SCGO 18th symposium, Phnom Penh, Nov 23 2019

Proposal for establishing guidelines for the management of gestational trophoblastic disease in Cambodia

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Investigation of management of gestational trophoblastic diseases in Cambodia

I. Results of questionnaire to participants at SCGO 16th Conference, November 2017

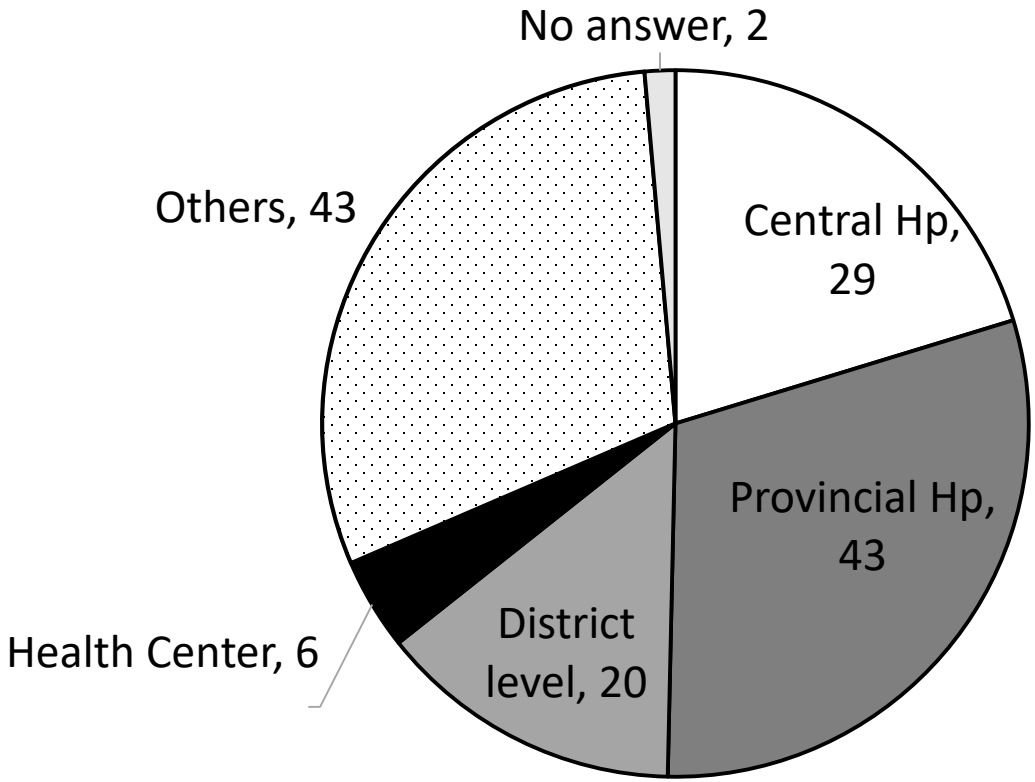
II. Analysis of Health Information System (HIS) data in 2014-2017

III. Interview doctors and midwives at hospitals, November 2017 - June 2019
   1. National Maternal and Child Health Center: Dr. Ung Mong Reaksmeg
   2. Khmer Soviet Hospital: Dr. Uy Kyna and Dr. Chhit Maryan, Prof. Kouy Samnag (Oncology Dept)
   3. Calmette Hospital: Dr. Korn Aum and Dr. Khann Sok Chann, Dr. Rath Beauta (Oncology Dept), Dr. Mary Nheb (Laboratory Dept)
   4. Kampong Cham Provincial Hospital: Dr. Nem Bunthoeun and Dr. Srey Kim Ehhorn
   5. Chamke Leu Referral Hospital: Dr. Thay Soklen and 7 midwives
   6. Takeo Provincial Hospital: Dr. Sou Vutha (main) and Dr. Soy Sokhoeum
   7. Bati Referral Hospital: Dr. Sao Chantha
   8. Battambang Provincial Hospital : Dr. Kak Seila, Dr. Ngeth Viphou and Dr. Sok Boraphen
   9. Moung Reusey Referral Hospital: Dr. Hosidara

Results of questionnaire to participants at SCGO 16th Annual Conference, November 2017

