Jurnal Anestesi Perioperatif
[**JAP**. 2025;13(3):155–62]

ORIGINAL ARTICLE

Analgesia Effect of 2.64% Alkalinized Lidocaine in 70% Alcohol Topically Before Phlebotomy

Joel Apriyanto Fejacreyo Huka,[1] Ony Wibriyono Angkejaya,[2] Achmad Tuahuns,[3] Cokorda Istri Arintha Devi,[2] Is Ikhsan Hataul,[3] Jilientasia Lilihata[2]

[1]Medical Professional Program, Faculty of Medicine, Universitas Pattimura, Ambon, Indonesia
[2]Departement of Anesthesia, Intensive Care and Pain Management, Faculty of Medicine, Universitas Pattimura, Ambon, Indonesia
[3]Departement of Surgery, Faculty of Medicine, Universitas Pattimura, Ambon, Indonesia

p-ISSN: 2337-7909
e-ISSN: 2338-8463
doi: 10.15851/jap.v13n3.4054

Received: July 28, 2024
Accepted: December 8, 2025
Available online:
December 29, 2025

Corresponding Author:
Joel Apriyanto Fejacreyo Huka
Medical Professional Program, Faculty of Medicine, Universitas Pattimura, Ambon, Indonesia
E-mail:
joelhuka@gmail.com

Abstract

Background: Phlebotomy is an essential procedure in healthcare, but it often causes pain due to its invasive nature. Although lidocaine is effective as a local anesthetic, the injectable formulation and low pH may induce pain before the anesthetic effect begins. Therefore, alkalinized lidocaine administered topically is considered a potential alternative to reduce pain and accelerate anesthetic onset. This study is essential to evaluate the effectiveness of this approach. This research aimed to assess the effect of 2.64% alkalinized lidocaine in 70% alcohol, applied topically, on phlebotomy pain levels, measured using the Numeric Rating Scale (NRS).

Methods: This study employed a single-masked randomized controlled trial (RCT) with a posttest-only control group design. Samples were obtained via simple random sampling, yielding 20 paired samples from 135 eligible participants. On the first day, participants underwent phlebotomy after the application of alkalinized lidocaine, and on the tenth day, phlebotomy was repeated using 70% alcohol as the control. Pain was measured using the NRS and analyzed using the Wilcoxon test.

Results: NRS scores in the control group were significantly higher than those in the experimental group, with a p-value of 0.001.

Discussion: Alkalinized lidocaine effectively reduced phlebotomy pain, likely due to an increased non-ionic fraction that enhances tissue penetration and accelerates anesthetic onset. These findings align with existing literature, although generalization remains limited by the small sample size and single-masked design.

Conclusion: Topically applied 2.64% alkalinized lidocaine in 70% alcohol is effective in reducing pain associated with phlebotomy.

Keywords: Alkalinized lidocaine; NRS Score; pain; phlebotomy; topical

Introduction

Blood collection is a medical procedure often performed in healthcare settings. The blood collection technique is known as phlebotomy.[1] Phlebotomy aims for laboratory blood testing, blood draws, drug therapy, and the establishment of the diagnosis.[2] The systematic review and meta-analysis show that phlebotomy is a routine and easily invasivea a procedure performed in about 80% of hospitalized patients worldwide,

p-ISSN 2337-7909; e-ISSN 2338-8463
https://doi.org/10.15851/jap.v13n3.4054

underscoring the importance of phlebotomy in healthcare.[3]

Phlebotomy is inherently invasive and frequently associated with patient discomfort. Pain is the most commonly reported complaint following this procedure.[4] According to the International Association For The Study of Pain (IASP) of 2020.[5] Pain is defined as an unpleasant sensory or emotional sensation that follows actual or potential damage or is described as the presence of damage. Pain measurement can use several scales, including the Numeric Rating Scale (NRS).

Pain during phlebotomy is not limited to the moment of needle insertion; repeated procedures may contribute to cumulative discomfort and reduce patient quality of life.[6] Treating pain side effects from phlebotomy is necessary to improve patients' quality of life and convenience. Previous studies have shown that increased phlebotomy frequency is associated with decreased quality of life and productivity, underscoring the need for effective pain management strategies.[7] One commonly used approach to manage pain associated with invasive procedures, such as phlebotomy, is the administration of analgesics.

