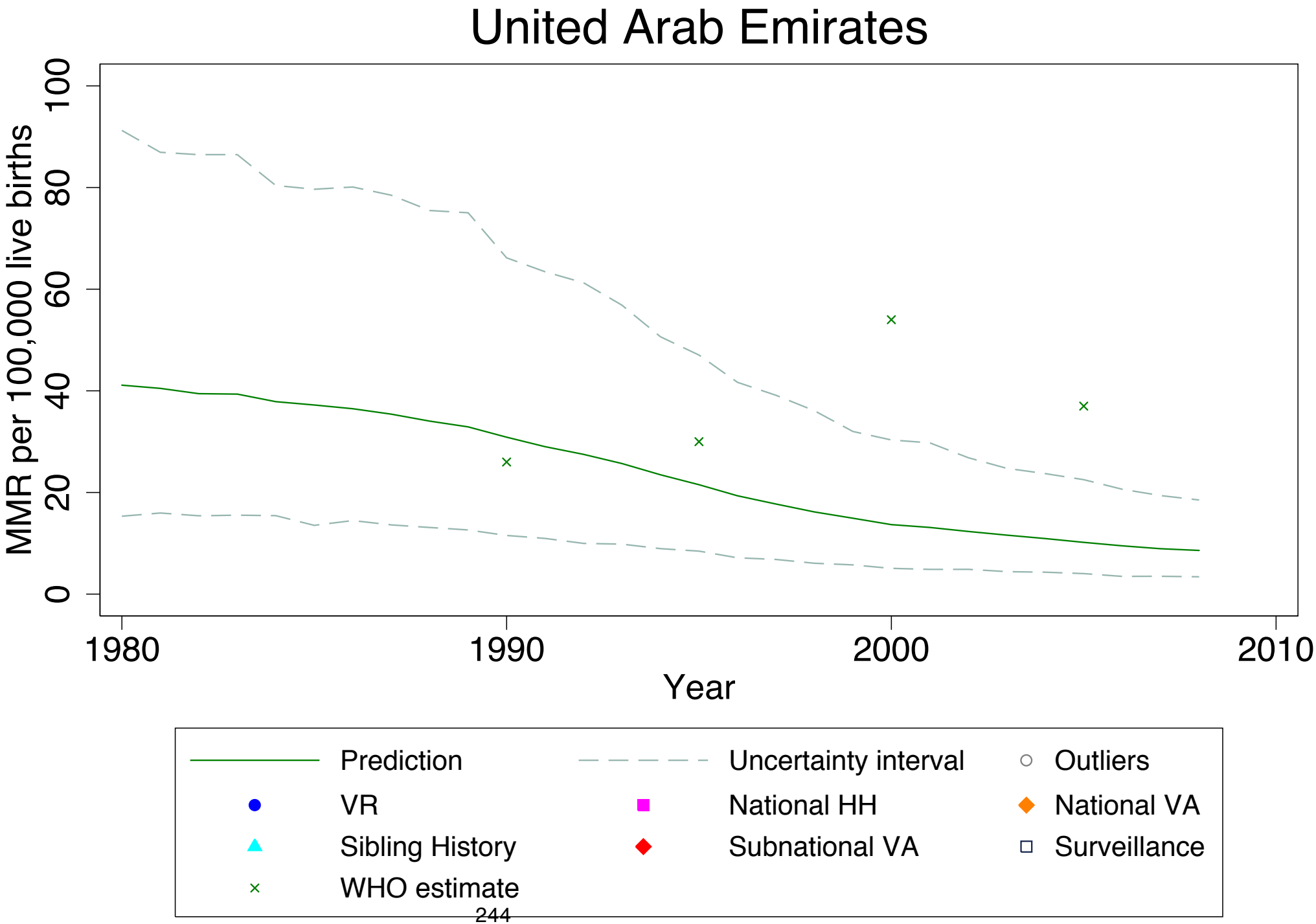

Argentina
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

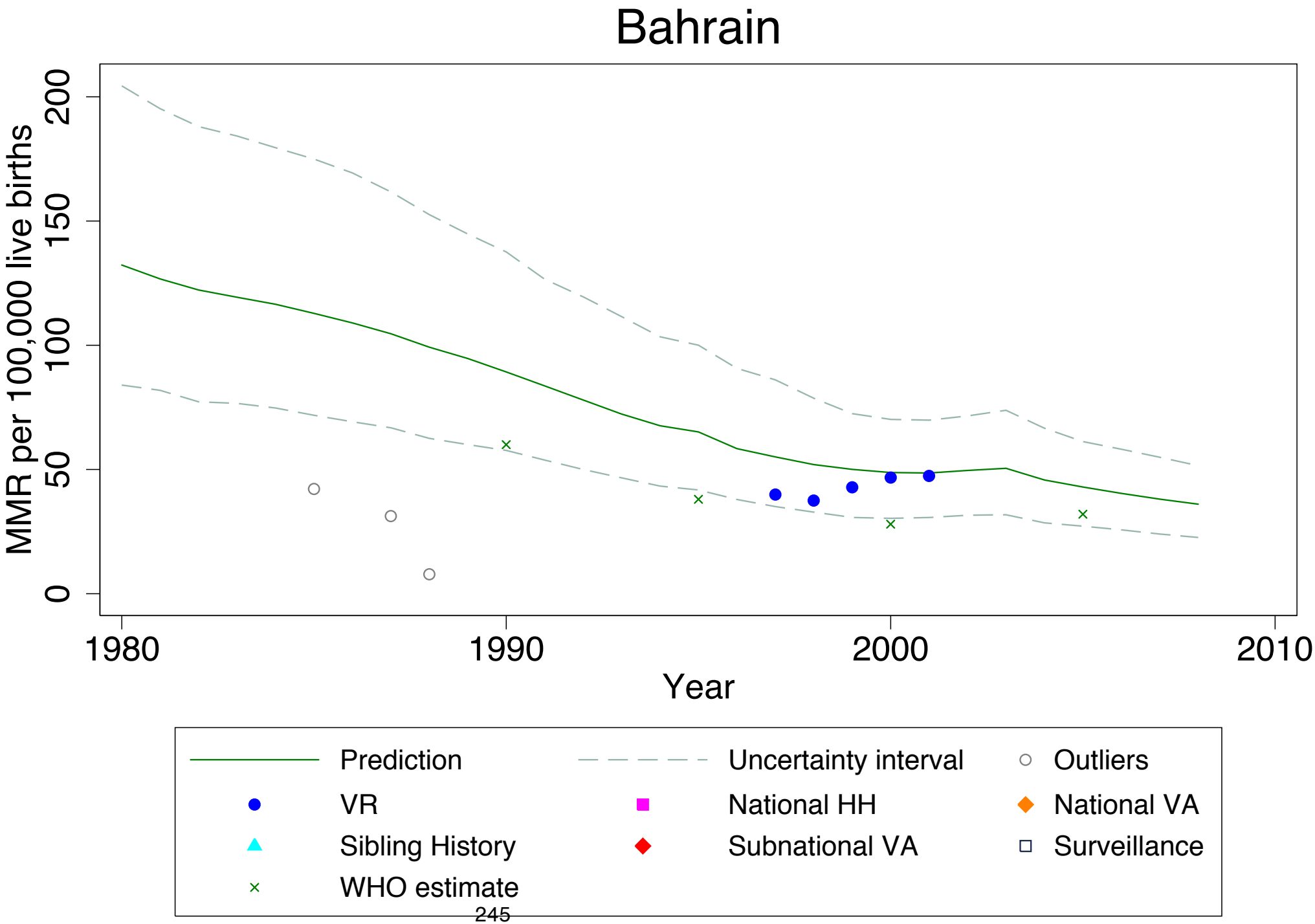

Chile
MMR per 100,000 live births
0
20
40
60
80
100
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

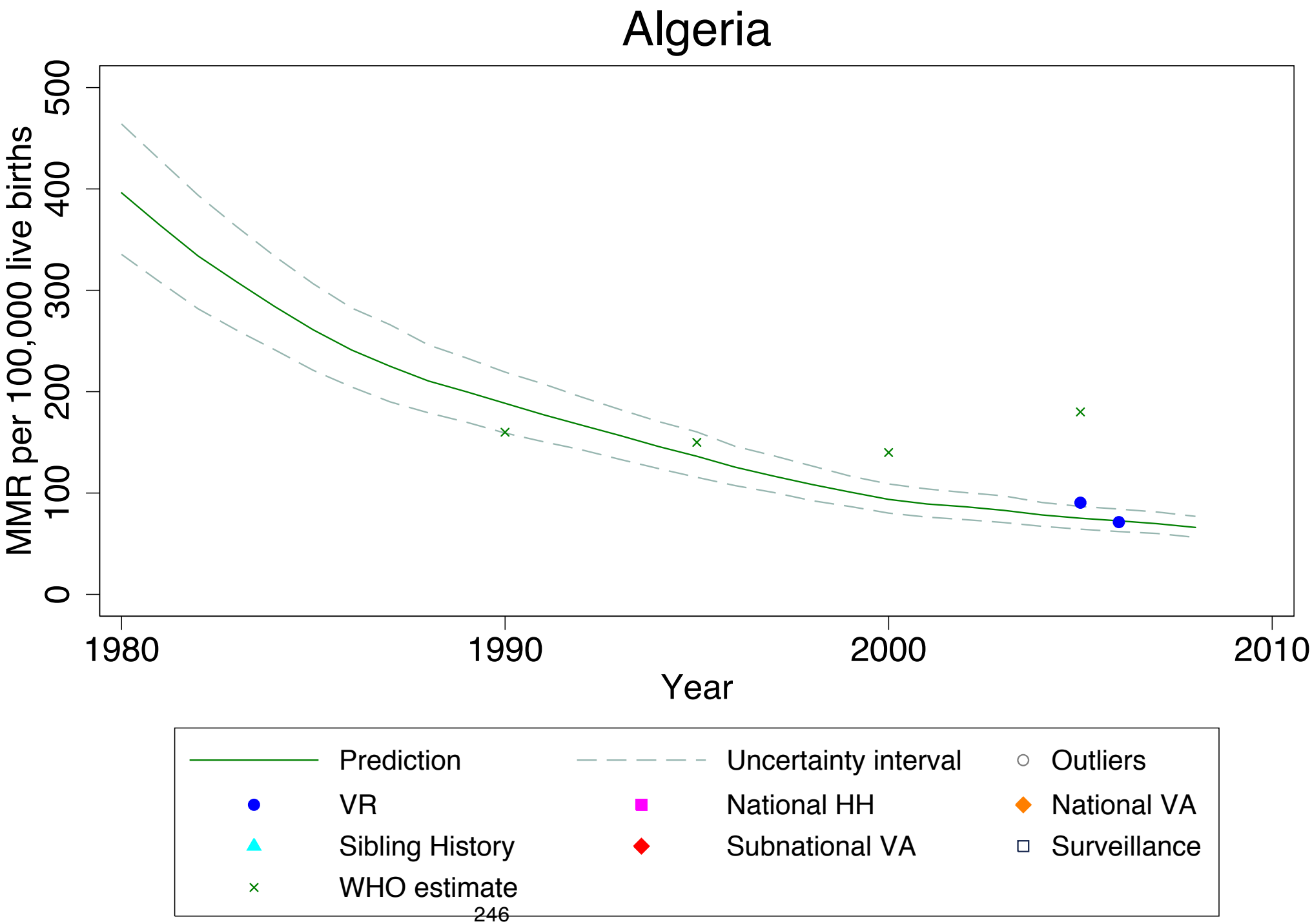

Uruguay
MMR per 100,000 live births
0
20
40
60
80
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

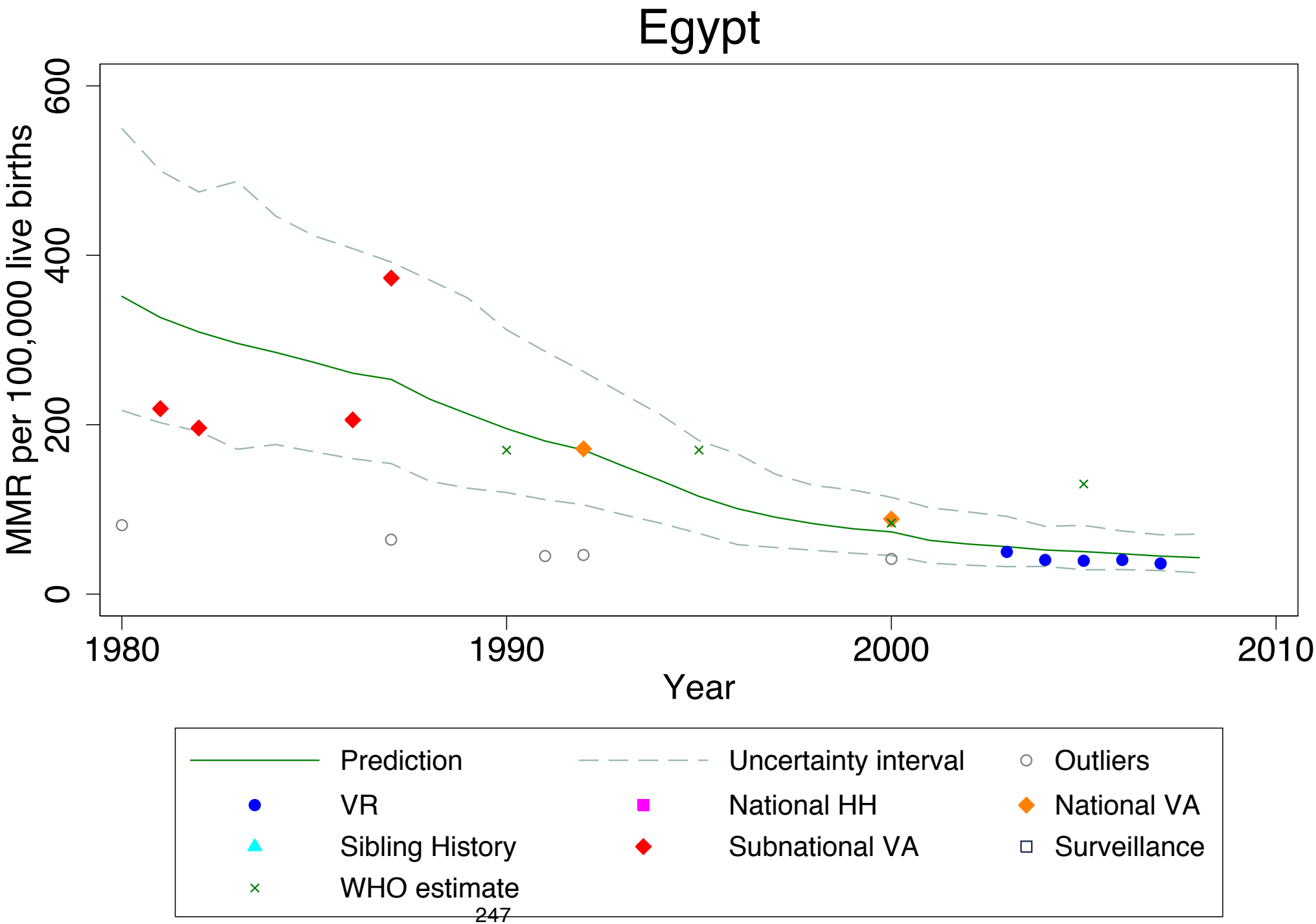

Brazil
MMR per 100,000 live births
0
50
100
150
200
250
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

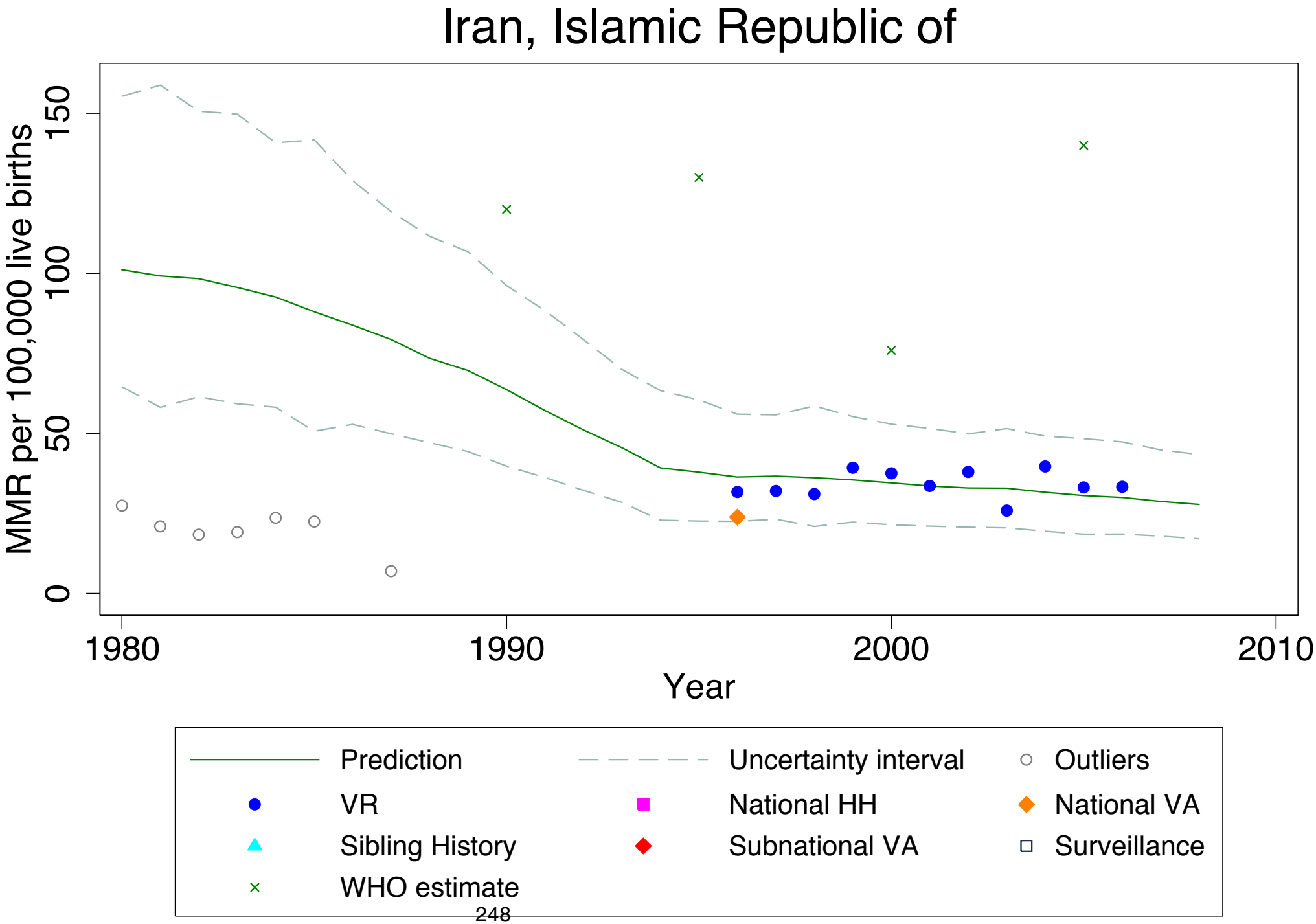

Paraguay
MMR per 100,000 live births
0
100
200
300
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

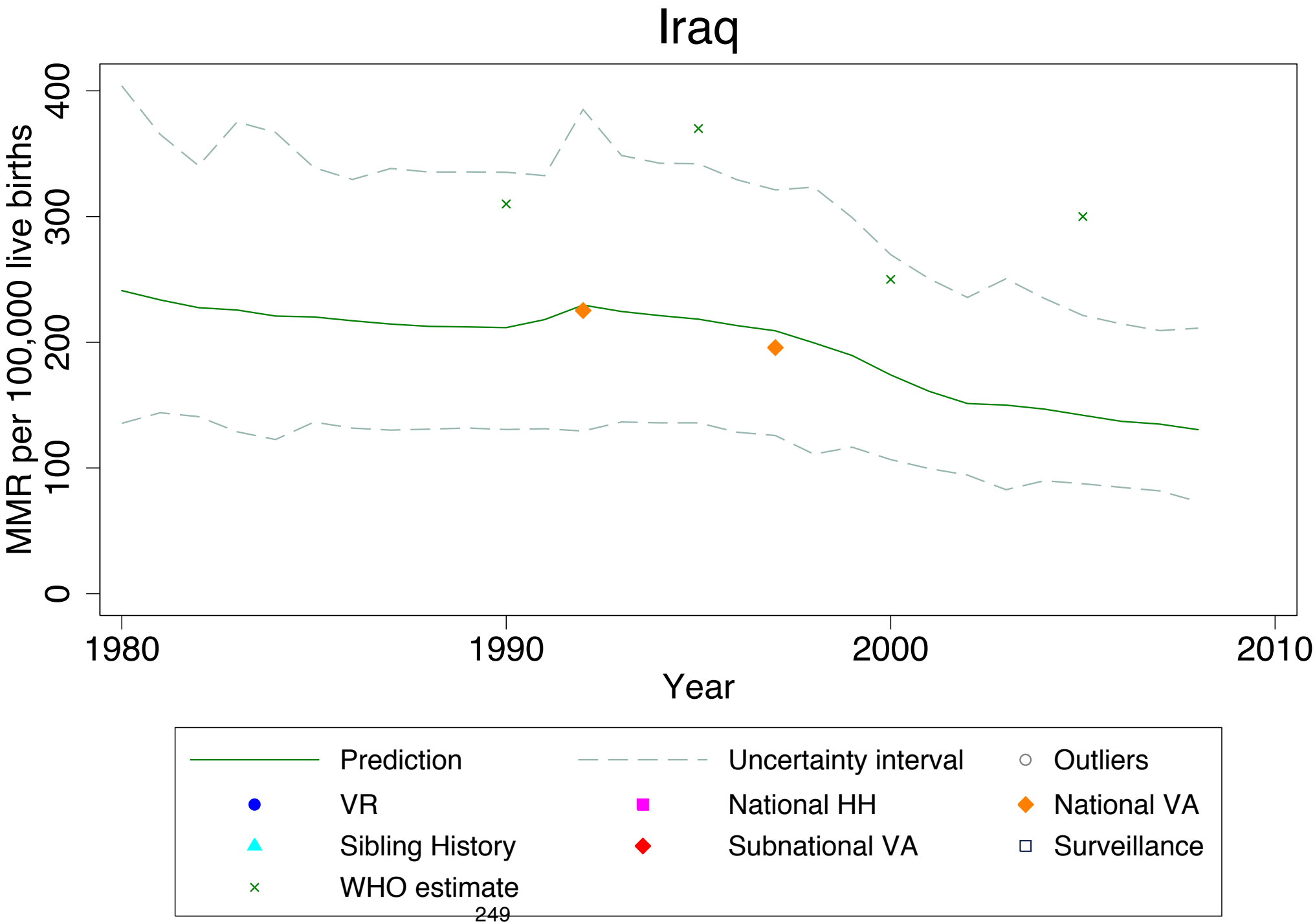

United Arab Emirates
MMR per 100,000 live births
0
20
40
60
80
100
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

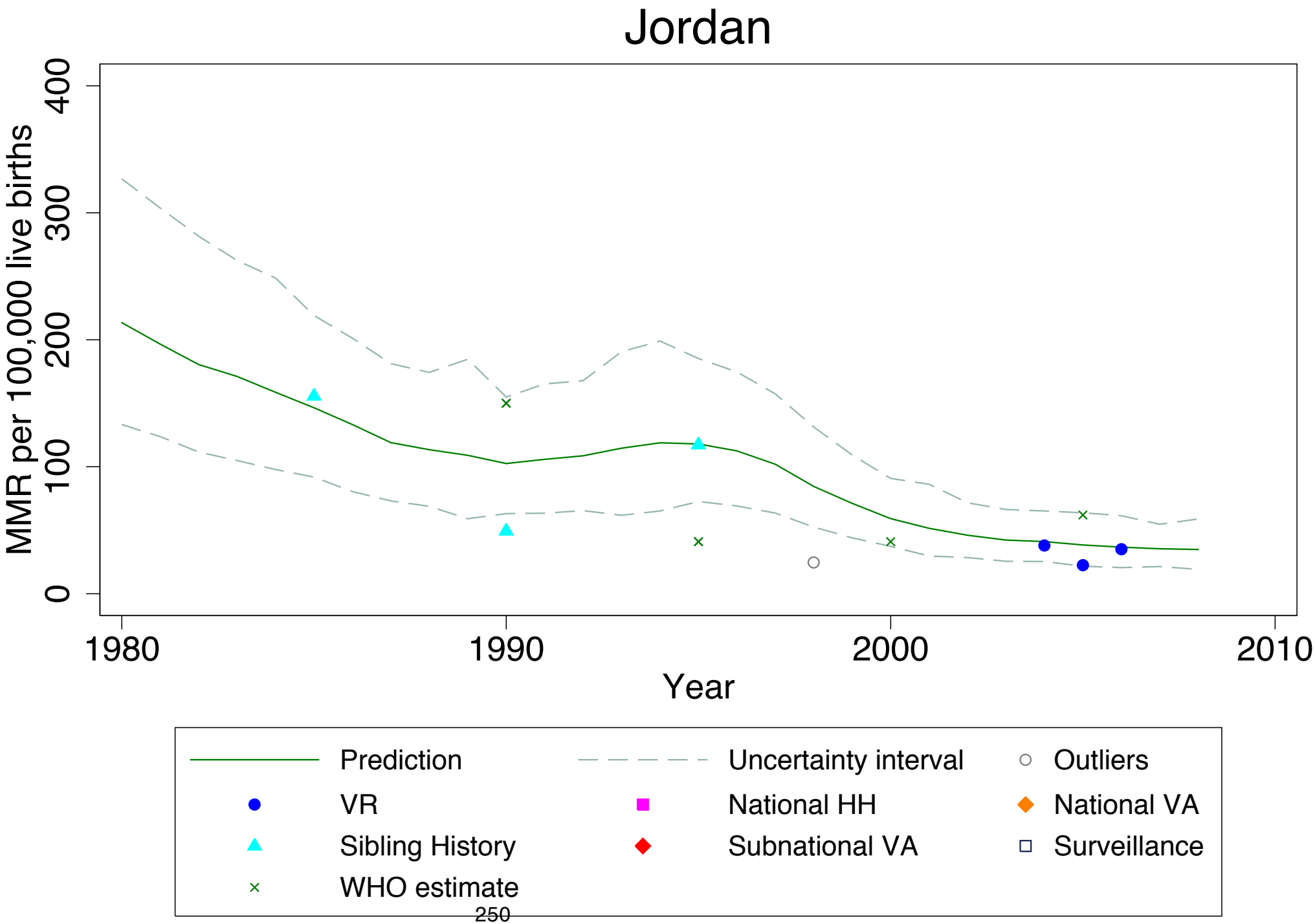

Bahrain
MMR per 100,000 live births
0
50
100
150
200
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