143 participants answered

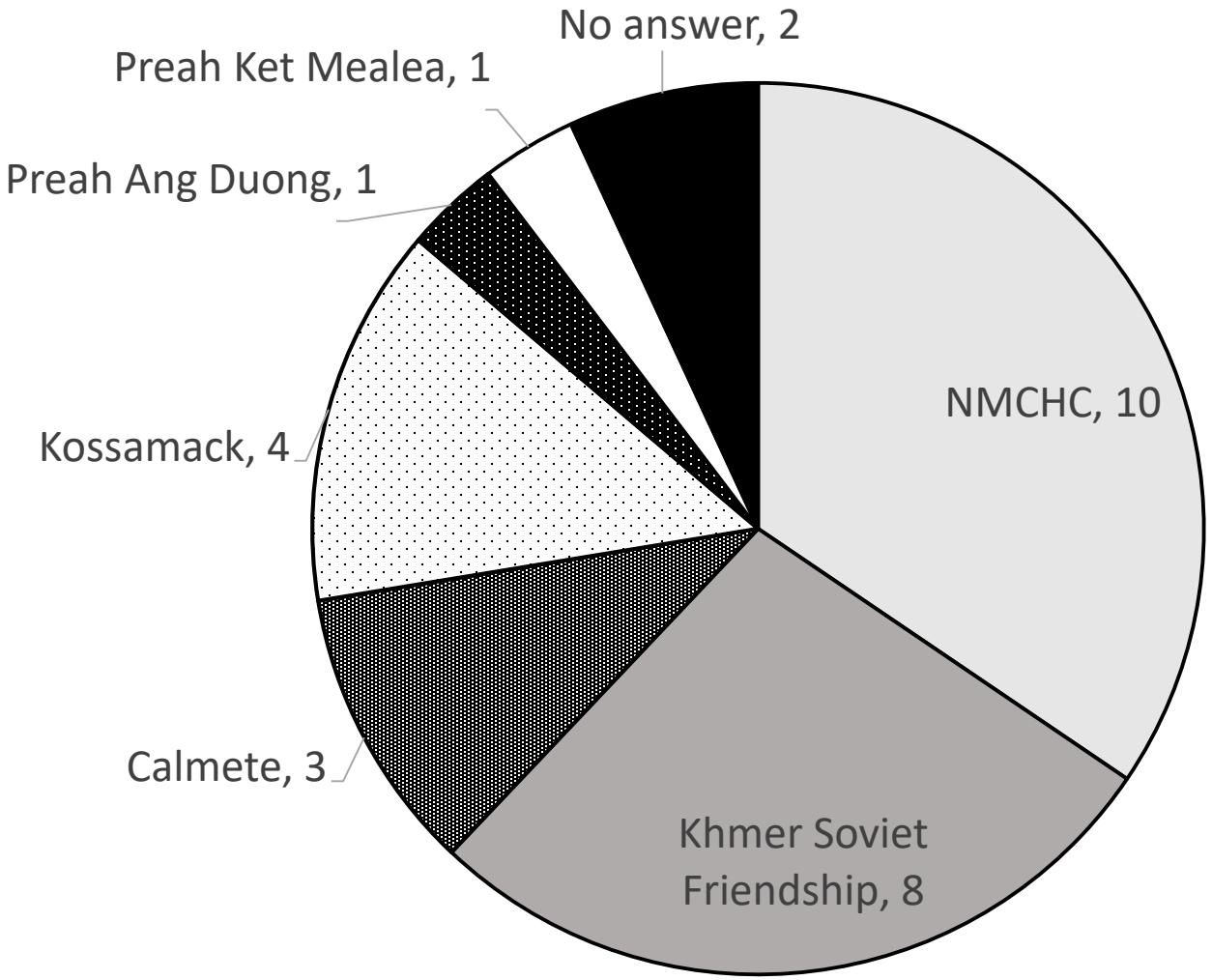
1. Level of Health Facility



2. Distributions of participants (N=143)

Province	N	Province	N
1.Phnom Penh	53	14.Preah Vihear	6
2.Banteay Meanchey	8	15.Prey Veng	1
3.BattamBang	3	16.Pursat	3
4.Kampong Cham	9	17.Ratana Kiri	0
5.Kampong Chhnang	2	18.Siem Reap	6
6.Kampong Speu	5	19.Stung Treng	1
7.Kampong Thom	2	20.Svay Rieng	3
8.Kampot	6	21.Takeo	4
9.Kandal	5	22. Paillin	3
10.Koh Kong	3	23. Tbong Kmon	3
11.Kratie	5	24. Kep	1
12.Mondol Kiri	1	25. Preah Sihaknouk	3
13.Otdar Meanchey	3	No answer	4

3. Participants from central hospitals in Phnom Penh (N=29)



4. Participants from provincial hospitals (N=43)

Name of Provincial Hospital	n
Mongkul Borey	3
Battambang	2
Kampong Cham	3
Kampong Chhnang	2
Kampong Speu	3
Chey Chamnes	5
Kho Kong	1
Kratie	2
Mondulkiri	1
Odomeanchey	3
16 Makara Hp	1
Prey Veng	1
Sampov Meas	2
Siem Reap	3
Svay Rieng	2
Takeo	2
Paillin	3
Preah Sihaknouk	2

5. Participants from district hospitals (N=20)

Name of District Hospital	n
Dongkor	1
Poipet	2
RH Poipet	1
Batheay	2
Srey Sothor	1
Batheay	1
Udong	1
Baray-Santuk	2
Kampong Trach	1
Chhouk	1
Snuol	1
Phnom Kravanh	1
Chi Phou	1
Memot	2
Tbong Kmom	1
No answer	1