Analgesics are classified into opioid, non-opioid, and adjuvant agents. Unlike opioid and non-opioid analgesics, which primarily relieve pain, adjuvant analgesics are not primarily analgesic but can produce analgesic effects, including local anesthetics.[8] Local anesthetics are effective adjuvant analgesics because they provide reversible anesthesia by blocking sodium channels in peripheral nerves. Their clinical effects are influenced by physicochemical properties, and, based on molecular structure, local anesthetics are classified into ester and amid groups.[9,10]

Lidocaine is the most used amide-type local anesthetic due to its effectiveness and favorable safety.[10, 11] As a weak base, its clinical performance is influenced by solution pH, which affects tissue penetration and anesthetic onset through sodium channel blockade.10 However, conventional lidocaine formulations are acidic and may themselves cause discomfort upon administration.[12] To overcome this, it is necessary to increase the pH of lidocaine through the Alkalinization process.

Alkalinization reduces the acidity of local anesthetic solutions and is commonly achieved by adding sodium bicarbonate.[13,14] This buffering process has been shown to accelerate anesthetic onset and reduce pain associated with acidic lidocaine formulations. Several studies have reported lower pain scores, reduced burning sensation, and greater patient preference for alkalinized lidocaine compared with non-alkalinized formulations, including significant reductions in Numeric Rating Scale (NRS) scores.[15–18] This study was conducted to evaluate the efficacy of 8.4% sodium bicarbonate-buffered local anesthetic solution and conventional local anesthetic in patients undergoing bilateral maxillary orthodontic extractions, with respect to pain on injection, onset of action, and duration of action. 102 patients requiring bilateral maxillary orthodontic extractions were included in the study. Buffered local anesthetic was administered on one side, while conventional local anesthesia (LA Beyond solution acidity, needle puncture itself is a major contributor to procedural pain. Therefore, non-invasive routes of lidocaine administration are desirable, particularly for alkalinized formulations, with topical anesthesia offering a practical alternative.

Topical anesthesia provides analgesia without needle puncture, making it particularly suitable for phlebotomy. Previous studies have demonstrated its effectiveness in phlebotomy and minor procedures, showing significant reductions in pain scores, including decreased Visual Analog Scale (VAS) values following topical lidocaine application.[19–21]

Pediatric dentists are constantly seeking more comfortable means of administering anesthesia. Topical anesthesia has proven to be a boon in this attempt. Literature shows that quite often, there is little pain relief from topical anesthesia, and one reason for failure may be that there is no consensus regarding the most appropriate time duration for topical

anesthesia to anesthetize intraoral tissue before injection.

Therefore, the aim and objectives of the study are as follows: (1 Phlebotomy procedures also require antiseptic skin preparation to prevent infection, with 70% alcohol being the most used disinfectant. Combining analgesic and antiseptic functions into a single topical preparation represents a practical and clinically relevant innovation. In this context, the topical application of alkalinized lidocaine formulated in 70% alcohol is proposed as a novel approach to maintain antisepsis and reduce pain during phlebotomy simultaneously. This study aims to evaluate the effect of topical 2.64% alkalinized lidocaine combined with 8.4% sodium bicarbonate in 70% alcohol on Numeric Rating Scale (NRS) scores before phlebotomy.

Subjects and Methods

Ethical approval for this study was obtained from the Commission of Ethical Research, Faculty of Medicine, University of Pattimura, Ambon, Indonesia, with approval ID number 023/FK-KOM.ETIK/VIII/2024.

The instruments in this study consisted of tools and materials, including 1 mL, 3 mL, and 10 mL syringes, solution containers, 7.5 cm2 sterile gauze, 1 L 70% alcohol, medical gloves, and 1 L 95% alcohol, 50 mL of 10% lidocaine (Xylocaine spray), 25 mL of 8.4% sodium bicarbonate that had been dissolved into 2.64% lidocaine alkalinized in 100 mL of 70% alcohol as the experimental solution, and 70% alcohol as the control solution.

A solution of 2.64% lidocaine is alkalinized in 70% alcohol by dissolving 10% lidocaine alkalized by 8.4% sodium bicarbonate into 95% alcohol. The equation M1V1 = M2V2 was used to determine the volume of 95% alcohol and the volume of 10% lidocaine diluted to become 2.64% lidocaine alkalinized in 70% alcohol.