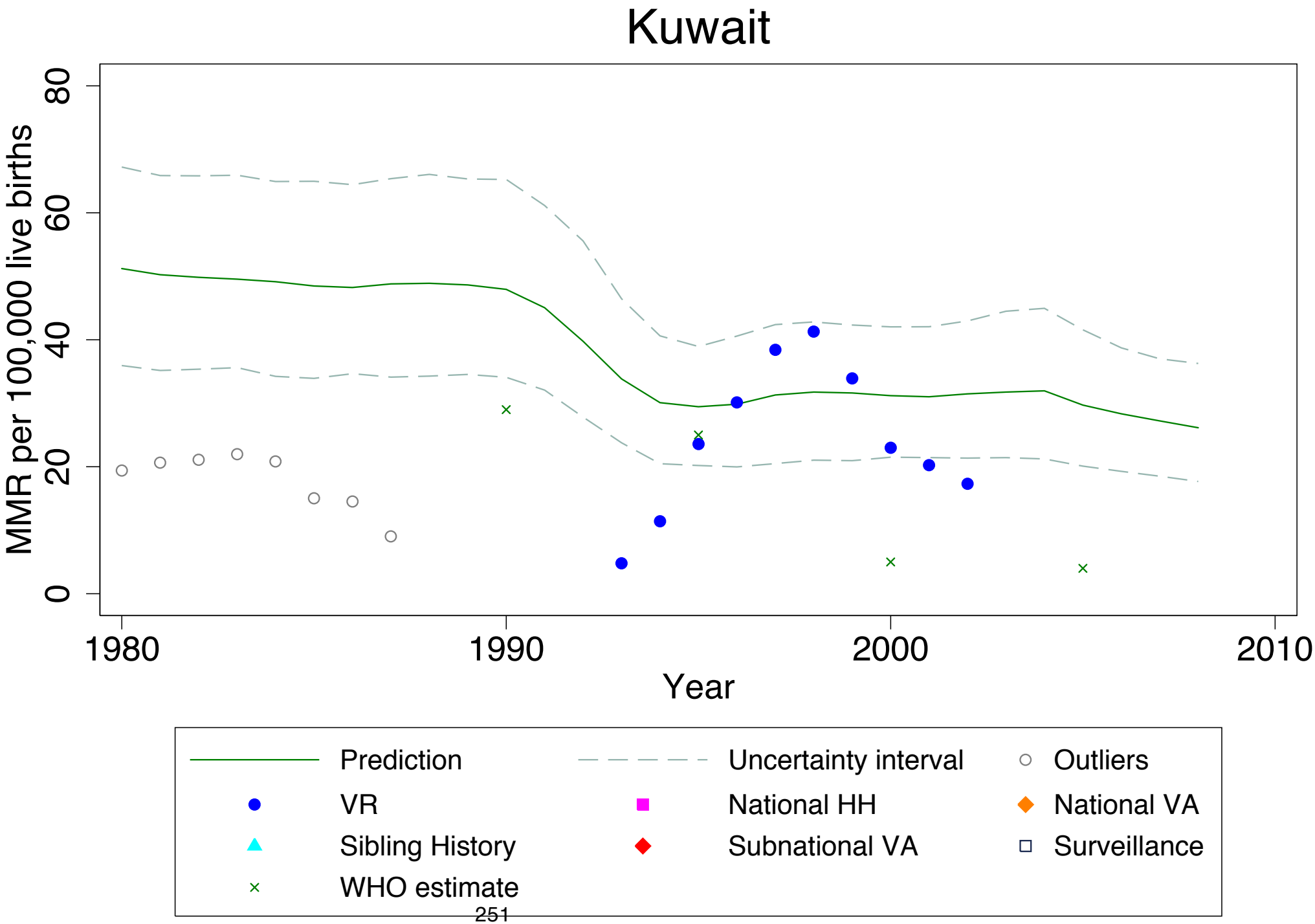

Algeria
MMR per 100,000 live births
0
100
200
300
400
500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Egypt
MMR per 100,000 live births
0
200
400
600
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Iran, Islamic Republic of
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Iraq
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Jordan
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Kuwait
MMR per 100,000 live births
0
20
40
60
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1980
1990
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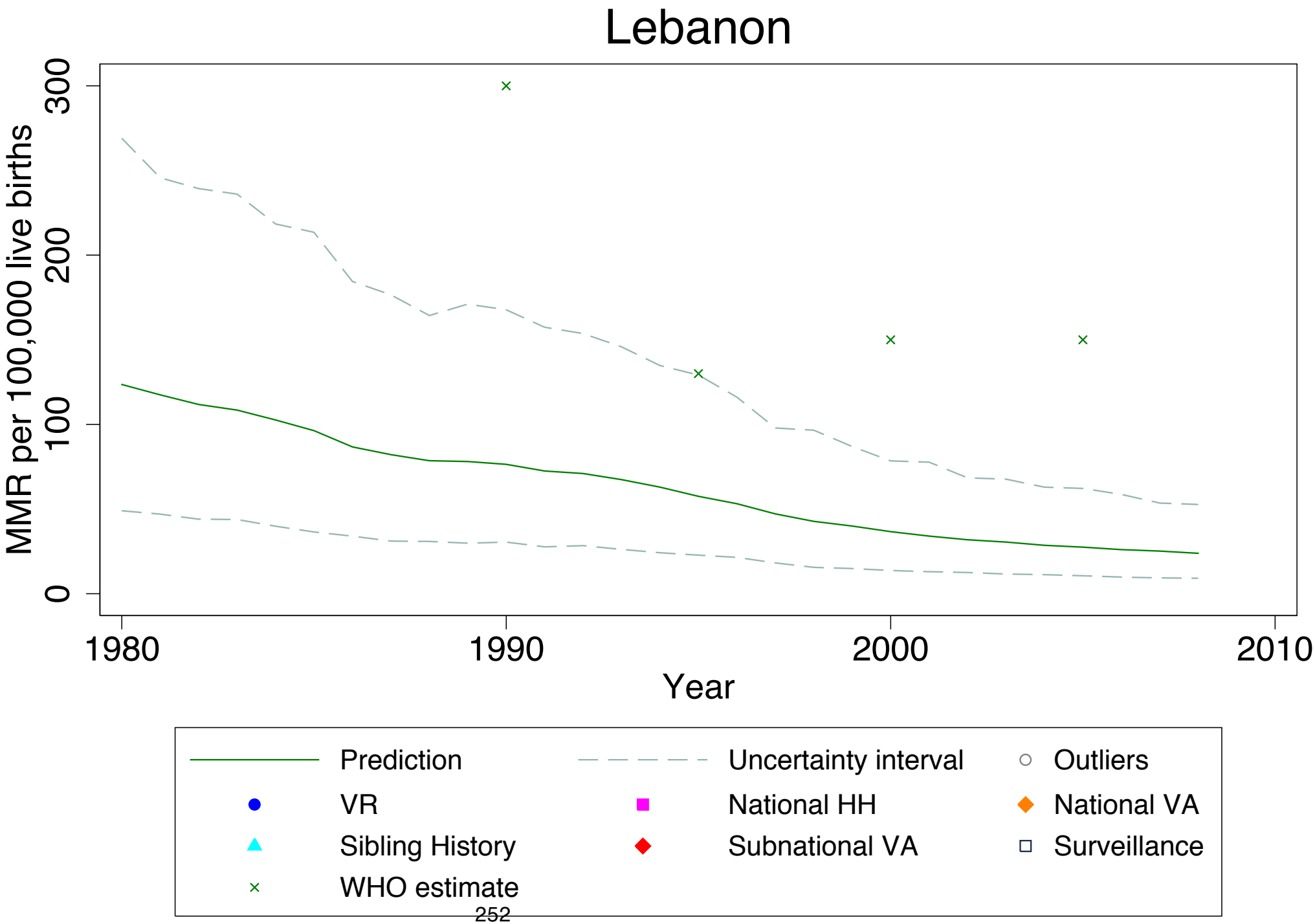
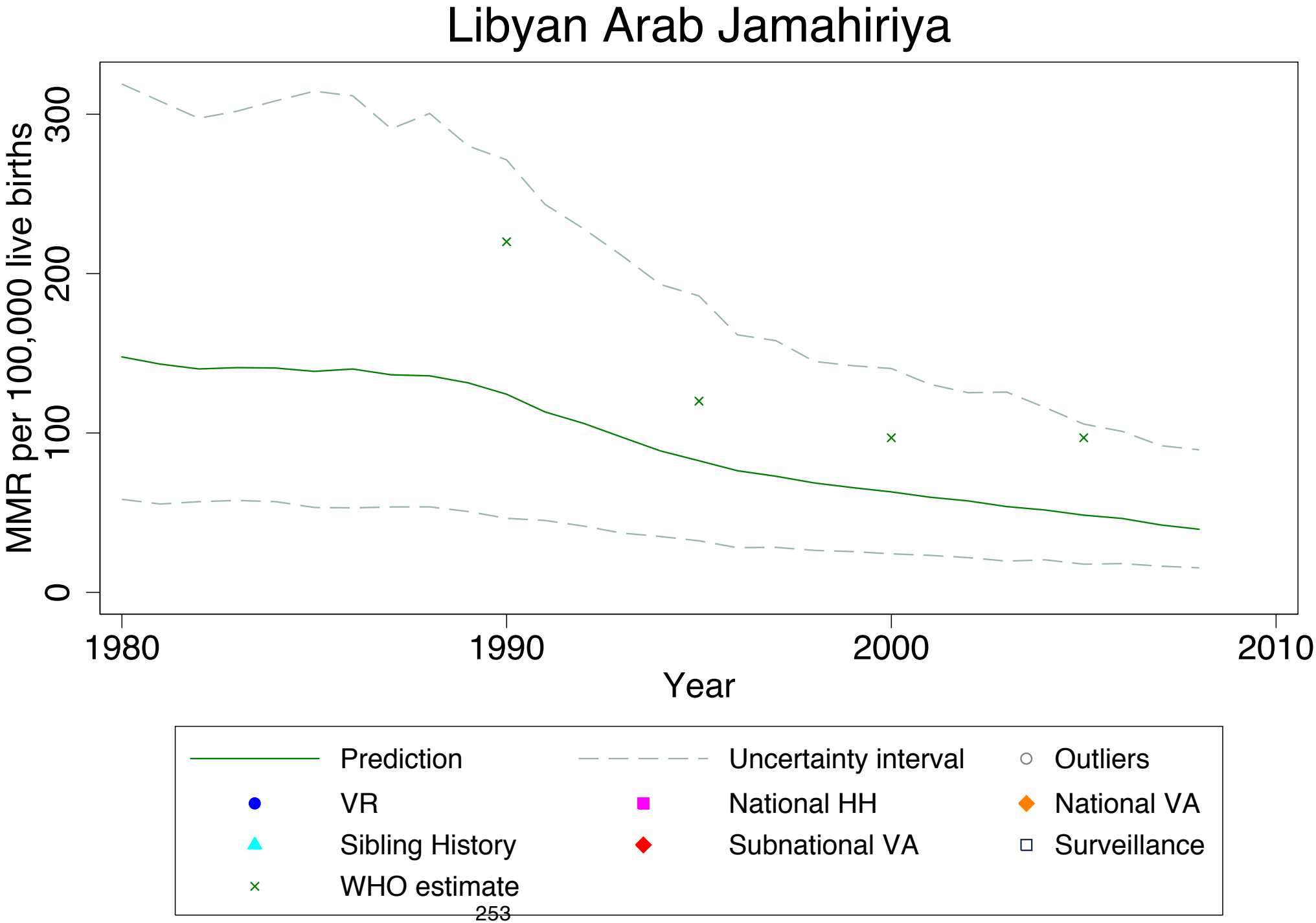
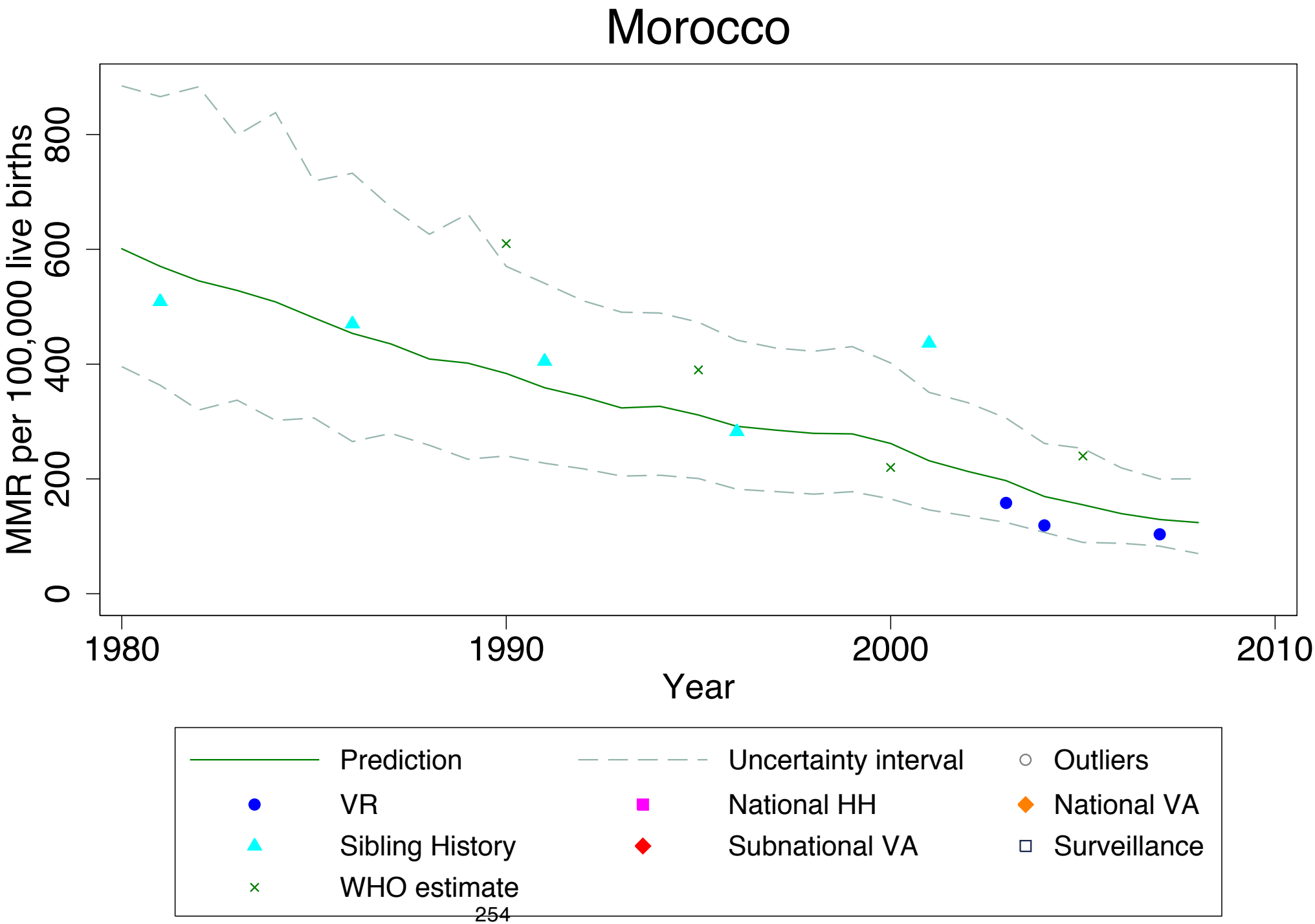
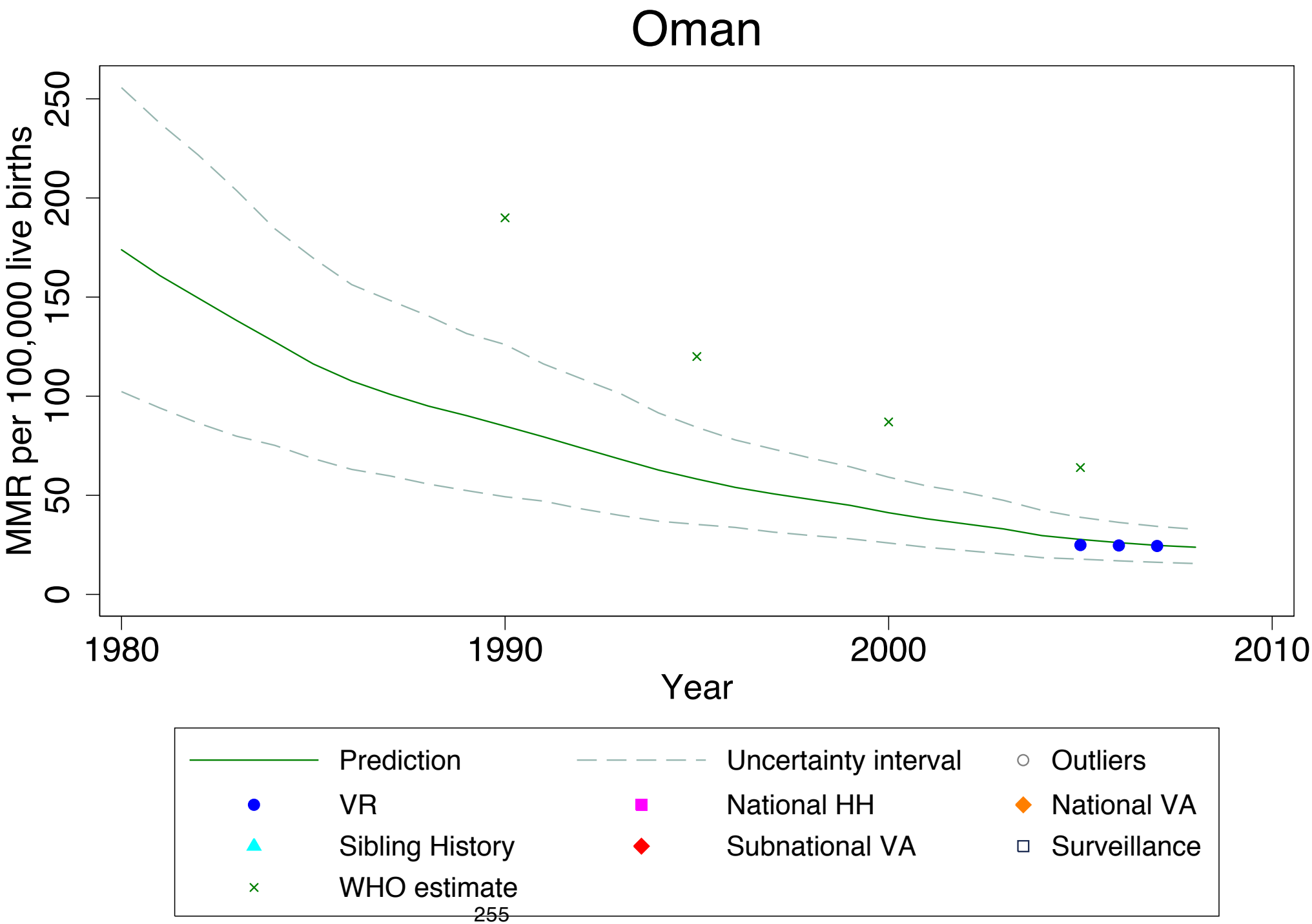
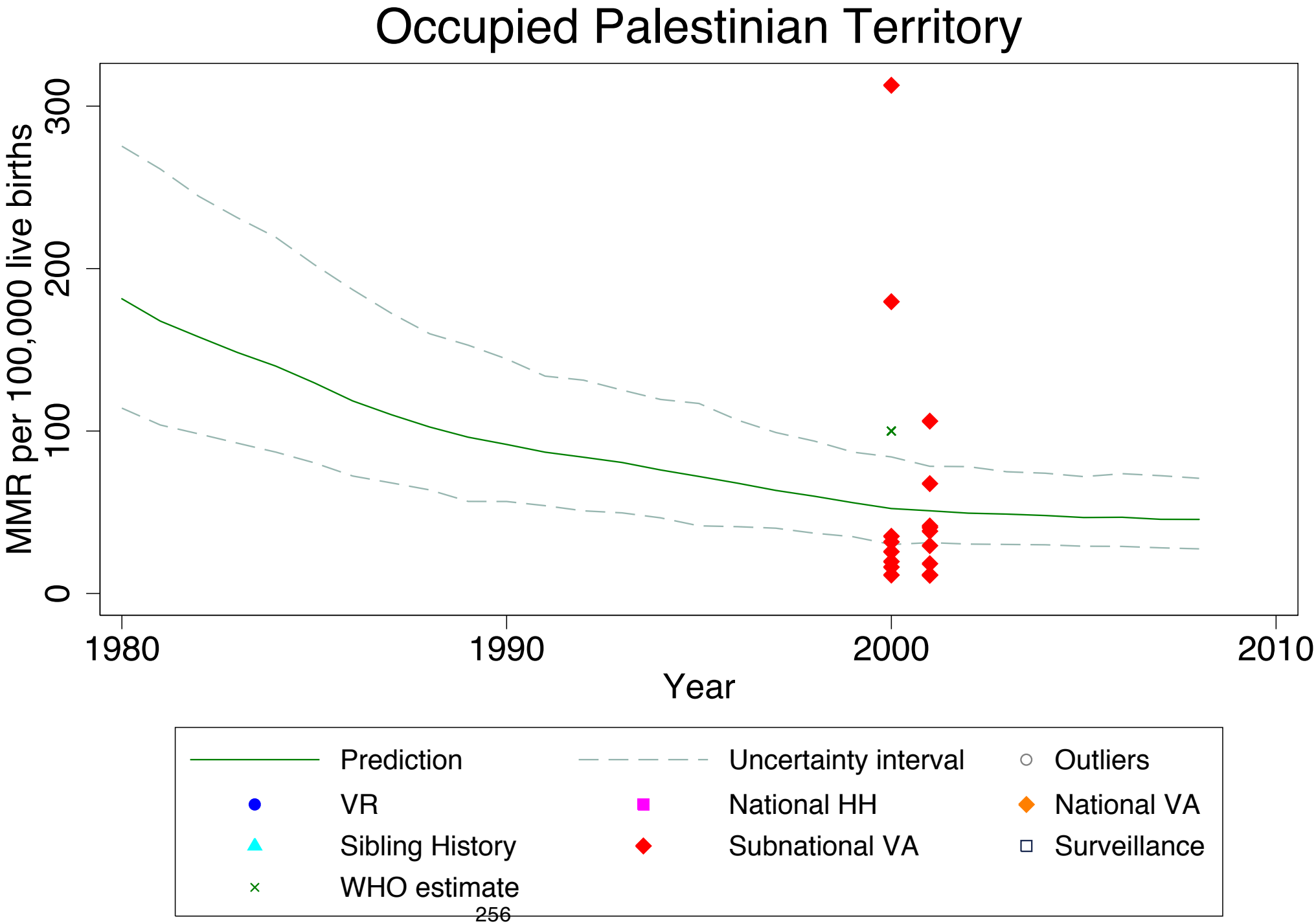
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

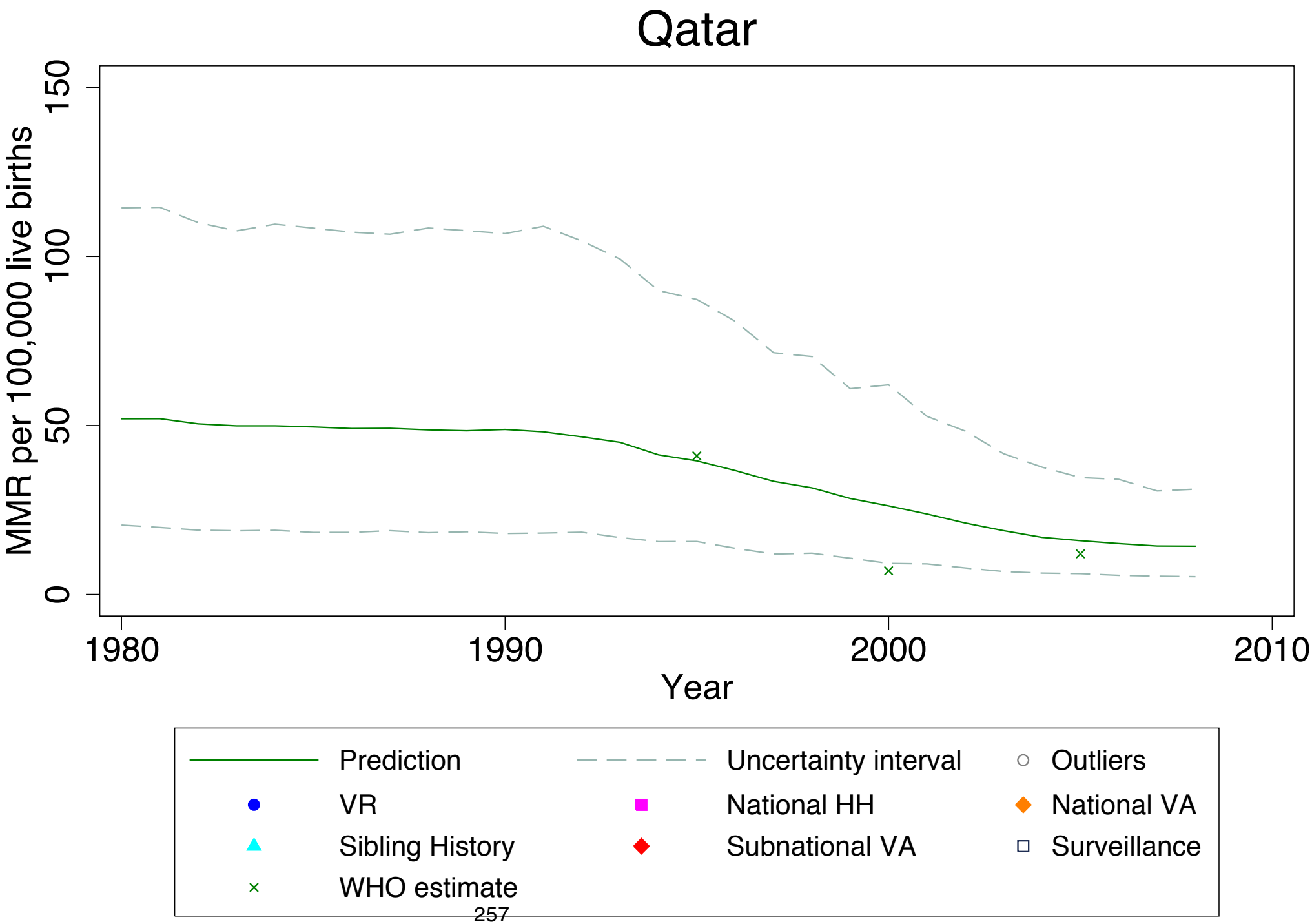

Lebanon
MMR per 100,000 live births
0
100
200
300
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

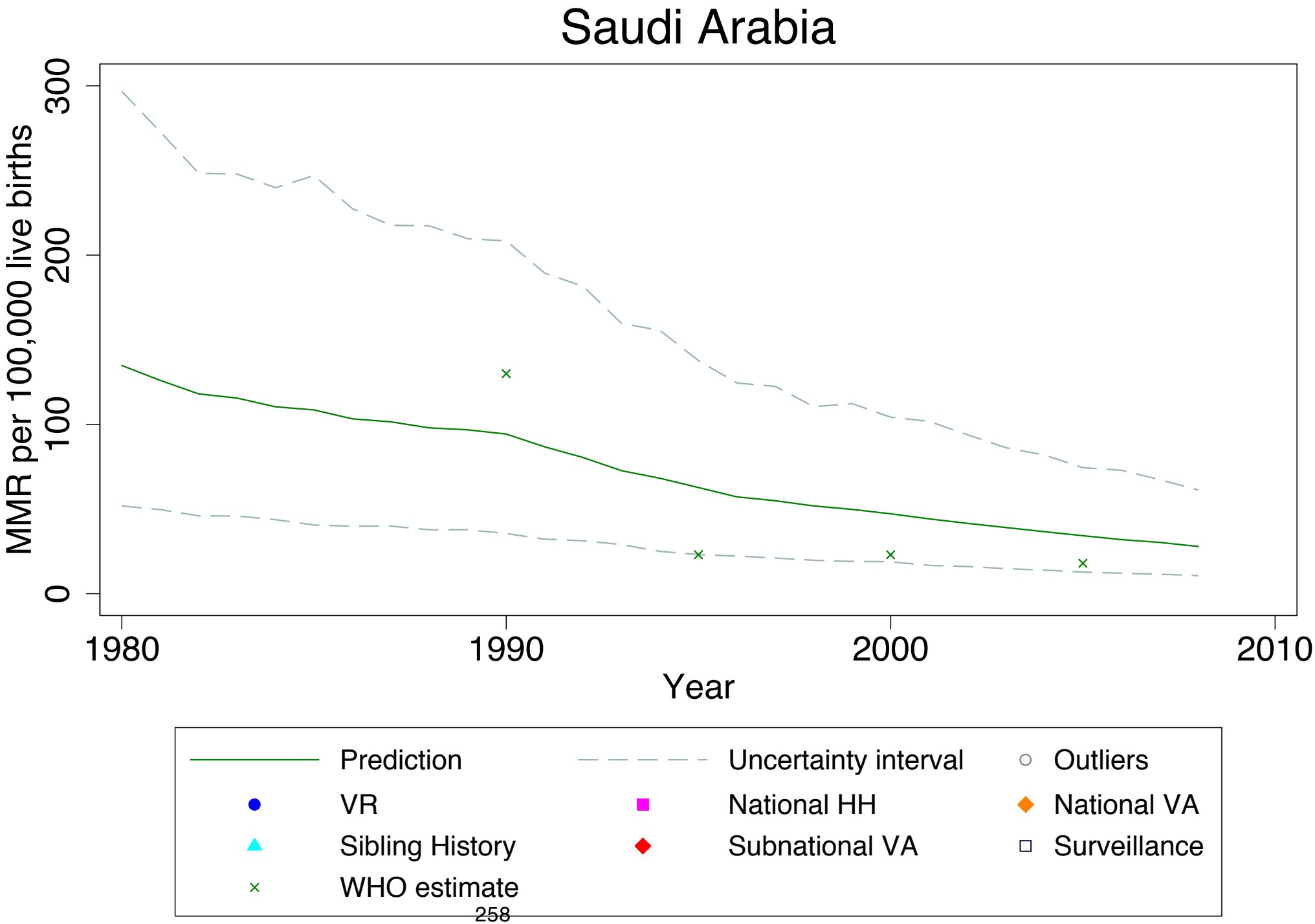

Libyan Arab Jamahiriya
MMR per 100,000 live births
0
100
200
300
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

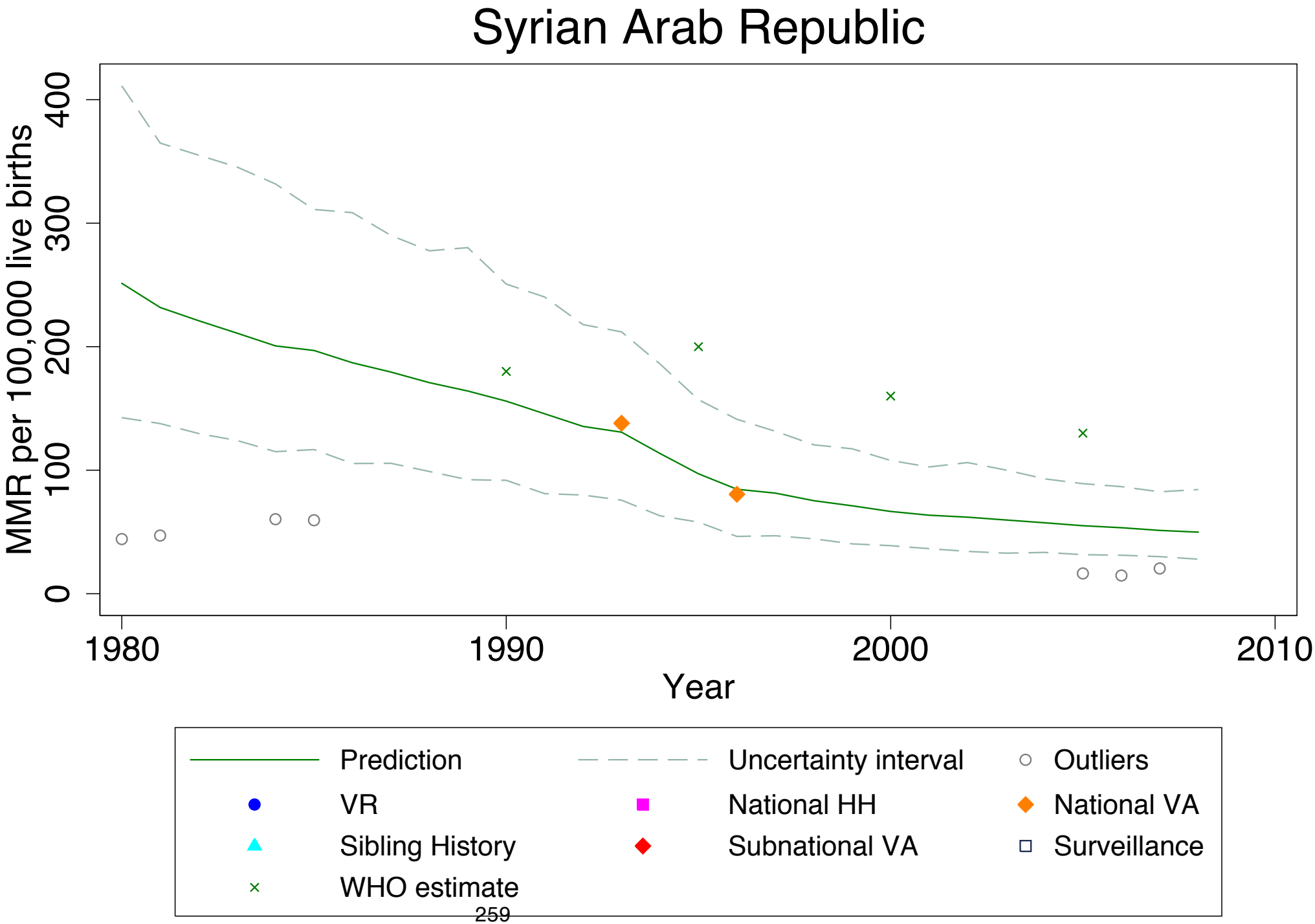

Morocco
MMR per 100,000 live births
0
200
400
600
800
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

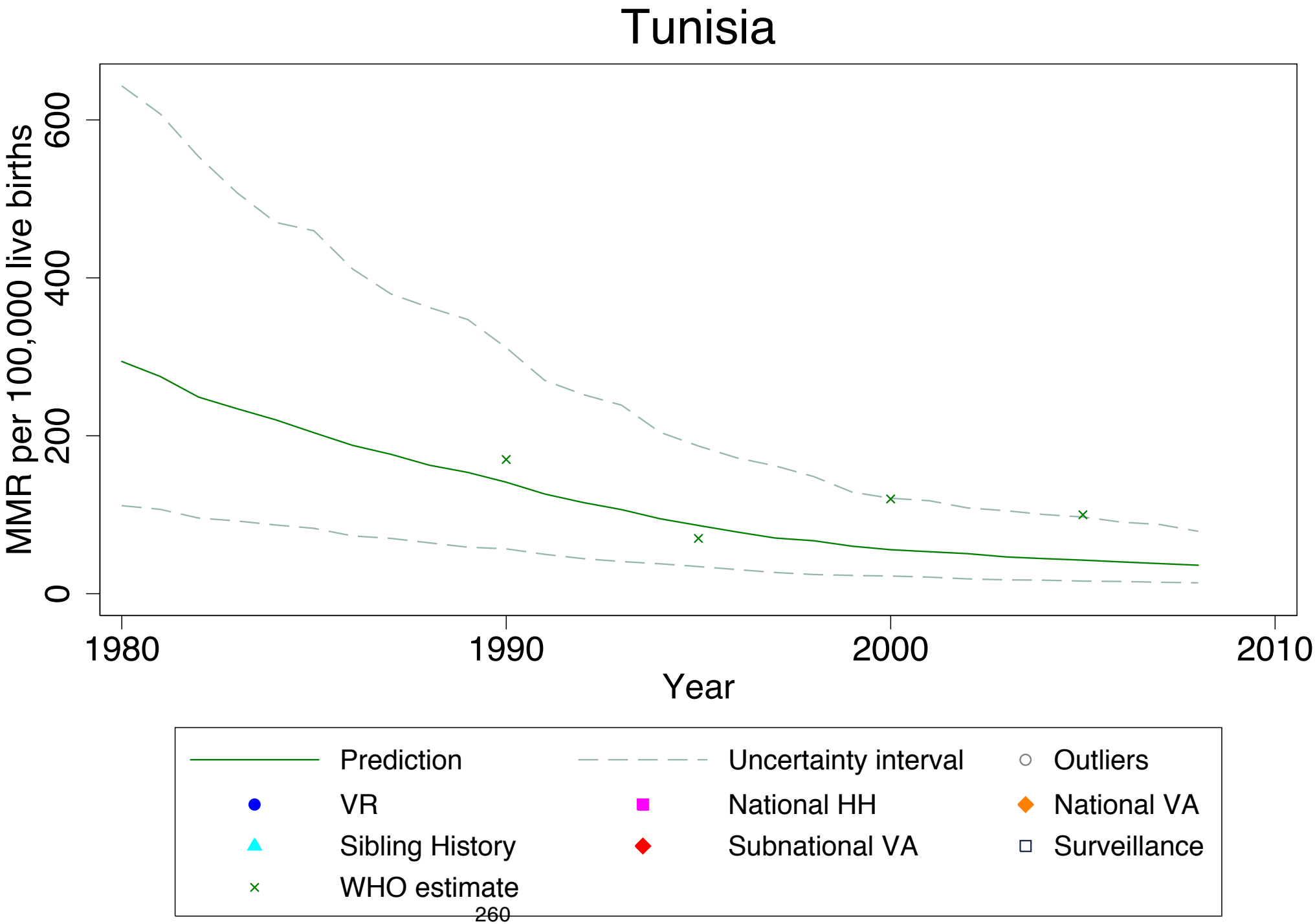

Oman
MMR per 100,000 live births
0
50
100
150
200
250
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

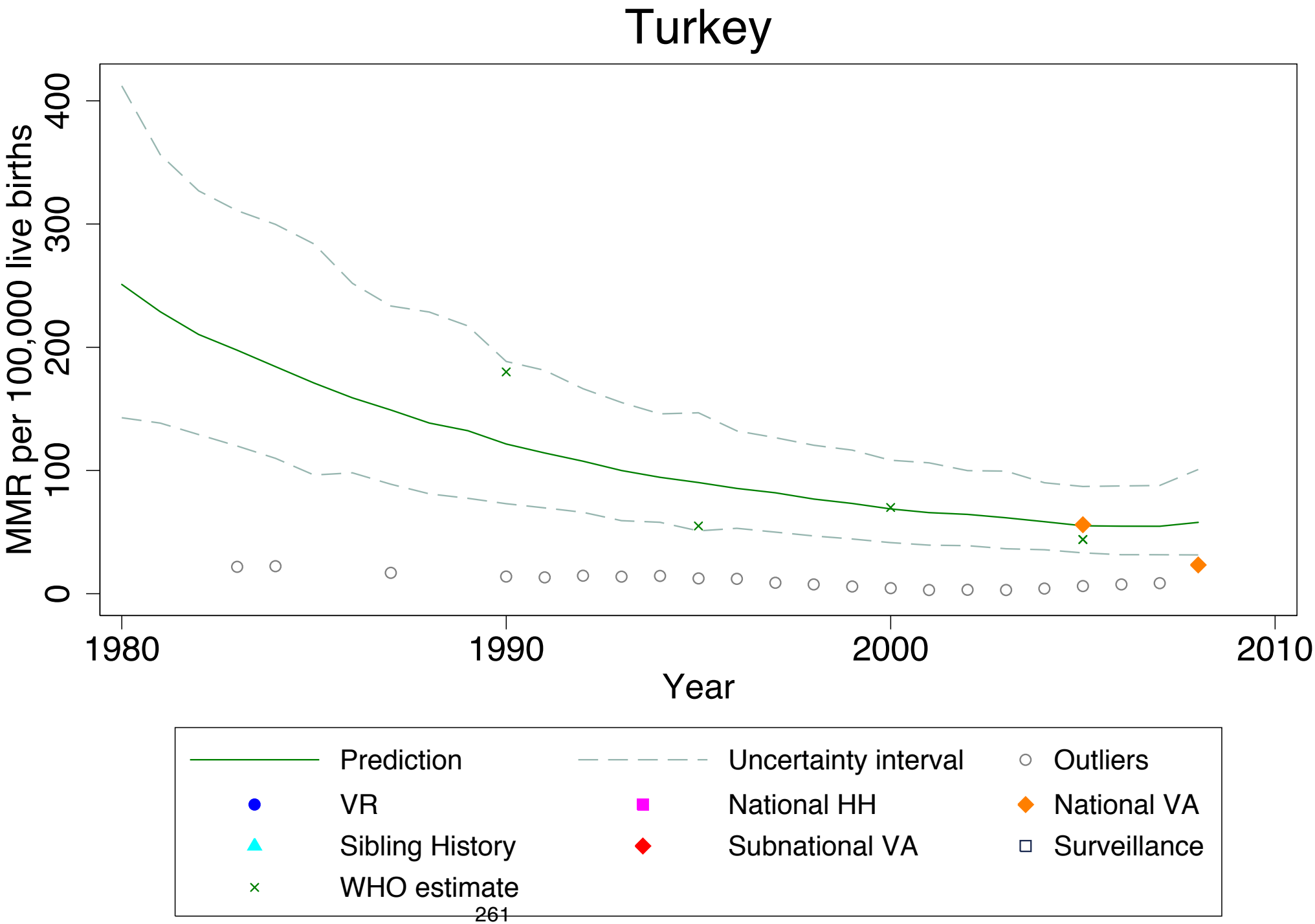

Occupied Palestinian Territory
MMR per 100,000 live births
0
100
200
300
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

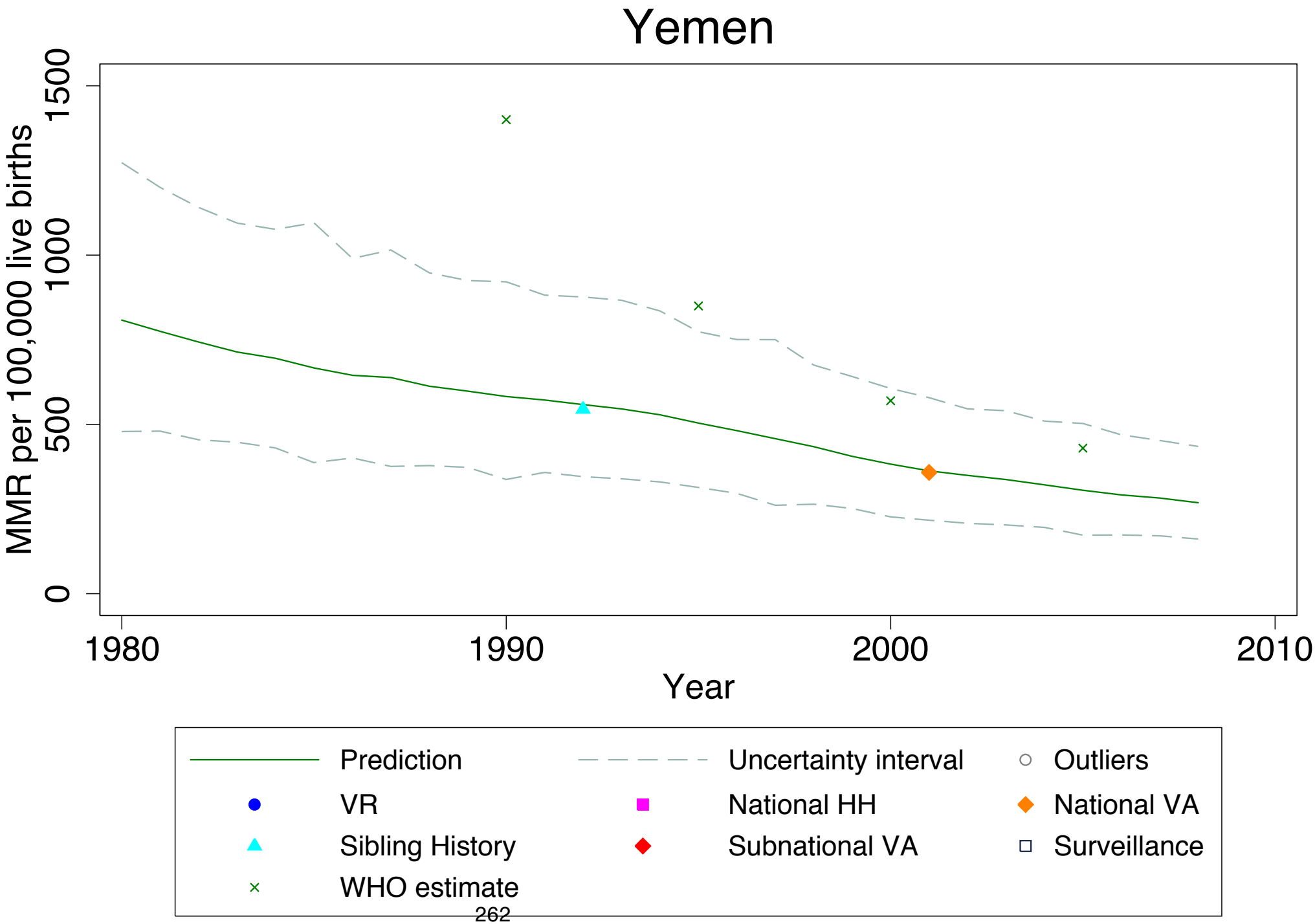

Qatar
MMR per 100,000 live births
0
50
100
150
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