6. Participants from health centers (N=6)

Name of Health Center	n
Bonsang	1
Chheb	1
Kulen	1
Kuhear Prampy	1
HC Angdong Rung	1
No answer	1

7. Participants from other working places (N=43)

Name of Working Place	n
RHAC	19
Clinic	4
NGO	1
Phnom Penh (Municipal Health Department)	2
PHD	4
OD	1
GIZ	1
Heng Daveth	1
Jayavarman VII	1
Ly Srey Vina	1
Mongkul Suor	1
Preah Vihear	1
PSIC	1
Serey Path Siem Reap Clinic	1
No answer	4

8. Number of delivery (N=143)

Q1. Does your health facility have baby delivery?

	Delivery			Number of Delivery (/year)
	Yes	No	No answer	
Central	28	1	0	250-12,000
Provincial	43	0	0	960-5,000
District	19	0	1	350-1,440
HC	6	0	0	30-360
Others*	16	29	0	24-2,640

*Others include 2 participants who did not answer the kind and name of health facilities .
HC, health center.

9. Number of miscarriage, abortion and hydatidiform mole

Q2. Does your health facility perform operations for miscarriage and abortion?
Q3. Does your health facility perform operations for hydatidiform mole?

	Miscarriage and abortion			N of abortion** (/year)	Hydatidiform mole (HM)			N of HM (/year)
	Yes	No	No answer		Yes	No	No answer	
Central	41	2	0	36-4,000	29	0	0	10-300
Provincial	43	0	0	24-1000	39	3	1	1-200
District	19	0	1	25-1200	8	11	1	1-30
HC	6	0	0	5-80	0	6	0	0
Others*	37	8	0	2-2,000	10	32	3	1-20

*Others include 2 participants who did not answer the kind and name of health facilities.
**Including miscarriage and abortion
HC, health center; N, number.

10. Available equipment and exams

Q4. Does your health facility have ultrasound?
Q5. Can you check hCG level at your health facility?
Q6. Can you order pathological examinations at your health facility?

	Ultrasound			hCG measurement				Pathological Exam		
	Yes	No	No answer	No	Preg. Check	Machine	No Answer	Yes	No	No answer
Central	26	0	3	4	7	15	3	21	2	4
Provincial	42	0	1	20	22	0	1	26	12	5
District	19	0	1	6	12	0	2	15	3	2
HC	0	5	1	3	2	0	1	2	2	2
Others	37	5	3	9	23	9	4	27	9	9

HC, health center.

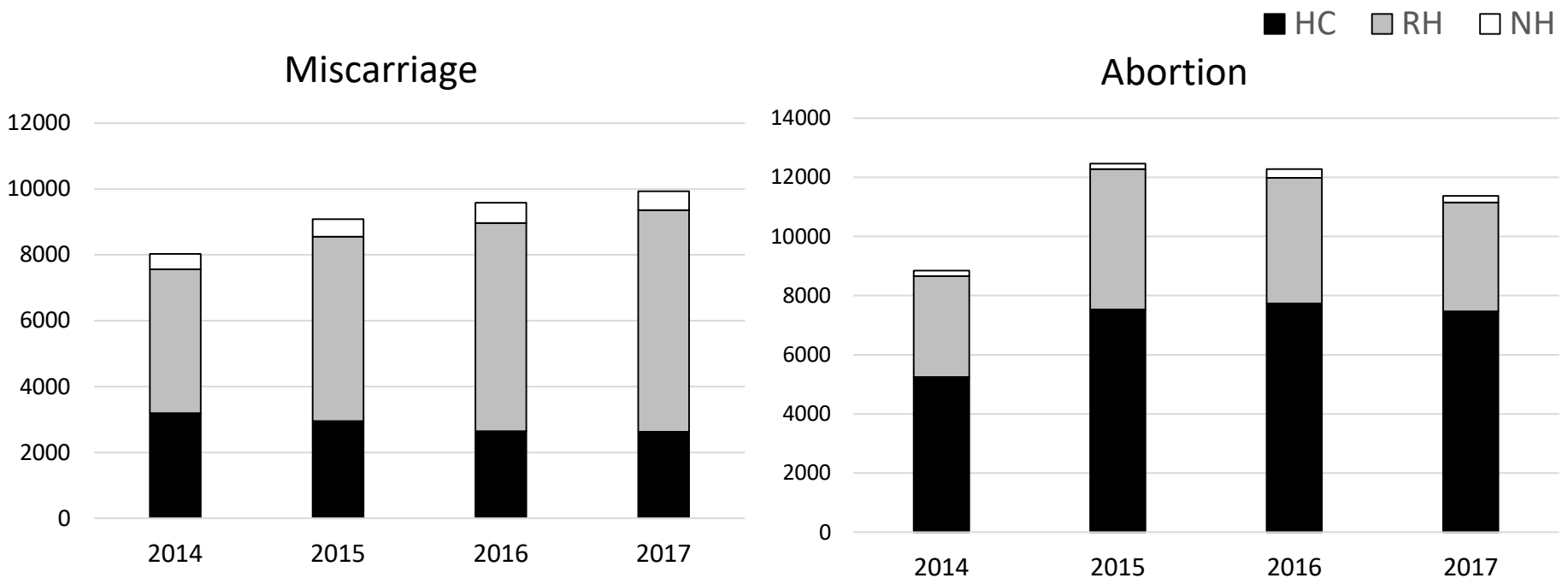
11. Experiences of hydatifirom mole (N=140)