The volume of 95% alcohol used is 73.6 mL, and the lidocaine concentration is 10%, yielding a maximum lidocaine concentration of 2.64% in 100 mL of 70% alcohol. The volume of 8.4% sodium bicarbonate is used in a ratio of 1:200 to minimize precipitation due to the dilution process, which takes longer because it is done manually, so that the volume of 8.4% sodium bicarbonate used to produce 2.64% lidocaine in 100 mL of 70% alcohol is 0.5 mL.

The subjects in this study are students of the Faculty of Medicine, Pattimura University, class of 2023. The sampling technique used is a probability sampling method of the simple random sampling type, which means that all members of the target population who meet the inclusion and exclusion criteria have the same chance of being selected at random. The randomization process uses Microsoft Excel to choose 20 random samples from 135 students who meet the inclusion and exclusion criteria.

The inclusion criteria are students who are willing to be respondents after informed consent was obtained, and the exclusion criteria are students who have a history of hypersensitivity to lidocaine, alcohol, and sodium bicarbonate and have unhealed wounds, trauma, signs of inflammation, or a mass at the site of injection.

Data collection was conducted using a simple random sampling technique. Informed consent was obtained from all participants before study initiation. Both experimental and control interventions were administered to each participant using a single-masked, crossover design.

The first stage was conducted on the first day of the study, during which the experimental solution was applied topically using a standardized 10×10 cm sterile gauze bandage, which was saturated by flipping the bandage three times to ensure uniform solution volume and distribution, followed by phlebotomy at the designated site. The second stage was conducted on the 10th day of the study, during which the control solution was applied using the same bandage size, saturation method, application duration, and injection site. A 10-day washout period was implemented to allow complete resolution of local anesthetic effects, normalization of tissue sensitivity, and prevention of potential carryover effects on

p-ISSN 2337-7909; e-ISSN 2338-8463
https://doi.org/10.15851/jap.v13n3.4054

pain assessment.

The data were analyzed using the Wilcoxon signed-rank test in SPSS version 23. This test was selected because the Numeric Rating Scale (NRS) measures ordinal data, the measurements were paired within participants, and the data were not assumed to follow a normal distribution. The independent variable was topical administration of 2.64% alkalinized lidocaine in 70% alcohol before phlebotomy, while the dependent variable was the NRS pain score during phlebotomy. Statistical significance was defined as a p-value <0.05.

Results

The Numeric Rating Scale (NRS) scores of respondents who received 2.64% alkalinized lidocaine in 70% alcohol topically (experimental solution) before phlebotomy were predominantly in the mild pain category (50%), followed by no pain (30%) and moderate pain (20%), with none reporting severe pain. In contrast, the NRS scores of

Respondents who received 70% alcohol topically (control solution) before phlebotomy mainly were in the mild pain category (60%),

Table 1 Distribution of Pain Intensity (Numeric Rating Scale) During Phlebotomy in Control and Experimental Conditions

Numeric Rating Scale	Control Solution		Experimental Solution	
	Frequency (n)	Percent (%)	Frequency (n)	Percent (%)
NRS 0 (No pain)	0	0	6	30
NRS 1–3 (Mild pain)	12	60	10	50
NRS 4–7 (Moderate pain)	6	30	4	20
NRS 8–10 (Severe pain)	2	10	0	0
Total	20	100	20	100