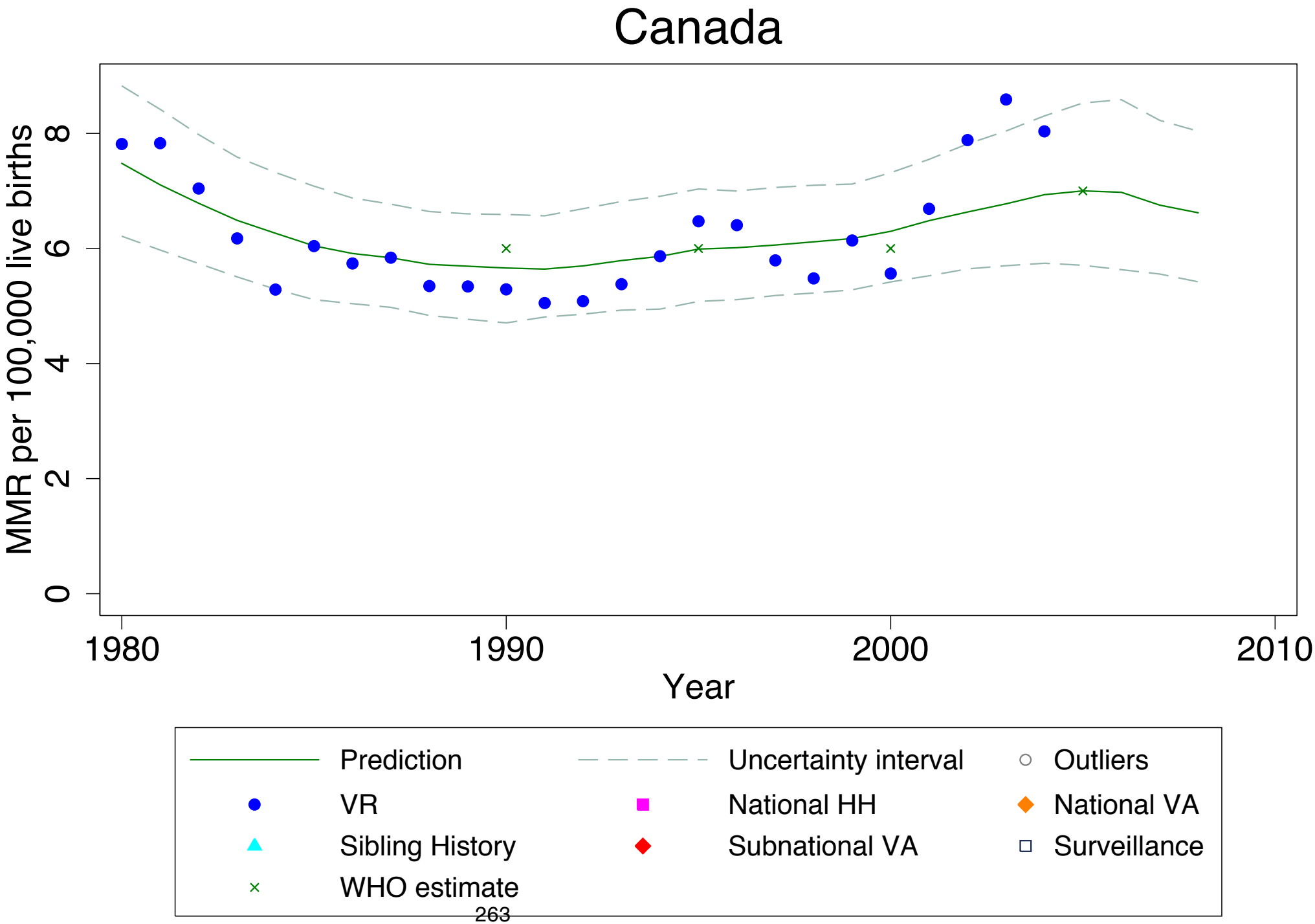

Saudi Arabia
MMR per 100,000 live births
0
100
200
300
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

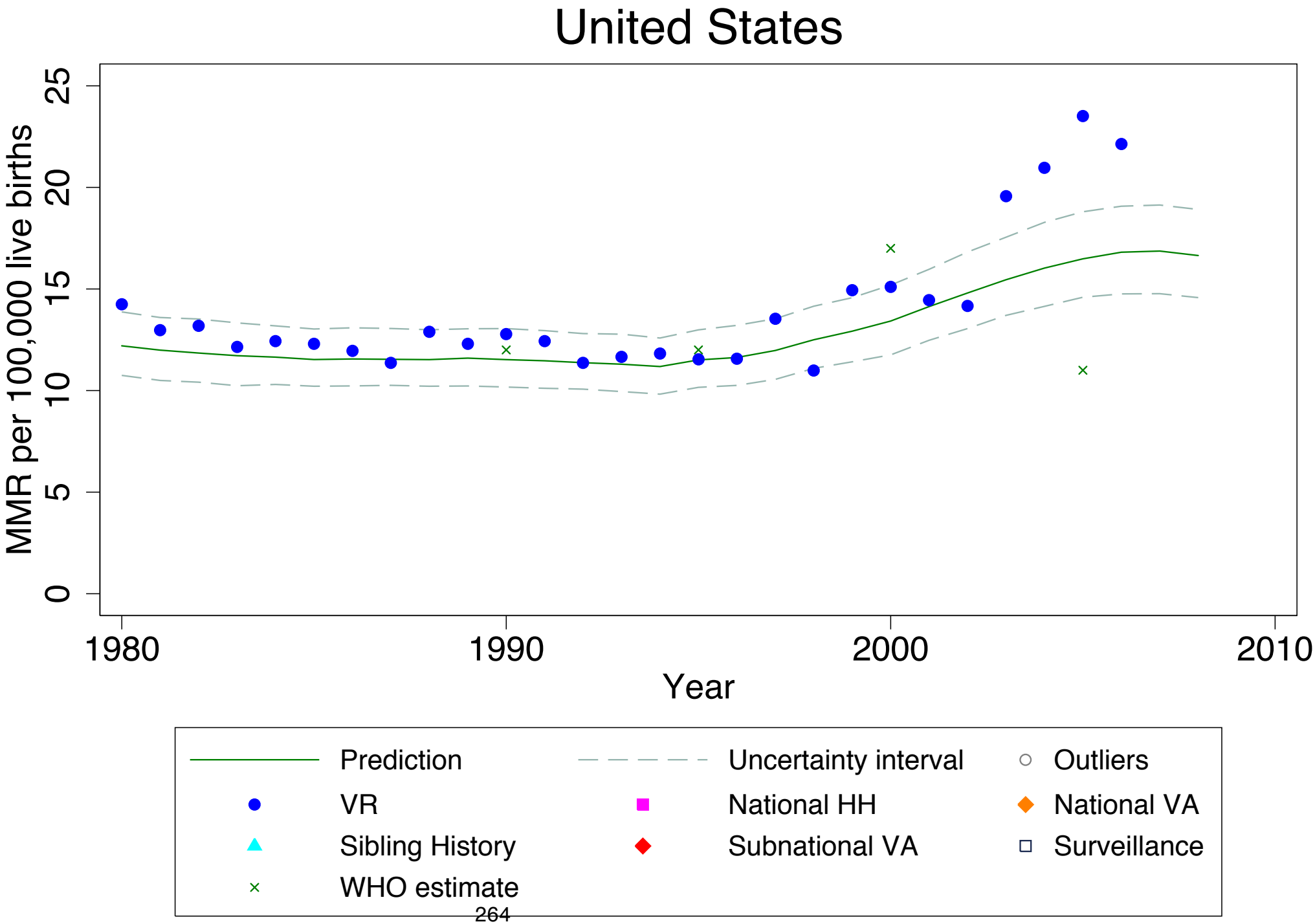

Syrian Arab Republic
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

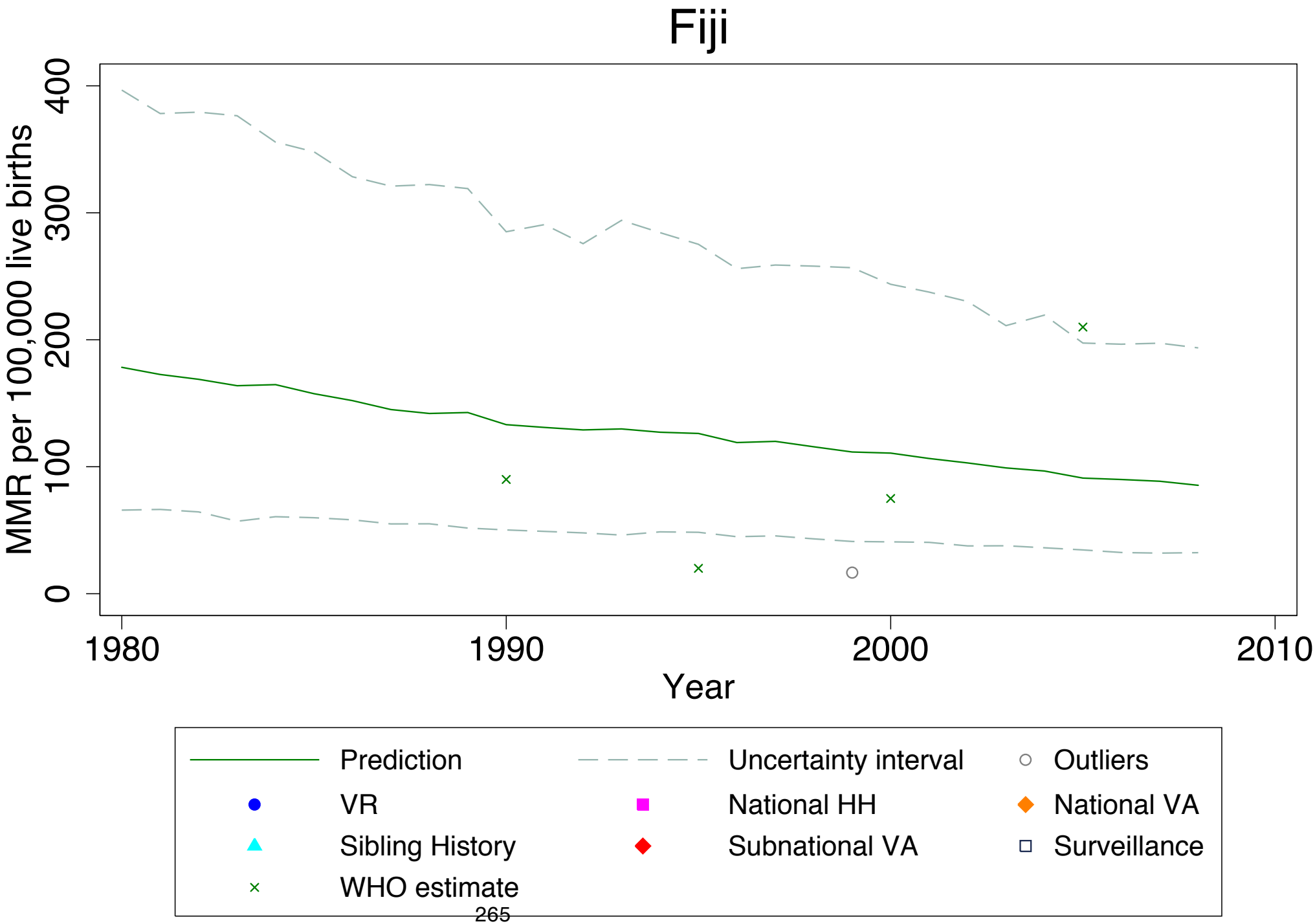

Tunisia
MMR per 100,000 live births
0
200
400
600
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

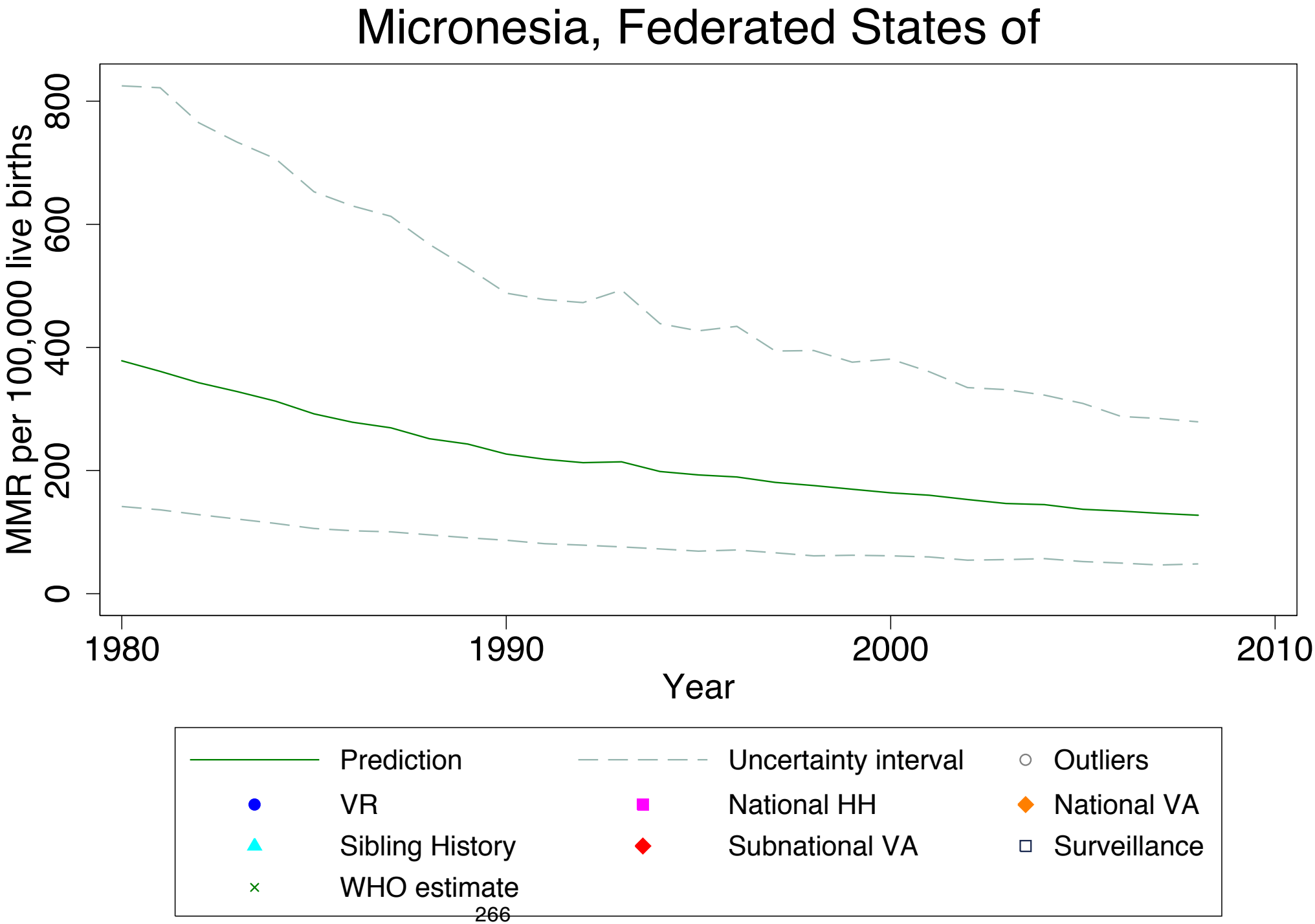

Turkey
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

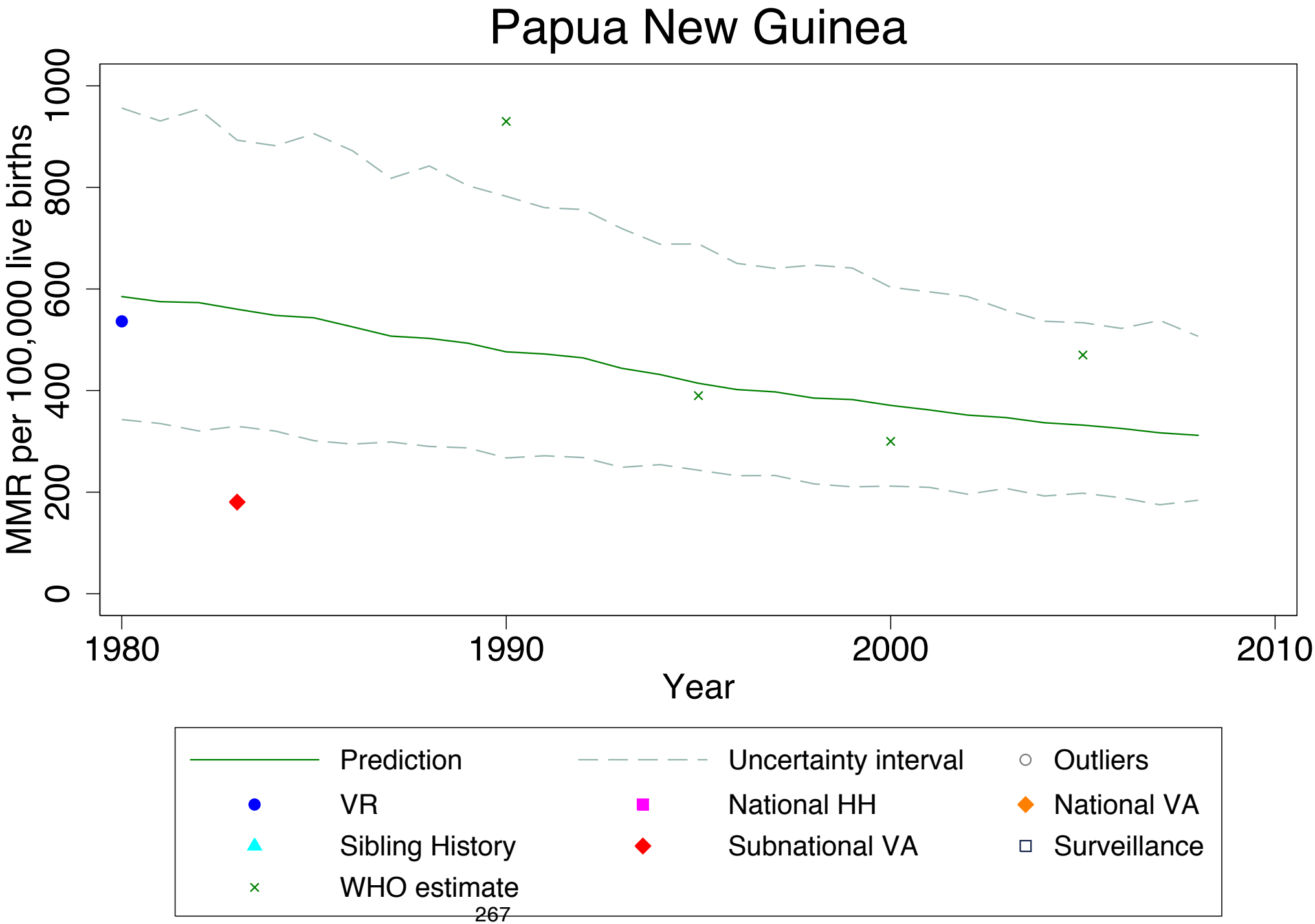

Yemen
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

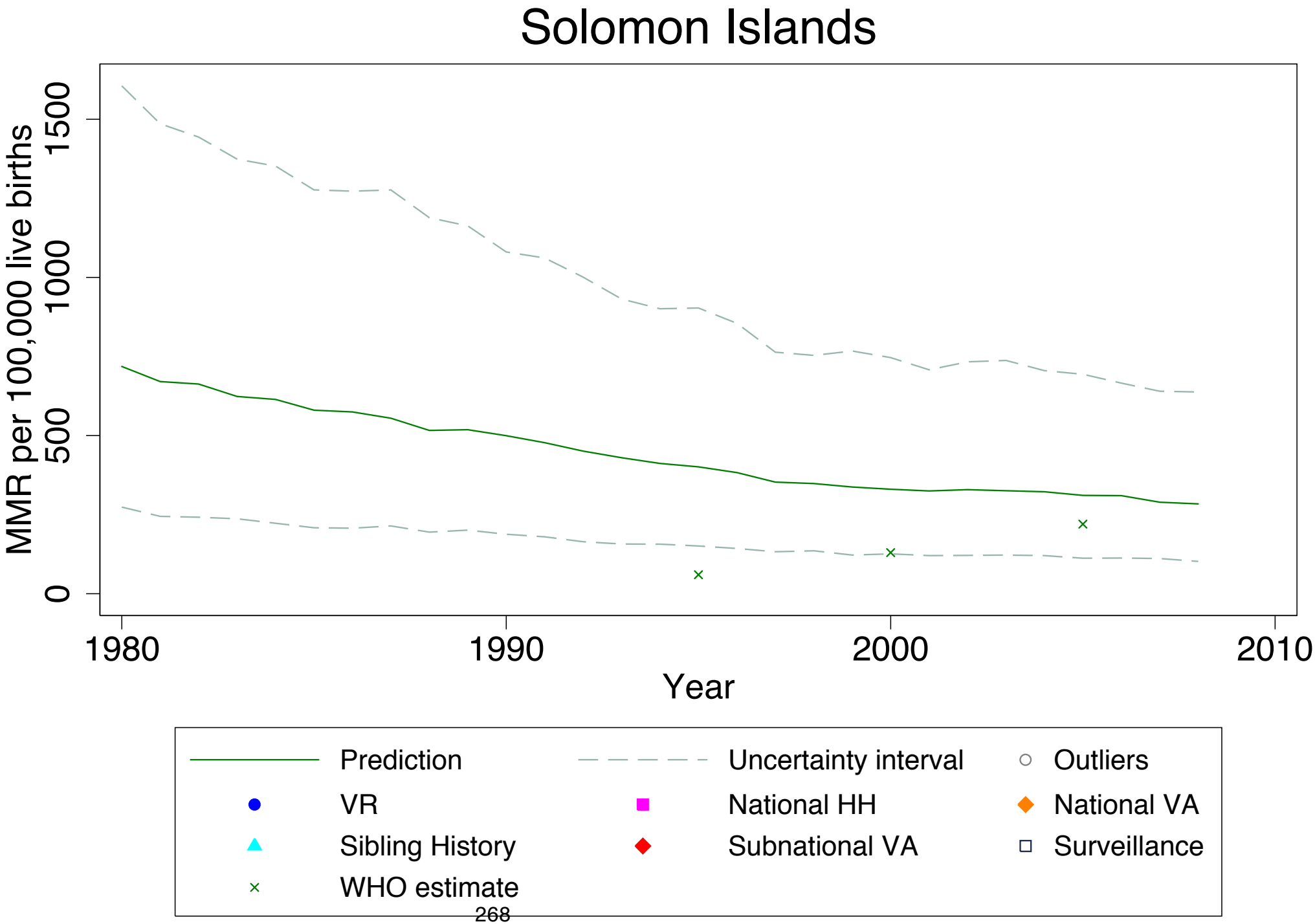

Canada
MMR per 100,000 live births
0
2
4
6
8
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

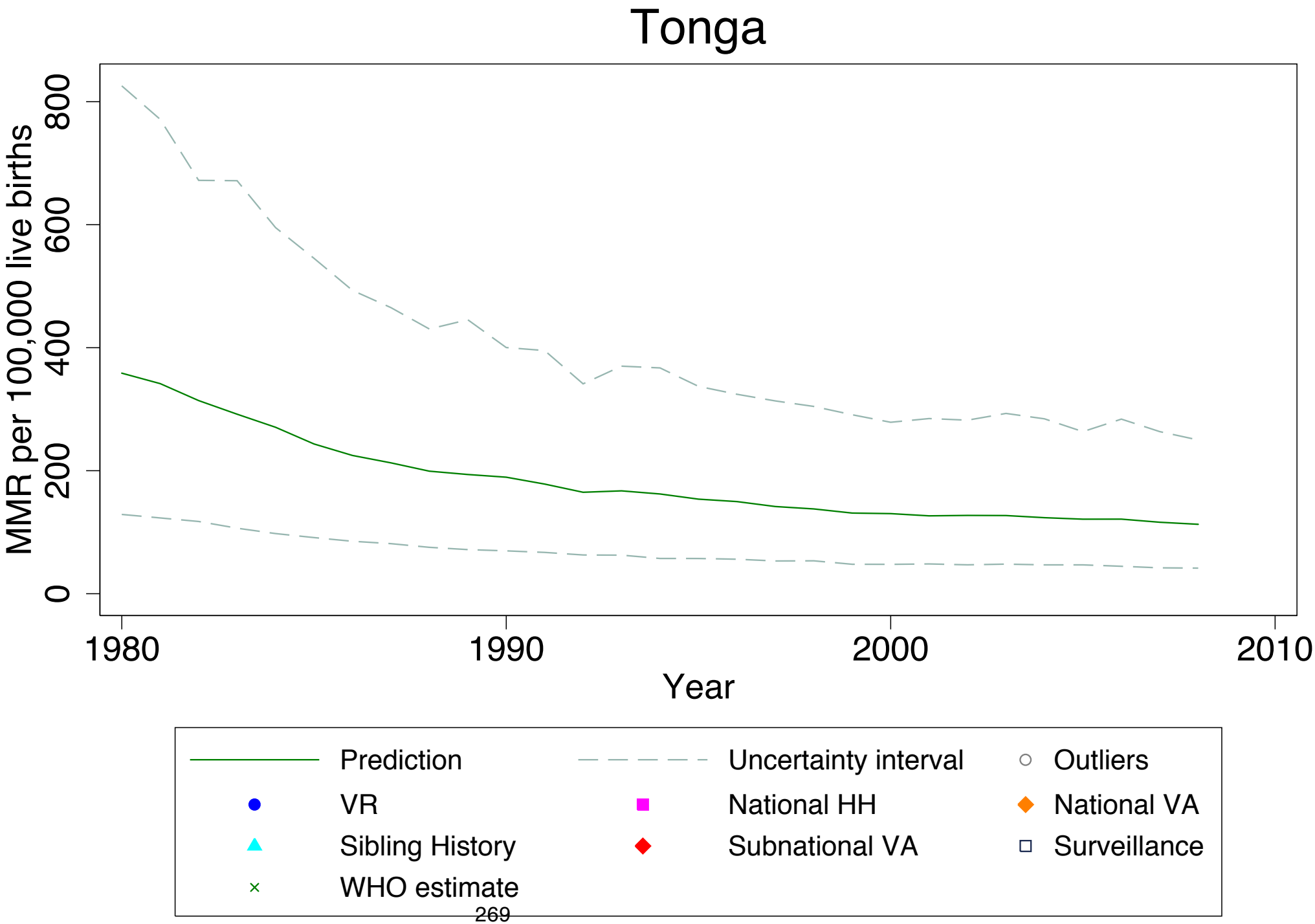

United States
MMR per 100,000 live births
0
5
10
15
20
25
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

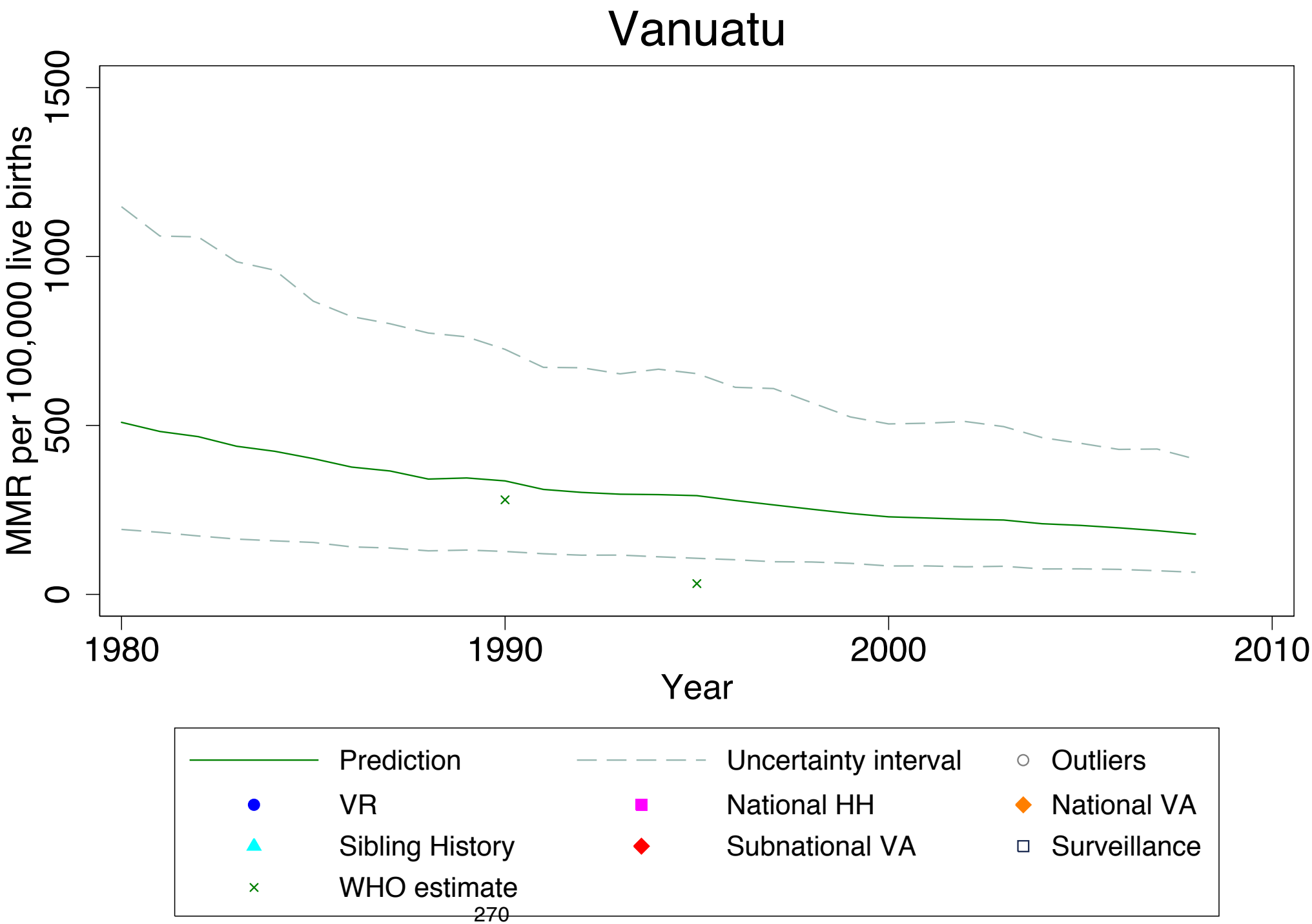

Fiji
MMR per 100,000 live births
0
100
200
300
400
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

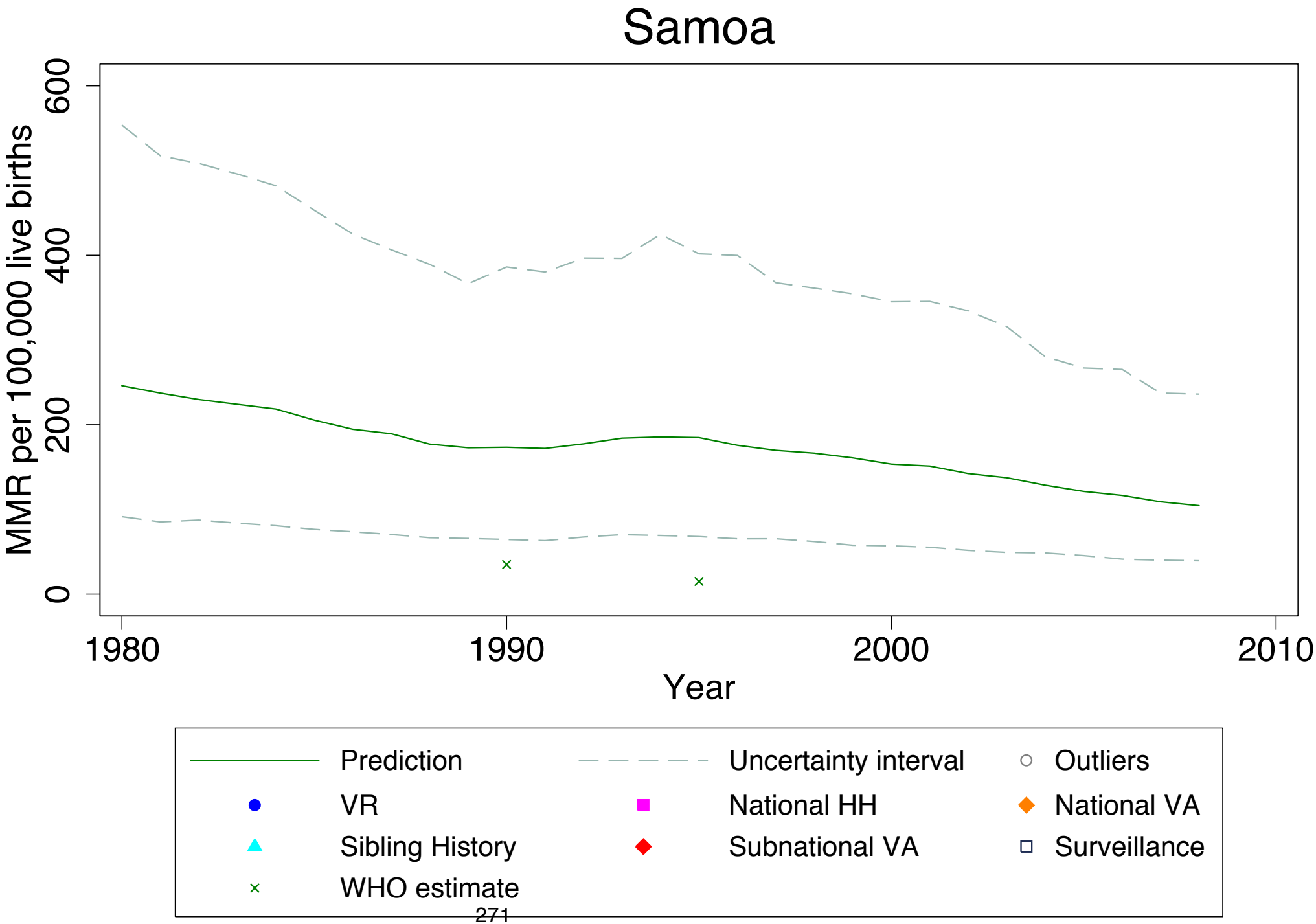

Micronesia, Federated States of
MMR per 100,000 live births
0
200
400
600
800
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

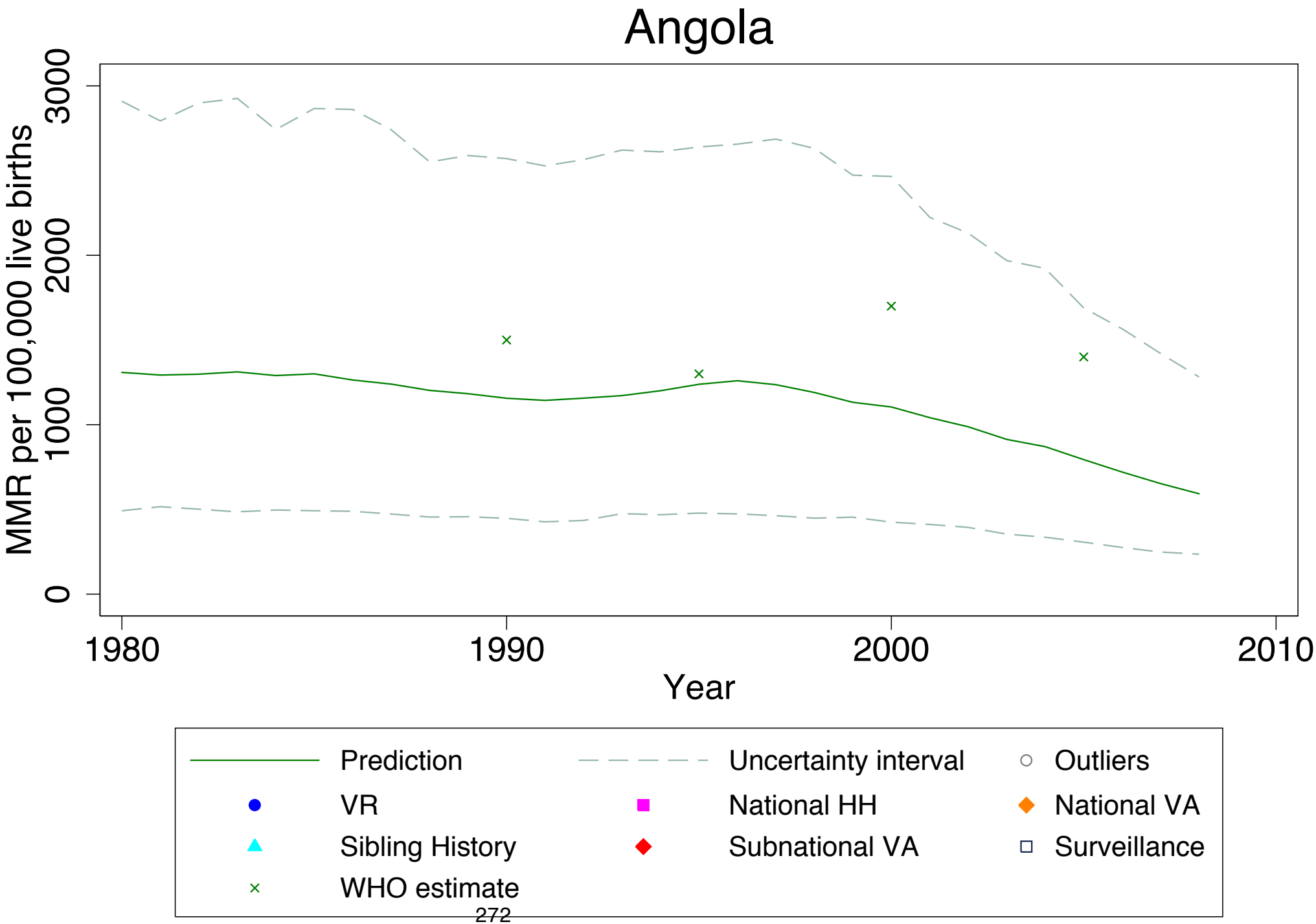

Papua New Guinea
MMR per 100,000 live births
0
200
400
600
800
1000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