Q7. Have you experienced treatment of hydatidiform mole?

	Experience of hydatifirom mole		
	Yes	No	No answer
Central	24	1	3
Provincial	21	19	3
District	3	16	1
HC	0	2	2
Others	10	31	4
Total	58 (41.4%)	69 (49.3%)	13 (9.3%)

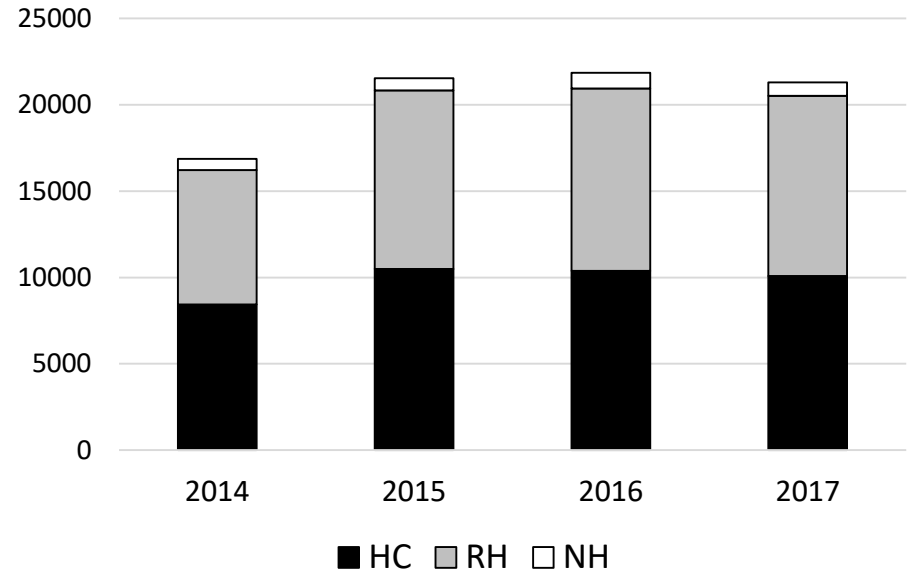
HC, health center.

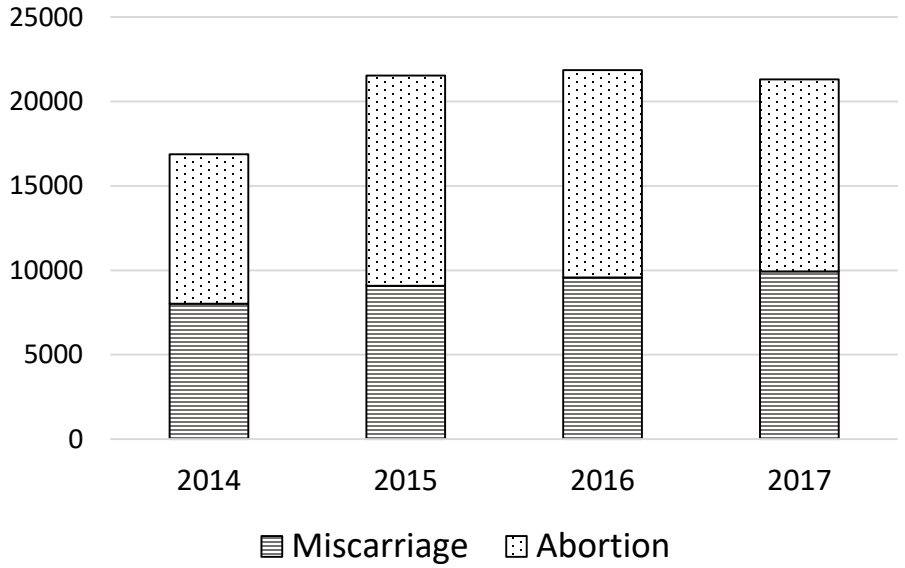
Miscarriage and abortion: HIS 2014-2017



- All levels of public health facilities had patients of spontaneous abortion and induced abortion.
- Referral hospitals had more spontaneous abortions than health centers.
- Health centers had more induced abortions than referral hospital.
- Total number of spontaneous abortions has been increasing, but the number of induced abortions has been decreasing.