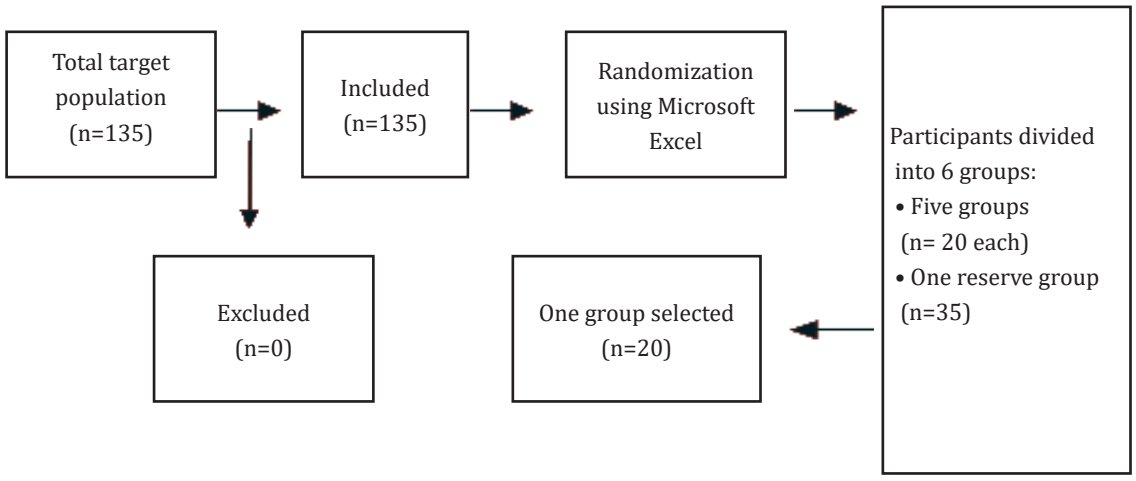

Figure 1 Flow Diagram of Participant Selection

Table 2 Effect of Topical 2.64% Alkalinized Lidocaine in 70% Alcohol on Pain Intensity During Phlebotomy

Variables	(Minimum-Maximum)	Effect size (r)	Wilcoxon	95% CI
Experimental solution pain intensity	2–4	0.72	Z = −3.207, p =0.001	0.40–0.88
Control solution pain intensity	1–3			

followed by moderate pain (30%) and severe pain (10%) (Table 1).

The analysis of 20 paired respondents who received an experimental solution of 2.64% alkalinized lidocaine in 70% alcohol topically before phlebotomy on the first day and a 70% alcohol solution topically before phlebotomy on the tenth day showed that the Wilcoxon signed- rank test revealed a significant difference between the control and experimental solution pain scores (Z=−3.207, p=0.001). The effect size was large, with r=0.72 (95% CI: 0.40–0.88), indicating that the experimental solution had a strong, clinically meaningful effect on pain reduction compared with the control solution (Table 2).

Discussion

The findings of this study indicate that topical application of 2.64% alkalinized lidocaine in 70% alcohol effectively reduces pain associated with phlebotomy compared with 70% alcohol alone. Participants receiving the experimental solution predominantly reported no pain or mild pain, with no occurrences of severe pain, whereas moderate-to-severe pain was observed only in the control condition. This pattern indicates a clinically meaningful analgesic benefit from adding alkalinized lidocaine to routine skin preparation before phlebotomy lidocaine to routine skin preparation prior to phlebotomy.

Quantitative analysis further confirmed that pain scores were significantly lower in the experimental condition, with a moderate-to- large effect size, supporting the robustness and consistency of the analgesic effect observed. Rather than reiterating individual pain categories, these results collectively demonstrate a clear shift toward lower pain intensity with the experimental intervention.

Compared with alternative topical analgesics, such as EMLA cream and vapocoolant sprays, the present findings are comparable in pain reduction but offer distinct practical advantages. Previous studies have reported that phlebotomy-related pain in placebo groups commonly ranged from moderate to severe. In contrast, pain in patients receiving EMLA cream or ethyl chloride vapocoolant spray was generally mild to moderate.[22] The NRS due to alkalinized lidocaine infiltration is lower than the pain due to non-alkalinized lidocaine infiltration.[15]

However, these agents typically require longer application times, additional materials, or separate procedural steps, which may limit their routine use in high-volume clinical settings. In contrast, the alkalinized lidocaine formulation in this study was integrated directly into the standard alcohol- based skin disinfection process, eliminating the need for additional analgesic preparations.