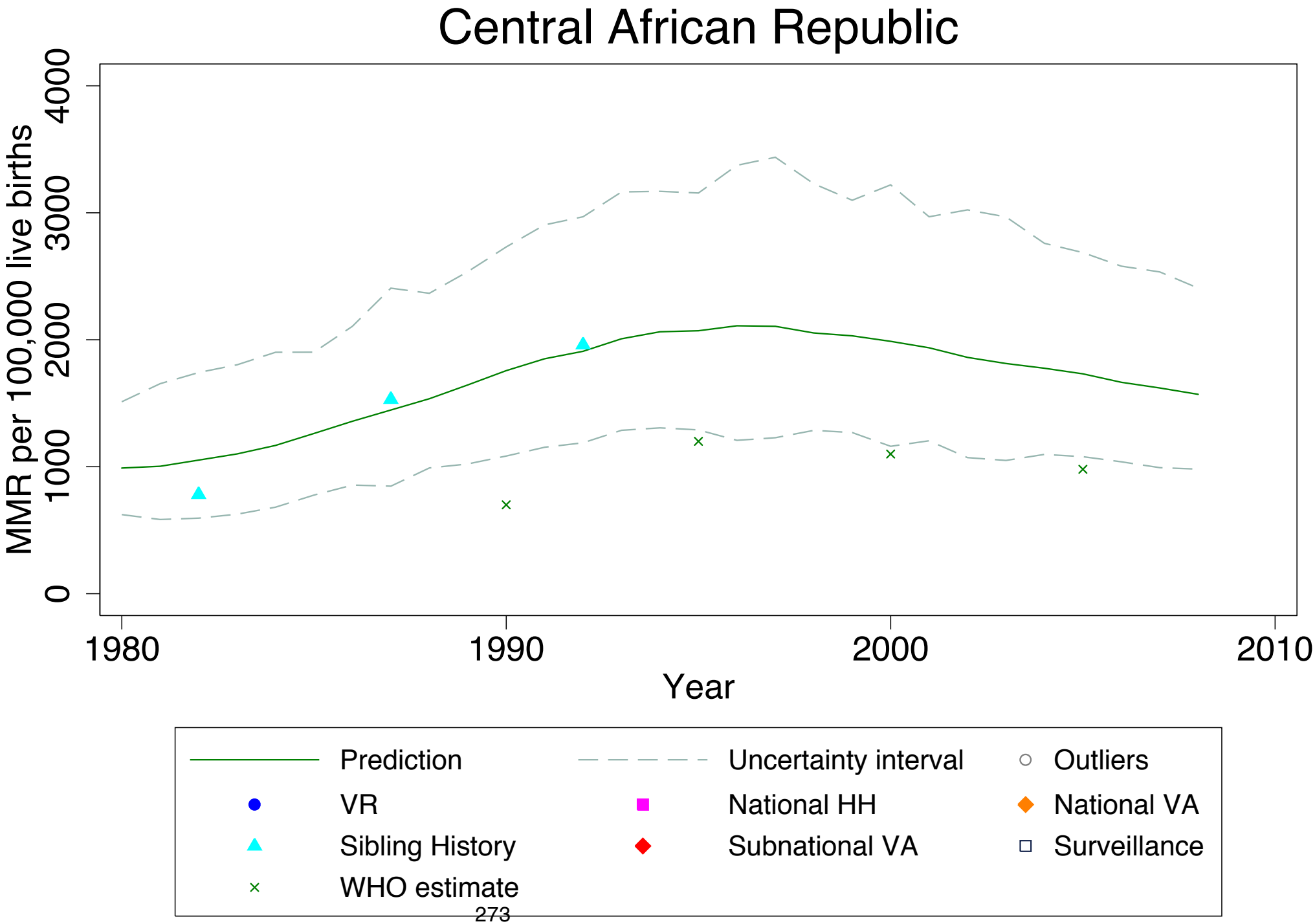

Solomon Islands
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

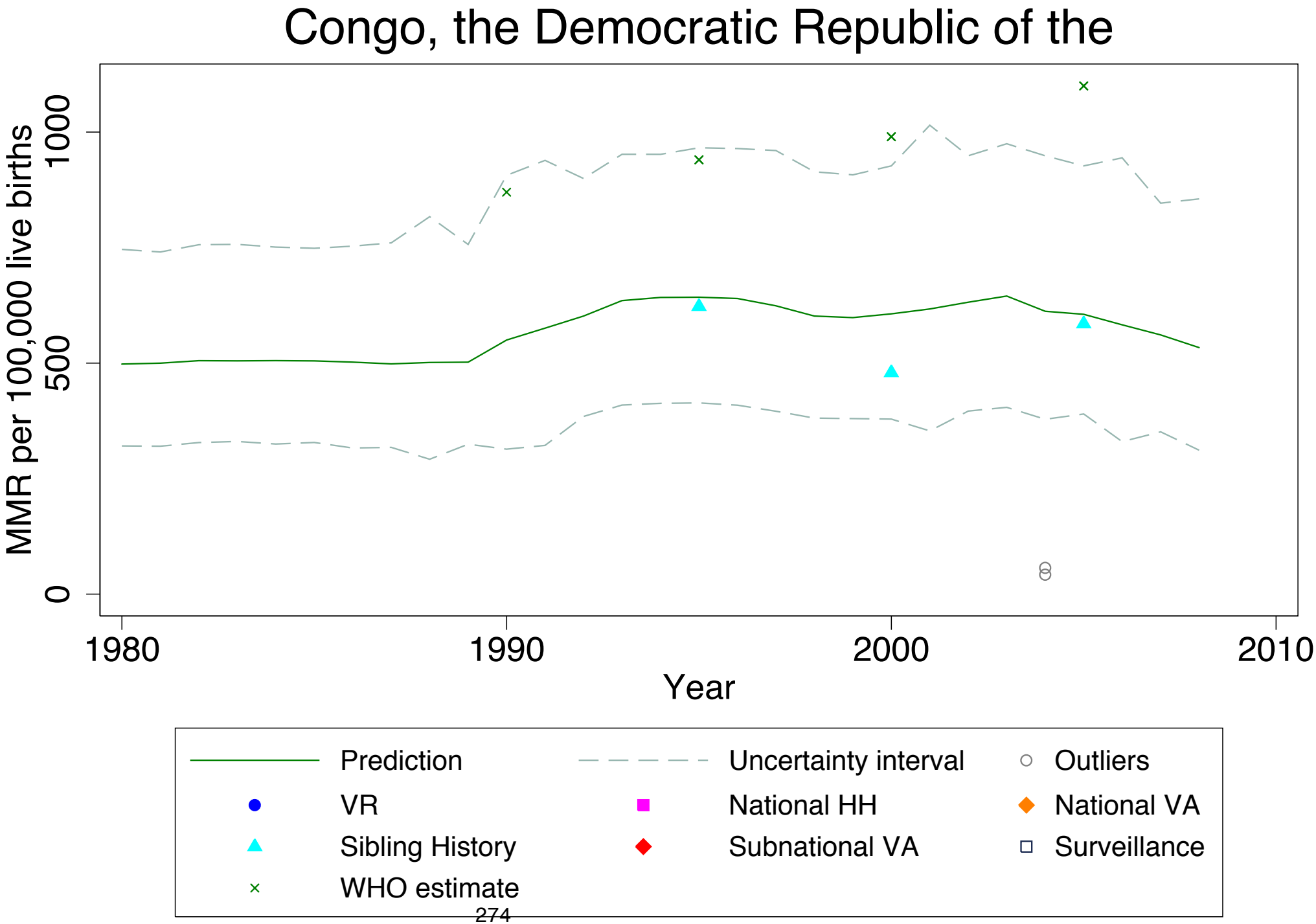

Tonga
MMR per 100,000 live births
0
200
400
600
800
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

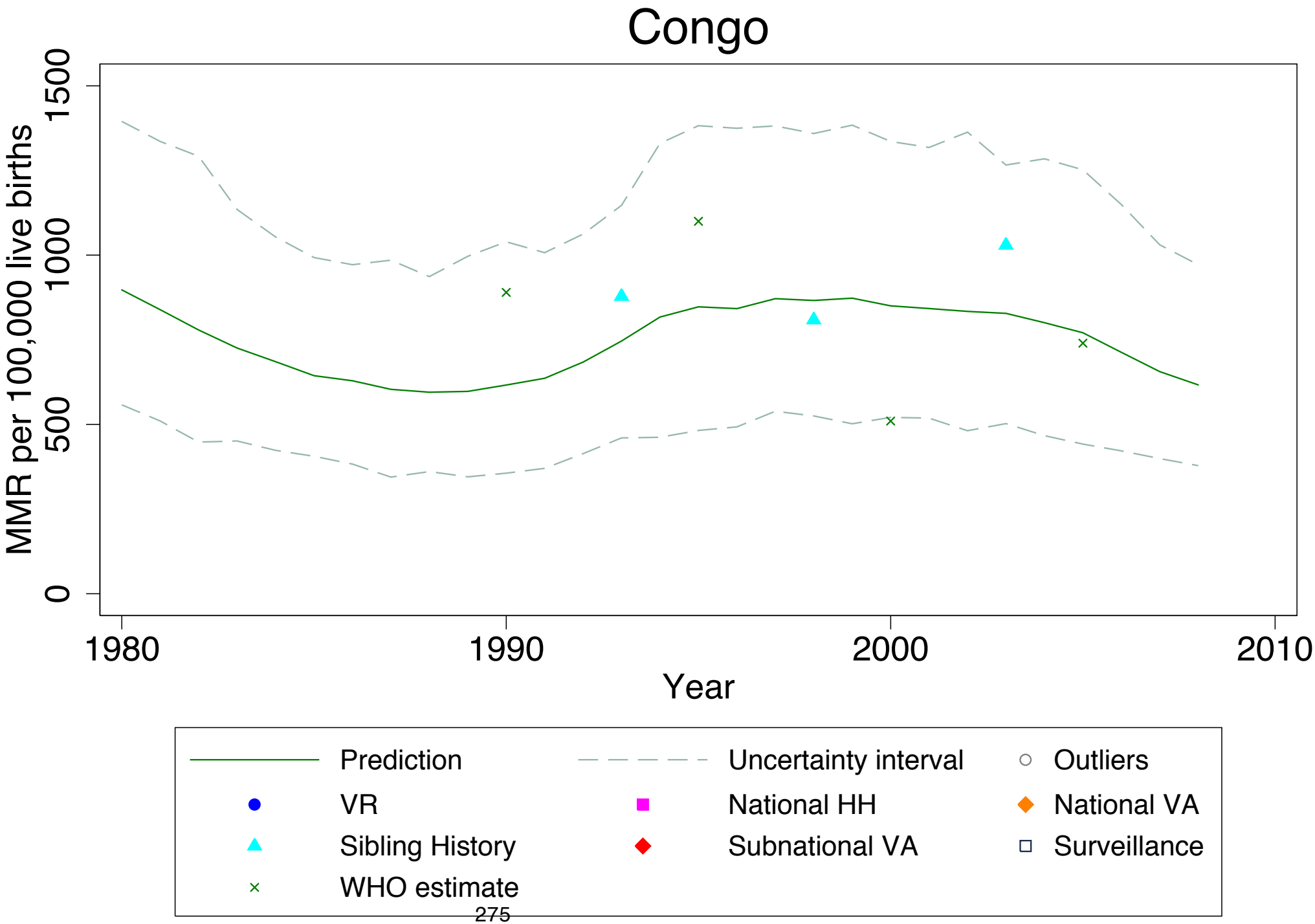

Vanuatu
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

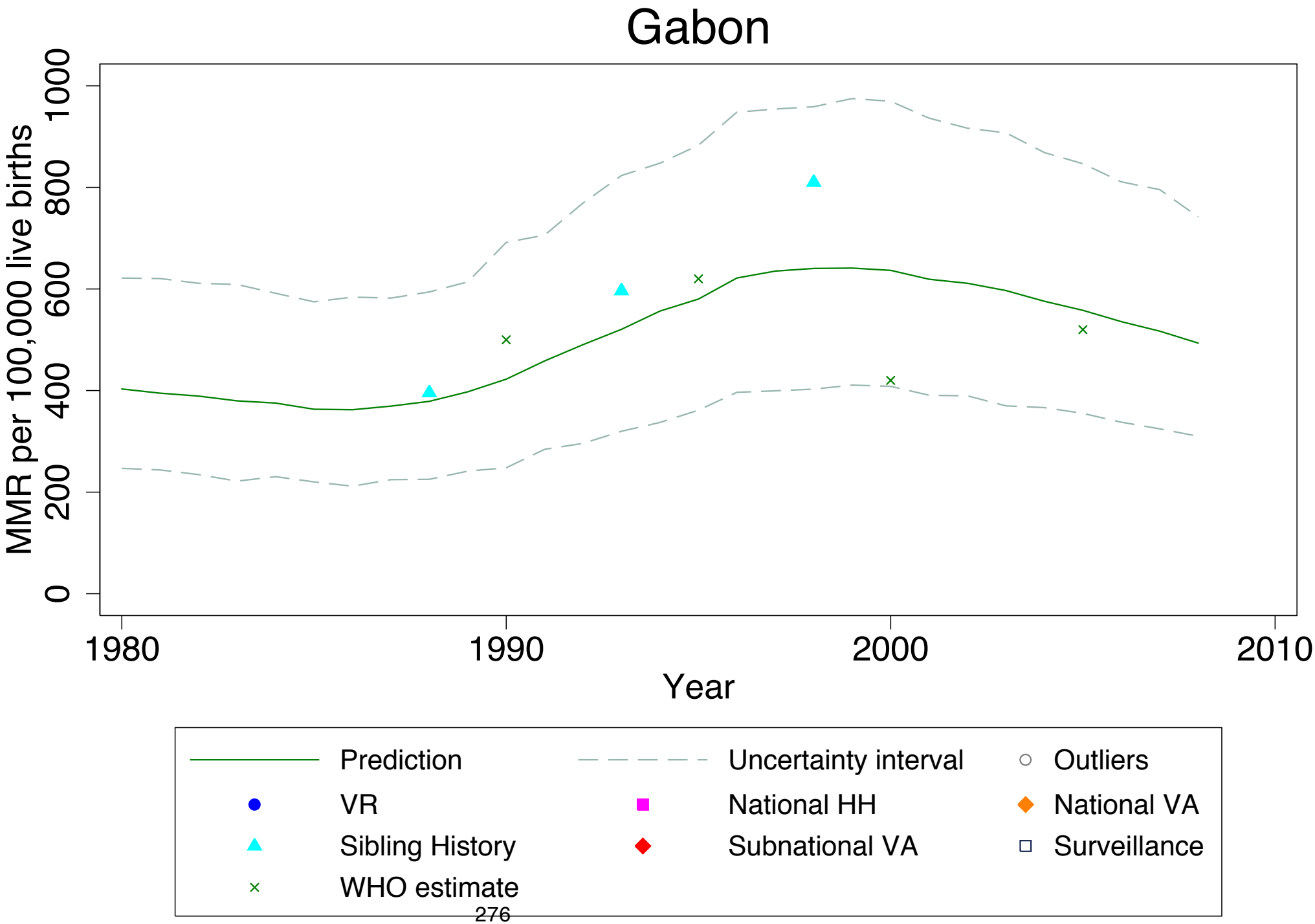

Samoa
MMR per 100,000 live births
0
200
400
600
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

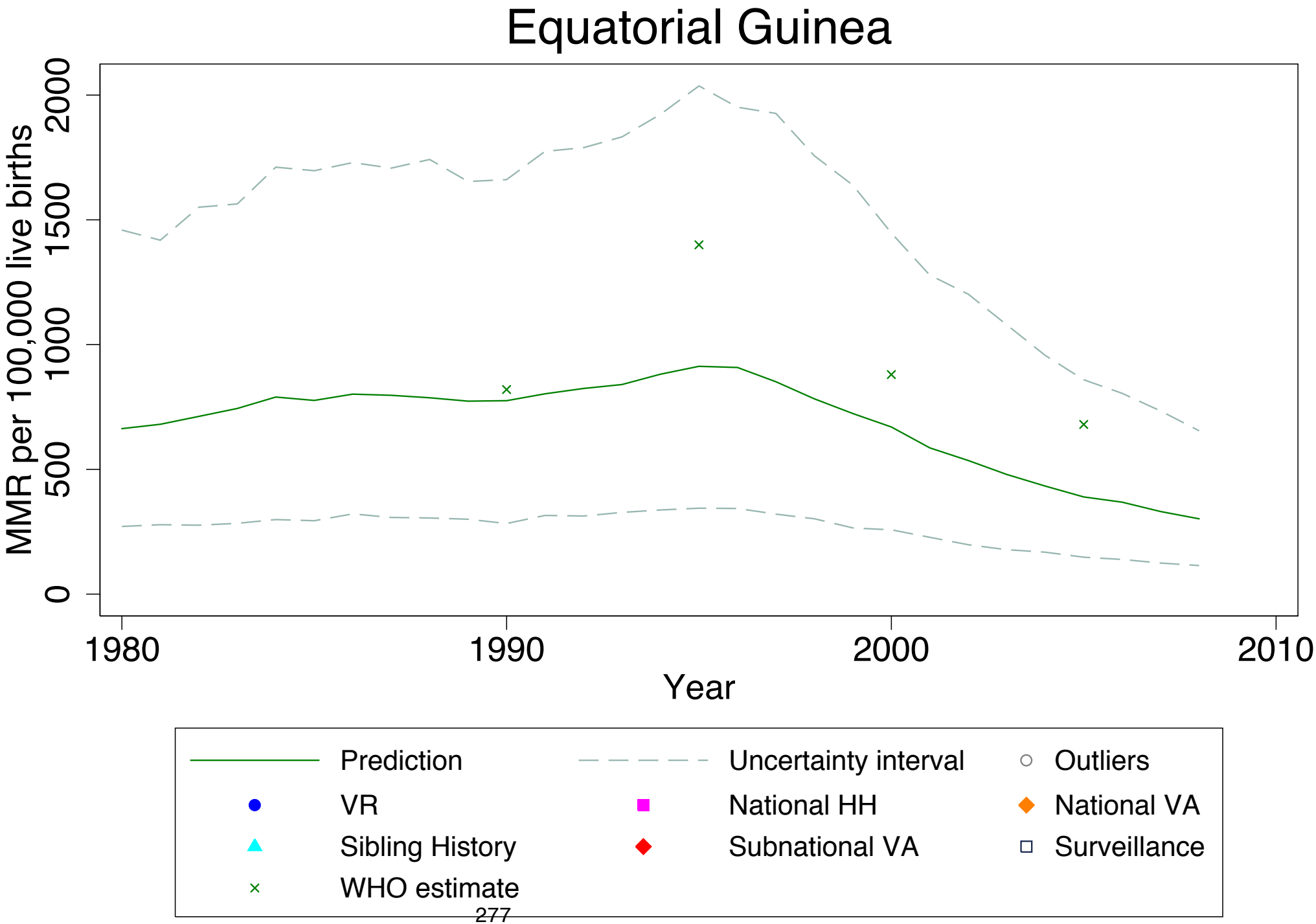

Angola
MMR per 100,000 live births
0
1000
2000
3000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

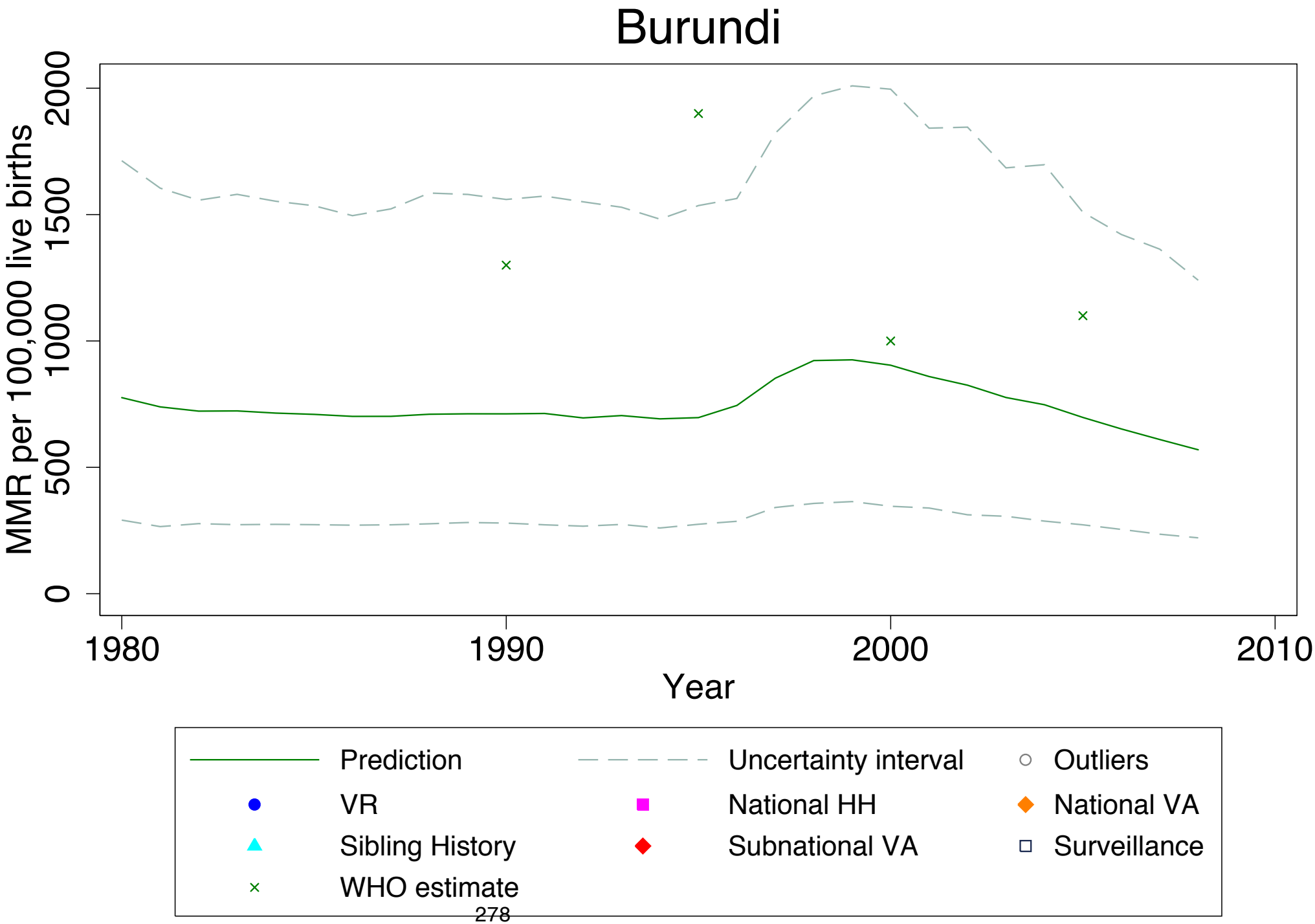

Central African Republic
MMR per 100,000 live births
0
1000
2000
3000
4000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