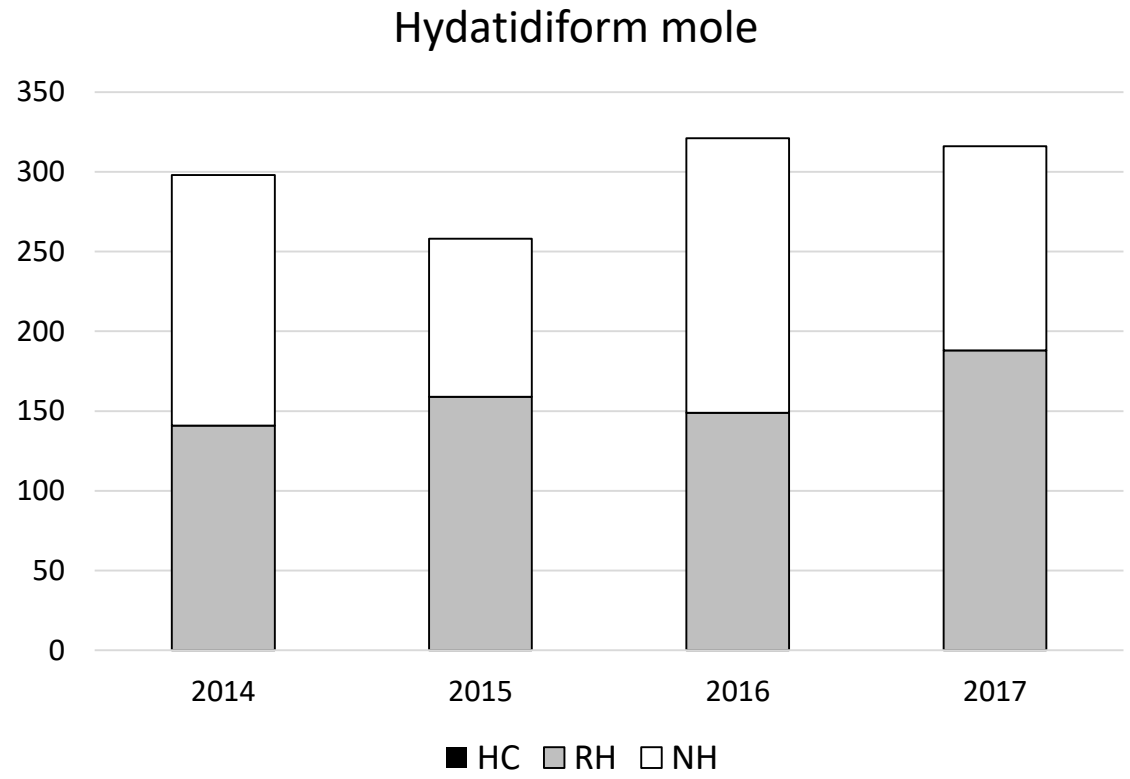
Miscarriage and abortion: HIS 2014-2017





- Almost half of cases (miscarriage and abortion) were treated at health centers.
- Number of abortions was higher than that of miscarriage.

Hydatidiform mole: HIS 2014-2017



- Referral hospitals (RH) and national hospitals (NH) had patients with hydatidiform mole.
- Health centers (HC) had no patients with hydatidiform mole.