The observed analgesic effect is consistent with lidocaine's known pharmacological action, which blocks sodium channels in peripheral nociceptors, thereby inhibiting pain signal transmission at the venipuncture site.[9] Buffering lidocaine further enhances this effect by increasing the proportion of non- ionized drug, facilitating faster tissue penetration and onset of anesthesia, even at lower concentrations than those typically used in injectable or conventional topical formulations.[14,23,24] These findings are consistent with previous studies showing that alkalinization of lidocaine significantly reduces pain scores compared with non-alkalinized lidocaine, including reductions in

p-ISSN 2337-7909; e-ISSN 2338-8463
https://doi.org/10.15851/jap.v13n3.4054

Numeric Rating Scale (NRS) values.[17]

From a clinical perspective, combining alkalinized lidocaine with 70% alcohol represents a feasible and practical strategy for routine phlebotomy. The formulation preserves the antiseptic efficacy of 70% alcohol, which is recommended by the Centers for Disease Control and Prevention (CDC) for skin disinfection due to its effectiveness in denaturing proteins and killing microbes.[25]

Despite these promising results, several limitations should be acknowledged. The relatively small sample size may limit generalizability, and pain assessment relied on subjective self- reporting. In addition, local skin reactions were not systematically evaluated. Future studies with larger sample sizes, double-masked designs, standardized application times, and direct comparisons with established topical analgesics are warranted to confirm efficacy, assess safety, and further define the role of this formulation in routine clinical practice.

Conclusion

Topically administering 2.64% buffered lidocaine in 70% alcohol before phlebotomy significantly reduced pain, as reflected in the change in the Numeric Rating Scale (NRS). However, the study has several limitations, including a small sample size, limited personnel who allowed only a single-masked design, the inherent subjectivity of pain assessment, and the use of a sodium bicarbonate–lidocaine ratio (1:200) that was lower than the recommended (1:10) due to manual preparation, increasing the risk of precipitation. These factors may have influenced the consistency and generalizability of the findings. Future research should employ larger and statistically powered samples, a double-masked design, and more objective pain assessment tools. Additionally, studies comparing alkalinized lidocaine with established topical analgesics such as EMLA cream or vapocoolant spray are recommended to determine its relative efficacy and practicality applicability in clinical settings.

AI Use Disclosure

During the preparation of this work, the authors used Grammarly and ChatGPT to improve readability and language. The authors have carefully reviewed and verified all content, and they take full responsibility for the accuracy, integrity, and originality of the final manuscript after using this tool/service.

References

1. National Cancer Institute. Phlebotomy [Internet]. NCI Dictionary of Cancer Terms. 2023 [cited 2023 Apr 30]. Available from: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/phlebotomy
2. Shlamovitz GZ, Rowe VL. Phlebotomy: Background, Indications, Contraindications [Internet]. Medscape. 2023 [cited 2024 Apr 30]. p. 1–3. Available from: https://emedicine.medscape.com/article/1998221-overview#showall
3. Webster J, Osborne S, Rickard CM, Marsh N. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. Cochrane Database Syst Rev. 2019;(1):327–77. doi: 10.1002/14651858.CD007798.pub4
4. Serra R, Lelapi N, Barbeta A, Buffone G. Adverse complications of venipuncture: A systematic review. Acta Phlebol. 2018;19(1):11–5.
5. IASP. IASP Announces Revised Definition of Pain [Internet]. International Association For The Study of Pain. 2020 [cited 2024 Feb 10]. Available from: https://www.iasp-pain.org/publications/iasp-news/iasp-announces-revised-definition-of-pain/
6. Kim IJ, Cho H, Yi MS, Park YH, Kim S, Kim DK, et al. Diagnosis and treatment of nerve injury following venipuncture-A report of two cases-. Anesth Pain Med. 2021;16(3):299–304. doi: 10.17085/apm.21010.
7. Visweshwar N, Fletcher B, Jaglal M, Laber DA, Patel A, Eatrides J, et al.