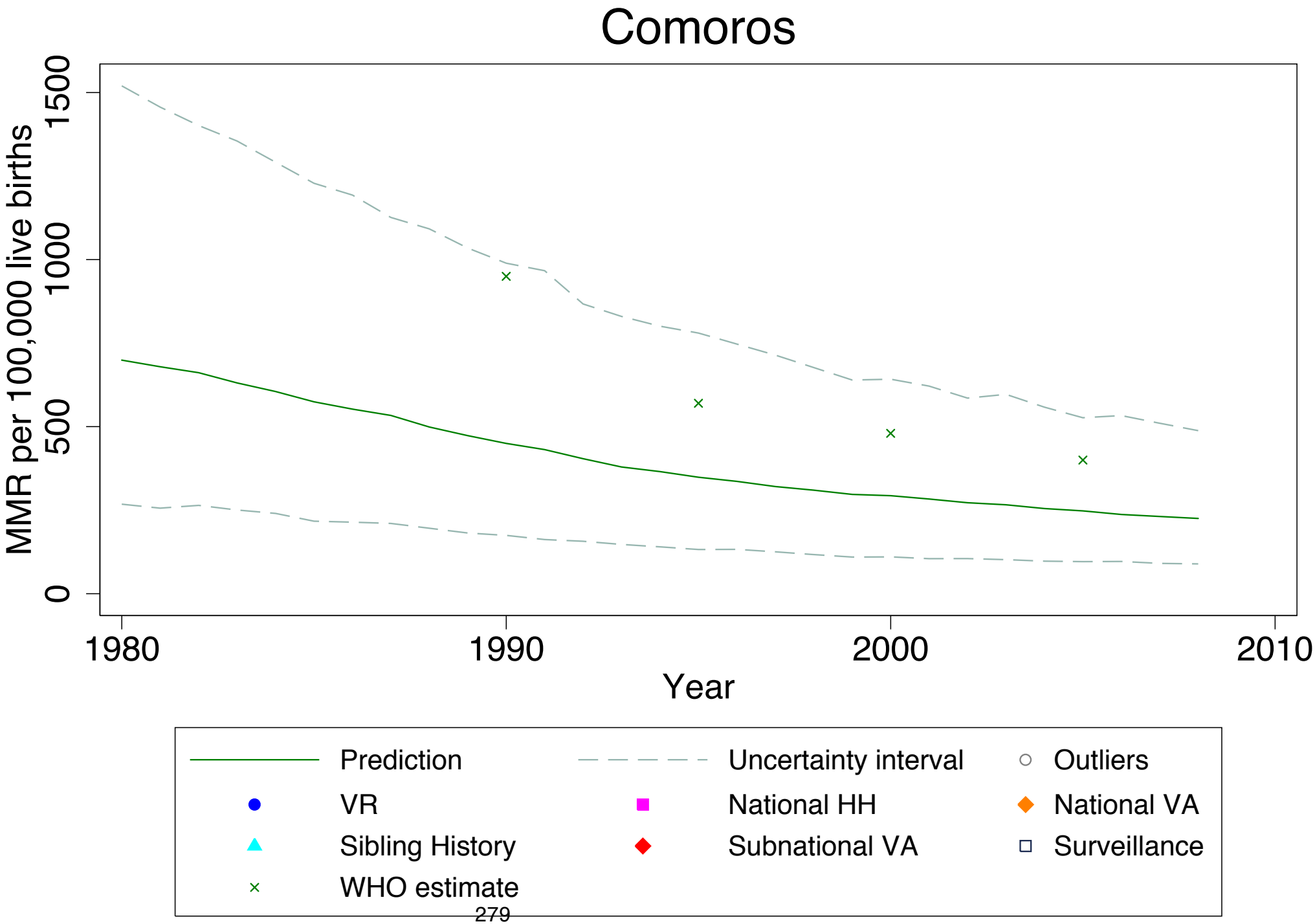

Congo, the Democratic Republic of the
MMR per 100,000 live births
0
500
1000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Congo
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Gabon
MMR per 100,000 live births
0
200
400
600
800
1000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Equatorial Guinea
MMR per 100,000 live births
0
500
1000
1500
2000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Burundi
MMR per 100,000 live births
0
500
1000
1500
2000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Comoros
MMR per 100,000 live births
0
500
1000
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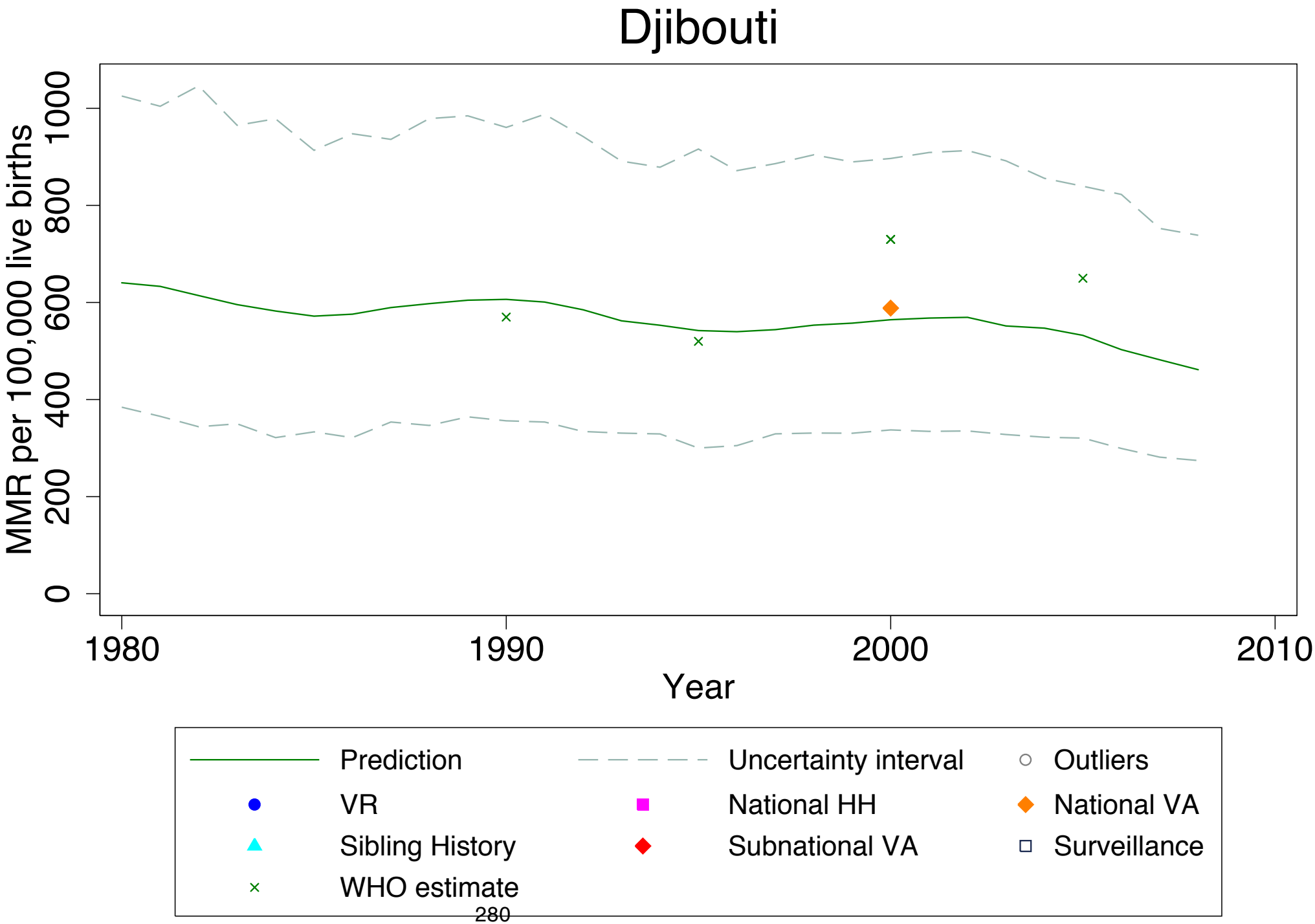
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Djibouti
MMR per 100,000 live births
0
200
400
600
800
1000
1980
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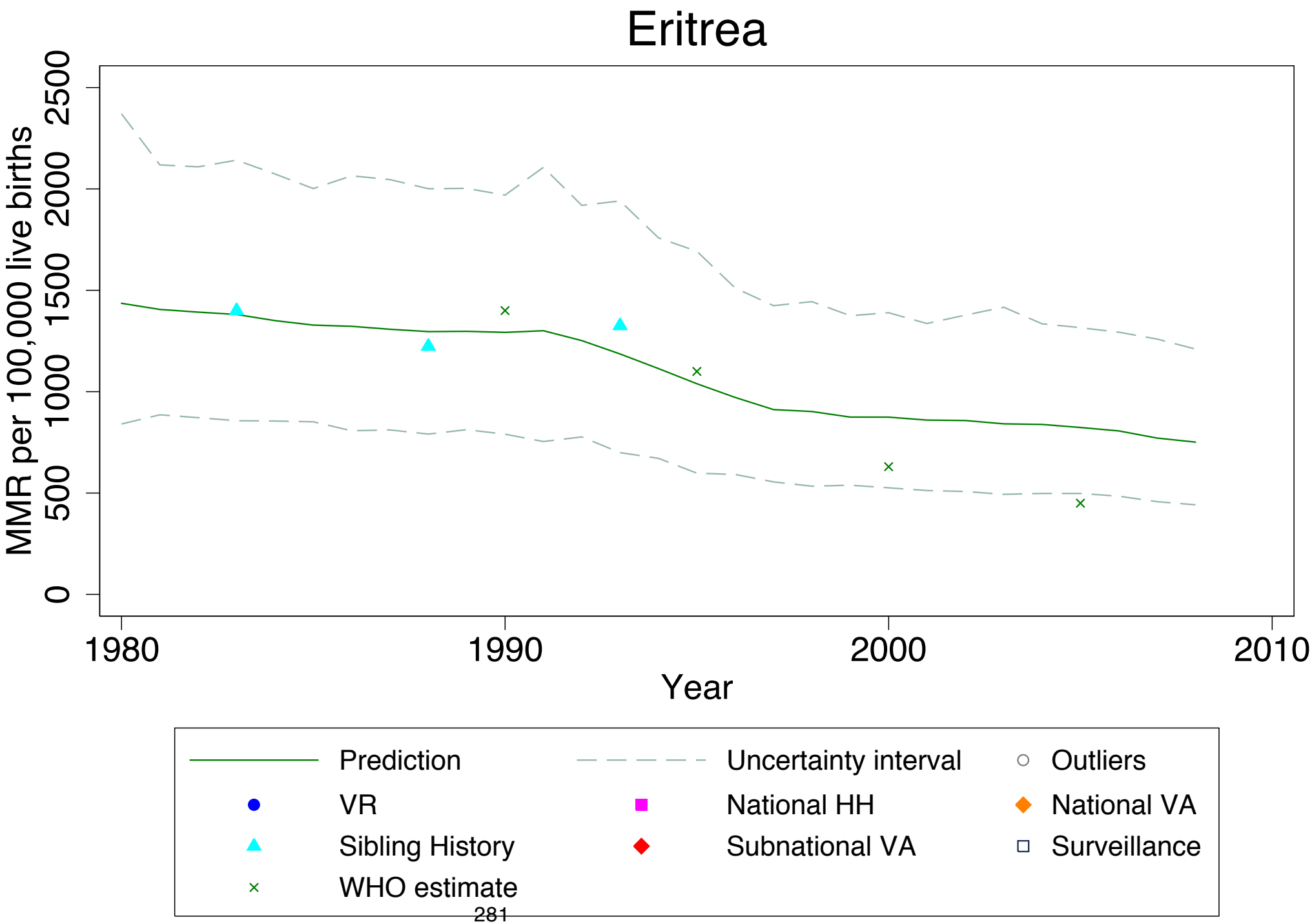
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Eritrea
MMR per 100,000 live births
0
500
1000
1500
2000
2500
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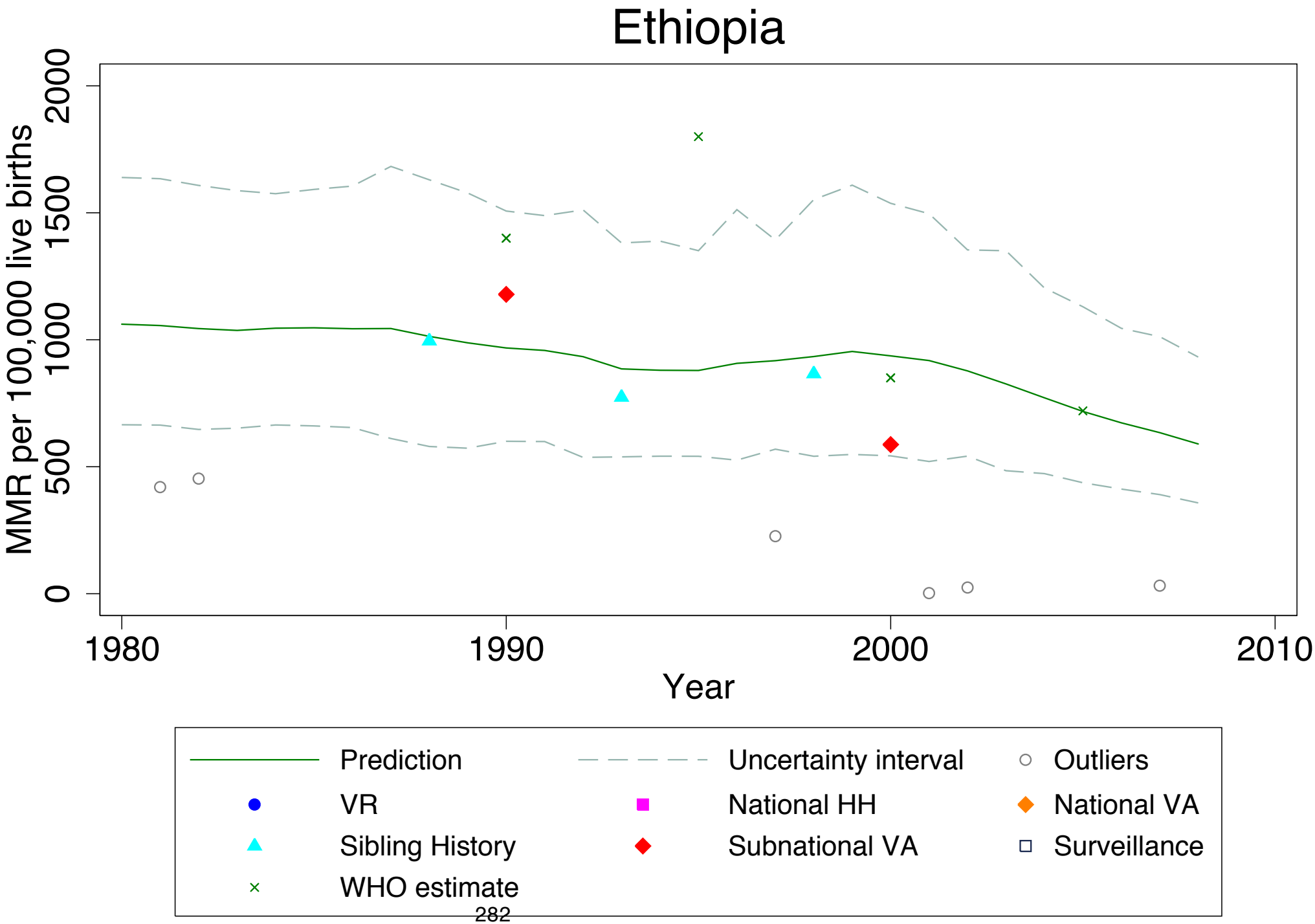
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Ethiopia
MMR per 100,000 live births
0
500
1000
1500
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1980
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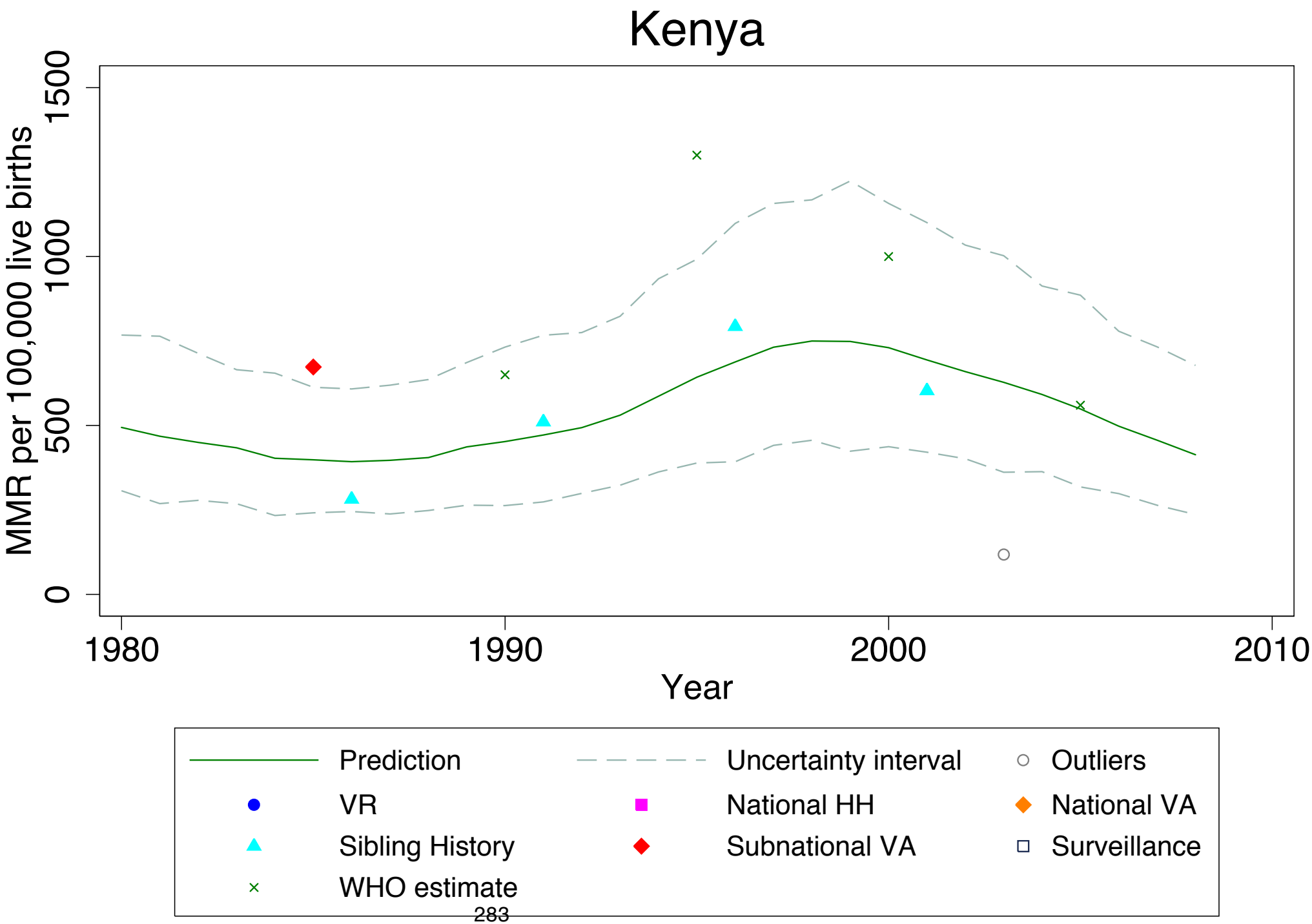
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Kenya
MMR per 100,000 live births
0
500
1000
1500
1980
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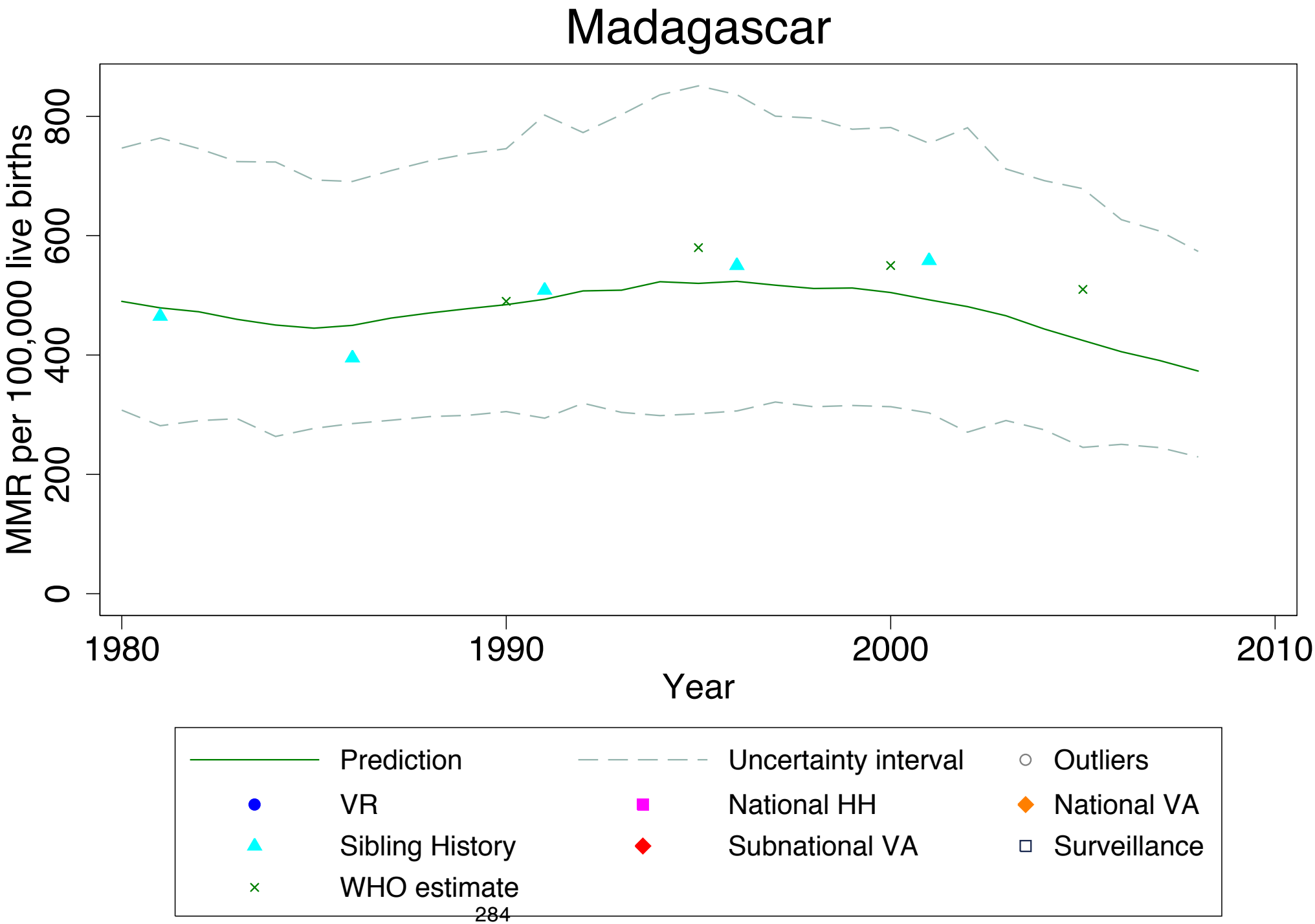
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Madagascar
MMR per 100,000 live births
0
200
400
600
800
1980
1990
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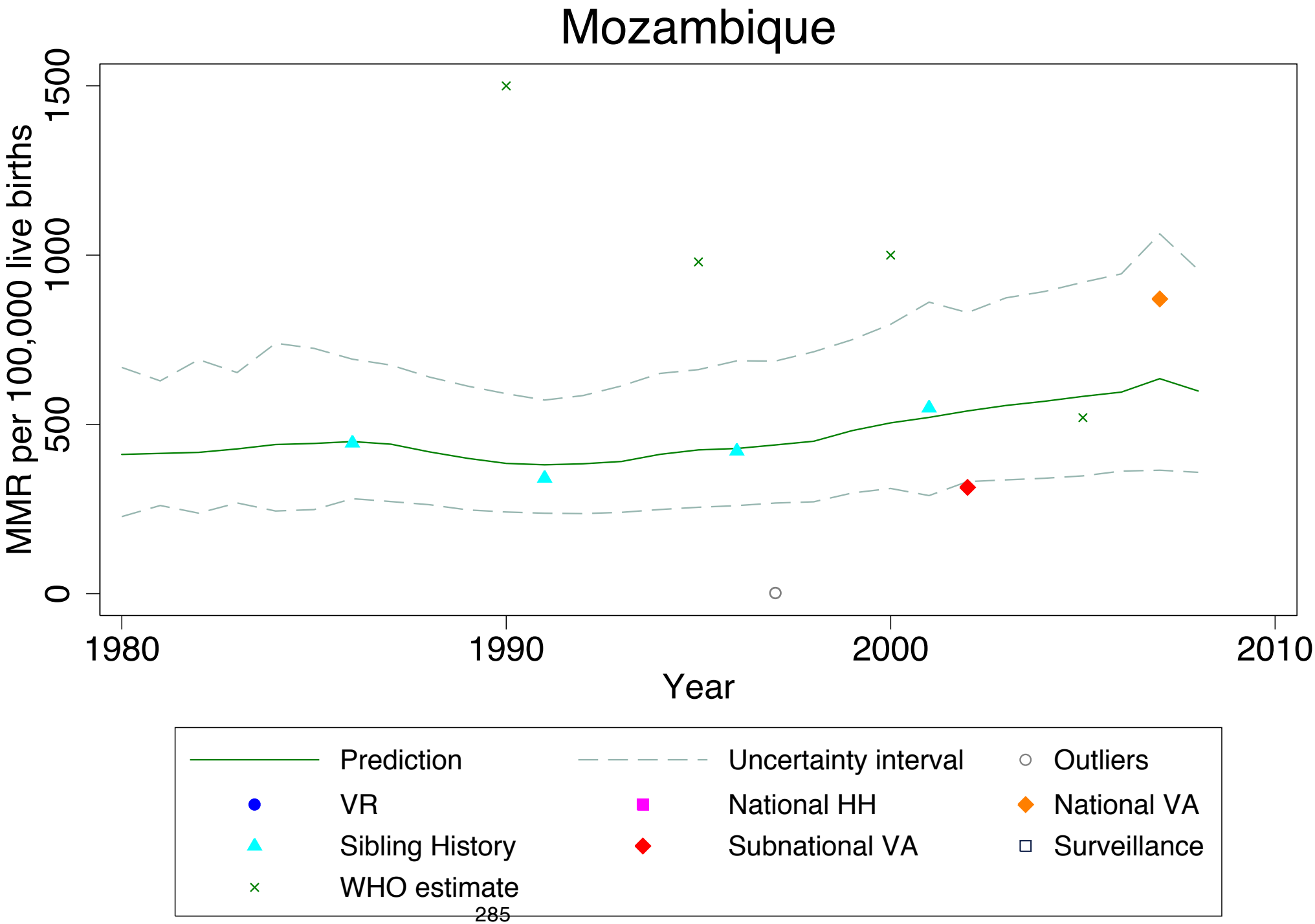
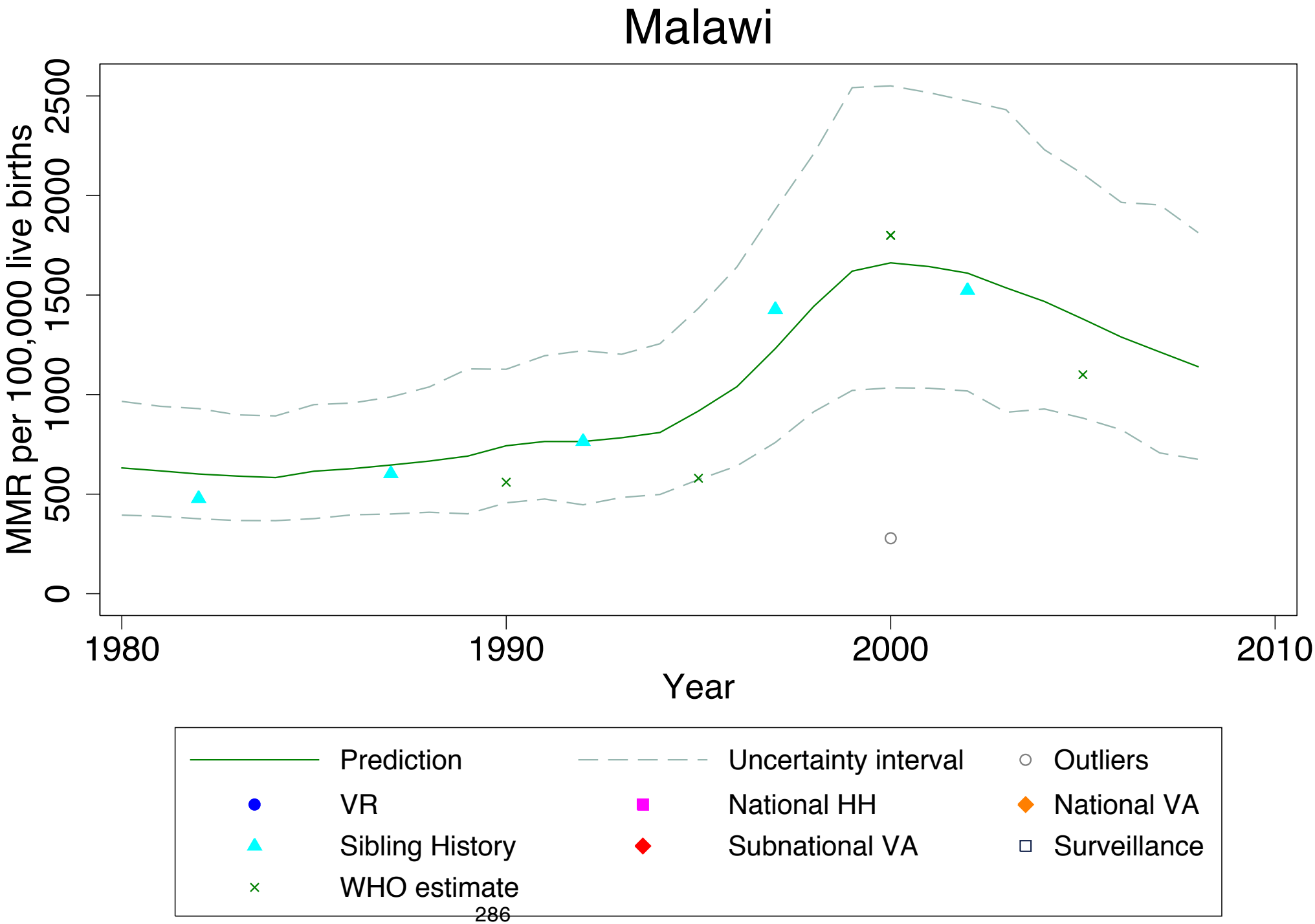
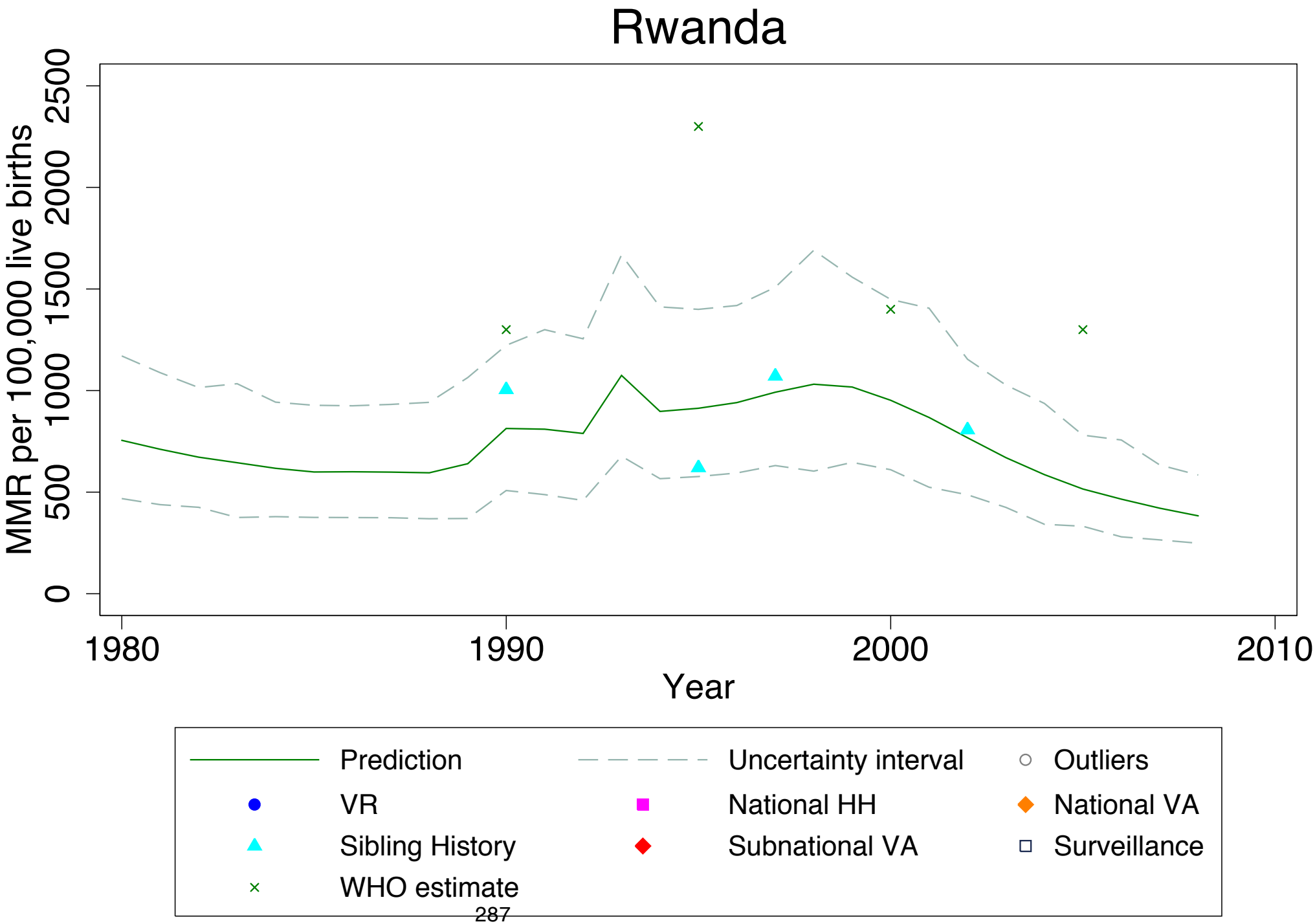
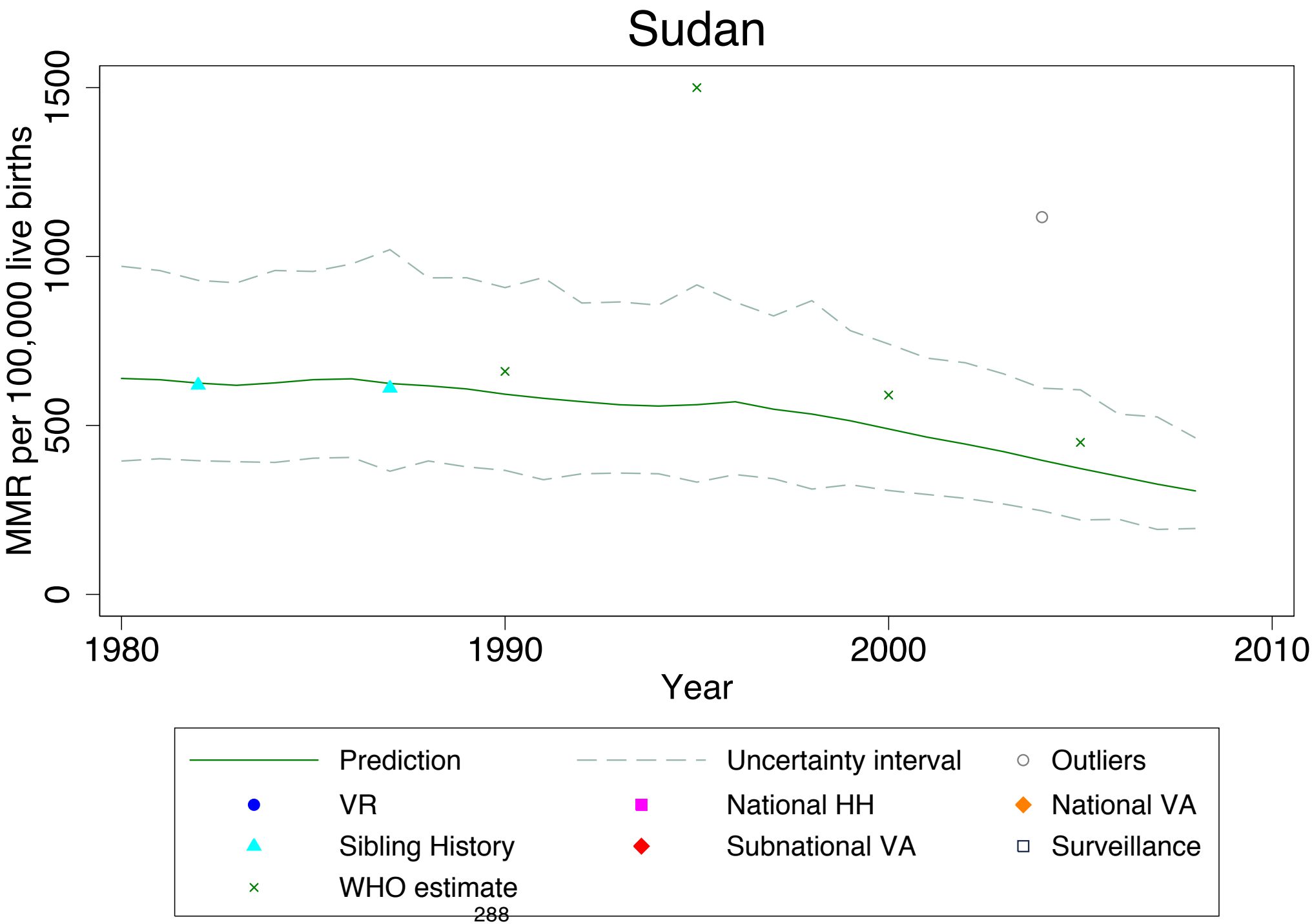
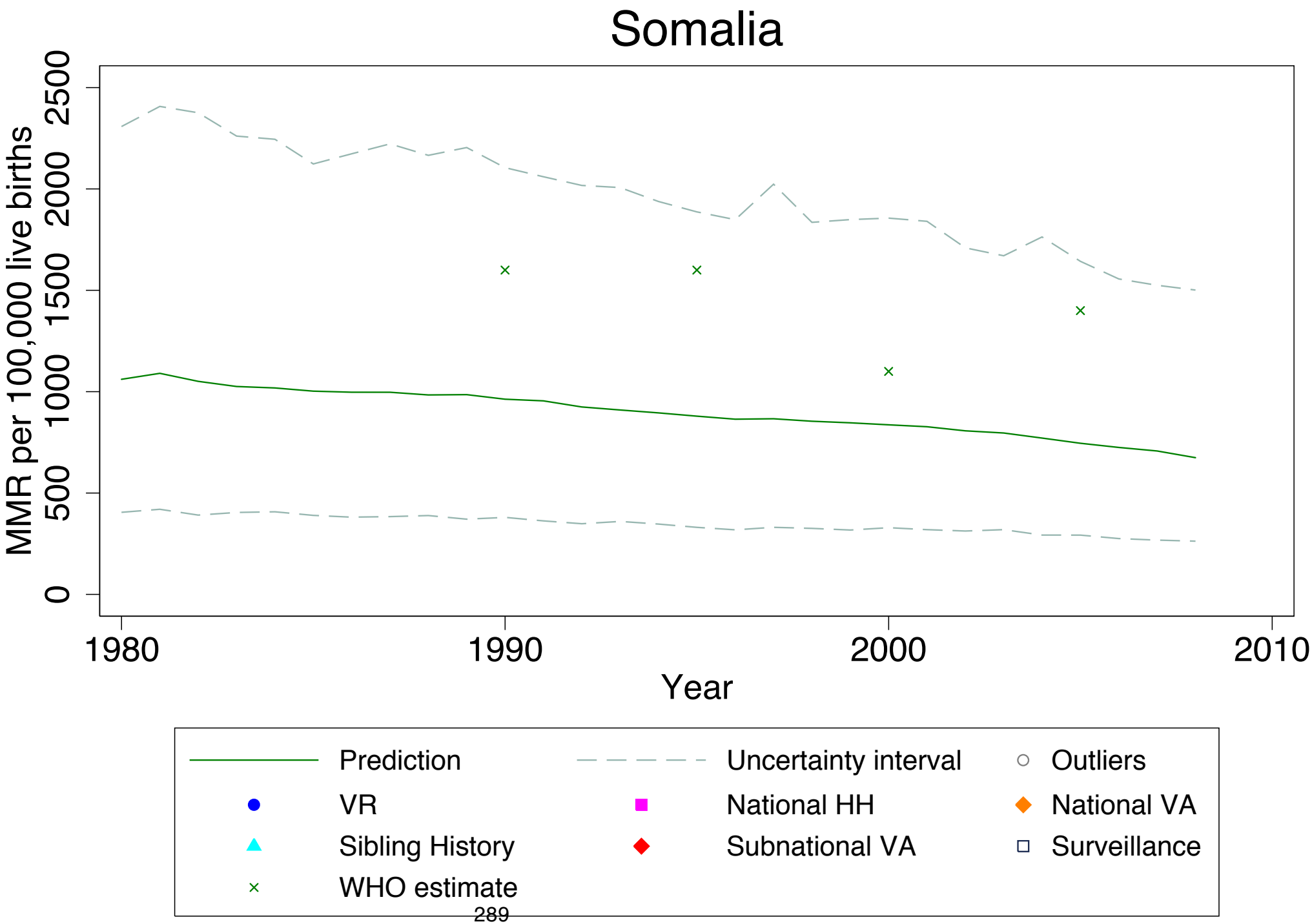
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

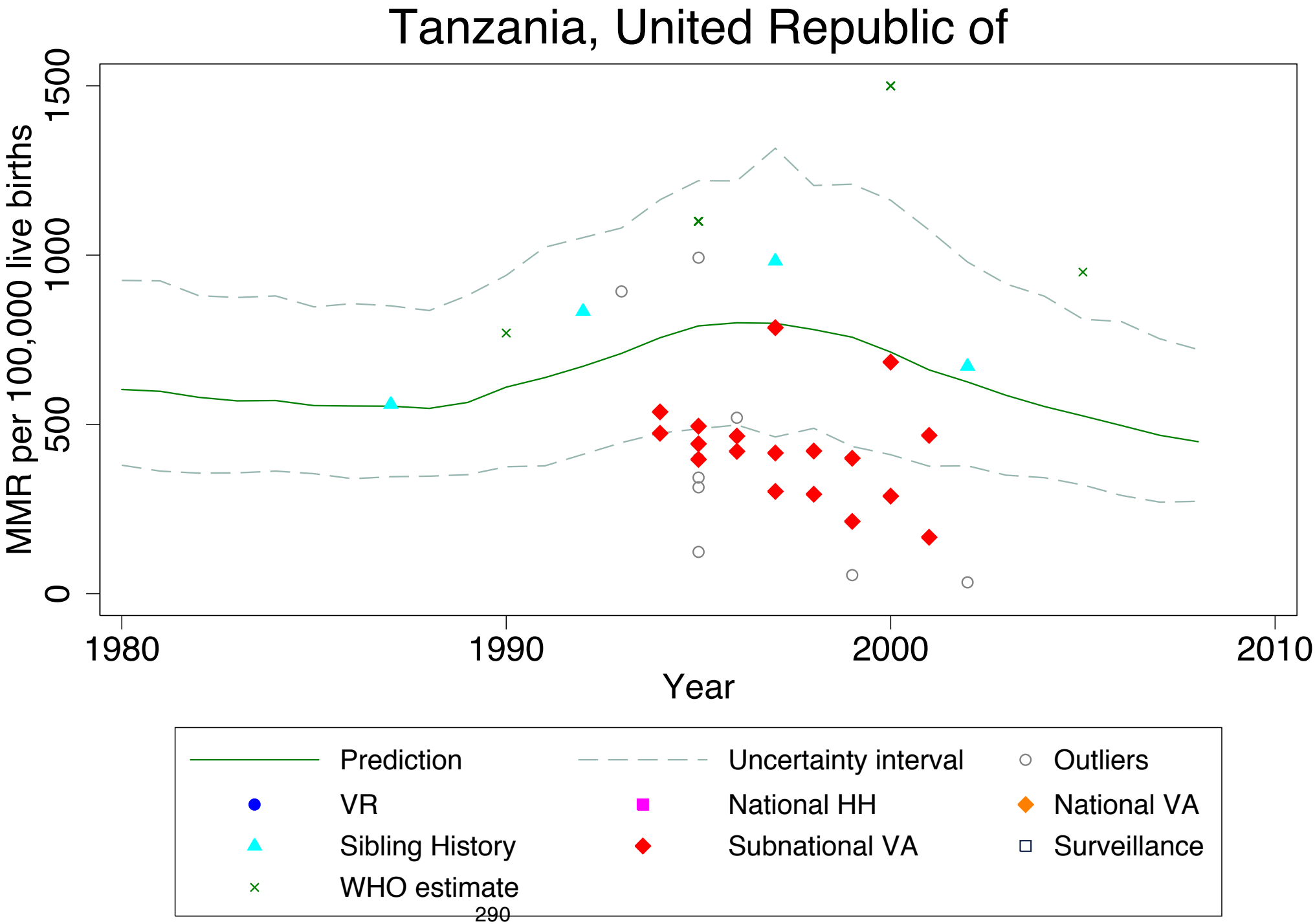

Mozambique
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

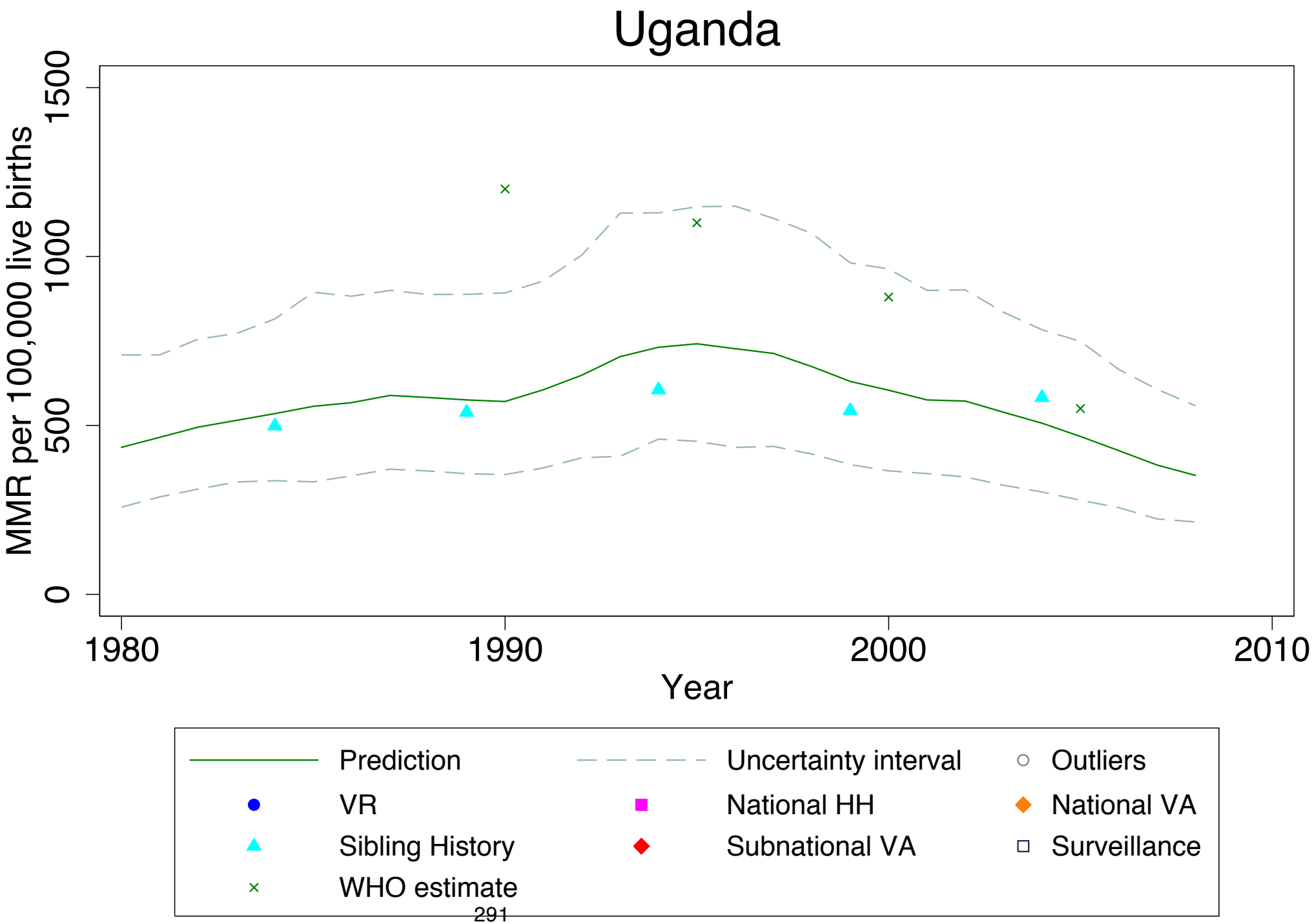

Malawi
MMR per 100,000 live births
0
500
1000
1500
2000
2500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