Incidence of hydatidiform mole: HIS 2014-2017

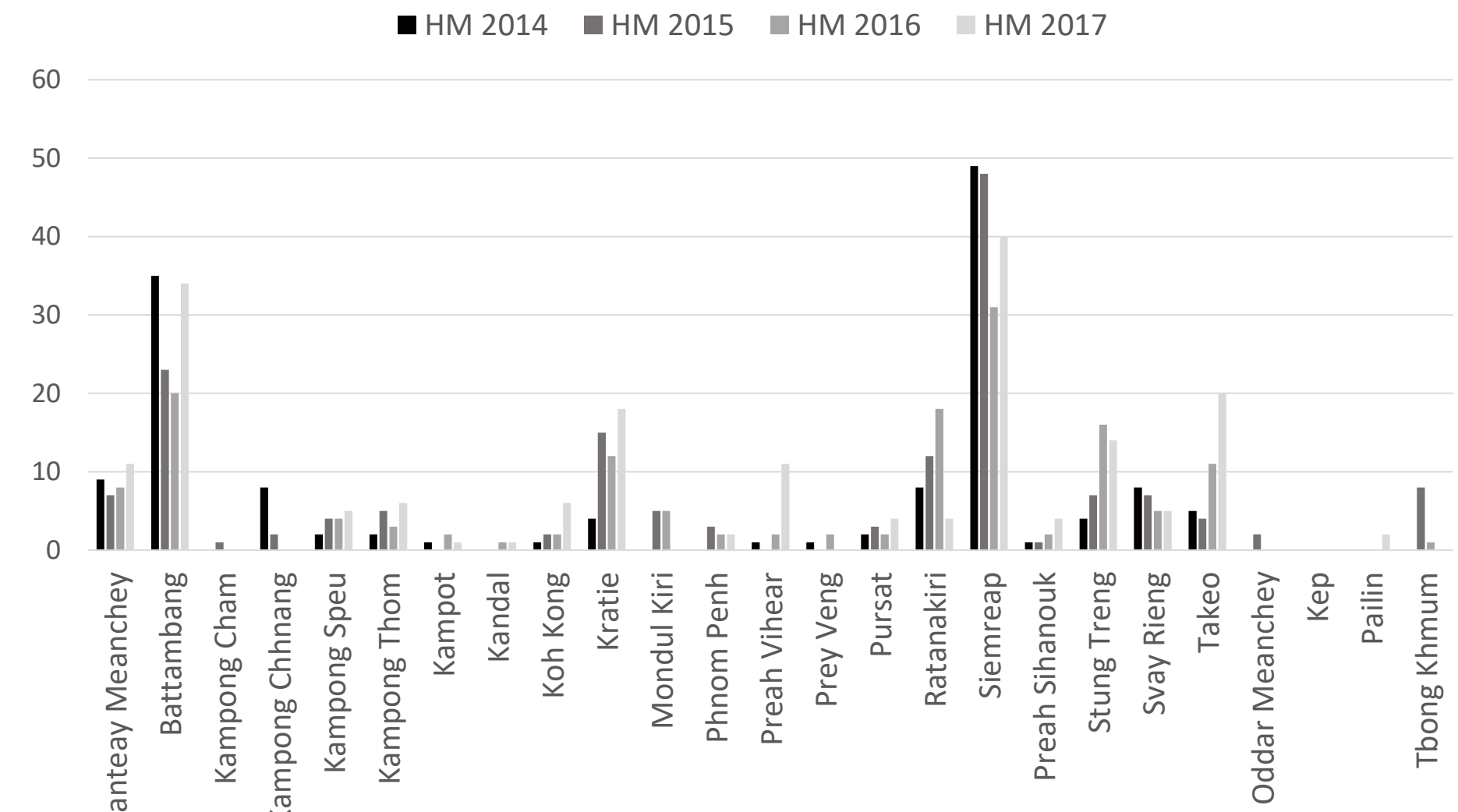
Incidence (per 1,000 deliveries)

	2014	2015	2016	2017
HM	298	258	321	316
Delivery	303,741	320,127	316,117	321,506
Incidence	0.98	0.81	1.02	0.98

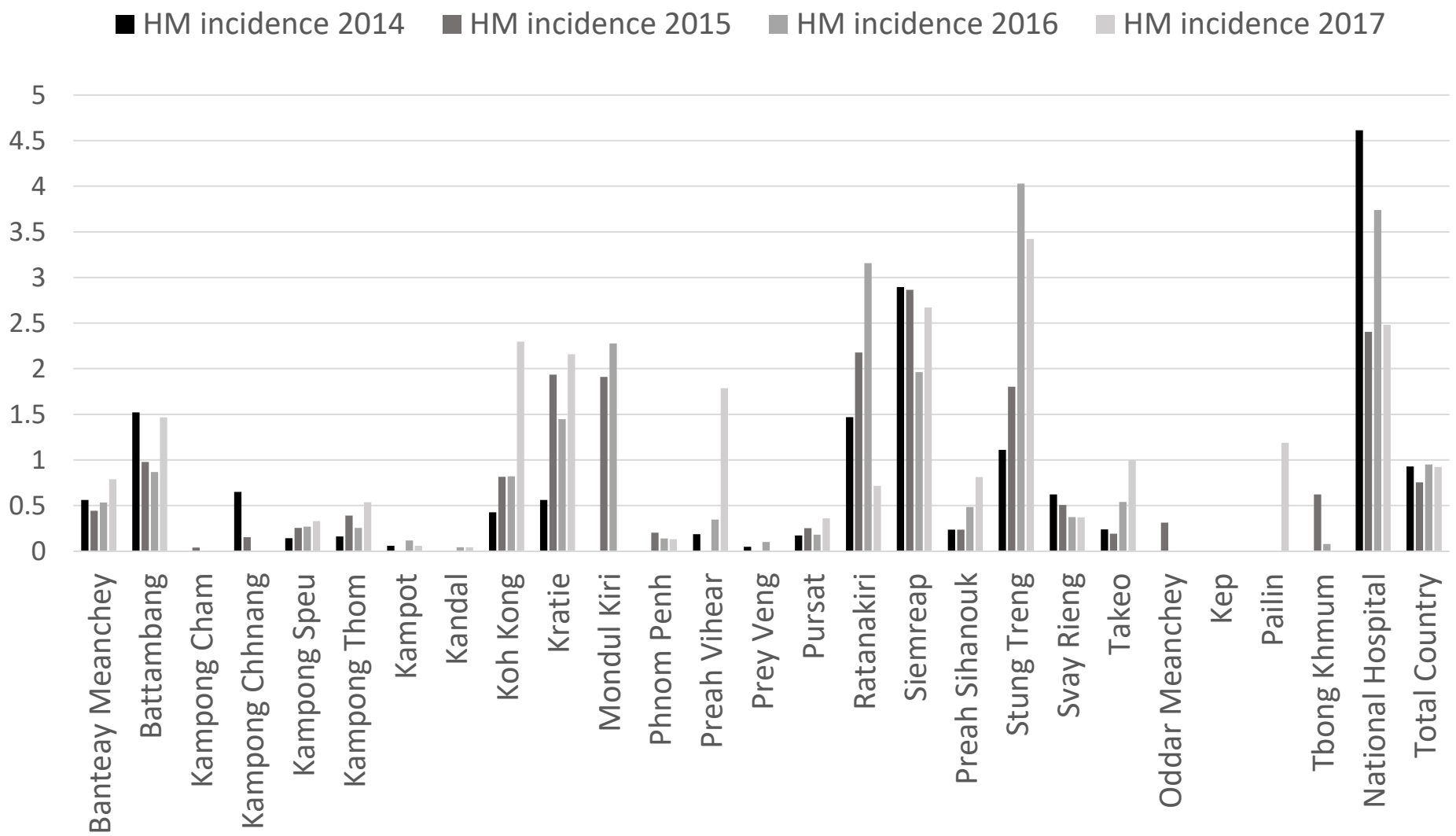
Incidence (per 1,000 pregnancies)