Impact of Phlebotomy on Quality of Life in Low-Risk Polycythemia Vera. J Clin Med. 2024;13(16)4952. doi: 10.3390/jcm13164952.
8. Daniel A, Milani Q, Davis DD. Pain Management Medications [Internet]. StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560692/
9. McLeod IK. Local Anesthetics [Internet]. Medscape. 2023 [cited 2024 Mar 28]. p. 1–8. Available from: https://emedicine.medscape.com/article/873879-overview#a2
10. Mumba JM, Kasandji F, Ngaka CT. Pharmacology of Local Anaesthetics and Commonly Used Recipes in Clinical Practice. In: Current Topics in Anesthesiology. Intech open science; 2017. p. 13.
11. Pardo JMC, Miler RD. editors. Basics of Anesthesia. 7th ed. Philadelphia: Elsevier; 2018. p. 149–51.
12. Strazar R, Lalonde D. Five Things to Know About: Minimizing injection pain in local anesthesia. Can Med Assoc J. 2016;184(18):2016. doi: 10.1503/cmaj.111780
13. National Cancer Institute. Alkalinization [Internet]. NCI Dictionary of Cancer Terms. 2023 [cited 2024 Mar 28]. p. 1. Available from: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/alkalinization
14. Angkejaya OW. Farmakologi Natrium Bikarbonat. In: Lisnawati, editor. Natrium Bikarbonat sebagai Adjuvan Anestesi Intratekal pada Seksio Sesaria. Purwokerto: Penerbit Amerta Media; 2023. p. 49–52.
15. Warren VT, Fisher AG, Rivera EM, Saha PT, Turner B, Reside G, et al. Buffered 1 % Lidocaine With Epinephrine Is as Effective as Non-Buffered 2 % Lidocaine With Epinephrine for Mandibular Nerve Block . J Oral Maxillofac Surg. 2017;75(7):1363–6. doi: 10.1016/j.joms.2016.12.045
16. Valiulla MUE, Halli R, Khandelwal S, Mittal A, Singh A, Bhindora K. Efficacy of Sodium Bicarbonate-Buffered Local Anesthetic Solution in Cases Requiring Bilateral Maxillary Premolar Orthodontic Extraction: A Comparative Split-Mouth Study. Cureus. 2023;15(4):4–11. doi: 10.7759/cureus.37934.
17. Vent A, Surber C, Graf Johansen NT, Figueiredo V, Schönbächler G, Imhof L, et al. Buffered lidocaine 1%/epinephrine 1:100,000 with sodium bicarbonate (sodium hydrogen carbonate) in a 3:1 ratio is less painful than a 9:1 ratio: A double-blind, randomized, placebo-controlled, crossover trial. J Am Acad Dermatol. 2020;83(1):159–65. doi: 10.1016/j.jaad.2019.09.088
18. Pereira e Silva R, Ponte C, Lopes F, Palma dos Reis J. Alkalinized lidocaine solution as a first-line local anesthesia protocol for intradetrusor injection of onabotulinum toxin A: Results from a double-blinded randomized controlled trial. Neurourol Urodyn. 2020;39(8):2471–9. doi: 10.1002/nau.24519.
19. Voute M, Venorique M, Pickering G. Topical Lidocaine for Chronic Pain Treatment. Dovepress. 2021;15:4091–103. doi: 10.2147/DDDT.S328228
20. Gupte T, Modi UA, Gupte S, Sawant A. Determination of onset of action and efficacy of topical lignocaine anesthesia in children: an in vivo study. Int J Clin Pediatr Dent. 2019;12(3):178–81. doi:10.5005/jp-journals-10005-1631.
21. Weilbach C, Hoppe C, Karst M, Winterhalter M, Raymondos K, Schultz A, et al. Effectiveness of various formulations of local anesthetics and additives for topical anesthesia–a prospective, randomized, double-blind, placebo-controlled study. J Pain Res. 2017;10:1105–9. doi:10.2147/JPR.S134222.
22. Wang L, Fang L, Zhou Y, Fang X, Liu J, Qu G. Efficacy and safety of vapocoolant spray for vascular puncture in children and adults: a systematic review and meta-analysis [Internet]. PLoS One. 2023;18(2):e0279463. Available from: http://dx.doi.org/10.1371/journal.

p-ISSN 2337-7909; e-ISSN 2338-8463
https://doi.org/10.15851/jap.v13n3.4054

pone.0279463.
23. Henry M, Lee Y, Kirkpatrick DL. Minimizing the pain of local anesthetic injection. Appl Radiol. 2024;53(1):16–21.
24. Jain TK, Jha R, Tiwari A, Agrawal N, Mali S, Sinha A, et al. A comparative study to evaluate the anesthetic efficacy of buffered versus non-buffered 2% lidocaine during inferior alveolar nerve block. Cureus. 2022;14(11). doi:10.7759/cureus.31568.
25. Gold NA, Mirza TM, Avv U. Alcohol sanitizer. In: StatPearls [Internet]. StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513254/.