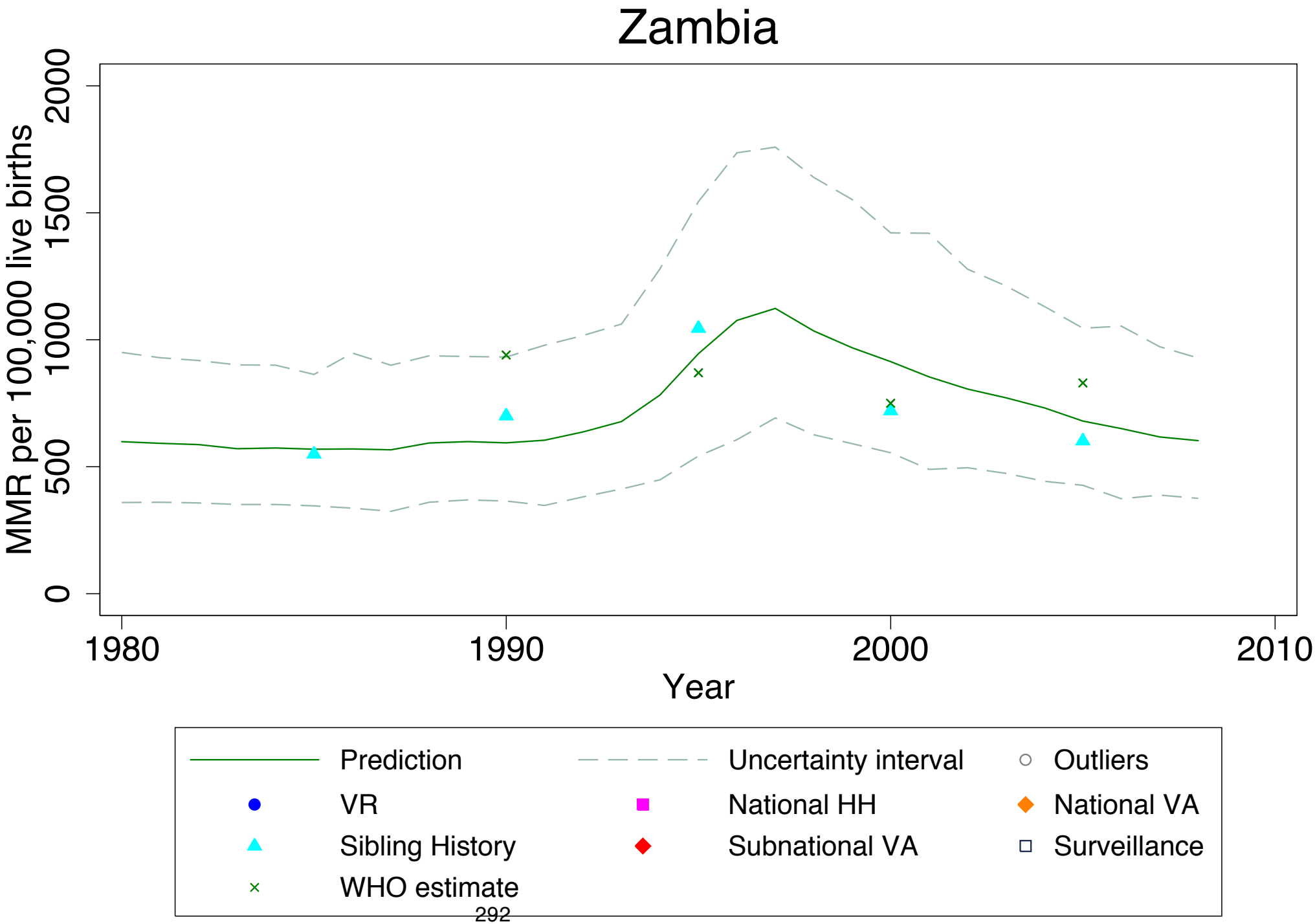

Rwanda
MMR per 100,000 live births
0
500
1000
1500
2000
2500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

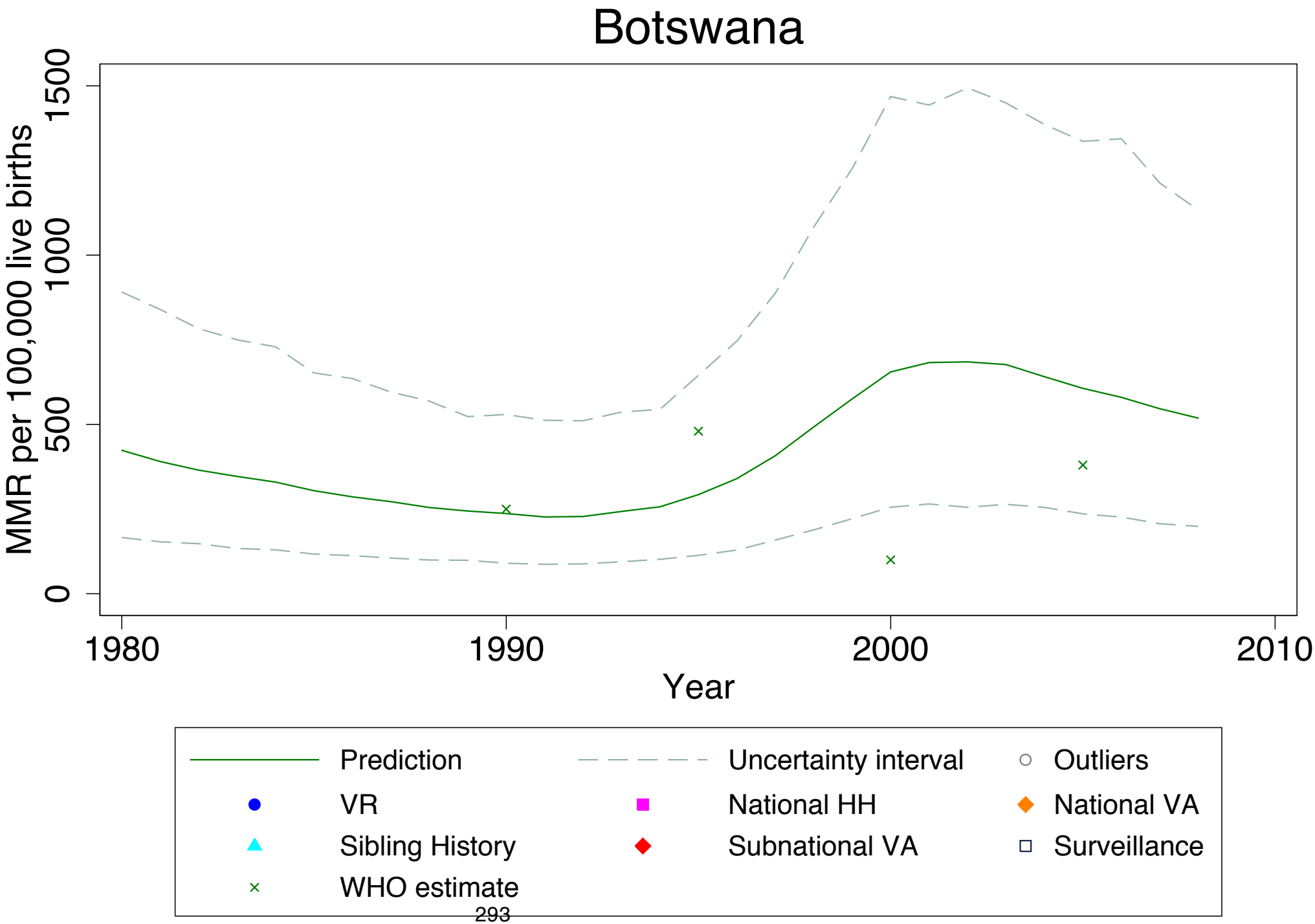

Sudan
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

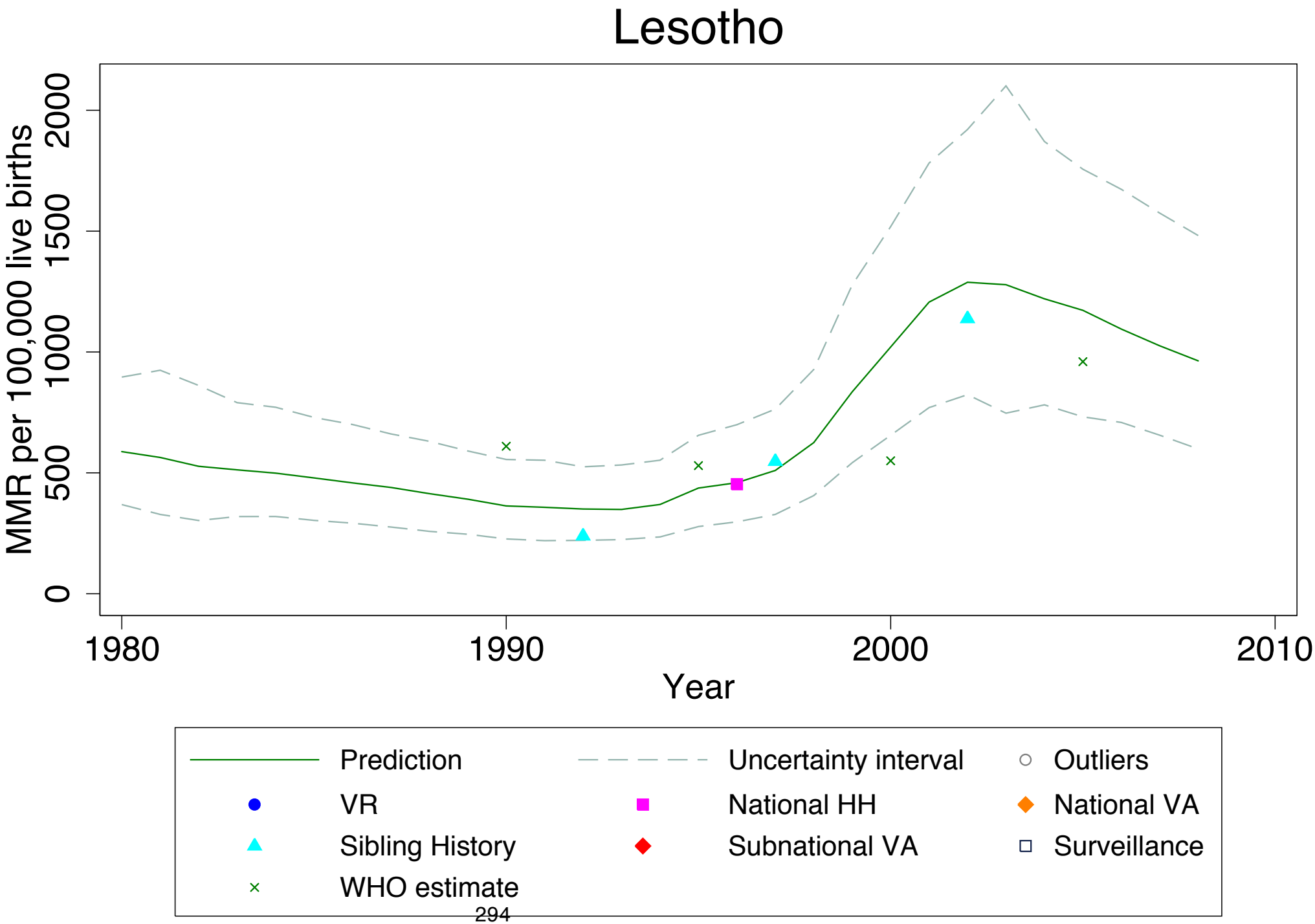

Somalia
MMR per 100,000 live births
0
500
1000
1500
2000
2500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

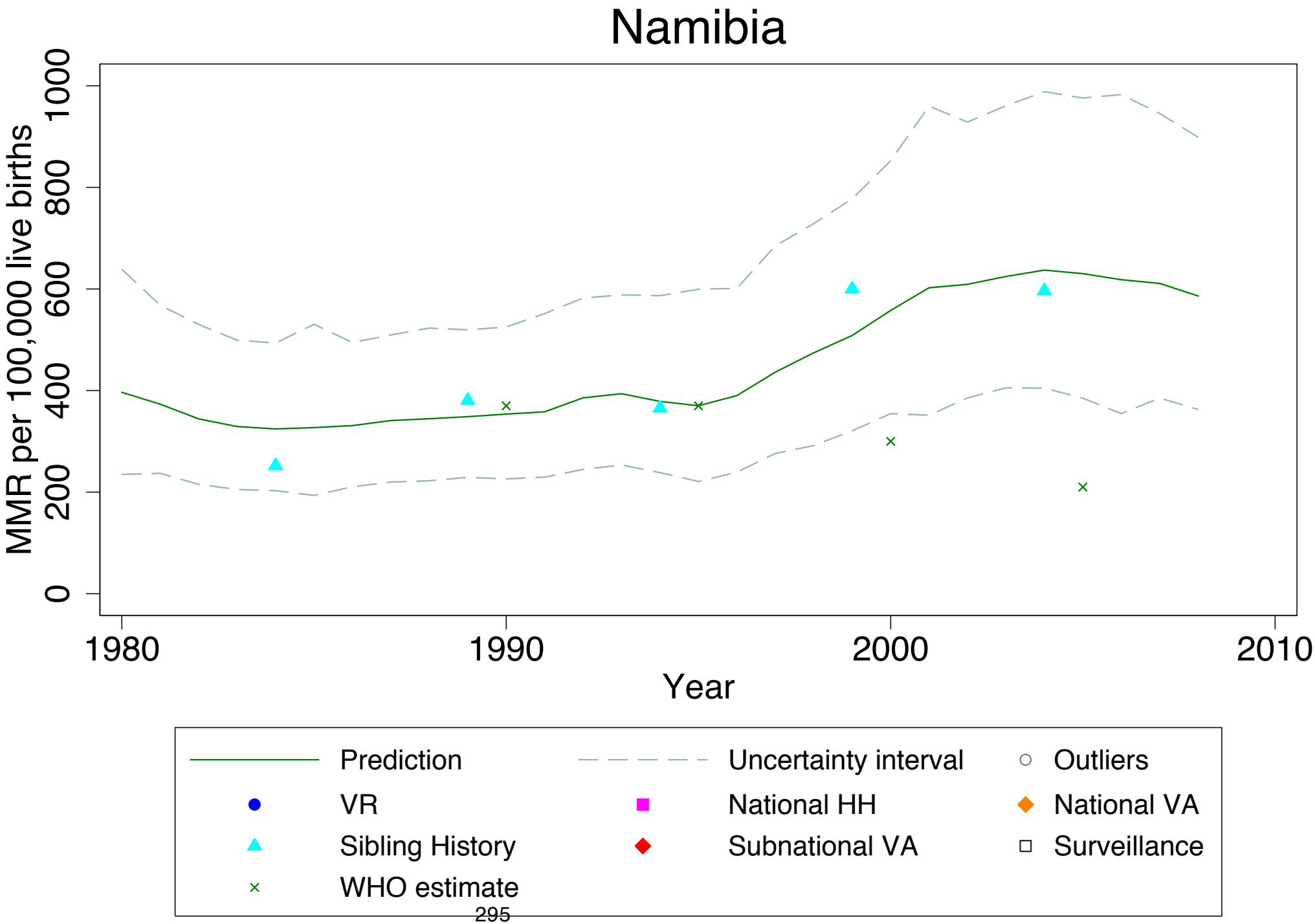

Tanzania, United Republic of
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

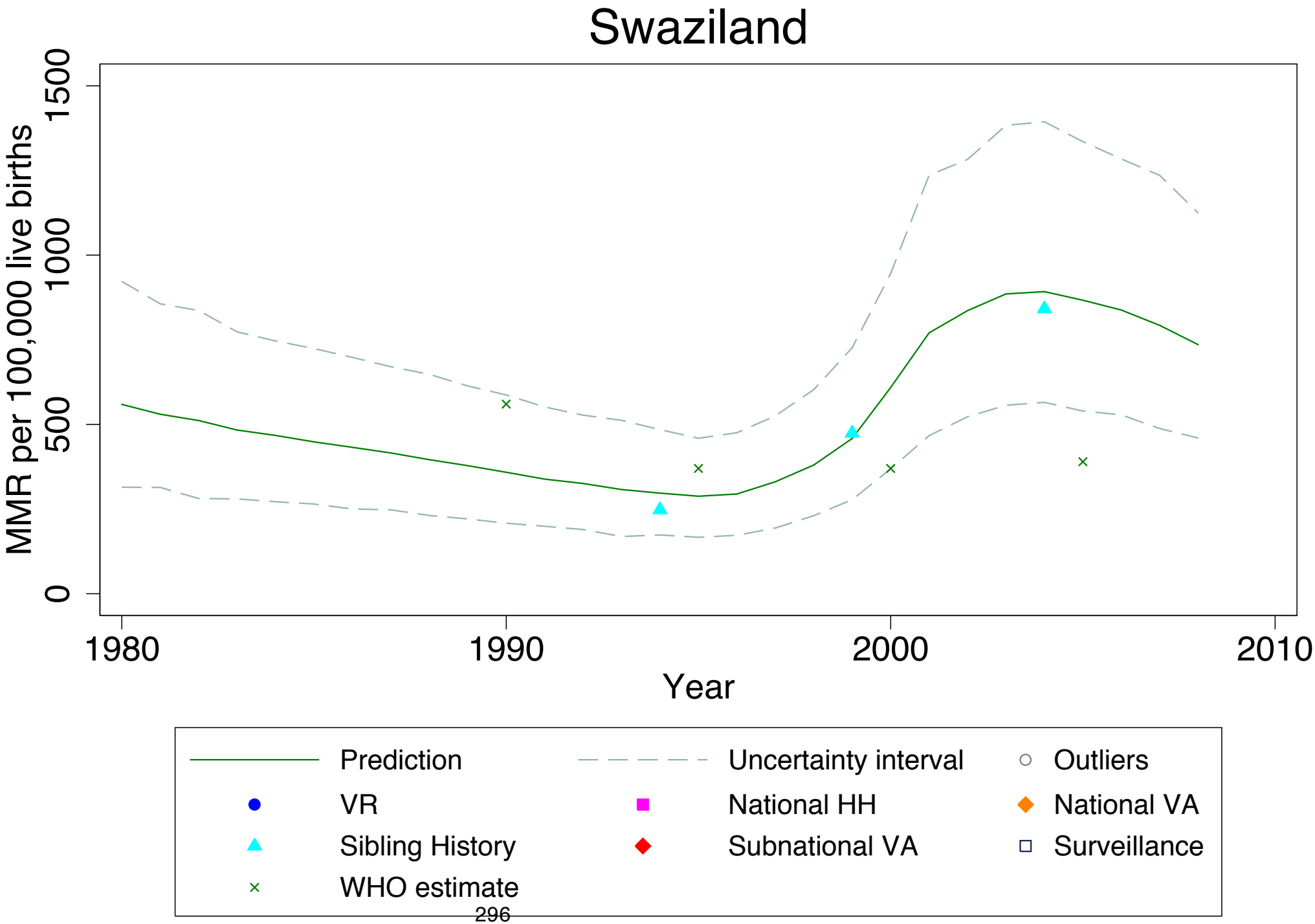

Uganda
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Zambia
MMR per 100,000 live births
0
500
1000
1500
2000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Botswana
MMR per 100,000 live births
0
500
1000
1500
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Lesotho
MMR per 100,000 live births
0
500
1000
1500
2000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Namibia
MMR per 100,000 live births
0
200
400
600
800
1000
1980
1990
2000
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Swaziland
MMR per 100,000 live births
0
500
1000
1500
1980
1990
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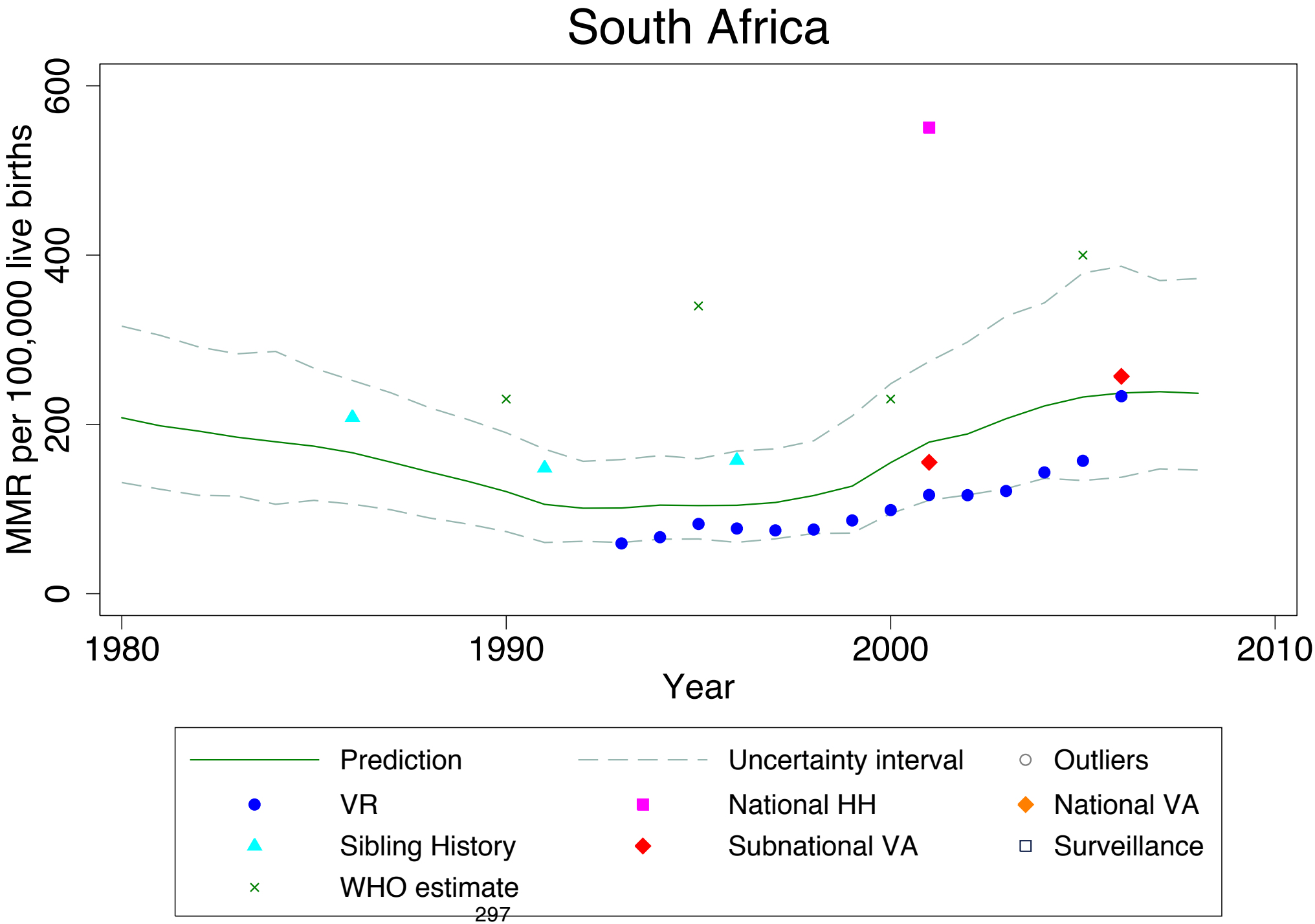
2010
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate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MMR per 100,000 live births
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200
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600
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2010
Year
Prediction
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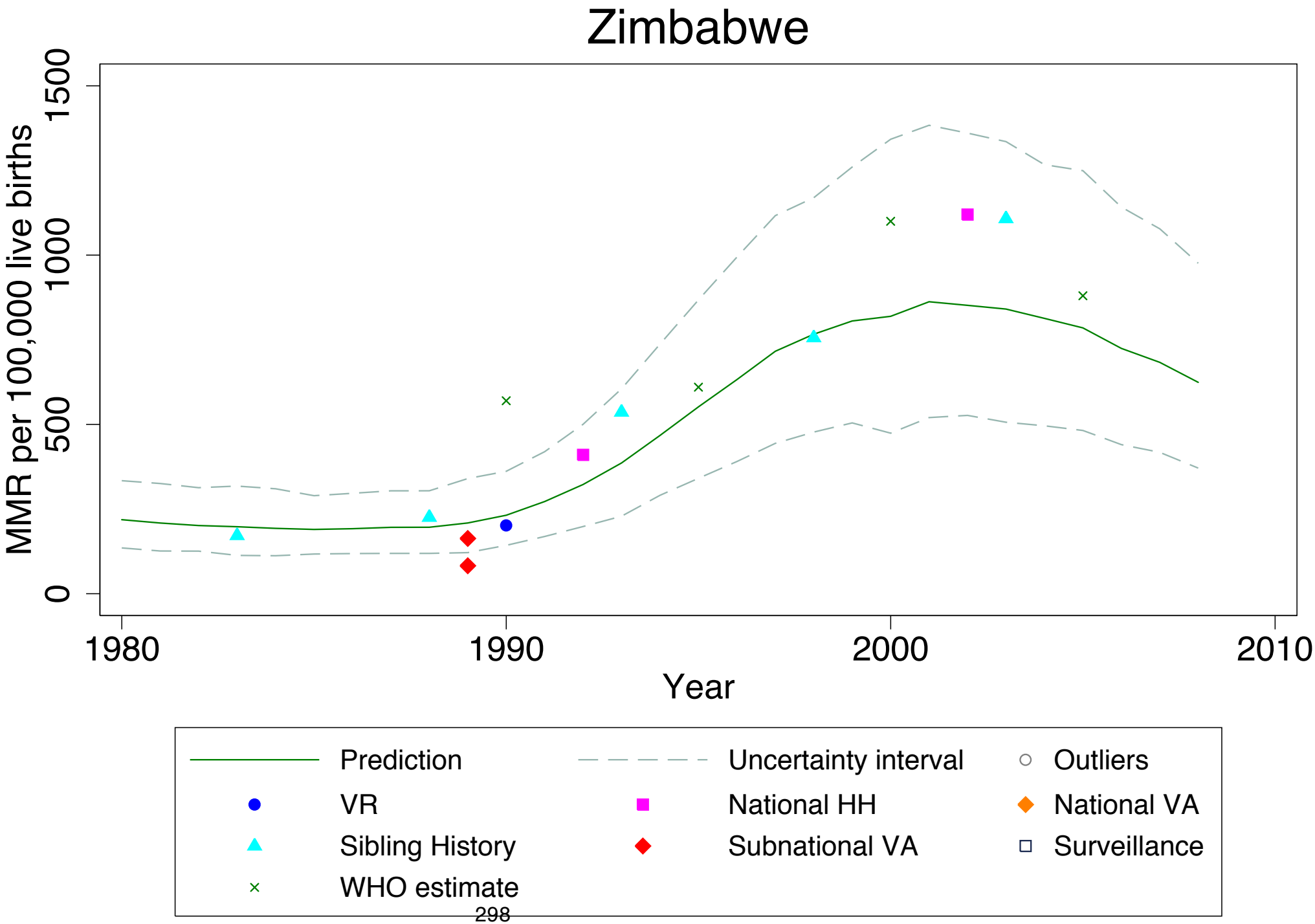
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate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MMR per 100,000 live births
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Prediction
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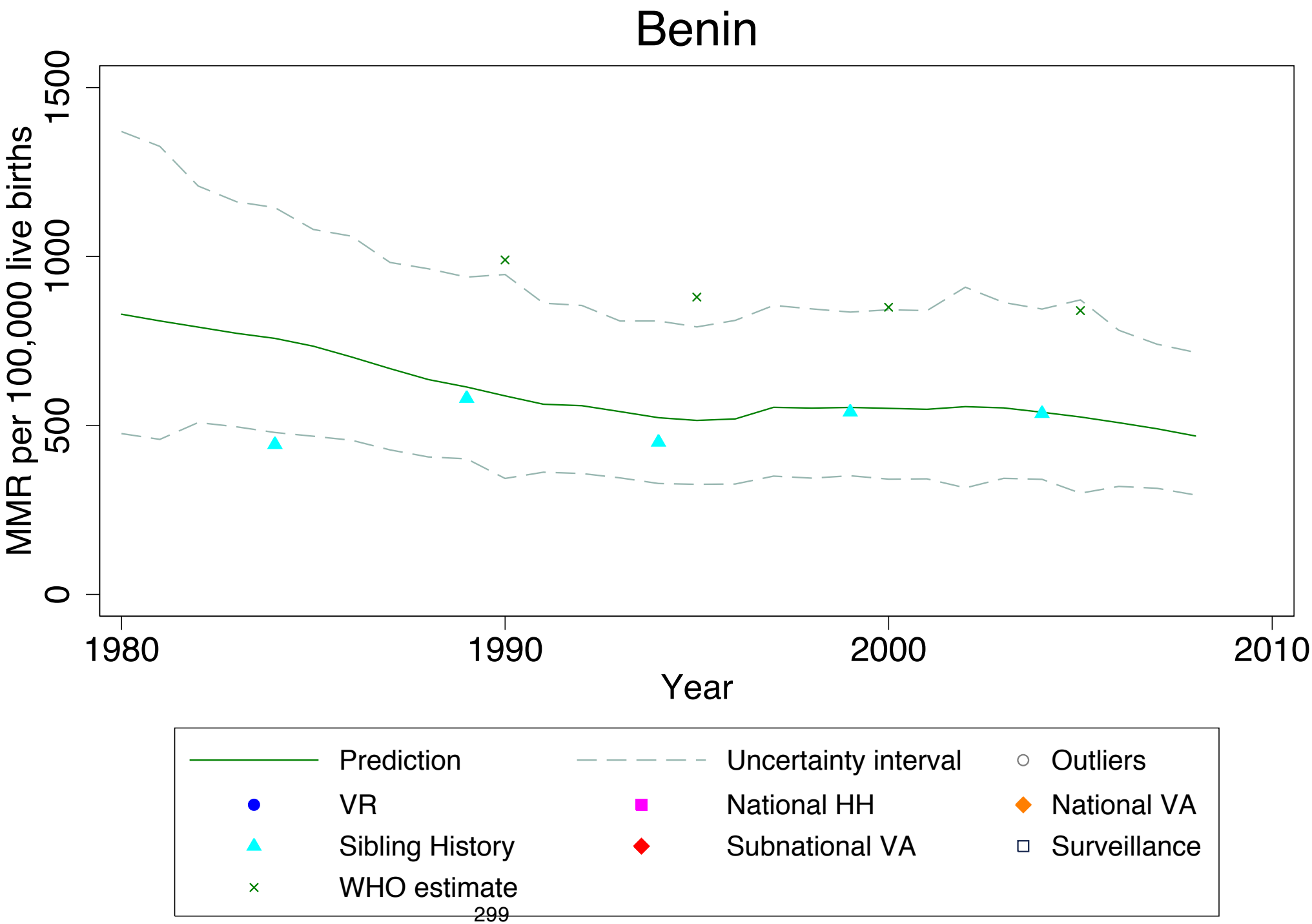
Surveillance
WHO estimate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MMR per 100,000 live births
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Prediction
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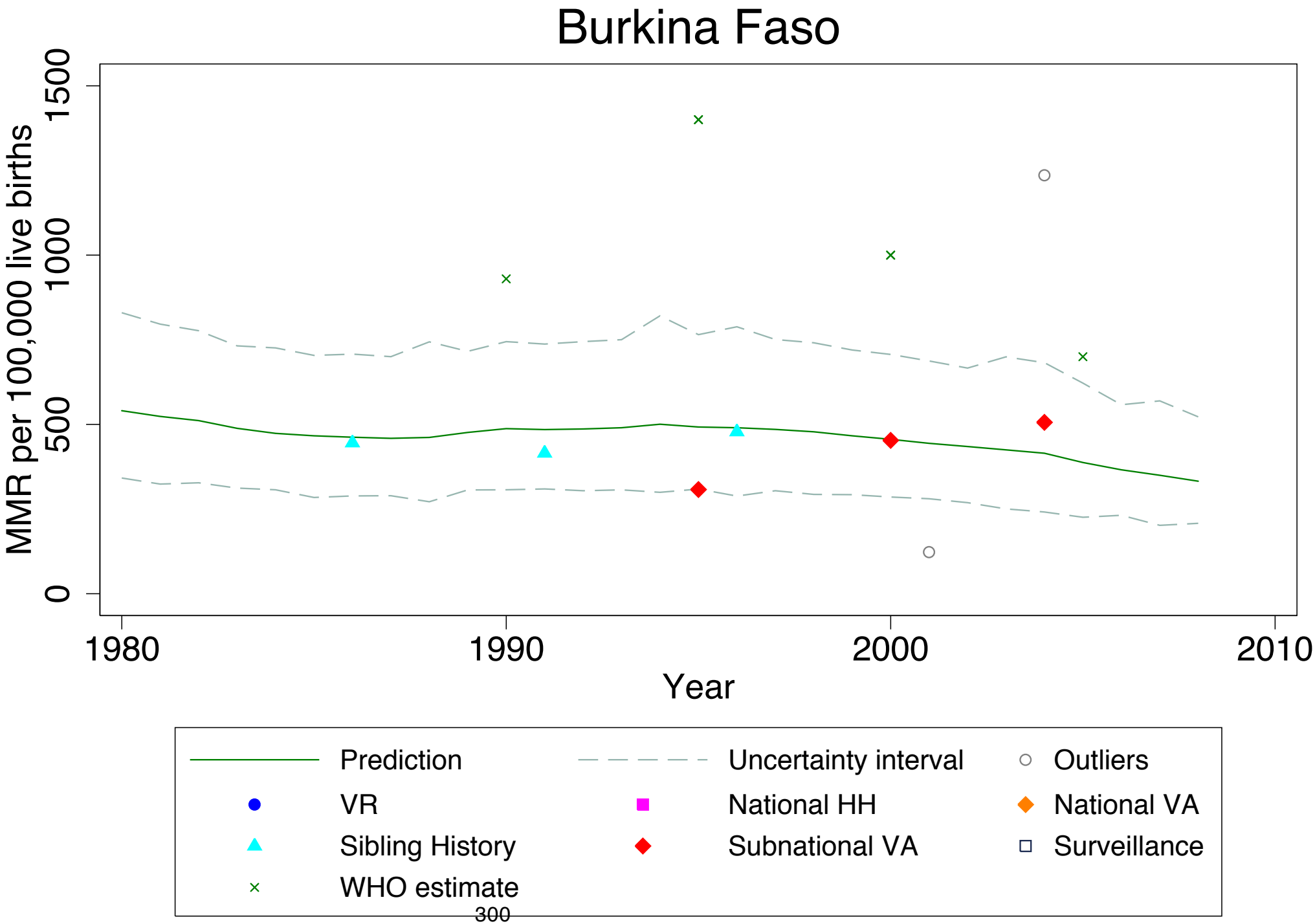
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate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Year
Prediction
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Outliers
VR
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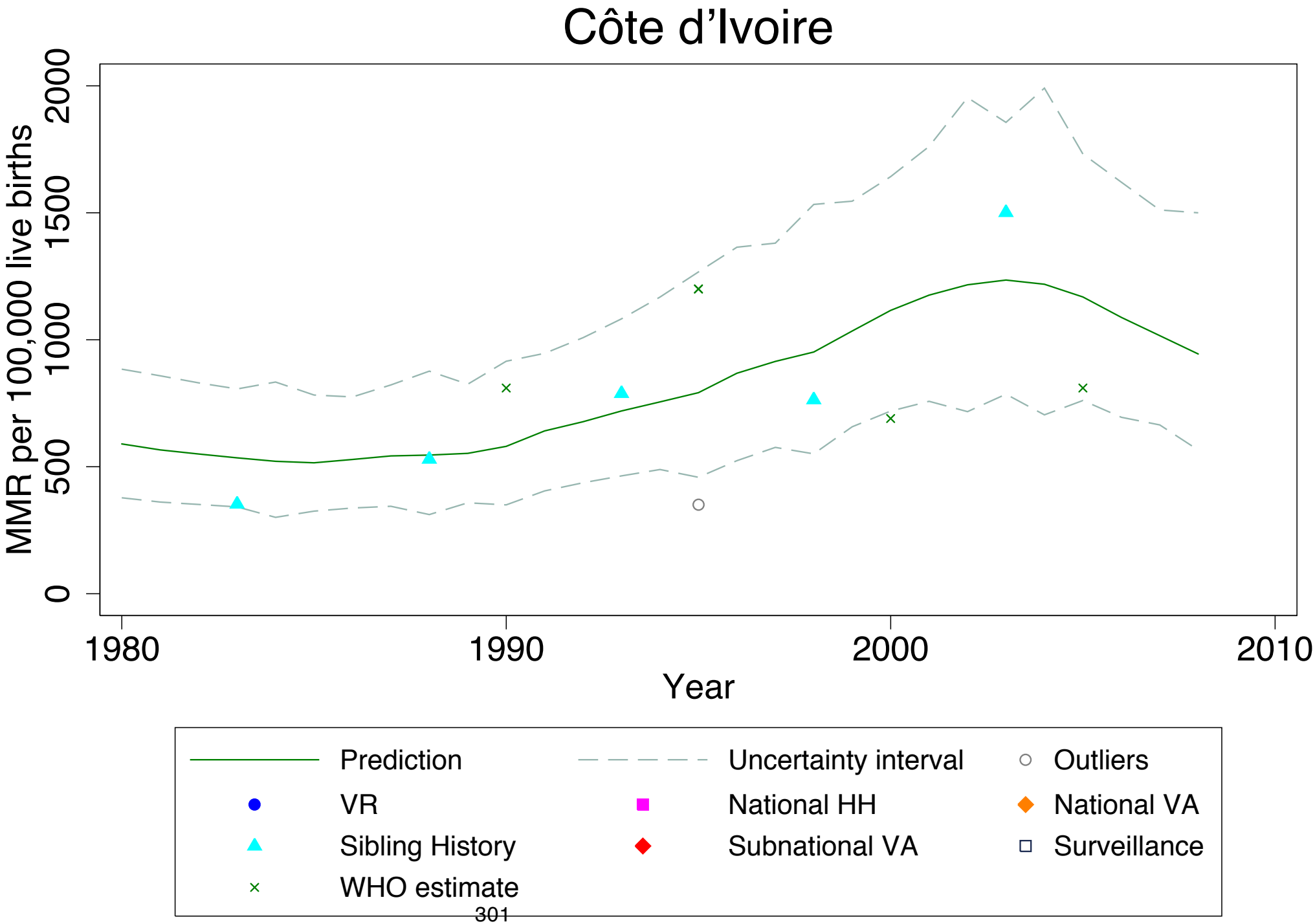
Sibling History
Subnational VA
Surveillance
WHO estimate