	2014	2015	2016	2017
HM	298	258	321	316
Pregnancy	320,612	341,672	337,972	342,811
Incidence	0.93	0.76	0.95	0.92

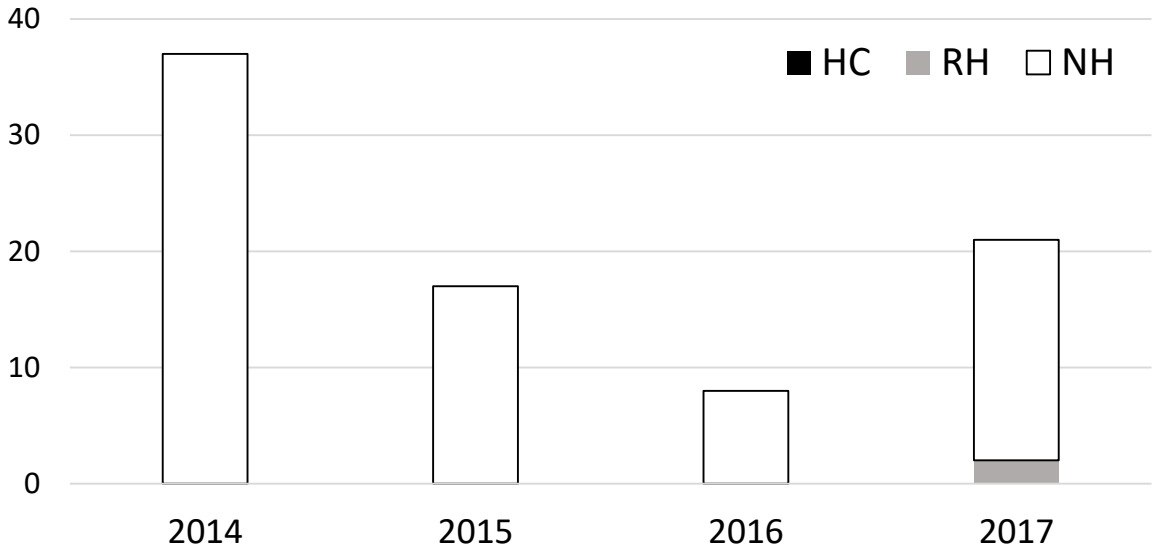
Number of HM in each province: HIS 2014-2017



Incidence of HM in each province (per 1,000 pregnancies): HIS 2014-2017



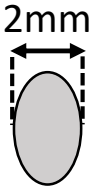
Gestational trophoblastic neoplasia (GTN) : HIS 2014-2017



- Most GTN patients were reported from national hospitals.
- In 2017, referral hospital in Kampong Chhnang and Takeo provinces reported two patients of GTN.

Management for hydatidiform mole in provinces

[Treatment] Evacuation should be performed after admission.
[Diagnosis] Evacuated tissues should be observed carefully. When the short diameter of cystic villi is over 2mm, the patient should be diagnosed as hydatifirom mole.