Côte d'Ivoire
MMR per 100,000 live births
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500
1000
1500
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Year
Prediction
Uncertainty interval
Outliers
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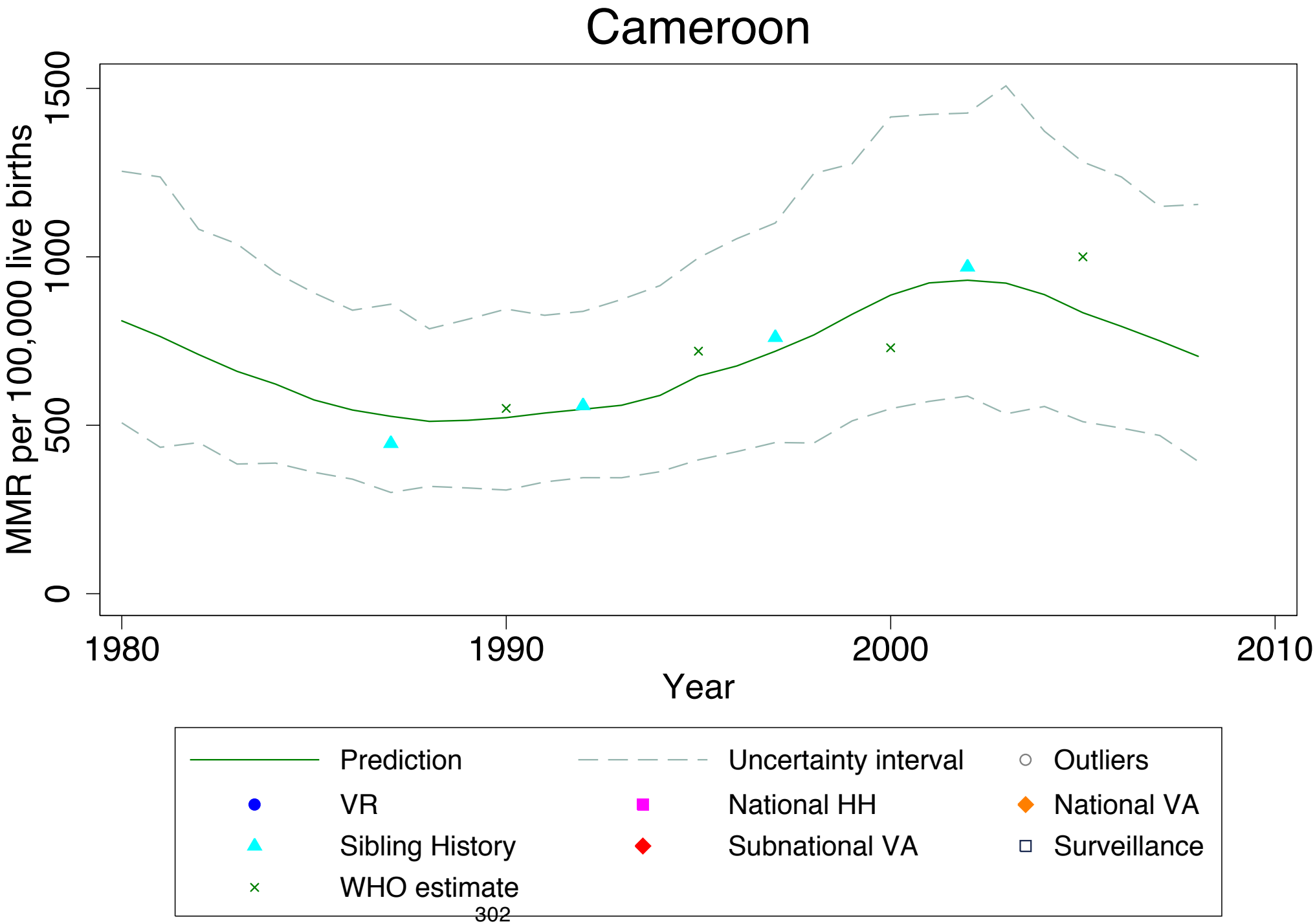
Subnational VA
Surveillance
WHO estimate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MMR per 100,000 live births
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Prediction
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VR
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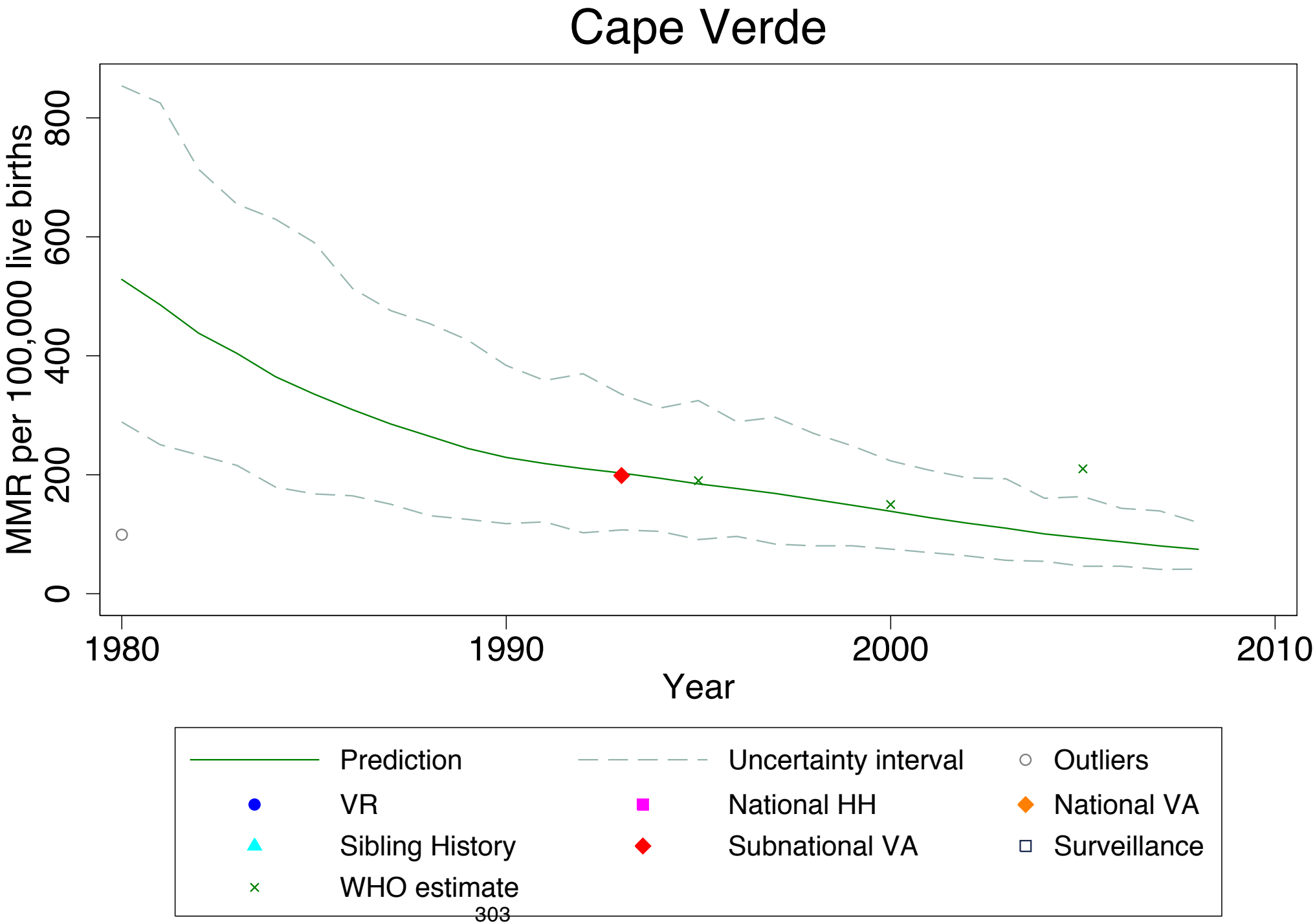
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Cape Verde
MMR per 100,000 live births
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Prediction
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Subnational VA
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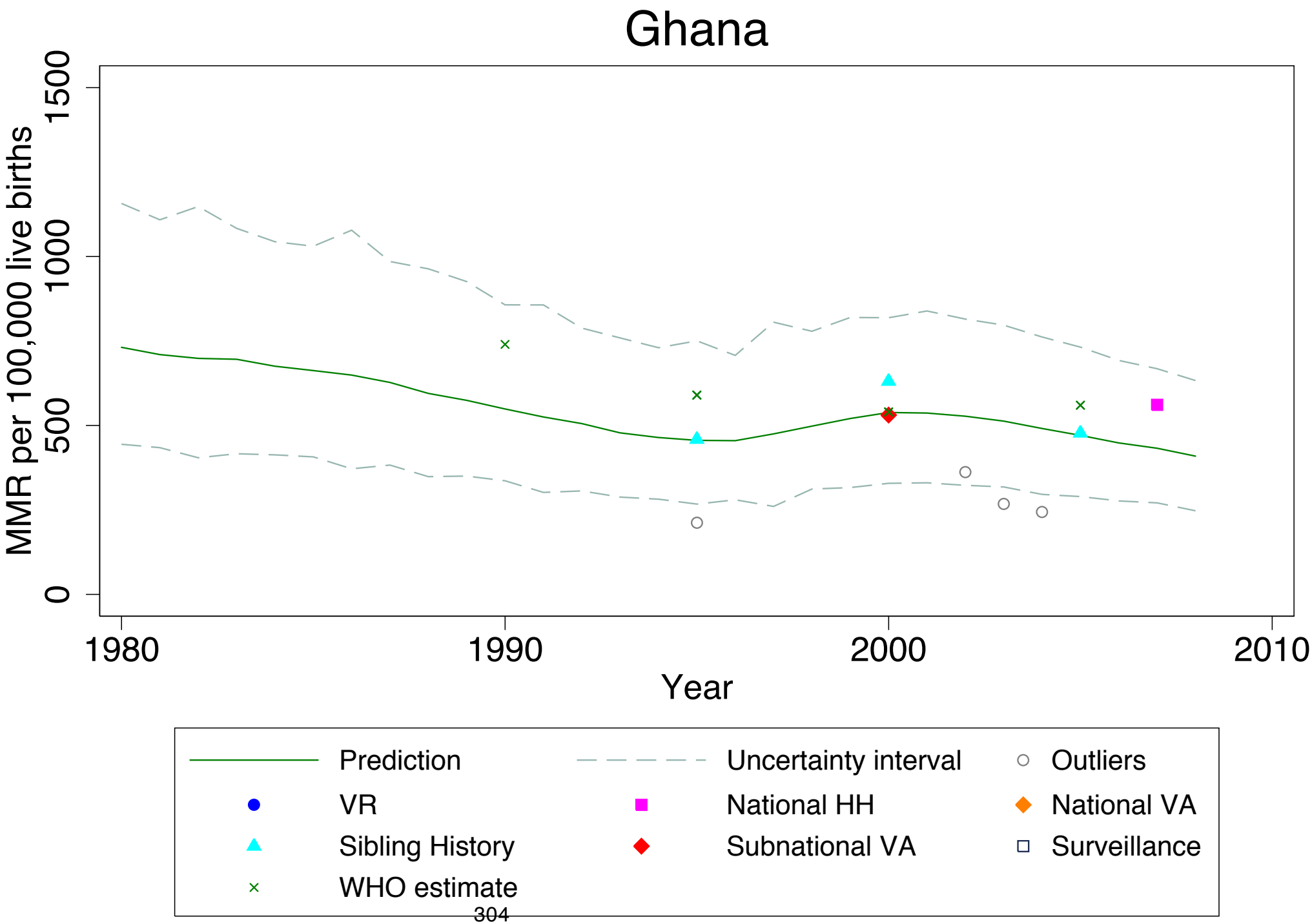
WHO estimate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Prediction
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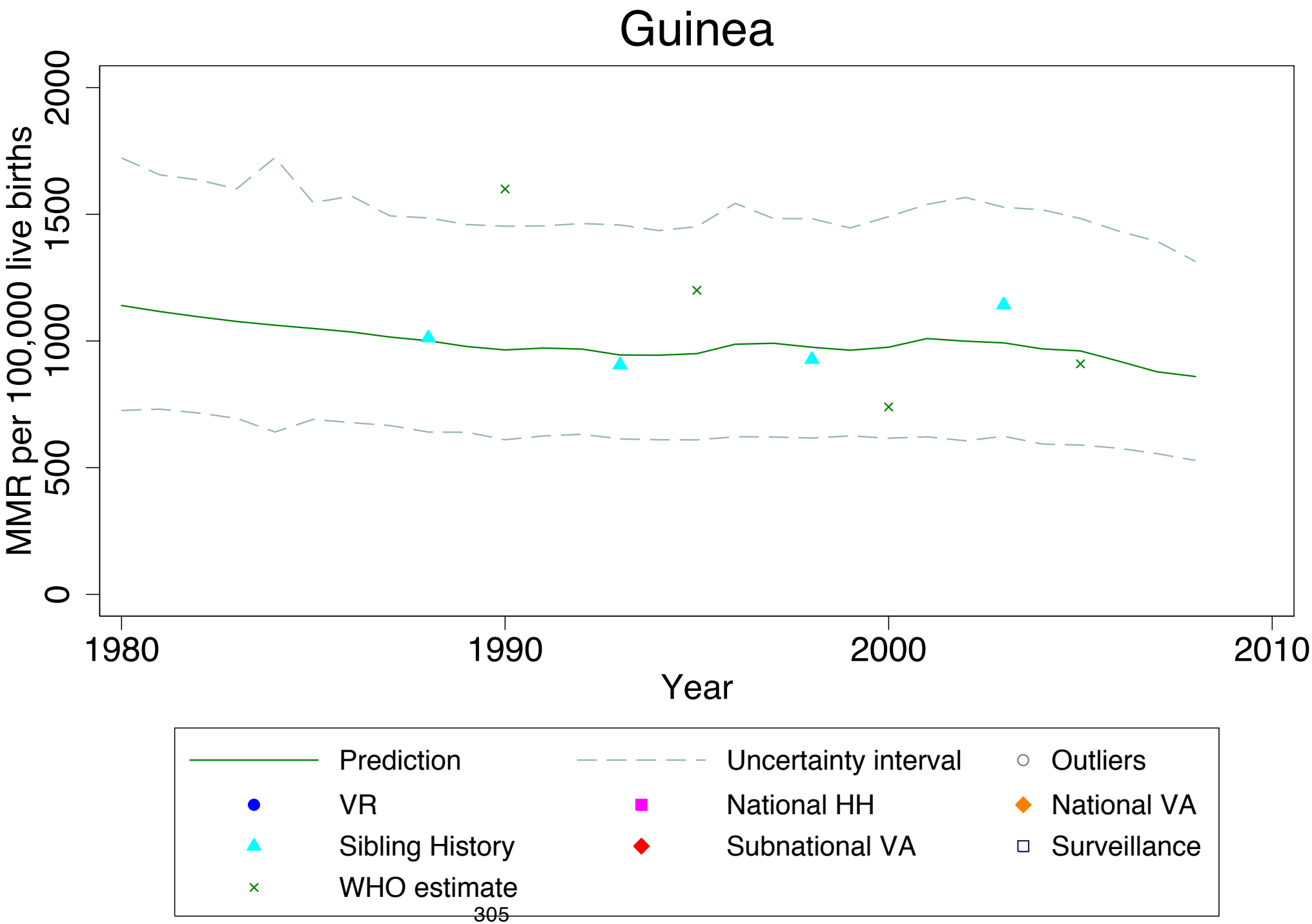
Subnational VA
Surveillance
WHO estimate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1990
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Year
Prediction
Uncertainty interval
Outliers
VR
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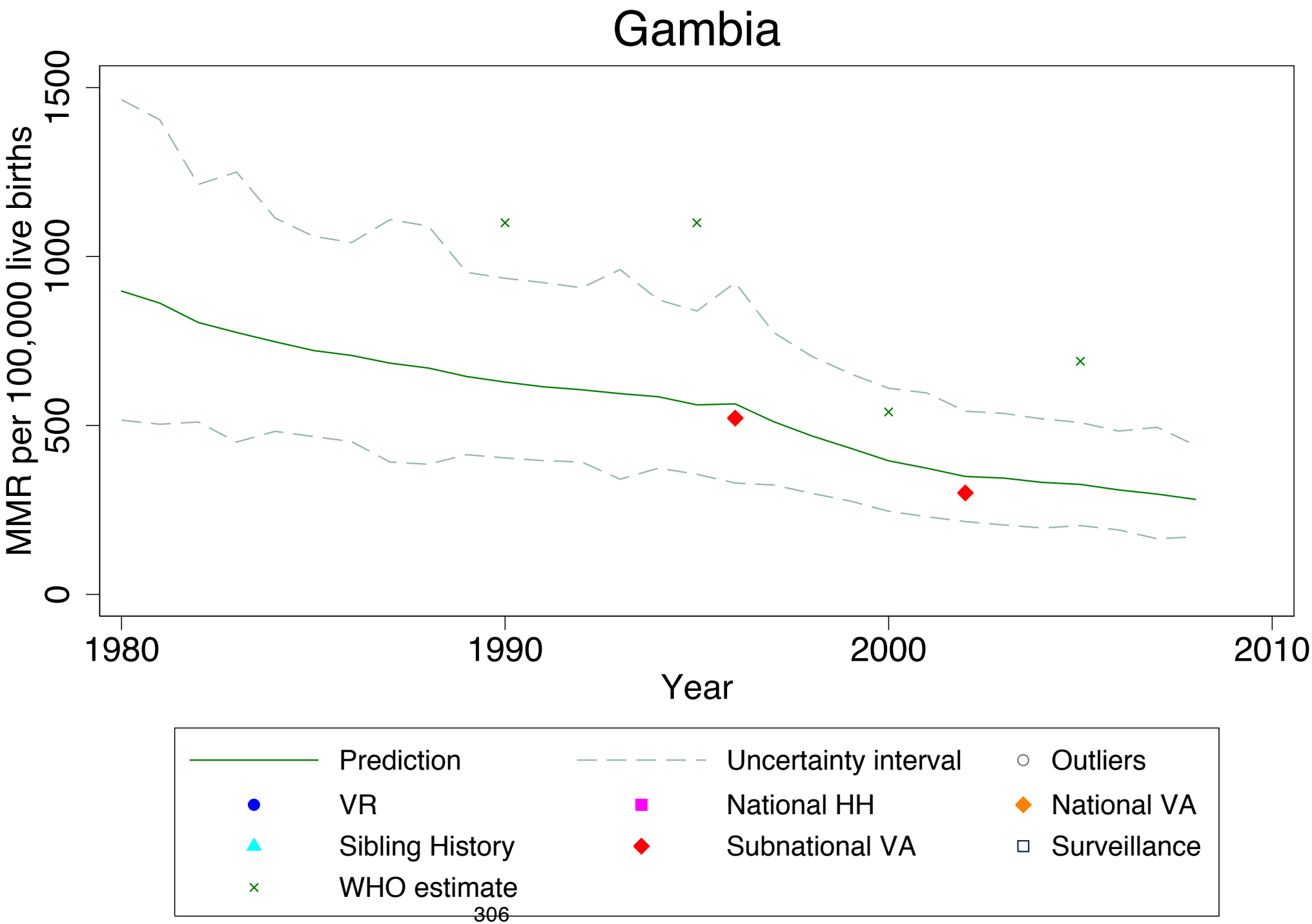
Subnational VA
Surveillance
WHO estimate


Gambia
MMR per 100,000 live births
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Year
Prediction
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VR
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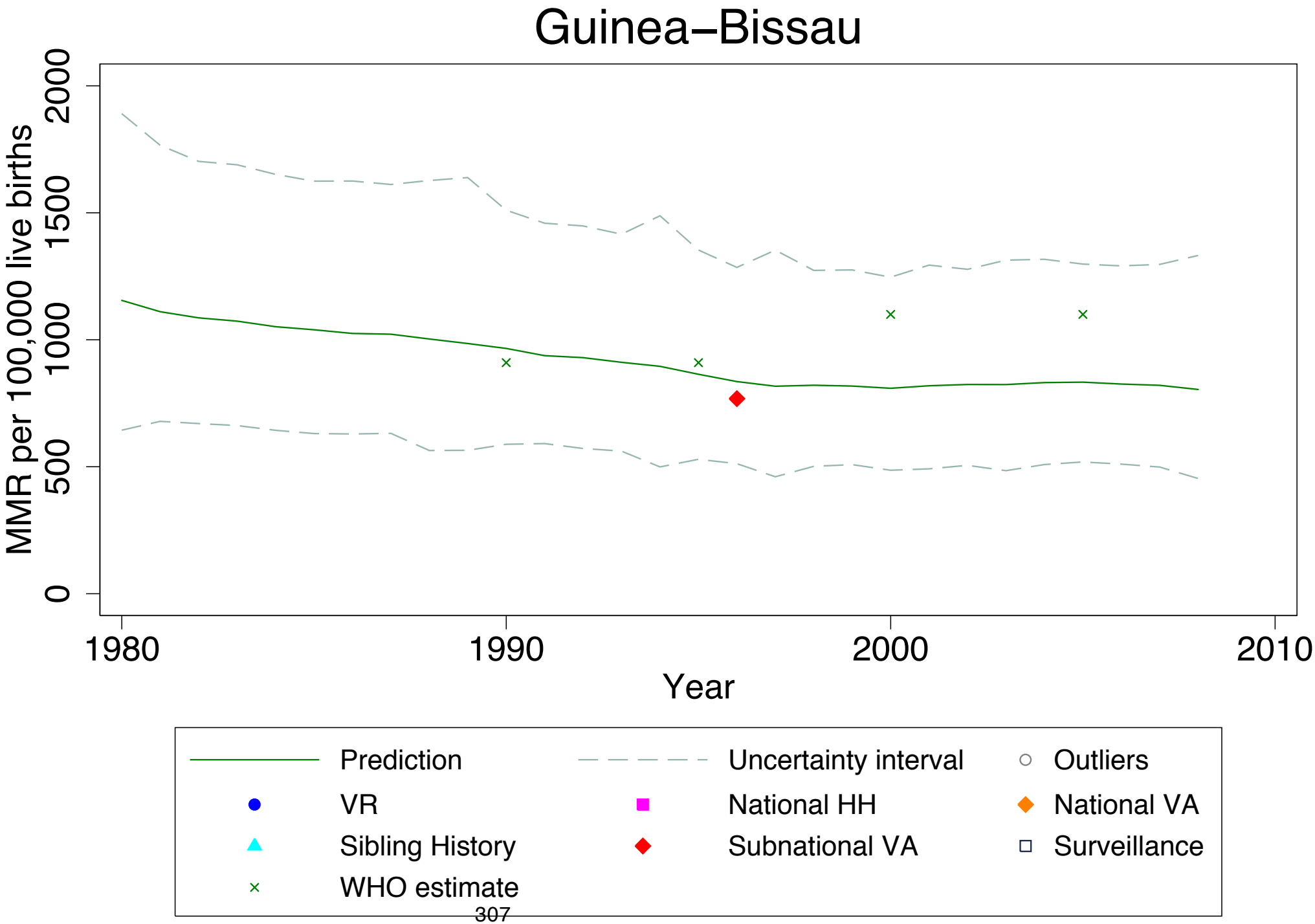
Subnational VA
Surveillance
WHO estimate


Guinea–Bissau
MMR per 100,000 live births
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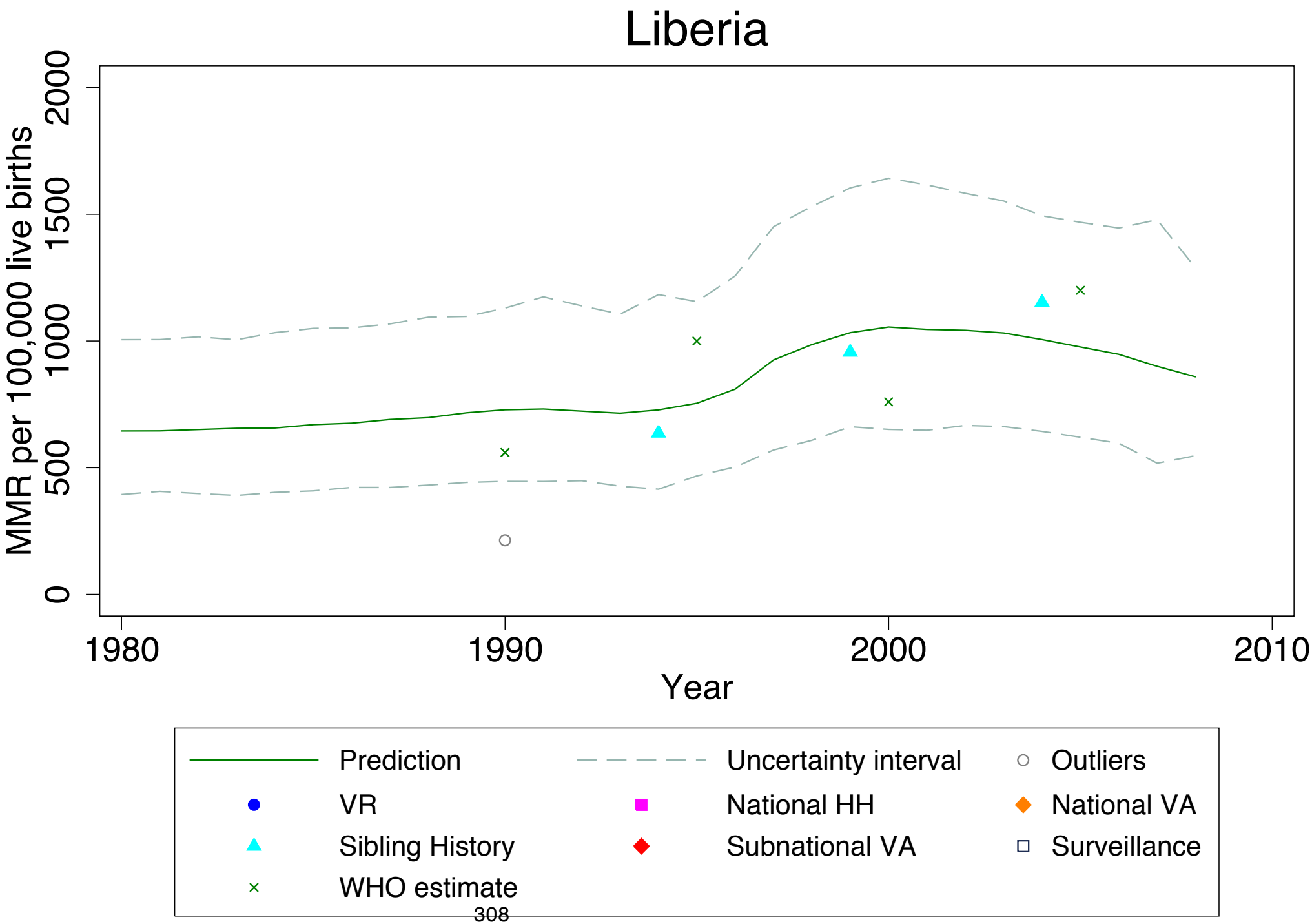
Subnational VA
Surveillance
WHO estimate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MMR per 100,000 live births
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Year
Prediction
Uncertainty interval
Outliers
VR
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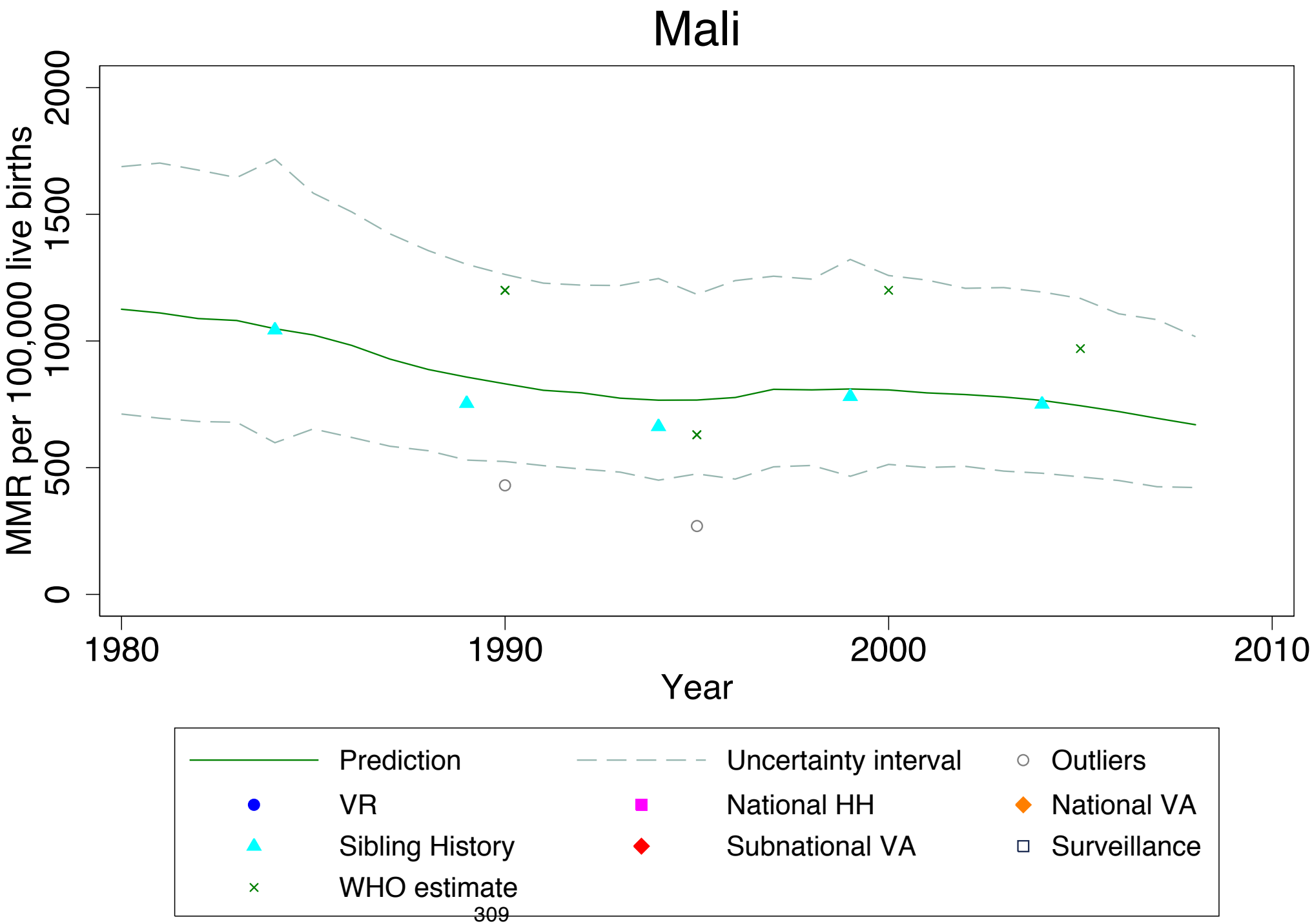
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate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MMR per 100,000 live births
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Uncertainty interval
Outliers
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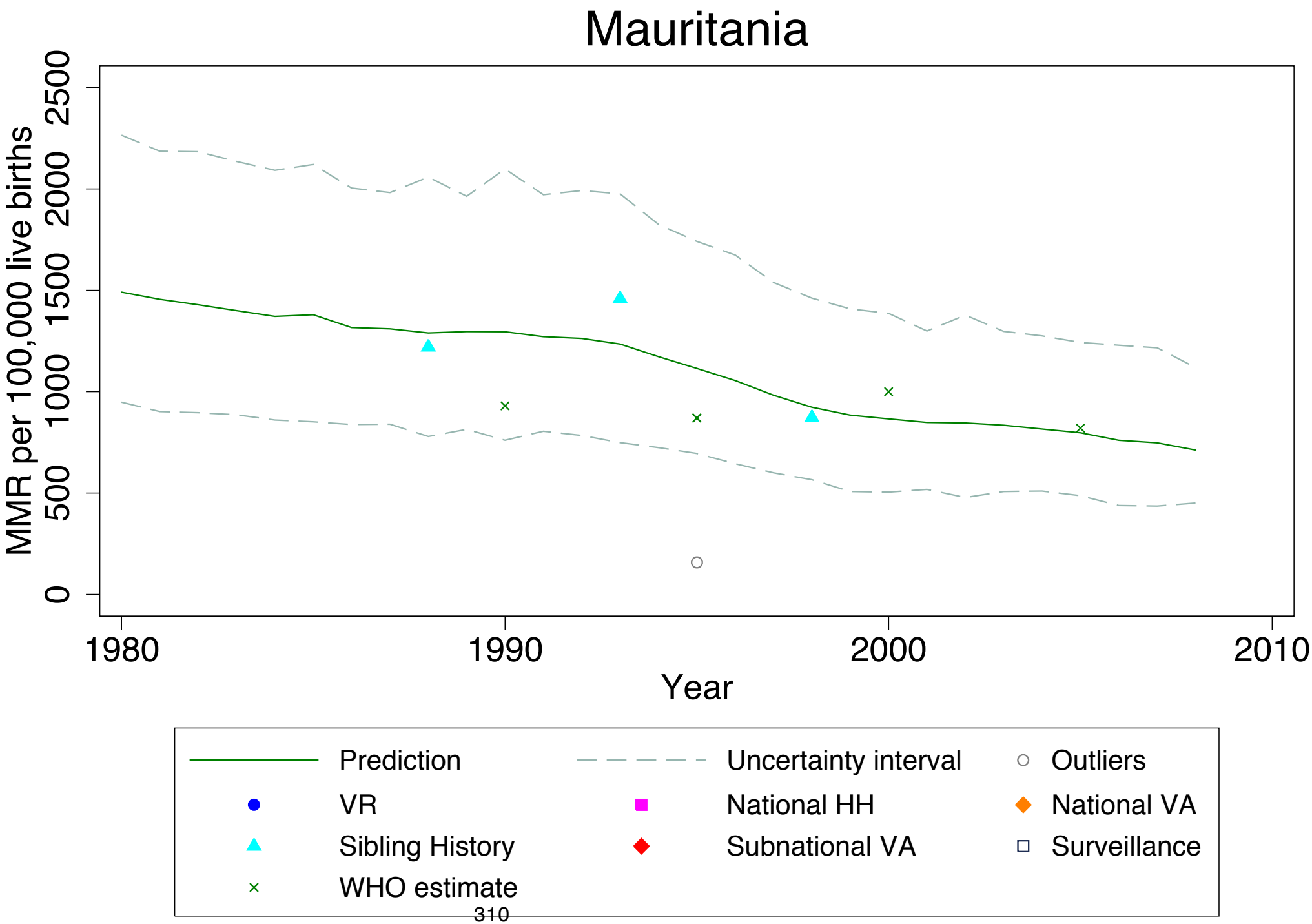
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate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Year
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Uncertainty interval
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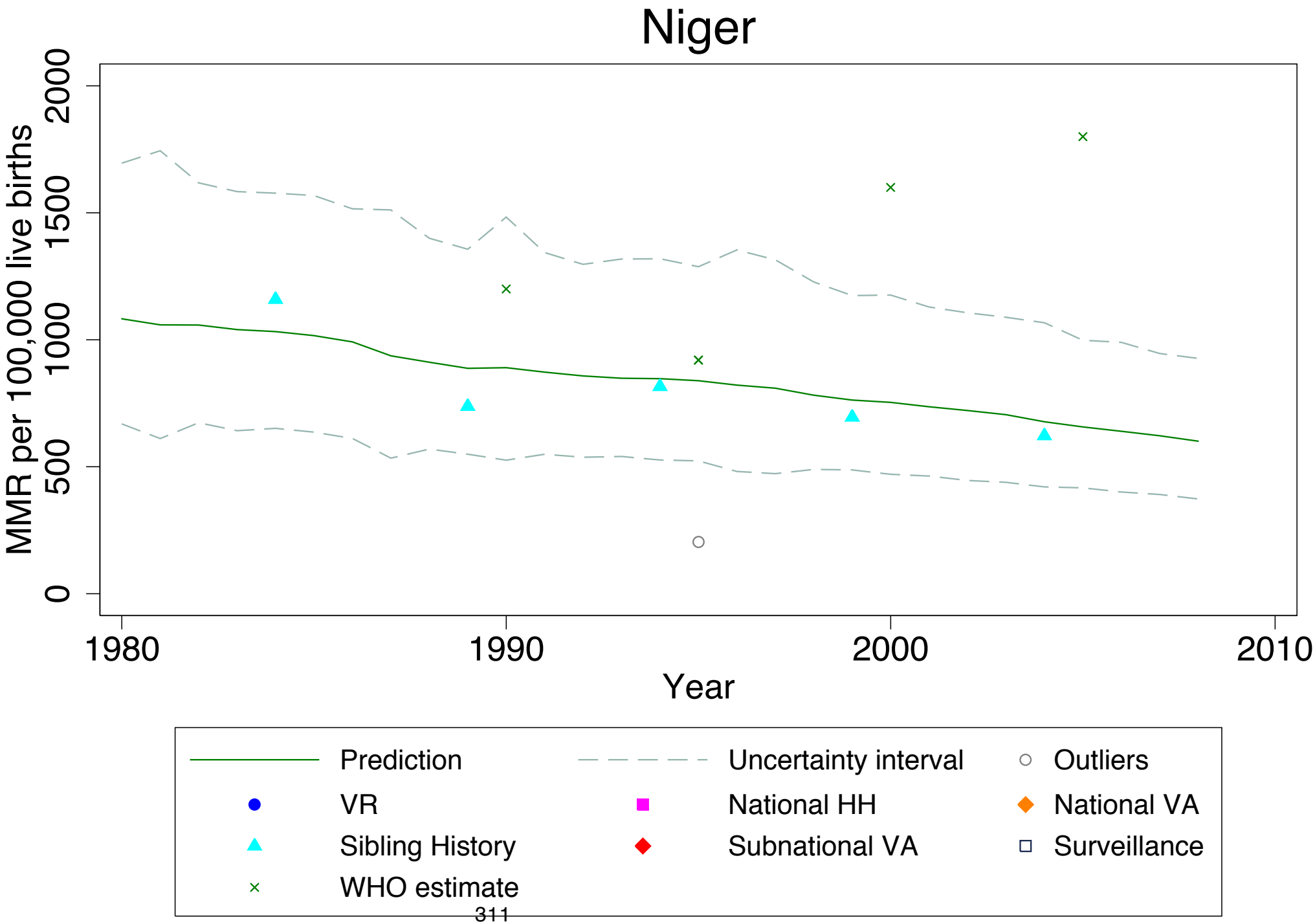
Surveillance
WHO estimate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MMR per 100,000 live births
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Prediction
Uncertainty interval
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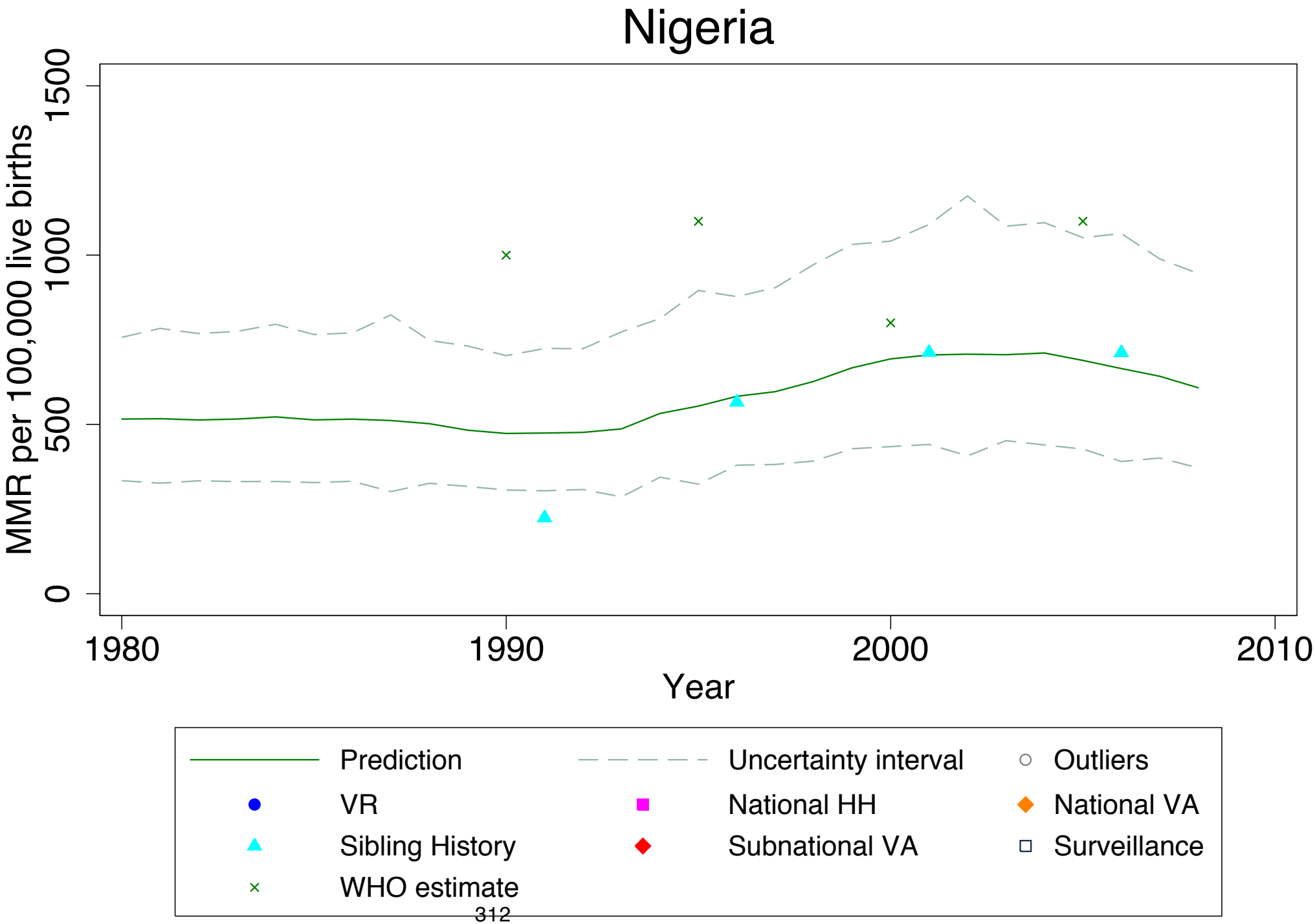
WHO estimate


Nigeria
MMR per 100,000 live births
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Outliers
VR
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National VA
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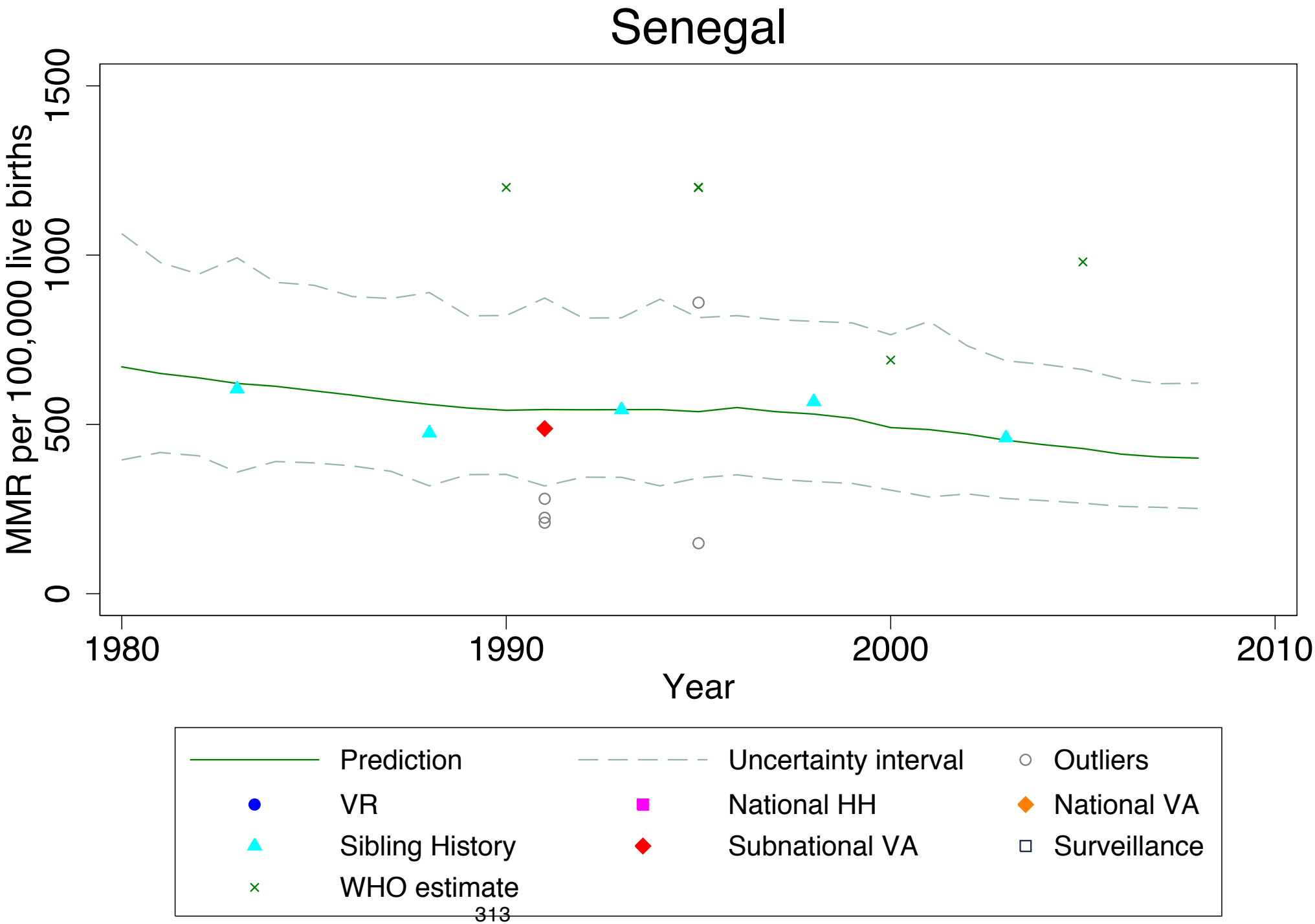
Subnational VA
Surveillance
WHO estimate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MMR per 100,000 live births
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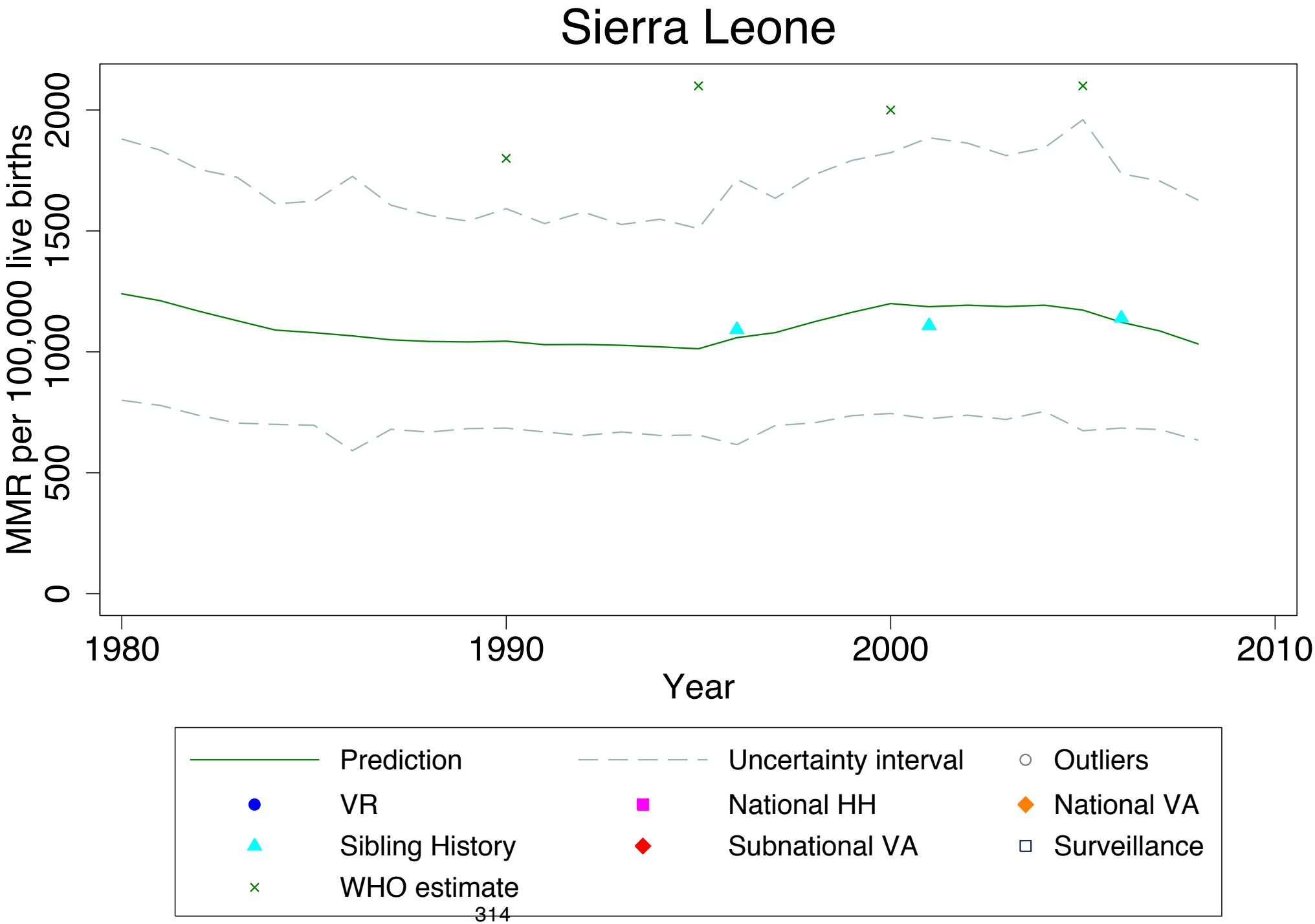
Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate


Sierra Leone
MMR per 100,000 live births
0
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Prediction
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Outliers
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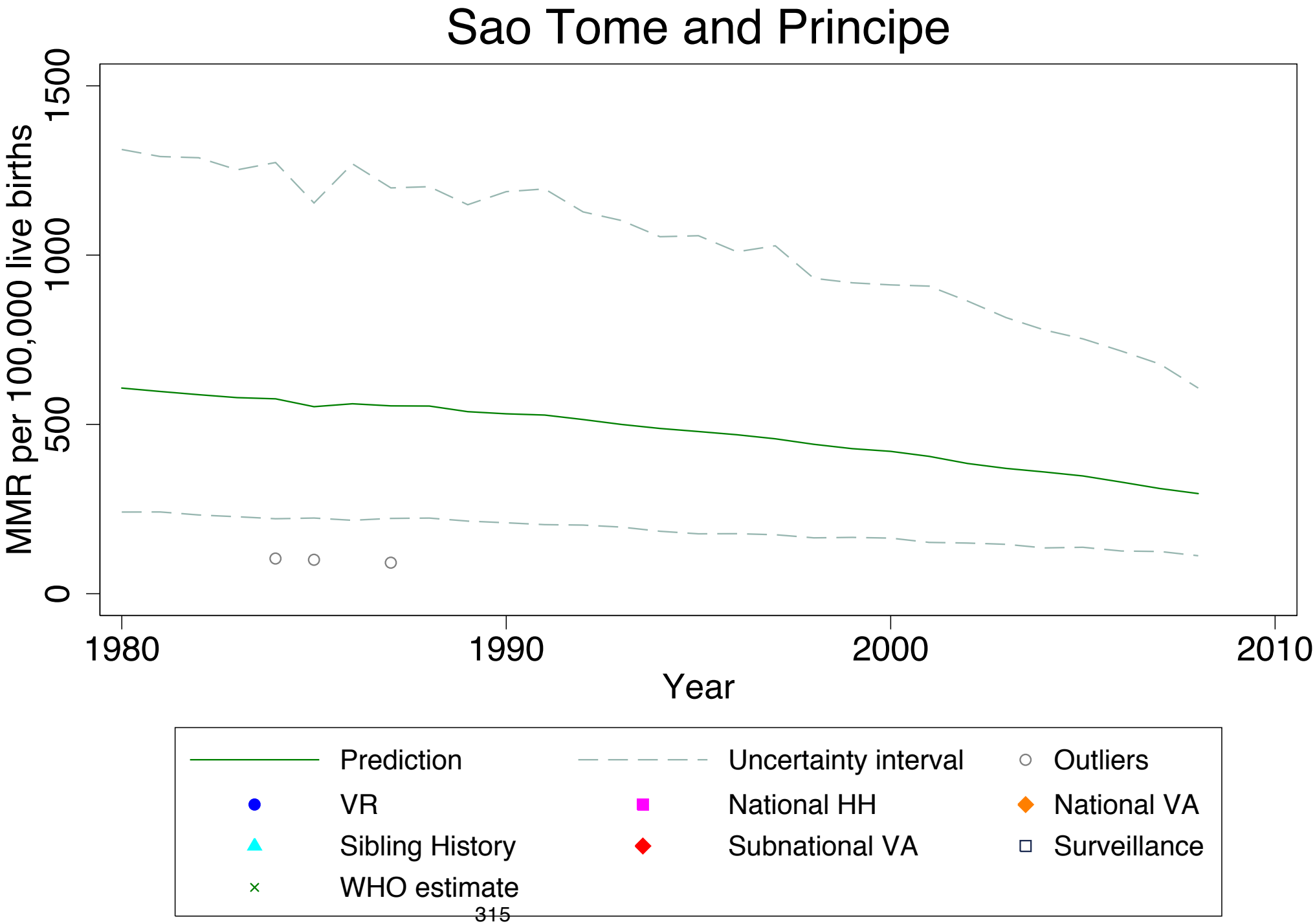
Surveillance
WHO estimate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MMR per 100,000 live births
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Subnational VA
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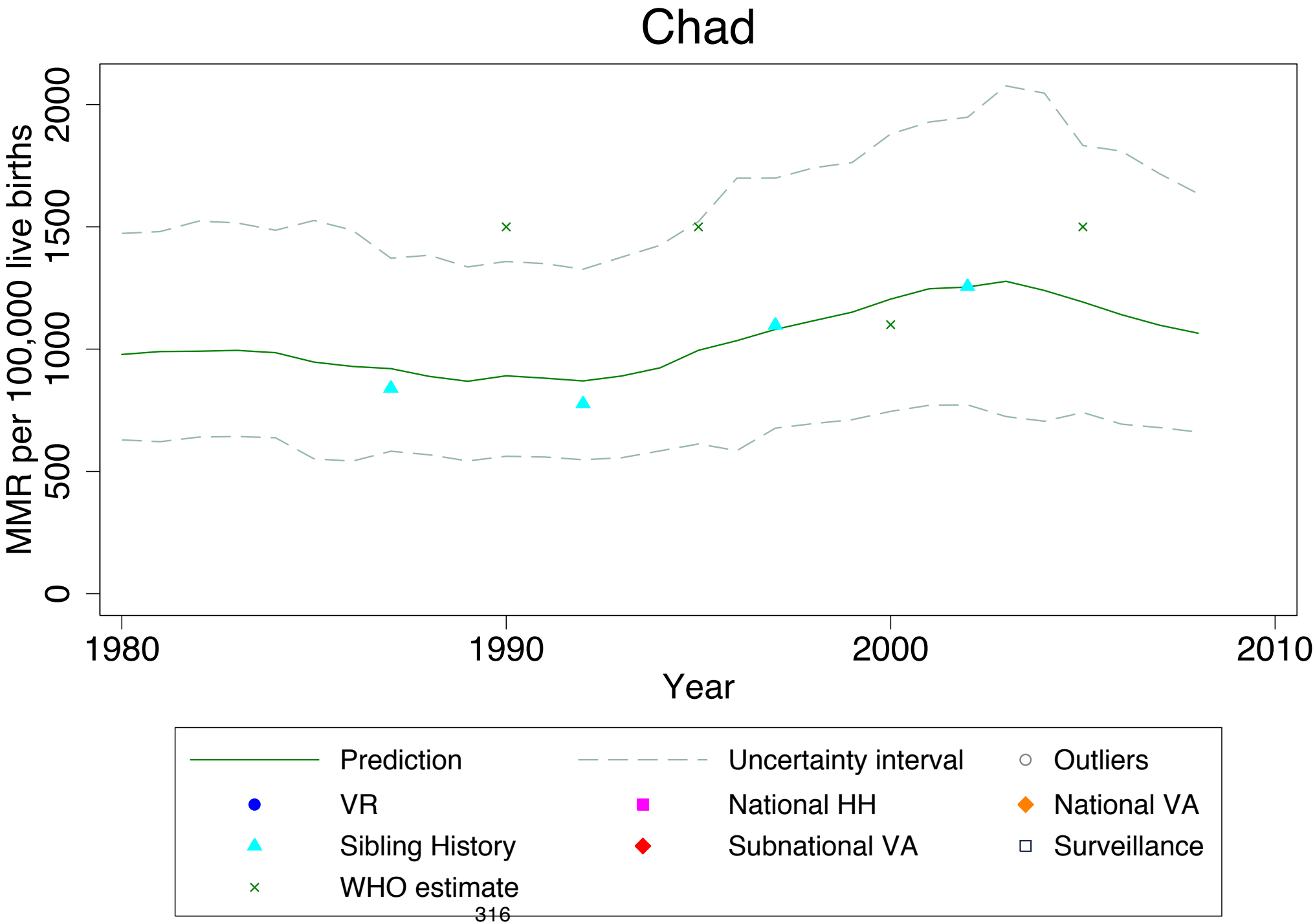
WHO estimate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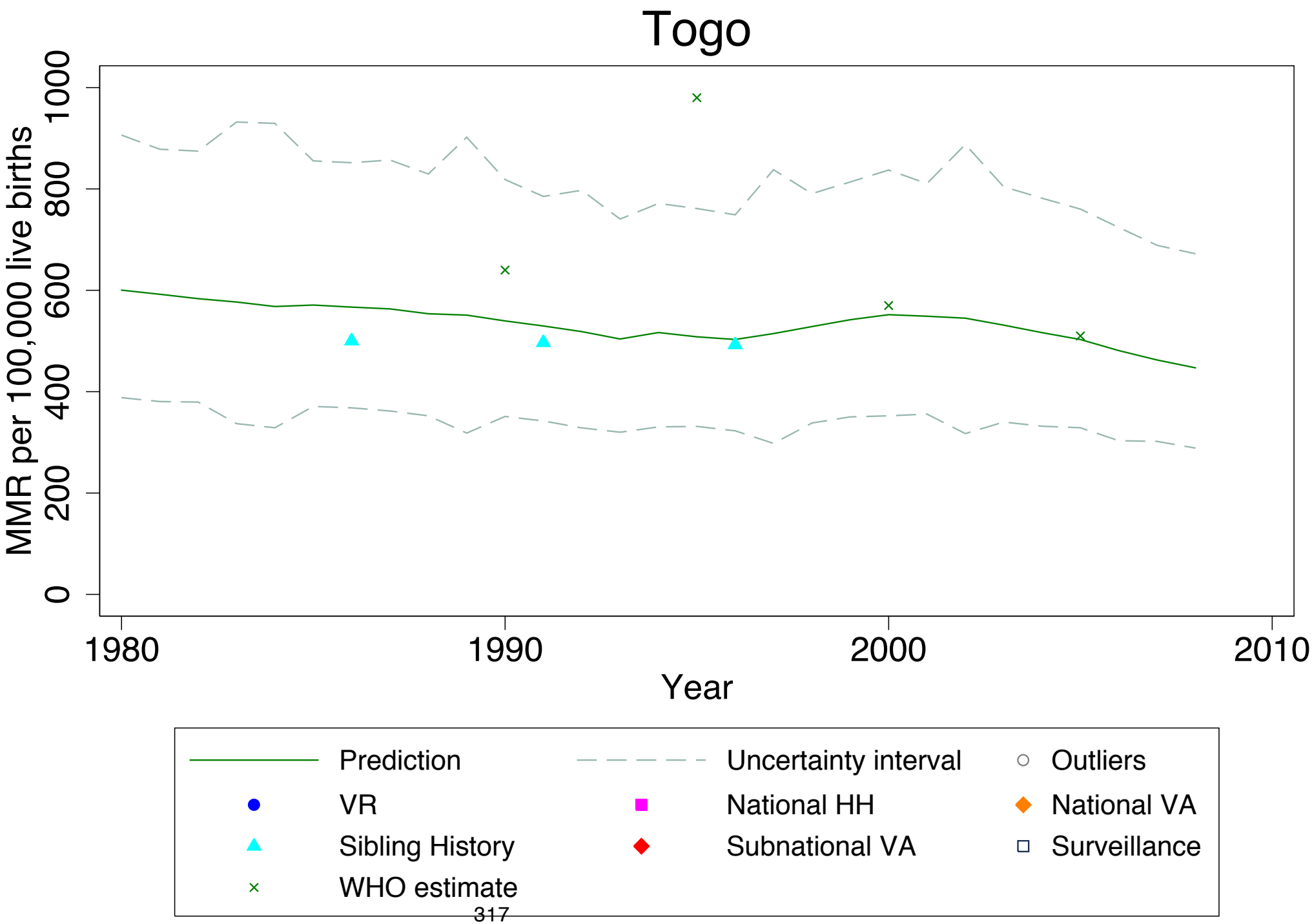
WHO estimate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1980
1990
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Year
Prediction
Uncertainty interval
Outliers
VR
National HH
National VA
Sibling History
Subnational VA
Surveillance
WHO estimate

Webtable 1. Correlation Matrix

	ln(TFR)	ln(GDP per capita)	Neonatal mortality	Education	HIV	HIV^2
ln(TFR)	1					
ln(GDP per capita)	-0.7544	1				
Neonatal mortality	0.772	-0.7649	1			
Education	-0.8273	0.7393	-0.7686	1		
HIV	0.16	-0.1835	0.094	-0.0684	1	
HIV^2	0.0675	-0.0809	0.0277	0.0022	0.9127	1

Webtable 2. Linear Model Regression Coefficients

	Ordinary Least Squares Regression		Generalized Negative Binomial Regression		Robust Regression	
	Coefficient	**Std. Error**	**Coefficient**	**Std. Error**	**Coefficient**	**Std. Error**
Intercept	5.044	0.107	-6.334	0.110	5.107	0.105
ln(TFR)	1.921	0.023	1.904	0.024	1.884	0.023
ln(GDP per capita)	-0.532	0.011	-0.514	0.011	-0.536	0.010
Neonatal mortality	13.777	0.757	11.568	0.796	13.994	0.741
Education	-0.102	0.003	-0.106	0.003	-0.101	0.003
HIV	0.116	0.005	0.144	0.005	0.119	0.005
HIV^2	-0.002	0.000	-0.003	0.000	-0.002	0.000
Age 15-19	-1.264	0.021	-1.174	0.020	-1.235	0.021
Age 20-24	-0.412	0.021	-0.360	0.020	-0.406	0.020
Age 25-29	-0.078	0.020	-0.091	0.021	-0.082	0.020
Age 35-39	-0.175	0.021	-0.153	0.024	-0.173	0.020
Age 40-44	-0.628	0.021	-0.543	0.026	-0.633	0.021
Age 45-49	-1.354	0.025	-1.302	0.029	-1.394	0.025

Webtable 3. Predictive Validity for Robust Regression and Generalized Negative Binomial Regression:

Out-of-sample model performance measured by root mean squared error (SE), root median SE, mean relative error (RE) and median RE for the following hold-out scenarios: (i) withholding all information for 20% of countries; (ii) withholding the first 20% of years of data for every country; (iii) withholding the last 20% of years of data for every country; and (iv) withholding 20% of all datapoints.

Robust Regression: 20% of Countries				
Regression	Root Mean SE*	Root Median SE	Mean RE**	Median RE
Linear	214.84	27.00	0.604	0.417
Spatio-Temporal	189.27	25.34	0.521	0.357

Robust Regression: First 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	208.28	22.04	0.702	0.437
Spatio-Temporal	129.32	11.92	0.392	0.199

Robust Regression: Last 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	158.86	13.23	0.538	0.421
Spatio-Temporal	104.08	7.46	0.284	0.213

Robust Regression: Random 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	215.44	24.22	0.619	0.419
Spatio-Temporal	125.34	10.36	0.286	0.165

Generalized Negative Binomal Regression: 20% of Countries				
Regression	Root Mean SE*	Root Median SE	Mean RE**	Median RE
Linear	241.59	27.67	0.783	0.472
Spatio-Temporal	183.57	25.57	0.518	0.355

Generalized Negative Binomal Regression: First 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	235.84	26.88	0.945	0.567
Spatio-Temporal	124.93	10.72	0.384	0.206

Generalized Negative Binomal Regression: Last 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	221.62	12.30	0.74	0.443
Spatio-Temporal	113.99	7.73	0.293	0.220

Generalized Negative Binomal Regression: Random 20% of Country Years				
Regression	Root Mean SE	Root Median SE	Mean RE	Median RE
Linear	256.72	24.73	0.820	0.480
Spatio-Temporal	123.81	10.11	0.284	0.163

*SE = Squared Error

** RE = Relative Error

APPENDIX A3

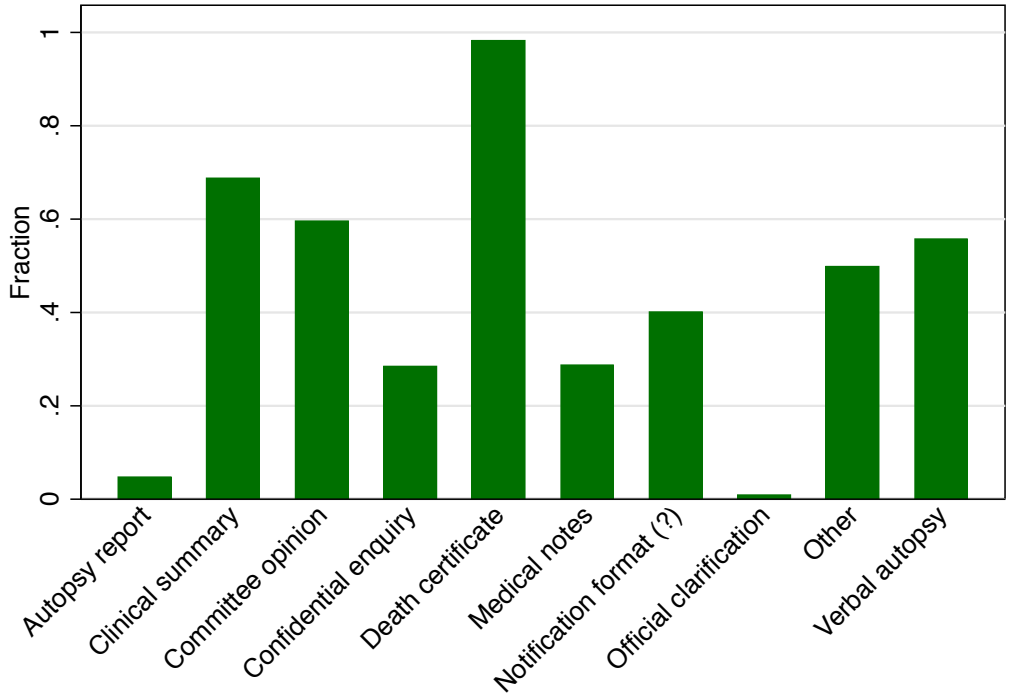

Figure A3.1: Sources of data used to review deaths, n=5886

Table A3.1: Tabulations of detailed indirect causes after recode completed

Cause	ICD code	2006	2007	2008	2009	2010	Total
Pre-existing essential hypertension complicating pregnancy, childbirth and the puerperium	O100	4	3	6	7	8	28
Pre-existing hypertensive heart disease complicating pregnancy, childbirth and the puerperium	O101	1	0	1	0	1	3
Pre-existing hypertensive renal disease complicating pregnancy, childbirth and the puerperium	O102	0	0	1	0	0	1
Unspecified pre-existing hypertension complicating pregnancy, childbirth and the puerperium	O109	2	0	1	0	0	3
All pre-existing hypertension		*7*	*3*	*9*	*7*	*9*	*35*
Diabetes mellitus in pregnancy: Pre-existing diabetes mellitus, insulin-dependent	O240	3	3	5	9	0	20
Diabetes mellitus in pregnancy: Pre-existing diabetes mellitus, non-insulin-dependent	O241	2	4	3	5	7	21
Diabetes mellitus in pregnancy: Pre-existing diabetes mellitus, unspecified	O243	1	1	1	0	0	3
Diabetes mellitus in pregnancy, unspecified	O249	0	1	0	1	1	3
All diabetes mellitus in pregnancy		*6*	*9*	*9*	*15*	*8*	*47*
Tuberculosis complicating pregnancy, childbirth and the puerperium	O980	12	9	6	12	18	57
Other infections with a predominantly sexual mode of transmission complicating pregnancy, childbirth and the puerperium	O983	0	0	0	1	0	1
Viral hepatitis complicating pregnancy, childbirth and the puerperium	O984	3	2	4	1	2	12
Other viral diseases complicating pregnancy, childbirth and the puerperium	O985	6	3	4	2	9	24
Protozoal diseases complicating pregnancy, childbirth and the puerperium	O986	1	0	0	0	0	1
Human immunodeficiency [HIV] disease complicating pregnancy, childbirth and the puerperium	O987	13	12	14	10	12	61
Other maternal infectious and parasitic diseases complicating pregnancy, childbirth and the puerperium	O988	6	2	5	7	11	31
Unspecified maternal infectious or parasitic disease complicating pregnancy, childbirth and the puerperium	O989	1	0	0	1	0	2
All maternal infectious or parasitic diseases		*42*	*28*	*33*	*34*	*52*	*189*
Anaemia complicating pregnancy, childbirth and the puerperium	O990	4	6	2	3	6	21
Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism complicating pregnancy, childbirth and the puerperium	O991	4	6	3	4	3	20
Endocrine, nutritional and metabolic diseases complicating pregnancy, childbirth and the puerperium	O992	14	9	5	4	7	39

Mental disorders and diseases of the nervous system complicating pregnancy, childbirth and the puerperium	O993	17	15	17	18	11	78
Diseases of the circulatory system complicating pregnancy, childbirth and the puerperium	O994	36	61	69	45	54	265
Diseases of the respiratory system complicating pregnancy, childbirth and the puerperium	O995	19	22	16	198	35	290
Diseases of the digestive system complicating pregnancy, childbirth and the puerperium	O996	22	31	33	35	24	145
Other specified diseases and conditions complicating pregnancy, childbirth and the puerperium	O998	72	65	63	68	69	337

Table A3.2: Missing rates for covariates

	2006	2007	2008	2009	2010
Number of pregnancies	8.1%	12.0%	3.2%	3.6%	3.1%
Marital status	1.7%	1.3%	1.7%	1.7%	1.8%
Education	5.0%	4.2%	6.0%	4.0%	5.2%
Any prenatal visit	25.9%	26.6%	19.1%	22.0%	25.2%
Place of death	100.0%	100.0%	0.2%	100.0%	0.7%
Place of delivery	14.1%	20.7%	16.2%	13.6%	12.9%
Place of care for first complication	20.1%	22.9%	17.9%	14.4%	15.4%
Age at death	0.4%	0.1%	0.0%	0.2%	0.2%
Deprivation index	0.3%	0.2%	0.6%	0.6%	0.4%
Skilled birth attendant	14.8%	16.1%	8.8%	8.0%	9.5%

Table A3.3: Multivariate logistic regression results comparing indirect deaths to direct deaths (n=5,553)

	Coef.	Std. Err.	p-value	95% Conf. Interval	
Marital status					
Single (comparator)					
Common law, divorced or widowed	-0.02	0.10	0.85	-0.21	0.17
Married	0.00	0.10	0.98	-0.19	0.20
Education					
< Primary (comparator)					
< Secondary	-0.10	0.10	0.32	-0.29	0.09
Secondary or higher	-0.24	0.10	0.01	-0.43	-0.06
Place of delivery					
Secretaria de Salud (comparator)					
IMSS	0.08	0.24	0.73	-0.44	0.61
IMSS Opportunidades	-0.23	0.38	0.57	-1.09	0.64
Public worker unit	0.18	0.18	0.32	-0.18	0.54
Private medical unit	-0.60	0.14	0.00	-0.87	-0.33

Home, street, other	-0.83	0.16	0.00	-1.15	-0.50
Place of care for first complication					
Secretaria de Salud (comparator)					
IMSS	0.30	0.23	0.22	-0.21	0.81
IMSS Opportunidades	-0.02	0.23	0.94	-0.51	0.47
Public worker unit	-0.04	0.22	0.87	-0.50	0.43
Private medical unit	0.01	0.13	0.91	-0.24	0.27
Home, street, other	-0.21	0.31	0.50	-0.82	0.40
Deprivation index, quintile (municipality)					
Q1-Rich (comparator)					
Q2	0.03	0.10	0.79	-0.17	0.22
Q3	-0.32	0.12	0.01	-0.56	-0.07
Q4	-0.33	0.12	0.01	-0.57	-0.09
Q5-Poor	-0.63	0.13	0.00	-0.88	-0.38
Skilled birth attendant					
None (comparator)					
Doctor, nurse or midwife	-0.19	0.22	0.40	-0.62	0.25
NA: no delivery	1.21	0.23	0.00	0.76	1.66
Year					
2006 (comparator)					
2007	0.25	0.11	0.02	0.04	0.46
2008	0.20	0.11	0.06	-0.01	0.41
2009	0.82	0.10	0.00	0.62	1.01
2010	0.45	0.11	0.00	0.24	0.66
Number of pregnancies	-0.05	0.02	0.01	-0.09	-0.01
Age	-0.01	0.01	0.06	-0.02	0.00
Any prenatal visit	0.20	0.10	0.05	0.00	0.40
Constant	-0.81	0.30	0.01	-1.39	-0.22