[Follow-up]

4th day : US perform → when remnant is suspected, 2nd MVA should be performed.
5th day : US perform → when normal, discharge
→ when abnormal, refer to central hospitals

2nd week: US → when remnant is found, refer to central hospitals

4th week: pregnancy test
6th week: pregnancy test
8th week: pregnancy test
10th week: pregnancy test
12th week: pregnancy test

When the result is negative in two consecutive tests,
→ the next visit is at 6th month
When the result is positive at 12th week
→ refer to central hospital

6th month: pregnancy test → (-) → permit the next pregnancy and finish follow-up
→ (+) → refer to central hospital (NMCHC)

- Whenever patients have abnormal bleeding, they should be referred to central hospitals.
- Patients should take contraception pills. Doctors should check if patients take pills correctly.
- The next pregnancy is allowed at 6th months when the pregnancy test was negative.

Management for hydatidiform mole at central hospitals

[Before treatment] US and β-hCG level should be checked.
[Treatment] Evacuation should be performed after admission.
[Diagnosis] Evacuated tissues should be observed carefully. When the short diameter of cystic villi is over 2mm, the patient should be diagnosed as hydatifirom mole. Pathological examination is recommended.
[Follow-up]
4th day : β-hCG level check, US → when remnant is suspected, 2nd MVA should be performed.
5th day : US perform and discharge
2nd week: β-hCG level, US
β-hCG level should be checked every 2 weeks until β-hCG < 5 IU/L
After β-hCG < 5IU/L, β-hCG level should be checked every month until 6th month.
6th month: β-hCG < 5IU/L → permit the next pregnancy
After 6th month, β-hCG level should be checked every 2 months until 12th month.

When β-hCG is stable or increased 3 consecutive tests before < 5IU/L,
→ US and chest X-P should be performed.
→ The patient is diagnosed as 'clinical invasive mole.'
→ When hysterectomy performed, pathological diagnosis should be made.

- Patients should take contraception pills. Doctors should check if patients take pills correctly.
- The next pregnancy is allowed at 6th months when the pregnancy test was negative.

Management for clinical invasive mole at central hospitals

Diagnosis

1. When β-hCG is increased or stable 3 times in a row after evacuation of hydatidiform mole, the patient should be diagnosed as 'clinical invasive mole'.
2. Abdominal or vaginal US for uterine lesion and X-P for lung metastasis should be performed.
3. When diagnosis is made by pathological examination after hysterectomy, diagnosis should be 'invasive mole'.

Treatment

1. MTX-FA for 8 days (interval 10 days) is given at inpatient ward or at OPD.
2. Hysterectomy can be performed when the uterus has tumor and patients do not need babies any more.
3. During chemotherapy, β-hCG should be checked at least once a course (before starting each course). When β-hCG is stable or increases in 2 consecutive courses, the regimen should be changed.
4. When MTX-FA is not effective, actinomycin-D is the 2nd regimen and etoposide is the 3rd regimen.
5. Chemotherapy should be given until β-hCG is <5IU/L and then 2 additional courses of chemotherapy is necessary.
6. After chemotherapy is finished, β-hCG should be checked every month for 12 months
7. Next pregnant is allowed 12 months after chemotherapy. Patients should take contraception pills and doctors should check if patients take pills correctly.

Regimens for invasive mole

MTX-Folinic acid				
Day 1, 3, 5, 7	MTX	1.0 mg/kg	i.m.	Every 2 weeks
Day 2, 4, 6, 8	FA	0.1 mg/kg	i.m.	

MTX, methotrexate, FA, folinic acid

Actinomycin D (ACTD)				
Day 1-5	ACTD	10 mg/kg (0.5 mg/body)	i.v.	Every 2 weeks

Etoposide (ETP)				
Day 1-5	ETP	60 mg/m^2 (100 mg/body)	div.	Every 2 weeks

Notes

1. When β-hCG > 100,000 IU/L, and/or age ≥40 years, hysterectomy after MVA is an option to reduce the incidence of invasive mole. However, the incidence of invasive mole cannot be zero after hysterectomy, and the patients should be followed using pregnancy test or β-hCG.
2. The duration of follow-up after HM treatment is the same for both patients who are diagnosed as complete hydatidiform mole and partial hydatidiform mole.
3. Most doctors in 3 provinces answered that they referred patients to KSF Hospitals when HM patients had some problems. However, NMCHC has better system for accepting HM patients from provinces and for keeping patient records.
4. MTX-FA can be given to patients after admission or without admission (visit OPD every day for injection).

Acknowledgement

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1. Prof. Koum Kanal and Prof. Sann Chansoeung, for collaborating on GTD research in Cambodia with me and giving a chance for presentation at SCGO 18th Symposium

2. Participants of SCGO 16th Annual, for answering the questionnaire

3. Doctors and midwives of NMCHC, KSF Hospital, Calmette Hospital, Kampong Cham Provincial Hospital, Chamke Leu Referral Hospital, Takeo Provincial Hospital, Bati Referral Hospital, Battambang Provincial Hospital, Moung Reusey Referral Hospital, for interviewing about GTD management

4. Dr. Sidonn Krang, Dr. Sim Sansam and Dr. Sothea Pho (Ministry of Health), for helping my visit hospitals